A Family Study of Major Central Nervous System Malformations in South Wales

C. O. CARTER, P. A. DAVID, and K. M. LAURENCE

From Clinical Genetics Research Unit, Institute of Child Health, London W.C. 1, and the Dept. of Paediatric Pathology, Welsh National School of Medicine, Llandough Hospital, Penarth, Glam.

This family study is based on an attempt to ascertain all patients with spina bifida cystica, anencephaly, and congenital hydrocephalus born between the years 1956 and 1962 inclusive in the mining valleys of Monmouthshire, in the mining valleys of Glamorgan up to and including the Neath valley, and in the Vale of Glamorgan. Details of the area, the population, and the methods of ascertainment are given in Laurence, David, and Carter (1968a). It is estimated that ascertainment was at least 95% complete except for 1956 where there was perhaps a 10% deficit. The urban areas of Cardiff, Newport, Barry, Penarth, and Neath were excluded. The district is shown in the Figure.

The estimate of the total population of the area (Registrar General's annual Review II) averaged 851,747 over the years of the survey, and the total births were 102,786 (52,715 male and 50,071 female), of which 2842 were stillbirths. Among these births there were ascertained 835 patients, 425 (200 male and 225 female) cases of spina bifida cystica (hereinafter referred to as spina bifida), 364 (91 male and 271 female and 2 not known) of anencephaly, and 46 (17 male and 29 female) of congenital hydrocephalus. Cases of hydrocephalus secondary to spina bifida were classed as spina bifida, cases of encephalocele were classed as spina bifida, cases of anencephaly with spina bifida as anencephaly, cases of iniencephalus, exencephalus, and microcephalus acrania as anencephaly. The completeness of ascertainment is discussed elsewhere (Laurence *et al.*, 1968a). The over-all incidence of the three malformations was 8.12 per thousand total births, and the individual incidences 4.13, 3.54, and 0.45, respectively; in male births 3.78, 1.73, and 0.32, and in female births 4.48, 5.40, and 0.58.

The spina bifida incidence is the highest reported for any series for a whole population; that for anencephaly is exceeded only in the Northern

Ireland series of Stevenson and Warnock (1959). The incidence of congenital hydrocephalus is unusually low, probably because in this survey all instances secondary to spina bifida were classed as spina bifida, only cases of truly congenital hydrocephalus were included, and instances where the presence of hydrocephalus was in doubt, for example in certain macerated stillbirths, were excluded. The eastern part of the district, East Monmouth, Ebbw Vale, Rhymney, and Caerphilly had a somewhat higher incidence than the western part, the comparative figures in the two areas being 4.61 and 3.85, 4.42 and 3.01, 0.42 and 0.46 for spina bifida, anencephaly, and hydrocephalus, respectively.

METHODS

For a detailed study of familial aggregation and epidemiological characteristics, cases ascertained for the whole period in four areas—6, 7, 8, and 9 (Rhondda, Aberdare, Caerphilly, and Merthyr)—were included, but only cases born in 1960–62 inclusive in the other 8 areas. This group selected for detailed study (hereinafter called the main group) numbered 551, including 278 cases of spina bifida, 247 of anencephaly, and 26 of hydrocephalus. Half of these patients, selected by random numbers for each area, were matched with 277 controls*; these controls were the nearest births of the same sex from the same town or group of villages as the index patient in the local authority's birth register.

Of this main group of 551 patients, 1 spina bifida and 1 anencephalus were not regarded as index patients for the family study, as they were not found in the original search but ascertained only through a sib who was an index patient. It was possible to visit the homes of the parents of all but 34 cases; however, at least partial family histories were obtained from health visitors, family doctors, or relatives for all but 1 patient with spina bifida and 1 with anencephalus, leaving 276 index patients with spina bifida, 245 index patients with anencephaly, and 26 with hydrocephalus. The parents of all but 15 of the 277 controls were visited, and again family

Received October 20, 1967.

* The number of patients in some areas was an odd number and hence come the extra $1\frac{1}{2}$ controls.

FIG.—Map of South East Wales. County boundaries shown by thick lines and district boundaries by thin lines. The survey districts are shaded and named in capital letters.

histories were obtained from other sources for all but 1 patient: this child was illegitimate, and another control was substituted and the family visited. One control had a spina bifida† and a second control was substituted for this child.

The visits were all carried out by one of us (P.A.D.), though several families of interest were visited in addition by one or by both of the other authors. Parents were told before the visit of the information needed and were asked to make inquiries from other members of the families. Information on the family was collected, usually from the mother alone but sometimes from other relatives, on sibs, parents, grandparents, aunts and uncles, and nephews and nieces of the index patients and controls. Details of the pregnancy and socioeconomic data were also recorded.

For the remaining 284 not selected for visiting, i.e. those born before 1960 from the areas other than 6, 7, 8, and 9 (hereinafter referred to as the subsidiary group), arrangements were kindly made by the medical officers of health for visits to the family by health visitors (public health nurses) who were instructed in the purposes and methods of the survey and collected a more restricted family history. One patient with anencephaly was ascertained

† This was one of 3 affected who were later found to have been missed in the original search for index patients. She (834), but not the other 2 who were traced through an affected sib, was included as an index patient.

only through an affected sib and so was not regarded as an index patient. Visits were made to the homes of the parents of all but 8, and data on the sibships were finally obtained for all but 1 hydrocephalic of the remaining 283 patients, leaving 147 with spina bifida, 116 with anencephaly, and 19 with hydrocephalus. Details of interviewing methods are given elsewhere (Laurence, David, and Carter, 1968b).

Histories of affected or possibly affected relatives were documented from hospital, death certificate, or other records.

The blood groups of the mothers in the main group and the controls were sought from hospital records or from the regional transfusion centre, and ABO and Rhesus blood types were found for all but 47 of the index patients; those missing were from home confinements in the earlier years of the survey.

Summary family histories for the main series are given in Appendix I and for the subsidiary series in Appendix II.

RESULTS

Some General Considerations

Sex Ratio. In this series the sex ratio was 0.89 for spina bifida, 0.34 for anencephaly, and 0.59 for hydrocephalus.

TABLE I
INSTANCES OF CONSANGUINITY IN CONTROL AND MAIN AND SUBSIDIARY SERIES

Relationship	Controls	Main Series			Subsidiary Series		
		Spina Bifida	Anen-cephaly	Hydro-cephalus	Spina Bifida	Anen-cephaly	Hydro-cephalus
1st cousins	0	0	1 (265)	0	2 (633)	1 (649)	0
1½ cousins	1 (393)*	1 (134)	0	0	0 (830)	0	0
2nd cousins	0	1 (202)	0	1 (341)	2 (824) (797)	1 (634)	0
Total	277	276	245	26	147	116	19

* Reference number of family is given in parentheses.

TABLE II
BROTHERS AND SISTERS OF INDEX PATIENTS WITH SPINA BIFIDA, DISTINGUISHING THOSE BORN BEFORE AND THOSE AFTER INDEX PATIENT

	Index Patient	Brothers						Sisters					
		Older		Younger		Total		Older		Younger		Total	
		Total	Affected	Total	Affected	Total	Affected	Total	Affected	Total	Affected	Total	Affected
Main series	Male 129	92	{ 6Sp. bif. 2An.	31	{ 2Sp. bif. 0An.	123	{ 8Sp. bif. 2An.	75	{ 3Sp. bif. 4An.	32	{ 1Sp. bif. 2An.	107	{ 4Sp. bif. 6An.
	Female 147	106	{ 4Sp. bif. 1An.	48	{ 1Sp. bif. 0An.	154	{ 5Sp. bif. 1An.	97	{ 3Sp. bif. 5An.	37	{ 0Sp. bif. 1An.	134	{ 3Sp. bif. 6An.
	Total 276	198	{ 10Sp. bif. 3An.	79	{ 3Sp. bif. 0An.	277	{ 13Sp. bif. 3An.	172	{ 6Sp. bif. 9An.	69	{ 1Sp. bif. 3An.	241	{ 7Sp. bif. 12An.
Subsidiary series	Male 67	45	{ 1Sp. bif. 0An.	46	{ 2Sp. bif. 0An.	91	{ 3Sp. bif. 0An.	43	{ 2Sp. bif. 0An.	28	{ 2Sp. bif. 0An.	71	{ 4Sp. bif. 0An.
	Female 80	42	{ 2Sp. bif. 0An.	39	{ 1Sp. bif. 1An.	81	{ 3Sp. bif. 1An.	49	{ 0Sp. bif. 4An.	44	{ 2Sp. bif. 0An.	93	{ 2Sp. bif. 4An.
	Total 147	87	{ 3Sp. bif. 0An.	85	{ 3Sp. bif. 1An.	172	{ 6Sp. bif. 1An.	92	{ 2Sp. bif. 4An.	72	{ 4Sp. bif. 0An.	164	{ 6Sp. bif. 4An.
Main + subsidiary series	Male 196	137	{ 7Sp. bif. 2An.	77	{ 4Sp. bif. 0An.	214	{ 11Sp. bif. 2An.	118	{ 5Sp. bif. 4An.	60	{ 3Sp. bif. 2An.	178	{ 8Sp. bif. 6An.
	Female 227	148	{ 6Sp. bif. 1An.	87	{ 2Sp. bif. 1An.	235	{ 8Sp. bif. 2An.	146	{ 3Sp. bif. 9An.	81	{ 2Sp. bif. 1An.	227	{ 5Sp. bif. 10An.
	Total 423	285	{ 13Sp. bif. 3An.	164	{ 6Sp. bif. 1An.	449	{ 19Sp. bif. 4An.	264	{ 8Sp. bif. 13An.	141	{ 5Sp. bif. 3An.	405	{ 13Sp. bif. 16An.

Parental Consanguinity. The information on parental consanguinity is summarized in Table I. The 2 spina bifida patients in the subsidiary series who had first cousin parents (633 and 830) were brother and sister.

Taking those sibships that were the product of cousin marriages, the spina bifida index patients had 11 brothers, of whom 1 had spina bifida; and 4 sisters, of whom 1 had spina bifida. The anencephalic index patients had 4 brothers, all unaffected, and no sisters. The hydrocephalic index patient had no sibs.

Twins. Even in such a large series there were few twins, and in retrospect it was not possible to determine the type of twinning. For spina bifida, 2 male index patients had normal male twins, and another had a normal female twin; 2 female index patients had normal female twins, and 2 had normal

male twins. For anencephaly, 2 male index patients had normal male twins, 3 female index patients had normal female twins, and 1 had a normal male twin. It is of interest that there was one family of triplets, 2 girls and a boy, in which both the girls were anencephalic index patients. For hydrocephalus 1 female index patient had an unaffected twin brother.

Sibs

Controls. The findings in the sibs of the 277 controls for main series index patients may be summarized as follows: of 256 brothers, 1 had spina bifida (this was an index patient in the main series), and of 243 sisters, 2 (not index patients and both in the same family) had anencephaly.

Spina Bifida. The findings in the sibs of the spina bifida index patients are shown in Table II.

TABLE III
BROTHERS AND SISTERS OF INDEX PATIENTS WITH ANENCEPHALY, DISTINGUISHING THOSE BORN BEFORE AND THOSE AFTER INDEX PATIENT

	Index Patient	Brothers			Sisters		
		Older	Younger	Total	Older	Younger	Total
		Total Affected	Total Affected	Total Affected	Total Affected	Total Affected	Total Affected
Main series	Male 61	48 { 0Sp. bif. 0An.	14 { 0Sp. bif. 0An.	62 { 0Sp. bif. 0An.	36 { 0Sp. bif. 2An.	15 { 0Sp. bif. 1An.	51 { 0Sp. bif. 3An.
	Female 184	120 { 2Sp. bif. 1An.	50 { 0Sp. bif. 0An.	170 { 2Sp. bif. 1An.	96 { 1Sp. bif. 1An.	45 { 5Sp. bif. 2An.	141 { 6Sp. bif. 3An.
	Total 245	168 { 2Sp. bif. 1An.	64 { 0Sp. bif. 0An.	232 { 2Sp. bif. 1An.	132 { 1Sp. bif. 3An.	60 { 5Sp. bif. 3An.	192 { 6Sp. bif. 6An.
Subsidiary series	Male 28	15 { 0Sp. bif. 0An.	11 { 0Sp. bif. 0An.	26 { 0Sp. bif. 0An.	29 { 1Sp. bif. 2An.	17 { 1Sp. bif. 0An.	46 { 2Sp. bif. 2An.
	Female 86	66 { 1Sp. bif. 2An.	42 { 0Sp. bif. 1An.	108 { 1Sp. bif. 3An.	64 { 1Sp. bif. 4An.	39 { 1Sp. bif. 0An.	103 { 2Sp. bif. 4An.
	Not known 2	0 { 0Sp. bif. 0An.	1 { 0Sp. bif. 0An.	1 { 0Sp. bif. 0An.	0 { 0Sp. bif. 0An.	0 { 0Sp. bif. 0An.	0 { 0Sp. bif. 0An.
	Total 116	81 { 1Sp. bif. 2An.	54 { 0Sp. bif. 1An.	135 { 1Sp. bif. 3An.	93 { 2Sp. bif. 6An.	56 { 2Sp. bif. 0An.	149 { 4Sp. bif. 6An.
Main + subsidiary series	Male 89	63 { 0Sp. bif. 0An.	25 { 0Sp. bif. 0An.	88 { 0Sp. bif. 0An.	65 { 1Sp. bif. 4An.	32 { 1Sp. bif. 1An.	97 { 2Sp. bif. 5An.
	Female 270	186 { 3Sp. bif. 3An.	92 { 0Sp. bif. 1An.	278 { 3Sp. bif. 4An.	160 { 2Sp. bif. 5An.	84 { 6Sp. bif. 2An.	244 { 8Sp. bif. 7An.
	Not known 2	0 { 0Sp. bif. 0An.	1 { 0Sp. bif. 0An.	1 { 0Sp. bif. 0An.	0 { 0Sp. bif. 0An.	0 { 0Sp. bif. 0An.	0 { 0Sp. bif. 0An.
	Total 361	249 { 3Sp. bif. 3An.	118 { 0Sp. bif. 1An.	367 { 3Sp. bif. 4An.	225 { 3Sp. bif. 9An.	116 { 7Sp. bif. 3An.	341 { 10Sp. bif. 12An.

In the visited main series there were 276 spina bifida index patients, and of 277 brothers, 13 (4.69%) had spina bifida and 3 (1.08%) had anencephaly. Of 241 sisters, 7 (2.90%) had spina bifida and 12 (4.98%) had anencephaly. Combining the two types of malformation, 5.78% of brothers and 7.88% of sisters were affected, and 6.76% of sibs of both sexes were affected. The abnormality in the affected sibs was documented in every case. One further later brother of a female index patient had a diastematomyelia with neurological involvement.

In the subsidiary series with 147 patients with spina bifida, of 172 brothers, 6 (3.49%) had spina bifida and 1 (0.58%) had anencephaly. Of 164 sisters, 6 (3.66%) had spina bifida and 4 (2.44%) had anencephaly. Again combining the two types of malformation, 4.07% of brothers and 6.10% of sisters were affected, and 5.06% of both sexes were affected.

Combining the main and subsidiary series of 449 brothers, 19 (4.23%) had spina bifida and 4 (0.89%) had anencephaly. Of 405 sisters, 13 (3.21%) had spina bifida and 16 (3.95%) had anencephaly. The total incidence of either type of malformation was 5.12% in brothers and 7.16% in sisters, and the total incidence in sibs of either sex was 6.09%. The abnormality in the affected sibs was documented in all but one instance.

Subdividing by sex of index patient shows no significant differences in the total proportion of sibs

affected. This is 27/392 (6.89%) for male, and 25/462 (5.41%) for female index patients. The proportion of sibs affected was higher in sibs born before the index patient, 37/549 (6.74%), than in those born after the index patient, 15/305 (4.92%), but again this difference is not significant.

Too few fathers were in socioeconomic groups other than skilled and semiskilled manual workers to make it possible to examine risks to sibs by socioeconomic group, and this was also true of the anencephaly and hydrocephalus index patients.

There is no indication that the proportion of sibs affected is raised in the families in which a relative other than a sib has a neural tube malformation. Of 18 brothers in such families, none was affected, and of 10 sisters, 1 had spina bifida and 1 had anencephaly.

Not a single brother or sister of an index patient with spina bifida had a hydrocephalus that was not associated with spina bifida.

Anencephaly. The findings in the sibs of the anencephalic index patients are shown in Table III.

In the main series with 245 index patients, of 232 brothers, 2 had spina bifida (0.86%) and 1 (0.43%) anencephaly. Of 192 sisters, 6 (3.13%) had spina bifida and 6 (3.13%) anencephaly. In total, 1.29% of brothers, 6.25% of sisters, and 3.54% of both sexes were affected with spina bifida or anencephaly. The abnormality in the affected sibs was

TABLE IV

BROTHERS AND SISTERS OF INDEX PATIENTS WITH HYDROCEPHALUS, DISTINGUISHING THOSE BORN BEFORE AND THOSE AFTER INDEX PATIENT

	Index Patient		Brothers						Sisters					
			Older		Younger		Total		Older		Younger		Total	
			Total	Affected	Total	Affected	Total	Affected	Total	Affected	Total	Affected	Total	Affected
Main series	Male	10	5	{0Hy. 0An.	1	{0Hy. 0An.	6	{0Hy. 0An.	11	{0Hy. 0An.	1	{0Hy. 0An.	12	{0Hy. 0An.
	Female	16	17	{0Hy. 0An.	4	{0Hy. 0An.	21	{0Hy. 0An.	17	{1Hy. 0An.	1	{1Hy. 0An.	18	{2Hy. 0An.
	Total	26	22	{0Hy. 0An.	5	{0Hy. 0An.	27	{0Hy. 0An.	28	{1Hy. 0An.	2	{1Hy. 0An.	30	{2Hy. 0An.
Subsidiary series	Male	7	9	{0Hy. 0An.	5	{0Hy. 0An.	14	{0Hy. 0An.	6	{0Hy. 0An.	2	{0Hy. 0An.	8	{0Hy. 0An.
	Female	12	12	{0Hy. 1An.	5	{0Hy. 0An.	17	{0Hy. 1An.	10	{0Hy. 0An.	3	{0Hy. 0An.	13	{0Hy. 0An.
	Total	19	21	{0Hy. 1An.	10	{0Hy. 0An.	31	{0Hy. 1An.	16	{0Hy. 0An.	5	{0Hy. 0An.	21	{0Hy. 0An.
Main + subsidiary series	Male	17	14	{0Hy. 0An.	6	{0Hy. 0An.	20	{0Hy. 0An.	17	{0Hy. 0An.	3	{0Hy. 0An.	20	{0Hy. 0An.
	Female	28	29	{0Hy. 1An.	9	{0Hy. 0An.	38	{0Hy. 1An.	27	{1Hy. 0An.	4	{1Hy. 0An.	31	{2Hy. 0An.
	Total	45	43	{0Hy. 1An.	15	{0Hy. 0An.	58	{0Hy. 1An.	44	{1Hy. 0An.	7	{1Hy. 0An.	51	{2Hy. 0An.

documented from hospital or public records in every case.

In the subsidiary series, with 116 index patients, of 135 brothers, 1 (0.74%) had spina bifida, and 3 (2.22%) had anencephaly; of 149 sisters, 4 (2.68%) had spina bifida, and 6 (4.03%) had anencephaly. In total, 2.96% of brothers, 6.71% of sisters, and 4.93% of both sexes were affected. In addition, one sister (674) had congenital hydrocephalus. In 6 instances in this subsidiary series, it was not possible to document that the sib was affected, but the mother's description left little doubt of the diagnosis.

Combining the main and subsidiary series, of 367 brothers, 3 (0.82%) had spina bifida, and 4 (1.09%) had anencephaly. Of 341 sisters, 10 (2.93%) had spina bifida, and 12 (3.52%) had anencephaly. The total incidence of either malformation was 1.92% in brothers and 6.45% in sisters, and the total incidence in sibs of either sex was 4.09%.

Subdividing by sex of index patient gives 7/185 (3.78%) of sibs of male index patients and 22/522 (4.21%) of the sibs of female index patients affected. It is noteworthy, though perhaps coincidental, that for these male index patients with anencephaly all 7 affected sibs were sisters and 5 had anencephaly, whereas the sibs of the female index patients included 11 with spina bifida and 11 with anencephaly. Among sibs born before the index patients 3.80% were affected and among those born after the index patient 4.70% were affected.

In the families in which a relative other than a sib

was affected, of 16 brothers and 12 sisters, none was affected, so there is no suggestion of an increased risk to sibs in these families.

Hydrocephalus. The findings in the sibs of the hydrocephalus index patients are shown in Table IV.

The hydrocephalus series is much smaller, comprising in the main series 10 male and 16 female index patients. Of 6 brothers and 12 sisters of male index patients, none was affected; none of 21 brothers but 2 of 19 sisters of the female index patients were affected with hydrocephalus: these 2 affected sisters came from the same sibship in which both were index patients. None of the sibs had either spina bifida or anencephaly.

In the subsidiary series of 7 male and 12 female index patients, none of the 14 brothers and 8 sisters of male index patients, and none of the 13 sisters of the female index patients was affected with a central nervous system malformation, but 1 (673) of the 17 brothers of female index patients had anencephaly.

Combining both series and index patients of both sexes, none of 58 brothers had hydrocephalus, but 1 had anencephaly, while 2 of 51 sisters had hydrocephalus.

Half-sibs

The numbers of half-sibs were, for controls, 11 maternal; for spina bifida, 12 maternal and 1

TABLE V
COUSINS OF CONTROLS AND OF MAIN SERIES INDEX PATIENTS, SHOWING NUMBER WITH SPINA BIFIDA, ANENCEPHALY, AND HYDROCEPHALUS

	Controls				Spina Bifida				Anencephaly				Hydrocephalus			
	Total	Sp. bif.	An.	Hy.	Total	Sp. bif.	An.	Hy.	Total	Sp. bif.	An.	Hy.	Total	Sp. bif.	An.	Hy.
Mother's brother's children	466	4	0	0	548	3	1	1	458	2	3	1	70	0	1	0
Mother's sister's children	765	2	2	1	566	6	1	0	577	3	0	1	108	0	0	3
Total Expected	1231	6 5.1	2 4.4	1 0.6	1114	9 4.6	2 3.9	1 0.5	1035	5 4.3	3 3.7	2 0.5	178	0 0.7	1 0.6	3 0.08
Father's brother's children	621	0	1	0	428	1	0	0	490	1	0	0	63	0	0	0
Father's sister's children	712	1	1	1	672	1	4	0	639	1	1	1	75	2	0	0
Total Expected	1333	1 5.5	2 4.7	1 0.6	1360	2 5.4	4 4.6	0 0.6	1129	2 4.5	1 4.0	1 0.5	138	2 0.6	0 0.5	0 0.06

paternal; for anencephaly, 22 maternal and 17 paternal; for hydrocephalus, 5 maternal. These were unaffected except in the case of 1 of 4 half-brothers of a male index patient with hydrocephalus (039). In this family the hydrocephalus was clearly X-linked, since a son of each of 2 sisters of the mother was proved to have died of congenital hydrocephalus, and there was a history of death from congenital hydrocephalus in 2 of the mother's brothers and 2 further mother's sister's sons.

Other Relatives

Information about the cousins, uncles and aunts, and nephews and nieces was collected only for the main series. There were not enough nephews and nieces yet born to provide useful information. The information on these relatives is less complete than for sibs, as hospital records were not sought and examined for all births to the grandparents and aunts and uncles of index patients, but only where there was a history suggestive of a neural tube malformation. It proved very difficult to document histories of affected aunts and uncles, as usually no records were available. Information on the cousins, since they are roughly contemporary with the index patients, is better, but here too ascertainment and documentation of affected subjects are far from complete. A woman who has an anencephalic child, for example, is often just told that her child is stillborn. Where a parent had no knowledge of the families of his brothers and sisters these were excluded from the analysis.

The findings on the cousins are summarized in Table V. Only those are shown as affected in whom there was documentary proof, and the majority of those documented as affected were also index patients. This was the case with 15 of the 25 cousins proved to have spina bifida, 11 of the 14

with anencephaly, and 3 of the 6 with hydrocephalus. A comparison is made in this Table with the numbers of neural tube malformations expected if the incidence had been that found in the general population of the area.

The control series shows that only 11 cousins were ascertained to be affected when 20 would have been expected. Only in the case of spina bifida in maternal cousins did the proportion affected approach the expected incidence, and it is only for spina bifida in maternal cousins that the observed number of cousins of spina bifida and anencephaly index patients who are affected (14 were found) exceeds the expected number 9, and the excess was largely confined to the mother's sister's children of whom 9 were affected when the expected number is 4.

Of the 3 instances of hydrocephalus in the cousins of hydrocephalus index patients, 2 were mother's sister's sons in the family with X-linked hydrocephalus mentioned above. The third, however, was in another family and was a girl.

Further Aspects

Maternal Age and Birth Order. The maternal age of the main series index patients is compared with that for the controls (who are controls for the main series index patients only), and with that for all births in South East Wales in 1960 in Table VI A. The comparisons indicate a significant excess of index patients born at maternal ages over 40 in all three conditions but especially in hydrocephalus. The maternal age distribution of the controls is closely comparable with that for South East Wales.

The birth order distribution (excluding half-sibs) of the main series index patients and the controls is given in Table VII A. Since birth order is not given for South East Wales, comparison is made

TABLE VI

MATERNAL AGE DISTRIBUTION OF (A) MAIN SERIES INDEX PATIENTS AND CONTROLS AND (B) ALL INDEX PATIENTS, COMPARED WITH THAT FOR ALL BIRTHS IN WALES I (SOUTH EAST) (1960)

		15-19	20-24	25-29	30-34	35-39	40 +	Total
(A) <i>Main Series Index Patients and Controls</i>								
Spina bifida	Observed Expected	27 20-72	86 83-95	79 79-55	48 52-16	21 28-83	15 7-78	276
Anencephaly (1 not known)	Observed Expected	24 18-52	70 75-03	62 71-10	52 46-62	25 25-77	12 6-96	245
Hydrocephalus	Observed Expected	2 1-97	7 8-00	4 7-58	7 4-97	3 2-75	3 0-74	26
Controls	Observed Expected	18 21-02	87 85-18	84 80-72	52 52-92	29 29-26	7 7-90	277
(B) <i>All Index Patients</i>								
Spina bifida	Observed Expected	35 32-10	136 130-08	116 123-26	75 80-81	41 44-68	20 12-06	423
Anencephaly	Observed Expected	30 27-40	108 111-01	91 95-20	77 68-97	37 27-13	18 10-29	361
Hydrocephalus	Observed Expected	4 3-42	13 13-84	11 13-11	9 8-60	3 4-75	5 1-28	45

TABLE VII

BIRTH ORDER (EXCLUDING STILLBIRTHS) IN (A) MAIN SERIES INDEX PATIENTS AND CONTROLS AND (B) ALL INDEX PATIENTS, COMPARED WITH THAT FOR ENGLAND AND WALES (1960).

		0	1	2	3	4	5 +	Total
(A) Main Series Index Patients and Controls								
Spina bifida (1 not known)	Observed Expected	128 103.63	58 85.25	36 44.07	27 21.00	12 10.23	15 11.82	276
Anencephaly	Observed Expected	110 91.61	65 75.36	31 38.96	20 18.57	6 9.05	13 10.45	245
Hydrocephalus	Observed Expected	7 9.76	9 8.03	4 4.15	2 1.98	3 0.96	1 1.11	26
Controls	Observed Expected	112 104.00	81 85.55	40 44.23	27 21.08	9 10.27	8 11.86	277
(B) All Index Patients								
Spina bifida	Observed Expected	195 158.82	100 130.65	49 67.55	38 32.19	15 15.68	20 18.12	423
Anencephaly	Observed Expected	163 135.54	89 111.50	45 57.65	33 27.47	12 13.38	19 15.46	361
Hydrocephalus	Observed Expected	14 16.90	13 13.90	7 7.19	1 3.42	4 1.67	6 1.93	45

with the birth order for all legitimate births to women married once only in England and Wales in 1960. The limitation to legitimate births of women married once only is not important since the proportion of illegitimate births among the patients, and indeed in South East Wales, is low, and relatively few of the index patients' parents have been married twice. The comparisons indicate a significant excess of first-born children among both spina bifida and anencephaly index patients.

The same comparisons (excluding controls) are shown for the whole series, main and subsidiary combined, of index patients in Tables VI B and VII B, and once again this shows the late maternal age effect in all three conditions and the primiparity effect in spina bifida and anencephaly.

Paternal Age. The paternal age distribution suggests no paternal age effect for any of the three conditions when compared with the maternal age

TABLE VIII
ABO BLOOD GROUP DISTRIBUTION OF MOTHERS OF PATIENTS
AND OF GENERAL POPULATION OF SURVEY AREA

Blood Group	Index Patients (main series)				General Population %	
	Spina Bifida		Anencephaly			Hydrocephalus
	No.	%	No.	%		
O	123	46.5	103	45.5	14	44.85
A	104	39.2	100	44.2	7	41.41
B + AB	38	14.3	23	10.2	3	13.74
Not known	13		21		2	
Total (excluding not known)	265		226		24	

TABLE IX
DISTRIBUTION OF PARENTAL AND GRANDPARENTAL
BIRTH PLACES (EXCLUDING THOSE NOT KNOWN) FOR
MAIN SERIES SPINA BIFIDA AND ANENCEPHALY INDEX
PATIENTS AND CONTROLS

	Parents				Great-grandparents			
	Patients		Controls		Patients		Controls	
	No.	%	No.	%	No.	%	No.	%
Glamorgan	663	65.6	360	68.1	2099	53.9	1217	58.8
Monmouth	244	24.1	115	21.7	823	21.1	418	20.2
Rest of Wales	14	1.4	6	1.1	141	3.6	56	2.7
Somerset	4	0.4	2	0.4	164	4.2	49	2.3
Rest of England	62	6.1	29	5.5	439	11.3	201	9.7
Ireland	10	1.0	6	1.1	160	4.1	83	4.0
Scotland	6	0.6	2	0.4	27	0.7	14	0.7
Elsewhere	8	0.8	9	1.7	40	1.0	30	1.5
Total	1011		529		3893		2068	

distributions. For spina bifida mean maternal age is 27.63 and mean paternal age 30.01 years, for anencephaly the means are 28.01 and 30.51, and for hydrocephalus 28.50 and 32.50. The difference is rather more than expected for hydrocephalus, but is not significant.

Blood Groups. The ABO blood group distribution for the mothers of the main series index patients is shown in Table VIII, and the observed percentage ABO group distribution is compared with those in the expected distribution in the survey area. The expected distribution in the survey area based on 2044 people has kindly been supplied by Dr. Ada Kopec of the M.R.C. Serological Population Genetics Laboratory, and she notes that there is no significant heterogeneity within the area. No significant difference exists between the mothers of patients and the general population.

The proportion of Rhesus negative mothers was 47 in 264 (17.8%) for spina bifida, 34 in 226 (15.0%) for anencephaly, and 6 in 24 (25%) for hydrocephalus. The proportion in the general population of Britain is of the order of 16%, and so again there is no difference between the findings in the mothers of patients and the general population.

Birth Places. Tabulation of the birth places of parents, grandparents, and great-grandparents showed no significant differences between main series index patients and controls. The tabulation for parents and great-grandparents of spina bifida and anencephaly index patients and controls is shown in Table IX.

DISCUSSION

Relatives

The proportion of sibs affected in this series may

TABLE X
STUDIES OF INCIDENCE IN GENERAL POPULATION AND PROPORTION OF SIBS
AFFECTED IN BRITAIN

	Index Patients	Population Incidence %	Sibs Affected with CNS Malformations	%	Relative to Population Incidence
Birmingham (Record and McKeown, 1950b) (subsequent sibs to index patients only)	Spina bifida Anencephaly	0.30 0.20	8 in 209 5 in 194 13 in 403	3.83 2.56	3.23 × 6.5
Southampton (Williamson, 1965) (all sibs)	Spina bifida Anencephaly	0.32 0.19	7 in 119 2 in 41 9 in 160	5.89 4.89	5.63 × 11.0
South Wales	Spina bifida Anencephaly	0.41 0.35	52 in 854 29 in 709 81 in 1563	6.09 4.10	5.18 × 6.8

be best compared with that in two other British population series, that of Record and McKeown (1950a, b) from the Birmingham area and that of Williamson (1965) from the Southampton area. The Birmingham series gives details of children born subsequent to the index patient; the Southampton series gives details on all the sibs of index patients. The comparison is shown in Table X.

The findings in the Birmingham and Southampton series do not differ significantly from the present South Wales study. All three studies are consistent in showing a somewhat higher risk of one or other malformation in a sib where the index patient has spina bifida. In the Birmingham and Southampton series no sibs in the families studied had hydrocephalus. In the South Wales series only one sib had congenital hydrocephalus which was not secondary to spina bifida.

One large hospital (rather than population) series has been reported in Britain for spina bifida index patients only (Lorber, 1965) based on patients referred for operation at the Sheffield Paediatric Surgical Centre. Taking only the first affected sib referred to the clinic as the index patient (a reasonable procedure since referral of a second affected child to such a centre might not be an independent event), the author found 76 of 1256 sibs affected with spina bifida or anencephaly, a proportion of 6.05%. In addition, and unlike the other studies, the Sheffield index patients had an excess of uncomplicated hydrocephalus (9 instances) among the sibs. From New York, Milham (1962) has reported a study based only on departmental records, but which probably represents a nearly complete ascertainment, since over 99% of births are in hospital and the great majority of malformations are recorded. Counting (as did the author) only one index patient per family, 10 in 338 sibs were affected; counting each family once for each patient independently

ascertained (this is probably preferable), 17 in 338 sibs were affected, a rate of 5.03%. Another hospital series from the United States (MacMahon, Pugh, and Ingalls, 1953) and series from Holland (Polman, 1951) and Denmark (Hindse-Neilson, 1938) give comparable results.

The suggestion of a raised incidence in maternal cousins, the only group on the evidence of the findings in the control series in which the reporting of malformed infants is likely to be at all complete, is also found in Williamson's (1965) series, where again raised incidences were in mothers' sisters' children. The same finding was seen in a series of families with at least 2 affected children (Carter and Roberts, 1967). In Hindse-Neilson's (1938) series again there was a raised incidence in maternal cousins, though here mothers' sisters' children are not distinguished from mothers' brothers' children. Whereas the higher incidence in maternal cousins as a group may well be due to lack of knowledge of the father's side of the family, the higher incidence in mothers' sisters' than mothers' brothers' children may be a real difference, and merits further study since it was not seen in the control series, and if real would suggest a special maternal influence.

Maternal Age and Birth Order

In this series there is an apparent clear-cut excess of first-born, and a strong indication of an effect of maternal age over 40 years, for spina bifida and anencephaly. There is no apparent effect of high parity in this series.

The increased proportion of first-born, first noted by Penrose (1964), is well seen for anencephaly in the Scottish stillbirth data (Edwards, 1958; Record, 1961) and in England and Wales since data became available in 1962 (Registrar General's annual Review I). The average rates for England and Wales for the years 1962-65 inclusive

are: 2.0 per thousand for first-born, 1.4 for second, 1.5 for third, 1.9 for fourth, 2.1 for fifth, and about 2.2 for later births.

The late maternal age effect seen in the present series for spina bifida and anencephaly was noted by Penrose in 1946, and is also present in the Birmingham series and for anencephaly in the two national series. The average rates for England and Wales for the years 1962-65 are: 2.2 per thousand for maternal age less than 20, 1.9 for 20-24 years, 1.6 for 25-29, 1.7 for 30-34, 2.0 for 35-39 years, 1.9 for 40-44 years (and 2.8 for over 45 years, though numbers here are small).

No exact standardization for birth order or maternal age can be made for the present series, but rough standardization based on national figures leaves the primiparity and late maternal age effects unaltered. In the national figures for anencephaly, as published, it is not possible to separate the effects of primiparity and maternal age. The Birmingham series showed independent effects of late maternal age and high parity for spina bifida, anencephaly, and hydrocephalus combined. A special tabulation of the anencephaly data of Scotland (Record, 1961) also showed independent effect of maternal age and high parity. It is possible, as Record notes, that this is due to social class. Large families are commonest in classes IV and V who have a high incidence of anencephaly. One reason for the apparent absence of a high parity effect in this series may be the small proportions in classes I and II and an apparently smaller class effect for spina bifida and its absence for anencephaly in South East Wales (Laurence *et al.* 1968b). However, in the Scottish data Record found that, though standardization for social class did increase the late maternal age effect and reduce that of high parity, both effects were still present.

The finding for hydrocephalus that there is a marked effect of maternal age, but little effect of parity, is the same as in other series.

Consanguinity

Consanguineous marriages are now rare in Britain. The suggestion of an increase in parental consanguinity for spina bifida and anencephaly in this series was also seen in Record and McKeown's (1950a) series where there were 3 first-cousin and 1 second-cousin marriages among parents of 742 patients with neural tube malformation, but only 1 first-cousin marriage among parents of 742 controls. More recently, suggestions of an increase in parental consanguinity for neural tube malformations have come from the WHO survey of congenital malformations (Stevenson *et al.*, 1966). In Alexandria, an

area with a high incidence both of neural tube malformations and of consanguineous marriages, the frequency of neural tube defects of all types was 14.2 per thousand (30 in 2109) among the offspring of first-cousin or closer marriages, and 5.7 per thousand among the children of unrelated marriages. A similar relationship was seen in Bombay.

Record and McKeown noted that little increase in consanguinity was to be expected for conditions as common as the neural tube malformations even if these were autosomal recessive traits. It has also been noted, however (Newcombe, 1964), that cousin marriage is a form of assortative mating; an increase in consanguinity is therefore to be expected with traits determined essentially by a polygenic predisposition with a threshold, as well as with those determined by reduction below an obligate level of heterozygosity.

With Newcombe's concept, that those affected are homozygous for all the genes concerned, the ratio of first-cousin marriages among parents of patients compared to that in the general population is similar to that with recessive inheritance—about 1.6 where the incidence of those at risk is about 1%. Models based simply on the one-sixteenth increase in variance in the offspring of first-cousin marriages give a smaller increase, a ratio of 1.2.

If the rise in paternal consanguinity were due to a proportion of cases which were the result of simple autosomal recessive inheritance (this has been suggested by Polman (1951) for anencephaly), we would expect a segregation ratio close to 1 in 4 among the sibs of index patients who have consanguineous parents. The few families in this series, with 2 in 19 sibs affected, provided no real support for this view. The 2 affected sibs were provided by a single family which included 2 index patients (633 and 830).

Blood Groups

Coffey and Jessop (1957) reported a raised incidence of blood group A among mothers of anencephalics in Dublin, but no such excess is seen in the present series, nor in a large unpublished series collected by one of us (C.O.C.).

Birth Places

When this survey was begun, it was thought that the birth places, particularly of the great-grandparents, might be of interest, particularly if areas now known to have a high incidence of neural tube malformations, for example Ireland, were a source of a relatively high proportion of great-grandparents. When it was found that South East Wales was itself a high incidence area no real differences were to be

expected. A subdivision of the great-grandparents into maternal and paternal also showed no differences between patients and controls.

Genetic Mechanisms:

Spina Bifida and Anencephaly

No conclusions may yet be drawn on the nature of the genetic predisposition to spina bifida and anencephaly. The suggestion which several authors have made of autosomal recessive inheritance is incompatible with the segregation ratio in sibships of about 1 in 20, unless it is assumed that the majority of affected zygotes abort. Further, such a mechanism for all but a minority of cases is ruled out by the apparent low concordance rates for monozygotic twins, particularly for anencephaly. Such a mechanism is also difficult to reconcile with the social class, maternal age, birth order, and possible seasonal effects. The social class and seasonal effects in this series are relatively small (Laurence, *et al.*, 1968b). It is, however, difficult to exclude the possibility that a minority of cases are straightforwardly autosomal recessive. Inspection of the array of sibships does suggest that the true segregation ratio is higher in some families than in others, and this is confirmed by the finding that the risk of recurrence in later sibs is higher after index patients who have an older sib with a neural tube malformation (Carter and Roberts, 1967); the variation, however, does not appear to be more than that which would be given by polygenic inheritance.

Polygenic inheritance, with much interaction with intrauterine environmental variables, is at present the most plausible hypothesis for the aetiology of these conditions, but more data are needed to confirm this. This mode of inheritance was suggested for neural tube malformations by Lamy and Frézal (1959). In particular, figures are needed on the proportion of second- and third-degree relatives affected, the proportion among the offspring of the increasing number of patients surviving affected with spina bifida, and the proportion affected of monozygotic and dizygotic twins of index patients.

Using the formula of 'p½' for the incidence in first-degree relatives (where 'p' is the incidence in the general population (Edwards, 1960)), with 'p' in the survey area for spina bifida and anencephaly combined being 7.7 per thousand, the expected incidence in sibs of index patients would be 8.8%, compared with the observed figure of 5.2%. Using Falconer's (1965, 1967) methods, an incidence of 5.2% for a character whose incidence in the general population is 7.7 per thousand would imply a heritability of approximately 60%. This estimate of heritability suggests that the proportion of mono-

zygotic co-twins also affected should be a little under 20%.

The recurrence risks to later children found in this study are appropriate to the survey area. They are probably not appropriate to other areas, particularly those with a lower incidence of central nervous system malformations. If the genetic predisposition to these malformations is in fact polygenic, then in low incidence areas it would be expected that the risk to sibs would be decreased, though the risk relative to the incidence in the general population will be increased.

SUMMARY

A family study of spina bifida, anencephaly, and hydrocephalus was based on 835 cases of these three malformations born in South East Wales (excepting the urban areas of Cardiff, Newport, Barry, Penarth, and Neath) between 1956 and 1962 inclusive. Except for the first year the ascertainment was estimated to be 96% complete. The population incidence of spina bifida, anencephaly, and hydrocephalus per thousand total births was 3.78, 1.73, and 0.32 for males, and 4.48, 5.40, and 0.58 for females.

Family data were collected by a visit by one of the authors to the homes of almost all of a defined main group of 551 cases. Visits were also made to the homes of almost all of a matched control series of 277 children. For the remainder, more restricted family data were collected by home visits by health visitors. Histories of affected relatives were, wherever possible, documented from hospital records or death certificates.

In the sibs of index patients with spina bifida and anencephaly, the proportion of sibs affected with spina bifida or anencephaly was over-all 5.2%, that is about 7 times the incidence (7.7 per thousand) in the general population of South East Wales. For spina bifida index patients the proportion of sibs affected was 6.1% and for anencephaly 3.5%. Estimates of incidences in other relatives are less reliable, but among mothers' sisters' children 9 were proved to have spina bifida when only 4 would be expected. Uncomplicated hydrocephalus showed no familial association with spina bifida or anencephaly.

There was a small increase in parental consanguinity for the spina bifida and anencephaly patients. An excess of first-born and a late maternal age effect were seen for spina bifida and anencephaly, and a marked late maternal age effect with hydrocephalus. The ABO blood group distribution of the mothers of the index patients was not dissimilar to that in the general population of the

same areas. The distribution of birth places of grandparents did not differ between index patients and controls.

The findings are compatible with the hypothesis that the genetic predisposition to spina bifida and anencephaly is polygenic, and that additional intrauterine environmental factors also play a part in causation. The risk of recurrence in this region of Britain would not necessarily apply to other regions with a lower incidence at birth of neural tube malformations.

This investigation could not have been carried out without the unstinting help of our hospital colleagues, the Local Health Authorities, and the local general practitioners, but we are particularly indebted to Dr. W. E. Thomas, County Medical Officer of Health for Glamorgan, Dr. G. Rocyn Jones, County Medical Officer of Health for Monmouthshire, and Dr. T. H. Stephens, Medical Officer of Health of Merthyr Borough, their Divisional Medical Officers, Health Visitors and Midwives, and to the Medical Records Officers of the various hospitals in the area. We would also like to thank the Registrar General for his help with case finding, and the Local Executive Councils, the Central National Health Service Register of the Ministry of Health, and the International Investigation Department of the Salvation Army for their help in tracing families; Mrs. K. Evans of the M.R.C. Clinical Genetics Research Unit, for visiting several families and Miss J. V. Dunscombe who helped us throughout and for a period as research assistant. We are grateful to Professor C. R. Lowe, Professor A. L. Cochrane, and Professor A. G. Watkins for their advice, and to Dr. H. Campbell for his constant statistical help.

This investigation was supported by generous grants from the Mental Health Research Fund and the Endowment Fund of the United Cardiff Hospitals.

REFERENCES

Carter, C. O., and Roberts, J. A. F. (1967). The risk of recurrence after two children with central nervous system malformations. *Lancet*, **1**, 306.
Coffey, V. P., and Jessop, W. J. E. (1957). A study of 137 cases of anencephaly. *Brit. J. prev. soc. Med.*, **11**, 174.
Edwards, J. H. (1958). Congenital malformations of the central nervous system in Scotland. *ibid.*, **12**, 115.

— (1960). The simulation of Mendelism. *Acta genet. (Basel)*, **10**, 63.
Falconer, D. S. (1965). The inheritance of liability to certain diseases, estimated from the incidence among relatives. *Ann. hum. Genet.*, **29**, 51.
— (1967). The inheritance of liability to diseases with variable age of onset, with particular reference to diabetes mellitus. *ibid.*, **31**, 1.
Hindse-Neilson, S. (1938). Spina bifida—Prognose; Erbllichkeit. Eine klinische Studie. *Acta chir. scand.*, **80**, 525.
Lamy, M., and Frézal, J. (1959). In *Malformations Congénitales du Cerveau* Ed. by G. Heuyer, M. Feld, and J. Gruner. Masson, Paris.
Laurence, K. M., David, P. A., and Carter, C. (1968a). The major central nervous system malformations in South Wales. I. Incidence with local variations and geographical factors. *Brit. J. prev. soc. Med.*, **22**. In the press.
—, —, and — (1968b). The major central nervous system malformations in South Wales. II. Pregnancy factors, seasonal variation and social class effects. *ibid.*, **22**. In the press.
Lorber, J. (1965). The family history of spina bifida cystica. *Pediatrics*, **35**, 589.
MacMahon, B., Pugh, T. F., and Ingalls, T. H. (1953). Anencephalus, spina bifida and hydrocephalus. Incidence related to sex, race, and season of birth, and incidence in siblings. *Brit. J. prev. soc. Med.*, **7**, 211.
Milham, S. (1962). Increased incidence of anencephalus and spina bifida in siblings of affected cases. *Science*, **138**, 593.
Newcombe, H. (1964). Summary. Congenital malformations—Papers and discussions. Presented at the Second International Conference of Congenital Malformations, p. 345. The International Medical Congress, New York.
Penrose, L. S. (1946). Familial data on 144 cases of anencephaly, spina bifida and congenital hydrocephaly. *Ann. Engen. (Lond.)*, **13**, 73.
Polman, A. (1951). Anencephaly, spina bifida and hydrocephaly. *Genetica*, **25**, 29.
Record, R. G. (1961). Anencephalus in Scotland. *Brit. J. prev. soc. Med.*, **15**, 93.
—, and McKeown, T. (1950a). Congenital malformations of the central nervous system. II. Maternal reproduction history and familial incidence. *ibid.*, **4**, 26.
—, and —, (1950b). Congenital malformations of the central nervous system. III. Risk of malformation in sibs of malformed individuals. *ibid.*, **4**, 217.
Registrar General's Statistical Review of England and Wales. Part II Tables, Population, years 1956–62. *ibid.* Part I Tables, Medical, years 1962–65.
Stevenson, A. C., Johnston, H. A., Stewart, M. I. P., and Golding, D. R. (1966). Congenital malformations. *Bull. Wld Hlth Org.*, **34**, Suppl.
—, and Warnock, H. A. (1959). Observations on the results of pregnancies of women resident in Belfast. I. Data relating to all pregnancies ending in 1957. *Ann. hum. Genet.*, **23**, 382.
Williamson, E. M. (1965). Incidence and family aggregation of major congenital malformations of central nervous system. *J. med. Genet.*, **2**, 161.

Appendix I
Main Series

M, male; F, female (*italics indicate affected relative*); m, miscarriage; sb, stillbirth; *, index patient; [], twins; (A), anencephalus; (S), spina bifida; (H) hydrocephalus.

Serial No.	Sibship	Date of Birth	
		Mother	Father
A: SPINA BIFIDA			
One-child families			
007	m 10/61; *M 9/62		
017	*M 7/62	1936	1935
022	*F 6/62	1943	1941
		1933	1924

Appendix I Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
046	m 11/61; *M 11/62	1940	1939
053	*M 9/61	1936	1934
056	*M 6/60	1932	1932
061	*M 4/62	1940	1938
062	*F 5/60	1938	1930
077	*M 2/62	1929	1927
078	*M 11/62	1943	1942
082	*M 6/62	1942	—
087	*F 6/62	1943	1942
091	*F 6/61	1936	—
104	*M 10/61	1942	1940
111	*M 12/60; m -/62	1929	1922
117	*M 3/62	1935	1930
118	*F 6/62	1939	1938
121	*M 8/62	1943	1940
136	*F 2/61	1934	1928
137	*M 8/57	1934	1934
138	*M 11/61	1939	1938
163	m -/56; *M 6/59; m -/60; m -/61	1931	1932
165	m -/58; m -/60; *F 12/62	1934	1931
189	*F 5/58	1936	1929
191	*F 10/61	1941	1929
197	m 1/60; m 11/60; m -/61; *F 9/62	1937	1936
203	*F 3/58	1921	—
214	*M 4/62	1939	1939
220	*F 4/57	1934	1924
223	*M 4/62	1943	1940
244	*M 5/60	1937	1934
255	*F 8/58	1929	1930
257	*F 9/61	1940	1936
262	*F 10/62	1937	1934
290	*M 3/60	1939	1929
299	*F 9/60	1941	1940
306	*M 3/62	1935	1931
319	*M 9/61	1940	1935
322	*M 4/57	1934	1932
323	*M 10/57	1928	1930
347	*M 8/58; m 5/59	1934	1933
357	*F 1/62	1941	1941
375	*F 2/58	1936	1936
376	*F 4/62	1943	1941
379	*F 10/62	1941	1940
381	*M 4/61	1939	1940
405	*M 3/62	1942	1938
410	*M 4/59	1934	1931
414	*F 12/60	1939	1935
417	m -/56; *F 9/57	1934	1929
438	*M 2/60	1932	1930
444	*F 4/62	1939	1937
446	*F 11/60	1925	1922
457	m -/60; *F 7/62; m -/63	1935	1933
461	*M 9/60	1931	1923
471	*M 7/60	1933	1921
474	*M 8/61	1939	1938
475	*M 9/61	1936	1932
481	*F 5/60	1933	1932
489	*M 6/62	1941	1939
501	*M 10/61; m -/62	1943	1942
509	*F 9/62	1944	1944
524	*F 7/62	1937	1935
528	*F 3/60	1929	1921
530	*M 4/62	1937	1932
539	*F 8/62	1931	1926
542	*M 7/62	1943	1942

Two-child families

005	F -/60; *M 10/62	1933	1936
011	m -/58; F 4/60; *M 1/62	1938	1937
013	m -/54; F -/55; *F 11/60	1934	1930

Appendix I Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
015	*M 6/60; F -/62	1939	1937
023	M -/58; *F 12/60	1937	1937
040	m 5/56; *F 7/60; M 6/63	1929	1928
043	*M 11/60; M 4/62	1941	1939
045	F 12/58; *F 2/60; m -/61	1931	1931
069	M(S) 4/55; *F 8/62	1933	1932
073	*F 2/60; m -/61; F 1/62	1938	1937
075	F 6/58; *M 6/62	1937	1935
083	F -/59; *M 11/61	1935	1932
088	M -/58; *M 11/61	1933	1935
102	F -/58; m -/60; *M 3/62	1921	1928
106	*M 7/60; M 1/62	1941	1940
109	m -/56; F 5/57; m -/59; *F 11/62	1929	1933
113	m -/51; M -/52; *M 5/61	1923	1918
122	*F 2/60; M -/61; m -/62	1938	1932
126	F -/53; *M 1/61	1929	1924
128	*F 8/61; M -/62	1926	1927
134	*F 12/57; m -/58; M 5/61	1931	1931
156	*M 9/60; M 3/62	1936	1934
160	*F 1/60; F 3/61	1935	1937
162	F -/55; *F 1/60	1934	1934
167	m -/59; F -/60; *M 9/62	1939	1933
169	*F 9/61; M 7/62	1937	1938
176	*M 7/60; M 5/62	—	—
178	M 9/60; *M 8/61	1930	1931
190	M -/46; *F 11/61	1930	1931
194	*M 2/58; F 3/59sb	1937	1935
213	F 11/54; *F 5/56; m -/61	1936	1934
215	F 3/52; *F 12/62	1931	1931
224	*M 12/62; F -/64	1933	1934
231	m -/56; *F 9/57; F 11/59	1931	1926
232	F 2/60; *F 3/62	1934	1931
237	*F 5/59; M 6/61	1938	1936
241	m -/53; M -/57; *F 8/60	1920	—
254	m -/59; *F 1/60; m -/61; M -/62	1938	1939
259	M(S) 11/54; m 8/58; *M 7/59	1932	1931
263	M 7/55; *M 10/56	1933	1929
264	*F 2/56; m 8/58; M 1/60	1931	1929
268	*M 7/61; F -/63	1935	1929
274	m -/54; *M 10/56; M 2/62	1932	1934
285	F 6/56; *F 3/61	1934	1933
301	*F 10/60; M 12/61	1935	1926
307	*F 8/61; m -/62; F -/63	1939	1937
308	m -/57; M 2/59; *F 6/61	—	1936
315	*M 9/59; M 6/60	1937	1935
334	M 3/55; *F 11/56	1934	1933
351	*F 5/58; M 1/62	1938	1936
370	*F 8/61; M 12/62	1940	1938
387	*M 2/56 No. 387; *F 4/57 No. 388	1928	1927
388			
399	[*M 1/61; M 1/61]	1939	1933
408	M 10/56; *M 10/57	1935	1935
411	F 3/58; *M 6/60	1926	1925
424	F 8/59; *M 1/62	1931	1930
425	M -/59; m -/60; *F 10/61; m -/62	1937	1935
437	M -/56; m -/57; *M 10/60	1934	1932
454	*F 6/61; M 5/62	1932	1926
484	*M 2/61; F -/63	1942	1940
487	m -/56; m -/57; m -/58; *F 9/60; F 12/62	1935	1920
488	m -/60; *M 12/61; M 11/62	1941	1941
503	M -/56; *M 3/61	1926	1924
513	M -/59; *M 3/61	1939	1938
523	F(A) 5/60 No. 832; m -/61; *M 4/62	1932	1934
525	*M 3/61; F(A) 9/62 No. 526	1937	1938
535	*M 3/61; M 8/62	1932	1930
536	*F 12/60; F 8/62	1942	1940
537	*F 9/61; m 4/62; F 3/63sb	1943	1942
538	M -/58; m -/60; *F 4/61	1937	1934
544	M 11/56; *M 3/60	1929	1926
545	*F 11/60; M -/62	1934	1936
546	M -/60; *M 1/61	1940	1940

Appendix I Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
Three-child families			
004	*M 12/60; F -/62; M -/64	1943	1941
009	*F 4/60; [F 5/61sb; F 5/61sb]	1934	1936
012	M 2/55; *F 8/61; M 10/62	1932	1930
014	*F 10/60; F 10/61; M 6/64	1937	1924
028	M -/56; M 12/60; *M 5/62	1937	1935
033	F 7/58; *F 5/60; M 4/62	1941	1936
041	*F 8/61; F 10/62; M 11/63	1940	1938
057	m -/59; m -/60; *M 10/61; F(A) 8/62 No. 058; M 8/63	1935	1937
070	F -/56; *F 2/61; M 8/62	1925	1925
074	M -/51; F -/53; [m -/57; m -/57]; m -/59; *F 12/60	1929	1926
080	M 6/57; M 9/58; *F 10/61	1938	1937
086	*M 3/61; F -/62; F -/64	1928	1922
089	M 11/52; M 5/54; m -/61; *M 12/62	1932	1928
092	F -/57; F -/59; *F 7/60	1937	1937
093	F 3/51; F 5/53; m 6/58; m 11/59; *M 7/61	1922	1920
094	M -/58; M -/60; *F 1/62	1940	1938
095	F -/55; m -/56; M -/57; m -/58; *M 4/60; m -/62	1936	1934
096	M -/58; F -/59; *M 11/61	1931	1928
097	M -/55; M -/58; *M 6/60	1934	1929
110	M -/54; [F 5/60sb; *M 5/60]; m -/62	1932	1930
114	*M 2/60; M 12/61; M(S) 11/63	1937	1933
145	F -/54; *F 7/56; M 5/61	1933	1928
166	F -/45; M -/51; m -/53; *F 3/59	1926	1924
170	F -/42; M -/49; *M 6/62	1919	1911
171	*F 5/58; F 4/60; m -/61; M 5/62	1929	1928
172	*F 3/58; F 6/60; F 10/61; m 6/62	1936	1936
183	*F 2/58; M 9/61; F 6/62	1929	1930
228	F 12/60; *M 9/62; F 9/63	1939	1940
249	F 8/54; m -/55; *M 6/58; F -/59	1928	1922
251	*F 5/57; M -/58; F -/61	1935	1933
253	m 2/56; F 2/57; *F 7/58; M 3/60	1928	1927
260	*M 8/58; F 7/60; F 9/62	1935	1936
266	F -/50; m -/55; [*F 5/59; M 5/59]	1928	1927
292	*F 3/57; F(A) 5/58 No. 293; F 10/60	1939	1933
297	*F 7/56; M 1/58; F 2/62	1933	1932
311	*F 3/59; F -/61; F -/63	1941	1935
324	F 12/46; M 11/47; m -/48; *F 5/57	1917	1915
327	*M 12/57; M -/60; m -/61; F 10/62	1941	1939
329	*F 2/61; F -/62; F -/64	1938	1937
333	M 10/55; F 1/57; m 2/58; *F 1/60; m 12/60	1921	1911
342	F(A) -/54; M -/56; *F 5/61	1931	1933
346	M -/54; M -/56; *F 1/57	1928	1925
350	F 3/61; *M 4/62; F 10/63	1932	1932
359	F -/55; F -/57; m -/58; *M 6/60	—	1934
382	M -/57; M -/59; *F 9/61	1939	1936
389	*F 7/56; [M 5/57; F 5/57]	1932	1933
391	M -/54; F -/56; *F 1/60	1933	1930
395	*M 1/59; M 2/60; M 2/61	1939	1939
401	F -/56; *F 11/58; M -/59	1931	1930
421	m -/59; M -/60; m -/60; *F 7/61; F 1/63	1940	1930
422	F -/48; M -/50; m -/56; *F 10/61	1924	1925
427	M 7/59; *F 9/60; M 1/62	1940	1935
435	F -/56; F -/58; *M 10/61	1933	1932
441	*M 6/60; F -/62; F -/64	1936	1936
448	M -/50; M -/55; *F 8/61; m -/62	1927	1919
483	F 7/59; *F 3/60; F 10/62	1931	1928
497	F -/47; F -/49; m -/59; m -/59; *F 10/60	1920	1920
515	M 6/48; M 6/55; *F 2/62	1928	1921
534	F -/47; M -/53; *F 9/60	1923	1924
540	F 2/60; *M 9/61; M(S) 7/62 No. 833	1940	1939
543	m -/57; m -/58; M -/59; *M 9/61; M -/63	1933	1926
834	M -/41; m -/45; F -/48; m -/50 [m -/54; m -/54]; m -/58; *F 1/60	1922	1925
Four-child families			
002	F 7/39; F(S) -/40; M -/41; *M 1/61	1919	1909
026	F -/54; F -/56; m -/57; F -/58; m -/60; *F 7/62	1929	1926
047	F -/51; M -/54; F -/58; *F 11/61	1931	1923
048	M -/47; M -/50; m -/52; M -/54; *F 5/61	1917	1922
049	F -/47; F -/49; m -/56; F -/60; *F 8/61	1924	1922
054	F -/51; M -/52; M -/53; *M 9/60	1920	1918

Appendix I Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
081	M -/53; F 6/55sb; M -/57; *F 8/62	1926	1926
133	F(A) 8/53; m -/54; F(S) 7/56 No. 707; M(A) 7/57 No. 708; *F 3/60	1928	1926
141	M -/48; M -/55; F -/58; *F 2/62	1928	1925
148	M -/54; M -/57; F -/58; *F 4/61	1932	1930
157	M 9/56; *M 5/59; M 10/60; M 7/62	1932	1931
164	M -/52; M -/57; [M 11/60; *F 11/60]	1929	1927
193	F -/56; M -/57; M -/59; *F 11/61	1936	1925
227	F -/45; F(S) -/50; M -/54; *F 9/62	1922	1921
240	m -/50; M 3/51; F 1/52; M 3/56; *M 7/61	1923	1911
247	*M 4/58; M 4/59; M 4/61; F 9/62	1938	1934
291	M -/50; F -/51; M -/52; *M 1/58	1924	1925
304	m -/56; *M 2/58; F 11/59; M 1/61; M 6/64	1928	1929
328	M 9/43; M 9/45; F 9/49; *M 8/59	1920	—
330	*F 8/57; m -/58; m -/59; M -/60; F 9/61; F 3/63	1937	1933
413	*M 6/58; M 6/59; F 9/61; M 10/62	1938	1934
440	F(S) 8/58 No. 650; F 6/61; *F 7/62; M 9/63	1935	1927
458	M -/52; M -/55; M -/57; *F 3/61	1932	1930
460	F -/51; M(S) 7/57 No. 551; F -/60; *F 1/62	1923	1928
480	F -/57; M -/59; *M 6/61; F -/62	1936	1933
500	M -/48; M -/58; *M 3/61; F 9/62sb	1930	1924
508	M -/41; F -/44; F -/47; *F 9/60	1920	1921
511	F 12/50; M 10/52; M 4/56; m -/59; *M 4/60	1929	1928
533	F -/56; m -/57; M -/59; M -/60; *F 10/62	1937	1910
<i>Five-child families</i>			
025	M -/48; F -/49; M -/50; M -/53; *F 10/60	1936	1921
140	m -/53; m -/54; F(A) -/55; M -/57; F -/59; *F 1/62; M -/63	1930	1928
202	M -/49; F -/52; F -/54; *F 7/58; M -/62	1928	1924
248	m -/55; M -/56; *F 5/57; M -/59; F -/60; F -/62	1933	1934
282	F -/48; m -/49; F -/54; F(S) -/55; F -/57; *M 5/59	1930	1927
300	F -/53; F -/56; m -/58; *F 1/59; M -/60; M -/62	1928	1927
314	M 10/54; F 11/55; *F 10/58; [M 2/61; M 2/61]	1936	1931
380	M 12/49; F 12/50; M 6/54; F 6/55; *F 3/58	1927	1922
397	M -/47; M -/48; m -/49; F -/51; m -/52; F -/55; *M 4/58	1927	1923
404	F -/49; F -/50; *M 7/57; M -/60; F 6/62	1928	1927
409	*F 10/57; M 11/59; M -/60; F -/61; M -/62	1938	1936
423	F -/54; F -/55; m -/56; M -/57; F(A) 1/60 No. 288; *F 12/61	1933	1927
450	M -/52; F -/55; F -/57; *F 2/60; F -/62	1928	1923
496	M -/48; M -/52; F -/55; *M 8/61; M -/62	1929	1928
519	M -/54; M -/57; F -/58; F -/59; *M 10/61	1931	1929
<i>Six-child families</i>			
101	F -/43; F -/44; M -/45; F -/46; M -/54; *M 5/62	1924	1919
120	M -/49; F -/51; M -/56; m -/57; M -/58; *F 7/62; F -/63	1930	1930
129	M -/51; M -/53; F -/54sb; F -/57; M -/58; *M 8/62	1921	1923
146	M -/56; M -/58; F -/59; *F 3/61; M -/62; M -/63	1936	1934
175	F -/54; *F 6/56; M(S) -/57; M -/59; M -/60; F -/62	1931	1932
321	m -/47; M 6/48; M 10/50; F 4/52; M 4/54; F(A) 6/59 No. 320; *F 12/61	1928	1927
332	F(A) -/46; F -/48; M -/49; F -/51; F(A) -/53; *M 7/60	1927	1924
335	F -/47; m -/48; M -/49; M 1/52; m -/53; M(S) 10/55; *F 3/57; F -/59sb	1921	1916
358	M 9/47; F 12/48; M(S) -/50; M 11/53; *M 6/56; M 9/59	1924	1922
378	M -/55; m 12/55; M -/57; F -/58; *M 2/59; M 9/59; F -/62	1929	1931
420	M -/43; F -/45; M -/48; M -/52; M -/55; *F 7/62	1922	1918
436	M -/54; M -/56; M -/57; M -/58; M(A) 4/60; *M 11/61	1929	1929
473	F -/48; M -/50; F -/54; M -/58; M -/60; *F 11/62	1930	1918
532	F -/51sb; m -/52; F -/53; M -/55; F -/59sb; *F 3/60; F -/61	1929	1924
<i>Seven (+)-child families</i>			
038	M 5/51; M 9/52; M 6/54; [F 6/56; F 6/56]; M 4/58; [*F 4/60; F 4/60]; F 7/62	1932	1927
084	M -/52; M -/53; F -/54; F -/56; F -/57; M -/59; M -/60; *F 1/62	1932	1928
198	M -/51; M -/52; F -/55; F -/56; F -/57; *F 2/60; M -/61	1927	1922
242	M -/43; M -/45; M -/49; M -/53; M -/54; M -/57; F -/58; F 2/60; *M 6/62	1921	1910
276	F 11/43; F -/45; M -/52; M -/55; *F 7/56; M 11/60; F 11/61	1920	1914
298	F -/45; M -/48; F -/50; F -/52; F -/54sb; m -/55; M -/56; *F 2/59; F -/60; M -/62; M -/63	1923	1923
303	M -/39; M -/40; F -/42; F -/44; M -/47; M -/51; M -/52; M -/54; F -/57; F -/59; M 1/60; *F 10/60; m -/61	1918	1917
338	M -/43; M -/46; M -/47; M -/51; F -/53; *M 4/58; F -/63	1931	1928
340	F 4/42; F(S) 4/43; F 10/44; M(S) 4/47; F 8/48; M(A) 2/50; *M 9/57; F 3/61	1918	1916
349	F -/43; M -/45; M -/46; F -/49; F -/51; F -/54; *M 5/58	1920	1925
383	M -/38; F -/39; M(S) -/42; M -/44; M -/47; F(A) -/48; M(S) -/49; M -/51; F -/54; *M 11/57; M -/60	1915	1911
385	M -/49; F -/51; F -/53; M(S) -/55; F -/56; *M 10/57; F -/59	1932	1931
392	M -/37; M -/46; M -/47; M -/49; F -/52; F -/54; *M 3/61	1920	1912
434	m 6/53; M 5/54; F 7/55; F 9/57; *M 6/60; F 8/61; [M 3/63; F 3/63]	1934	1933
485	F -/54; M -/57; M 9/58; *M 11/60; M -/61; [M 6/62; M 6/62]; m 5/63	1931	1927

Appendix I Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
B: ANENCEPHALUS			
One-child families			
001	*F 11/62	1943	1943
018	*F 7/62	1940	1939
019	*F 6/61	1944	1941
031	*F 12/60	1940	1938
044	m -/60; *F 9/61	1942	1938
065	*M 10/62	1940	1933
066	*F 10/62	1945	1942
079	*M 3/61	1937	1935
105	*F 11/62	1941	1933
107	*M 7/61	1939	1937
112	*F 7/62	1938	1938
115	*F 7/61	1941	1940
116	*F 10/62	1940	1938
125	m -/61; *F 11/62	1934	1934
147	*F 7/62	1939	1940
150	*F 12/56	1925	1924
151	*F 12/59	1934	1932
161	*M 10/59	1915	1914
177	*F 1/60	1928	1931
187	*F 10/61	1943	1940
212	*F 8/61	1935	—
218	*M 12/62	1938	1939
230	*F 7/57	1925	1921
243	*M 2/59	1937	1933
273	*F 5/56	1927	1923
275	*F 3/61	1939	1934
284	*F 11/56	1930	1910
317	*M 9/62; m 7/63	1938	1934
325	*F 4/60	1925	1926
348	*M 5/60	1932	1928
354	*F 12/62	1939	1932
361	*M 3/62	1939	—
363	*F 8/62	1936	1934
377	*F 4/61; m 12/61	1939	1938
396	*F 7/60	1919	1923
407	*F 8/60	1939	1937
416	*F 11/62	1944	1941
418	*F 5/57	1927	1931
419	*M 8/61	1920	1936
432	*M 5/62	1940	1937
433	*M 10/62	1942	1940
443	m -/59; *M 4/60	1927	1928
453	*F 9/62	1942	1940
456	*F 12/62	1946	—
463	*F 4/62	1941	1942
466	*F 5/62	1936	1931
478	*F 5/62	1931	1923
479	*F 8/61	1928	1935
486	*F 11/62	1934	—
492	*M 7/61	1938	1938
493	*F 11/60; m -/61	1926	1917
495	*F 10/62	1941	1940
505	*F 8/61	1922	1917
510	*F 3/62	1943	1931
529	*F 6/62	1941	1938
547	*M 6/60	1932	1925
Two-child families			
006	F 6/60; *F 5/62	1937	1938
016	M 10/54; *M 3/62	1930	1928
024	M -/53; *M 3/62	1932	1931
027	*M 6/61; F -/63	1940	1940
037	M 3/60; *F 10/62	1937	1936
042	*M 4/60; M 4/61; m 11/62	1938	1932
068	*F 5/61; F 7/62	1940	1938

Appendix I Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
103	*F 11/61; M -/63	1941	1929
108	F -/58; m -/59; *M 4/61; m -/62	1931	1926
123	F 5/56sb; *F 12/61	1935	1932
127	*F 9/60; M 11/61	1930	1927
131	M -/56; *F 3/60	1933	1933
143	F -/59; *F 12/62	1934	1931
152	*F 3/62; F -/63	1941	1933
153	*F 2/59; m 1/60; F 5/61	1935	1924
155	M -/50; *F 3/61	1930	1929
168	M 10/57; *M 3/60	1935	1933
174	*F 11/56; M 7/58	1937	1932
186	*F 12/59; M 5/61	1939	1937
192	F -/60; *F 5/62	1937	1937
199	F -/49; m -/57; *M 2/61	1926	1925
201	m -/57; *F 8/59; M 3/60	1938	—
204	*F 8/59; F 10/62	1939	1937
209	*F 2/59; M 6/61	1938	1934
210	M -/56; *F 4/57	1938	1935
216	*F 11/58; M 4/61	1926	1923
221	*F 4/60; M 8/61	1920	1924
222	F 11/56; m -/58; *F 1/60	1929	1923
235	*F 12/57; M 12/60	1930	1930
236	F -/56; *M 4/60	1938	1938
239	*F 10/58; M -/64	1937	1937
246	*M 8/60; M 2/62	1942	1940
250	*F 1/61; M -/64	1939	1934
252	M 12/52; *F 6/57	1933	1927
256	*M 6/59; F -/62	1936	1933
265	*F 5/60; M 1/62	1940	1933
269	*M 8/57; M 8/59; m 4/62	1935	1932
270	M -/52; *M 12/61	1931	1931
271	F 10/57; *F 3/62	1931	1931
283	F -/54; *F 10/56	1924	1926
289	F 4/57; *F 7/61	1934	1934
295	M 10/48; m -/52; *M 3/58; m -/61	1926	1921
296	*M 3/57; M -/58; m -/60	1931	1925
336	M 5/54; *F 11/60	1918	1910
343	F 12/56; *F 11/59	1934	1925
345	*M 11/56; M 4/61	1937	1931
352	F 2/58; *F 12/61; m 9/62	1933	1928
360	*M 3/60; F 5/62	1942	1939
364	M 5/58; *F 1/60	1934	1932
371	M 1/54; m 7/60; *M 5/61; m 2 62	1930	1929
373	M -/49; *F 10/57	1924	1926
374	m 3/58; *F 1/59; F 1/60	1925	1920
390	M 4/61; *M 4/62	1940	1931
393	M 1/49sb; *F 5/57	1927	1926
394	M -/41; *M 6/59	1924	1924
403	M 8/59; *F 4/62	1935	1931
430	M -/53; *F 12/60	1930	1929
442	F -/55; *F 6/60	1932	1928
451	*F 10/61; M 12/62	1941	1939
455	M -/59; m -/60; *F 11/61; m 9/62	1935	1934
459	*F 9/61; F -/62	1940	1941
462	*F 2/60; M 12/61	1934	1933
464	*F 10/60; M -/63	1941	1937
465	F -/59; *M 6/61	1930	1930
468	M -/53; *F 5/60	1925	1923
469	[F 7/62sb; *F 7/62]	1942	1930
476	*F 1/60; M 12/60	1935	1934
477	M -/60; *F 12/62	1938	1933
491	F -/54; *F 7/61	1931	1924
498	M -/54; *F 3/61	1931	1930
504	M 5/59sb; *F 9/60	1940	1935
514	*F 9/61; m -/62; F -/63	1941	1939
526	M(S) 3/61 No. 525; *F 9/62	1937	1938
541	*F 10/60; F 7/62	1939	1937

Appendix I Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
Three-child families			
003	F 3/58; F 12/59; *M 8/62	1933	1932
021	*F 5/60; F 5/62; M 11/63	1941	1938
030	F -/52; F -/55; *M 9/62	1932	1932
032	*F 1/60; F 2/61; F(S) 2/63	1938	1936
058	m -/59; m -/60; M(S) 10/61 No. 057; *F 8/62; M 8/63	1935	1937
072	F 12/52; F 9/54; *F 4/61	1931	1936
076	M -/50; M -/52; *M 1/61	1922	1918
085	F -/60; [F 1/61; *F 1/61]	1935	1931
090	M -/53; M -/58; *F 7/61	1931	1929
130	M -/58; M -/59; *F 6/61	1933	1933
135	M -/49; F -/53; *F 7/60	1929	1925
139	F 9/48sb; M -/52; *F 1/61	1925	1924
142	F -/42; F -/45; *F 3/58	1919	1920
144	m -/57; F 1/60; m 1/61; m 9/61; *M 7/62; F 8/63	1935	1937
149	M 7/55; F -/58; *F 1/62	1930	1927
154	M 11/54; *F 4/59; M 3/62	1934	1931
181	M -/50; M -/57; *F 10/61	1925	1917
188	*F 3/56; F 9/57; M 4/60	1926	1919
206	*F 11/56; F -/57; M -/59	1935	1934
207	M -/47; F -/49; *F 11/57	1926	1924
211	F -/52; F -/56; *F 11/59	1930	1929
217	F 12/45; m -/50; F 7/53; *M 4/61	1925	1924
225	M -/48; M -/50; *F 11/62	1924	1923
238	M 12/57; M 7/60; *F 6/61	1936	1936
245	M 12/57sb; *F 10/59; F 9/60	1934	1933
258	M -/53; *M 4/57; M -/58	1925	1914
287	m -/55; M 8/57; *F 8/58; F 7/60	1923	1919
293	F(S) 3/57 No. 292; *F 5/58; F 10/60	1939	1933
294	M 11/57; *M 1/58; M 2/61	1934	1933
302	m -/57; *F 1/59; F 8/60; M 3/63	1936	1931
305	*F 1/58; M 2/59; M 2/61	1929	1920
309	F 10/55; F 4/59; *F 1/62	1935	1935
310	m -/57; *F 10/58; M -/59; F 3/61	1936	1933
313	*F 5/56; M 6/58; F 2/60	1934	1933
326	M 6/52; *M 5/57; M 6/61	1925	1925
331	*M 7/56; F 12/57; M -/60; m -/61	1933	1932
337	F -/49; F -/58; *M 8/60	1928	1924
339	m -/53; M -/55; *F 2/58; m -/60; F(A) 11/61	1931	1930
356	M -/49; F -/52; *F 4/57; m -/61	1920	1915
365	F -/51; F -/52; *F 7/56	1932	1928
369	M -/47; M -/49; m -/54; m -/55; *F 10/58	1926	1922
372	M 7/56; *F 9/58; M 6/62	1937	1937
398	M 3/48; M 8/49; *M 9/58	1926	1921
406	F 11/53; *F 8/57; F 11/58	1928	1926
415	F 7/48; M 12/50; *F 4/57	1923	1923
426	M -/57; *F 9/60; M 6/62	1936	1931
428	M -/58; *F 8/60; M -/62; m -/64	1936	1938
447	*F 4/61; M -/62; F(A) 12/63	1935	1934
449	M -/46; F -/52; m -/56; *F 2/60	1923	1920
452	M -/54; m -/57; *F 5/61; M -/62	1934	1932
467	F -/61; *F 11/62; M -/64	1943	1941
482	M -/56; *F 7/61; F -/62	1935	1934
499	F -/50; M -/53; *F 9/60	1927	1923
506	m -/59; *F 2/60; F -/62; M -/64	1941	1937
518	M -/58; [*F 9/62; M 9/62sb]	1937	1938
520	M -/51; M 5/60; *F 12/62	1927	1927
521	*F 8/61; M -/62; M -/63	1936	1922
527	F 1/57sb; M -/59; *F 7/60	1923	1921
Four-child families			
059	F -/52; M 1/56; F -/57; m -/60; *F 9/62	1928	1926
063	*M 2/60; F -/61; M -/62; M -/63	1928	1921
067	M 9/52; M 12/53; M 3/57; *F 11/62	1930	1930
071	M -/59; *M 4/61; F -/62; F -/64	1935	1931
099	F -/50; M -/52; M 9/56; *F 6/60	1924	1926
159	M 4/49; M 4/50; F 11/53; *F 3/57	1929	1919
173	*F 6/56; F 11/57; F 7/61; F 7/62	1933	1931
179	F -/50; m -/55; *M 7/57 No. 179; *F 7/58 No. 180; M -/60	1929	1927
180			

Appendix I Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
200	M -/46; M -/48; F -/50; *F 11/57	1919	1918
226	m -/55; m -/56; m -/56; *F 3/57; M 6/59; F 6/60; M 8/62	1923	1923
272	M -/41; F -/43; M -/47; m -/48; *F 11/57	1920	1918
277	M -/56; *F 3/57; F -/59; M -/61	—	—
281	F 8/52; M 4/55; F 9/56; *F 10/60	1932	1930
286	M -/53; *F 2/56; M 12/56; M -/61	1930	1927
318	M -/52; F -/55; F -/59; *M 8/61	1928	1922
344	M 12/46; M 3/48; F 5/54; *F 6/59	1921	1914
353	M -/51; m -/53; M -/54sb; m -/55; m -/55; F -/56; m -/57; *F 9/58	1933	1931
362	F -/47; F -/50; *F 8/57; M 9/60	1923	1921
366	m 10/56; m 2/57; *F 1/58; M 11/59; F 1/61; F 8/62	1937	1931
384	F 6/54; M 4/60; [M 8/61; *M 8/61]	1930	1927
402	M -/57; M -/60; *F 8/61; F -/63	1936	1935
431	M -/47; F -/49; m -/51; m -/53; F -/56; *F 5/62	1926	1923
445	F(A) 11/55; M 12/56sb; F -/60; *F 12/61; m 10/62	1928	1927
490	M 1/59; F 1/60; M 7/61; *F 2/62	1937	1936
494	M -/47; F -/48; M -/54; *F 10/61	1924	1920
507	*F 7/60; M 1/62; M 7/63; F(S) 9/64	1942	1936
522	M -/59; *F 4/60; m -/61; F -/61; m -/62; F(S) -/63	1939	1931

Five-child families

034	M -/40; M -/42; M -/44; F -/49; *M 10/61	1921	1915
055	F -/50; F -/51; F -/55; *F 9/60; F -/61	1931	1928
060	M -/56; M -/58; *F 10/60; F -/62; F -/63	1934	1918
119	M -/40; M -/44; M -/45; F -/57; m -/58; *F 6/62	1917	1917
185	M -/52; M -/56; M -/58; *F 3/59; M 12/59	1932	1932
288	F -/54; F -/55; m -/56; M -/57; *F 1/60; F(S) 12/61 No. 423	1933	1927
312	F 7/53; M 7/55; M 11/56; *M 12/57; F 5/59	1920	1922
367	M 4/40; F 7/46; M 5/48; F 11/55; *F 3/57	1917	1911
386	M 12/58; M 12/59; M 12/60; *M 8/62; F 8/63	1932	1929
412	*F 3/58; M -/59; M -/60; [F -/62; F -/62]	1937	1937
470	M -/57; F -/58; F -/59; *M 7/61; F -/63	1925	1931

Six-child families

020	m -/47; M -/48; m -/48; M -/49; M -/51; M -/52; m -/54; [m -/55; m -/55]; F -/57; *M 5 61	1927	1924
064	F -/52; M -/53; M -/55; F -/57; F -/59; *F 8/60	1929	1927
196	F -/41; m -/42; F -/43; M -/44; M -/45; F -/53; *F 12/57	1913	1911
208	M 3/54; M 4/55; F 11/56; F 9/58; *F 8/60; m 7/61; F 8/62sb	1937	1932
267	M -/53; F -/54; F -/55; F -/57; M -/60; *F 5/62	1935	1932
320	m -/47; M 6/48; M 10/50; F 4/52; M 4/54; *F 6/59; F(S) 12/61 No. 321	1928	1927
355	M -/53; F -/54; M -/55; *M 3/56; F -/58; F -/61	1934	1933
439	F -/43; F -/44; F -/46; M -/51; *F 7/60; m -/61; M 12/62	1923	1919
512	F -/48; M -/50; F -/53; F -/56; F -/58; m -/60; *F 8/61	1920	1926
517	F 6/44; [F 3/49; F 3/49]; F 4/53; M 6/55; *F 3/62	1919	1918
531	M -/52; M -/54; M -/57; *F 8/60; F -/61; F -/62	1930	1933

Seven (+)-child families

029	M 11/41; M 3/43; F 5/53; F(A) 2/55; F(A) 1/57 No. 808; F 7/58sb; *M 1/61	1922	1921
036	F 5/36; F -/38; m -/40; M -/42; m -/42; M -/43; F -/45; F -/50; M -/54; F -/57; *F 6/61	1917	1915
050	F -/39; M -/43; M -/44; F -/46; M -/48; m -/50; m -/52; F -/54; F -/55sb; M -/61; *M 3/62	1919	1916
051	M -/42; M 6/45; F -/46; M 5/47; F 6/49; M 6/51; M 9/54; F 2/59; *M 10/61; m 3/62; F 3/63	1922	1920
052	F -/42; [F -/43; F -/43]; M -/47; M -/50; F -/55sb; M -/56; M -/58; *F 1/60	1920	1919
316	M 3/43; M 11/44; M 10/46; M 3/48; F 2/49; F 5/53; *M 3/56; M 10/57; M 12/59	1923	1921
400	M -/43; M -/46; F 9/47; M -/48; M -/50; F -/51; M -/56; m 11/58; *F 5/61; M -/62	1918	1918

C: HYDROCEPHALUS

One-child families

008	*F 3/60	1939	1936
039	*M 11/62	1921	1915
158	*F 3/62	1940	—
182	*F 4/59	1936	1934
341	*M 1/62	1936	1931
502	*M 1/62	1944	—

Appendix I Continued

Serial No.		Sibship	Date of Birth	
			Mother	Father
<i>Two-child families</i>				
010	F -/55; *F 12/60		1926	1926
184	M -/50; *F 10/60		1924	1922
219	M 3/59sb; *M 1/62		1937	1936
261	F -/46; *M 9/62		1926	1920
368	M 5/59; *F 8/62		1932	1932
<i>Three-child families</i>				
195	F 2/52; F 3/53sb; *M 1/56; m 12/61		1932	1928
205	*M 9/57; M 6/59; F 4/61		1935	1930
233 } 234 }	F -/56; *F 3/59 No. 233; *F 12/61 No. 234		1928	1925
278	M -/59; *F 4/61; M -/62		1941	1936
280	M 12/54; *F 1/56; m -/57; M 11/59; m -/61		1935	1932
472	M -/46; M 7/52; *F 10/62		1920	1919
<i>Four-child families</i>				
100	F -/56; M -/58sb; F -/61; *M 9/62		1936	1937
124	F -/57; M -/58; *F 4/60; M -/61; m 9/63		1933	1922
<i>Five-child families</i>				
132	F -/48; F -/50; M -/53; M -/55; *M 9/61		1929	1926
429	F 11/40; M -/42; F -/46; F -/49; m -/53; *F 1/60		1919	1912
<i>Six-child families</i>				
035	F 10/52; M 8/54; F 1/56; F 6/57; F 10/58; *M 2/62		1935	1931
229	F -/48; F -/50; M -/51; M -/53; m -/57; M -/59; *F 5/61		1926	1923
<i>Seven (+)-child families</i>				
279	F -/43; M -/45; F -/49; M -/50; F -/55; *F 8/58; M -/59		1924	1923
516	M -/45; F -/47; F -/49; F -/50; M -/51; M -/54; F -/55; M -/56; *F 6/60		1921	1921

Appendix II

Subsidiary Series

M, male; F, female (italics indicate affected relative); m, miscarriage; sb, stillbirth; *, index patient; [], twins; (A), anencephalus; (S), spina bifida; (H) hydrocephalus.

Serial No.	Sibship	Date of Birth	
		Mother	Father
A: SPINA BIFIDA			
One-child families			
552	*F 4/59	1919	1924
576	m 11/52; *M 3/57	1926	1924
596	m -/57; *F 11/58	1927	1929
617	*M 12/56	1937	—
669	*F 9/58	1929	1928
670	*M 3/56	1928	1918
677	*F 8/56	1933	1931
697	*F 6/59	1932	1930
709	*F 9/56	1921	1911
742	*M 11/56; m 10/60	1929	1914
779	*F 10/57	1914	1908
781	*F 3/57	1920	1916
794	*M 6/58	1937	1933
829	*F 7/59	1924	1917

Appendix II Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
Two-child families			
550	*M 5/58; F 1/60	1937	1933
554	*M 7/58; M 4/60	1934	1926
560	*F 6/59; M 11/61	1936	1929
570	F 6/55; *M 2/57	1919	1928
572 } 573 }	*M 9/57 No. 572; *F 9/58 No. 573	1939	1932
574	M 8/53; *M 5/58	1931	1928
587	*F 6/59; M 6/60	1922	1921
592	*M 12/59; M 10/62	1925	1927
600	*F 1/58; M 8/62	1937	1933
602	*M 4/58; F 3/60; m 9/63	1936	1933
612	*M 3/57; M 4/60	1936	1929
618	*M 12/56; M 12/57; m 7/60; m 12/60; m 7/62	1934	1930
619	M -/52; *M 7/58	1924	1923
622	F 5/47; *F 7/58	1918	1916
637	*M 5/56; M 10/60	1936	1934
644	M 7/53; *F 11/56	1929	1933
661	M 1/48; *F 11/58	1926	1927
664	*F 11/56; F -/59	1934	1930
696	*F 11/59; F 7/61	1936	1936
698	M 4/49; *F 11/57	1930	1925
716	*F 11/59; F 3/61	1932	1934
717	*M 4/58; m -/58; M 10/59sb	1933	1932
721	M 3/58; *M 10/59	1935	1934
725	*M 9/58; F 9/60sb	1932	1929
734	*F 4/59; M 8/61	1935	1934
741	M 9/47; *F 7/57	1923	1921
749	*F 1/58; M 10/60	1932	1931
762	*F 7/57; F 5/59	1929	1920
785	*F 3/59; M 2/61	1928	1926
792	M 7/47; *F 3/57	1916	1907
802	m 1/57; *M 7/58; F 6/62	1931	1929
815	*F 9/57; F 9/60	1935	1936
816	M 3/57; *M 6/58	1925	1921
817	*M 9/57; M 2/63	1934	1933
Three-child families			
553	F 9/55; *F 2/58; M 6/61	1938	1937
556	*F 11/57; F 9/58; M 1/64	1929	1922
557	F 11/56; *F 10/58; F 11/62	1930	1925
558	M 6/51sb; *F 8/56; M -/59	1918	1924
568	M 7/45; M 5/48; *M 5/57	1920	1916
579	*F 11/58; F 1/60; F -/64	1933	1930
589	M 5/52; F(A) 9/57 No. 588; *F 1/59	1930	1930
594	M 1/53; *F 3/56; F 10/61	1929	1929
599	M 7/41; F 10/43; *F 5/57	1914	1915
606	F 1/44; F -/47; *M 2/56	1918	1916
609	F 1/56; [M 2/57; *M 2/57]	1937	1935
615	M 3/54; *M 10/56; F 6/60	1932	1930
633 } 830 }	*F 2/58 No. 633; *M 6/59 No. 830; M 11/61	1937	1936
636	F 1/52; m -/53; F -/54; *F 4/58	1923	1926
663	*M 5/56; M -/57; F -/61	1933	1931
667	F 4/57; *F 12/59; F 2/62	1935	1932
672	*F 6/59; M -/62; F 11/63	1936	1936
675	*M 2/58; M -/59; M(S) -/62	1929	1925
684	*F 3/57; M 4/58; F 10/59	1931	1929
685	m 2/53; F 4/55; *F 10/59; M 3/62	1924	1925
689	*M 11/59; F 3/61; M 8/62	1935	1933
701	M 1/52sb; *F 6/56; F 8/59	1927	1926
714	*M 3/56; M 9/57; m -/59; M 2/61	1923	1927
715	M 3/55; *M 1/59; F 11/61	1930	1924
720	*M 2/56; M 12/57; F 3/59	1938	1920
723	*M 7/58; M 7/59; F 5/62	1937	1933
735	M 10/54; *M 12/56; M 1/58	1929	1926
736	F 6/52; [*M 9/58; F 9/58]	1927	1927
747	m -/56; *F 1/57; M 12/57; m 1/60; F 6/62	1932	1930
748	*M 8/59; M 1/61; F 8/62	1935	1934

Appendix II Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
760	F 7/53; *F 9/58; M 9/61	1934	1929
767	F 11/53; [*F 6/57; F 6/57]	1933	1929
778	F 2/55; m -/56; *F 5/58; M 3/60	1929	1927
799	*F 8/58; F 12/59; M 1/61	1935	1934
806	*F 3/58; M 7/59; F 4/62	1932	1929
810	*M 7/56; M 1/58; M 9/61	1935	1935
821	M -/51; F(A) 4/57 No. 820; *F 9/59	1935	1932

Four-child families

548	M 10/52; M 4/54; *M 5/59; M(S) 2/63	1931	1930
551	F -/51; *M 7/57; F -/60; F(S) 1/62 No. 460	1923	1928
555	*M 9/59; M 3/61; M 2/62; F 8/63	1937	1937
561	F 4/40; F 7/42; F 6/45; *F 12/56	1918	1909
581	F 4/58; *F 4/59; F 3/60; F 7/62	1937	1933
593	F 4/49; M 6/53; *M 11/58; M 6/61sb	1925	1923
601	M 12/53; *M 10/59; F 10/60; M 1/62	1931	1925
610	M 8/53; M 4/55; *F 7/58; M 7/60	1920	1921
613	M 10/48; M 10/51; M 6/53; *F 2/59	1925	1925
616	*M 7/59; M 1/61; M 1/62; F 7/63	1938	1937
625	F 7/55; *F 8/56; F 2/58; M 6/61	1934	1932
638	*M 6/58; [M 5/59; M 5/59]; M 2/62	1939	1935
650	*F 8/58; F 6/61; F(S) 7/62 No. 440; M 9/63	1935	1927
681	M 10/56; *F 8/59; m -/60; F 8/61sb; M 10/63	1934	1932
691	F 3/41; F 10/43; M 7/53; *F 8/56	1921	—
699	F 10/49; F 1/56; *F 1/57; F 6/59	1924	1925
707	F(A) 8/53; m -/54; *F 7/56; M(A) 7/57 No. 708; F(S) 2/60 No. 133	1928	1926
711	M 4/40; F 6/42; M 2/52; *M 5/58	1925	1921
722	M 1/51sb; M 10/53; M 6/55; *F 12/58	1924	1929
730	F 2/55sb; *M 11/56; F 10/59; F 8/60	1932	1926
738	M 9/42; M 1/44; M 7/50; m -/52; *M 12/58	1921	1920
744	*F 4/56; F 2/59; M 10/60; M 6/62	1933	1932
750	M 10/54; m 10/56; *F 3/58; F 8/60; F 8/63sb	1933	1932
758	*M 9/59; F 1/61; m -/61; M 5/62; F 7/63	1940	1935
771	F 7/55; *F 6/57; F 12/58; m -/60; M 11/61	1935	1932
773	F 7/55; *F 6/57; F 12/58; m -/59; M 11/61	1936	—
775	*F 6/56; F 5/58; M 6/60; F 5/63	1933	1927
784	M(S) 8/55; *M 3/57; F 11/58; M 12/60	1930	1932
788	M 5/56sb; *F 10/59; F 3/61; M 1/63	1933	1931
790	F 6/50; F 4/53; m -/54; F(A) 7/55; *F 3/58	1931	1927
796	M 8/53; F 10/54; *M 7/59; F 4/61	1929	1929
797	m -/57; *M 9/59; M 5/61; F 4/63; M 9/64	1936	1927
801	M 11/51; *M 8/56; M 1/58; M 12/58sb	1932	1931
807	M 5/54; *M 12/57; M 12/59; F 12/60	1930	1929
822	*F 7/56; F -/58; F -/61; F -/63	1936	—
824	M 1/56; *F 1/58; M 12/59; M 6/62	1937	1930

Five-child families

621	M 4/42; M 5/43; M 5/46; F 10/49; *M 3/56	1914	1899
632	F 3/47; F 4/48; F 12/54; *M 9/57; M 5/62	1923	1923
647	F 10/42; M 2/44; F 12/50; M 2/56; *F 5/57	1921	1911
660	F 7/55; *F 7/56; F 9/58; F 3/61; M 3/63	1932	1932
710	F 1/47; F 6/48; M 3/51; *F 6/59; M 9/61	1923	1919
746	F 7/54; *F 5/56; F 3/58; F 2/60; M 2/61	1932	1924
753	M 7/38; F 7/40; F 9/46; F 5/49; *M 2/59	1919	1910
764	M 2/47; m -/47; F 3/48; F 7/49; *M 10/58; M 3/63	1925	1924
766	F 3/54; M 7/55; *M 10/56; M 4/58; M 2/61	1934	1934
809	M 5/50; F 5/52; F 12/53; M 1/56; *M 11/59	1930	1928
811	M 3/45; F -/48; F 1/50; F -/52; *F 1/58	1926	1927

Six-child families

630	F 3/51; M 6/53; M 6/55; *M 10/57; F 1/59; F 12/60	1930	1925
704	m -/47; F 4/51; M 6/52; F 3/54; F 10/55; F 8/57; *M 7/59	1928	1924
726	m -/41; F -/47sb; m -/48; F 12/49; M(S) -/54; m -/54; *F 6/56; [M 2/58; F 2/58]; m 11/61	1921	1912
745	F(S) 2/52; M 7/53; M 9/54; F 12/55; *M 12/57; M 4/61	1931	1926
768	F -/42; M -/44; M -/46; F -/49; M -/52; *F 1/56	1921	1916
803	M 9/50sb; F 3/52; F 5/54; F 6/55; *F 5/58; F 6/62	1927	1924

Appendix II Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
Seven (+)-child families			
564	m 12/51; M 12/52; F 12/53; M 12/54; M 1/56; *F 1/57; M 12/59; M 1/61	1932	1925
578	M 7/52; F 4/54; F 4/55; F 9/56; m -/57; *F 8/58; F 11/60; M 6/62	1916	1915
586	F 8/42; M 2/44; F 4/46; F 6/48; M 5/51; F 12/52; M 8/55; M 11/57; *M 10/59; M 4/61	1922	1923
652	M 1/50; F -/51; F 12/53; F 3/55; M 2/56; M 6/57; *M 2/59; m 2/61; M 2/63	1925	1909
656	F 10/48; F 1/51; M 3/54; M 11/56; *M 3/58; M 1/61; M 11/62	1930	1926
724	M -/46; M -/48; F -/49; *F 1/56; M 4/57; M 4/58; F 2/60	1924	1918
763	F 1/47; F 5/48; F 6/49; M 12/51; F 11/54; *M 9/58; F 12/60	1921	1922
B: ANENCEPHALUS			
One-child families			
549	*F 3/58	1931	—
591	*M 3/56	1929	1924
604	*F 3/57	1931	1927
608	*F 12/59	1934	1932
645	*- 8/59	1939	1938
657	*M 5/57	1930	1927
688	*F 4/59	1928	1929
754	*M 3/59	1937	1931
756	*M 12/56; m 11/62	1927	1923
761	*F 1/56	1920	—
774	*F 4/57	1932	1925
782	*F 6/57	1926	—
798	*F 3/56	1933	1916
805	m -/54; *F 1/56; m 3/58; m -/61	1929	1913
Two-child families			
559	*F 12/58; F 12/60	1936	1935
580	m -/54; F(A) 6/55; m -/56; m -/57; m -/58; *F 7/59	1931	1930
584	M 2/49; *F 11/56; m 12/62	1924	1917
595	*F 9/58; F 11/59	1934	1935
603	*F 3/58; M 4/60	1937	1935
623	*F 1/57; F 11/58	1931	1931
629	m -/49; m -/51; m -/53; m -/54; F 2/56; F 12/58	1925	1924
634	*M 7/57; M 6/60	1935	1935
646	M 11/55; *F 10/59	1933	1931
649	m -/57; *F 7/59; M 12/60	1934	1931
654	*F 6/59; M 6/61	1926	1912
694	F 10/56; *F 11/57	1925	1924
700	*F 8/59; F 4/61	1940	1939
713	M(A) 3/56; m -/57; *F 10/59	1923	1926
719	*F 7/57; F 8/59; m -/63; m -/64	1936	1930
728	*F 3/57; F 4/60	1933	1930
783	*F 12/57; M 6/60	1930	1929
786	*F 9/59; M 2/62	1931	1929
791	M 8/57; *F 10/59	1930	1936
812	F 6/48; *F 10/57	1926	1924
823	*- 9/59; M 11/62	1939	1936
826	*F 1/59; M 10/60	1933	1931
Three-child families			
562	m -/55; *F 11/56; F 12/58; F 3/61	1935	1932
566	*M 12/56; M 1/58; M 9/59	1938	1934
569	M 9/57; *F 10/59; F 6/62	1939	1933
577	*F 8/57; F 11/58; M 5/63	1938	1933
582	F 10/47; F 5/53; *M 3/59	1926	1921
583	F 9/47; F 7/51; *M 4/57	1924	1916
588	M 5/52; *F 9/57; F(S) 1/59 No. 589	1930	1930
605	*F 2/58; M 11/59; F 10/61	1937	1933
611	m -/43; M 3/54; M 4/55; *F 12/56	1923	1920
620	M 8/51; M 4/56; *F 12/59	1923	1912
624	F 8/54; *M 4/59; F 4/62	1931	1931
631	*F 6/56; M -/57; m -/59; F 6/61	1932	1934
651	M 7/56; *F 5/59; M 8/61; m -/62; m -/63	1934	1934
655	*M 1/57; m -/58; F -/60; F -/62	1936	1935
665	*F 3/56; F 1/58; F 2/60	1929	1922

Appendix II Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
670	*F 5/57; M 9/58; M 8/59	1936	1936
676	F 8/47; M 5/50; m -/54; *F 1/57	1924	1920
679	M 12/40; F 7/43; *F 1/57	1916	1915
680	*F 12/59; F -/61; F -/62	1939	1936
682	M 1/53; *M 7/57; M 7/58	1933	1930
702	F 8/56; *F 8/57; F 2/60	1933	1931
712	*M 9/57; F 5/59; F 7/62	1936	—
718	M -/56; m -/57; *F 5/59; M 8/61	1929	1926
731	F 2/55; *F 6/57; M 9/60	1929	1929
732	m -/54; *F 9/56; M 11/58; F 6/60	1933	1930
739	M 5/47; F 11/48; *F 8/56	1923	1921
751	M 11/49; M 11/51; *M 12/58	1915	1912
759	M 11/45; M 12/48; *F 11/57	1919	1913
776	*M 9/58; F 11/59; F 8/62	1932	1921
777	*F 4/56; M 5/60; M 12/62	1935	1926
814	m 12/57; *M 12/58; F 3/60; M 6/63	1936	1931
818	F 5/54; *F 3/56; F 5/58	1934	1934
820	M -/51; *F 4/57; F(S) 9/59 No. 821	1935	1932
825	F 3/51; *F 11/56; M 8/62	1929	1928
828	*F 12/58; M 5/60; F 2/63	1938	1936
<i>Four-child families</i>			
567	m 11/56; F -/57; *F 5/59; M -/60; F -/62	1937	1936
642	M 3/53; M 8/56; *M 8/59; M 10/60	1932	1922
659	*F 1/58; F 4/60; F 2/62; M 7/63	1935	1934
662	F(A) 9/54; *M 5/56; F 3/58; M 2/60	1929	1927
671	F 9/45; F 2/47; M 1/50; *F 9/57	1921	1919
673	F 9/53; F 2/55; m -/57; *M 2/56; F(H) 6/59 No. 674; m 7/63	1935	1931
678	*F 1/58; F 4/59; F 12/60; F 11/63	1935	1933
683	*M 9/59; F 7/61; F 4/62; M 9/63	1939	1937
706	M 4/56; *F 9/58; M 7/60; M 6/62	1938	1934
708	F(A) 8/53; m -/54; F(S) 7/56 No. 707; *M 7/57; F(S) 2/60 No. 133	1928	1926
727	M 4/57; *M 9/59; M 12/60; M 3/63	1936	1936
743	F 7/51; M 10/52; M 10/54; *F 6/59	1929	1929
752	F 6/56; *F 4/58; M 8/59; F 10/62	1936	1926
755	M 7/44; F 7/45; m -/52; F 7/54; *M 3/57	1913	1912
769	M 1/45; F 5/46; F 12/47; *M 4/59	1924	1923
770	F 10/55; *F 4/58; M 8/59; F 7/61	1934	1933
772	M 6/51; M 4/55; *M 11/57; F 8/59	1925	1924
789	F 11/51; M 5/53; M 10/55; *F 9/57	1920	1905
800	*F 9/58; F 9/59; M 11/60; M 8/62sb	1940	1940
813	F 2/47; F 4/48; F 11/52; *F 10/57	1928	1926
819	M 6/55; *F 8/57; M 12/58; M 1/62; m 5/63	1935	1927
827	*M 2/56; M 2/57; F 1/59; F 4/60	1929	1924
<i>Five-child families</i>			
571	M -/39; M -/42; F -/44; F -/47; *F 10/59	1921	1920
590	*F 8/56; F 2/58; M 8/60; M 4/61; M 7/63	1934	1930
607	F(A) 12/52; F 1/54; M 4/55; *F 11/56; F 3/60	1921	1922
626	M 7/45; F 4/47; M 11/52; F 5/56; *F 11/58	1928	1920
627	M(S) 2/47; M 6/48; M 12/50; M 6/53; *F 4/58	1929	1925
640 } 641 }	F -/56; [*F 7/57 No. 640; *F 7/57 No. 641; M 7/57]; m -/59; M -/60	1926	1928
648	F 11/43; M 9/46; M 2/54; *F 1/57; M 10/61	1923	1918
658	M 2/42; F 2/44; M 2/47; F 2/48; *F 11/59	1915	1914
737	F 12/46; M 5/49; m 6/53; M 2/55; *F 3/56; M 8/59	1920	1916
<i>Six-child families</i>			
705	F 2/44; M(A) 8/45; F(A) 3/46; F 6/48; F 5/51; *F 9/59	1924	1919
793	F 12/51; F 1/53; F 4/54; [*M 12/59; M 12/59sb]; F 10/61	1922	1918
<i>Seven (+)-child families</i>			
597	F 5/43; M -/44sb; F 2/45; F 12/46; F 4/48; F 8/49; M 11/52; *F 10/57	1921	1925
598	M 11/47; M 7/49; F 8/52; M 3/54; F 11/56; [*F 3/59; F 3/59]	1931	1924
628	F 7/50; M 10/51; F 2/53; M 8/54; *F 3/57; M 2/58; M 4/59; F 7/61; F 3/63	1922	1920
635	F -/33sb; F 5/37; F -/40sb; M 10/41; M 5/43; F 5/44; F 9/52; F 5/53; *M 4/57	1913	1911
639	F -/50; F -/51sb; F 7/52; M -/54sb; F 7/56; M 8/57sb; *F 11/59	1926	1924
643	F -/43; M -/44; F -/46; F -/48; M -/50; F -/54; *F 4/57; M 9/59	1923	1919
668	M 10/33; F 4/35; F 3/37; M 3/39; F 9/41; F 5/43; F 10/46; M 11/50; F 4/52; *M 1/57	1915	1906
757	M 7/46; F -/49sb; F 8/50; M 5/52; F 9/54; F 2/55; F 12/56; *F 5/58; F 2/60	1926	1925
780	M 3/50; M 3/51; M 2/52; M 10/53; *F 3/56; M 1/58; [M 4/60; F 4/60]	1922	1919
787	M 10/44; M 11/45; M 2/47; M 3/48; F 5/50; M 6/51; F 9/54; M 3/56; *F 4/59; F 9/61; F 4.63	1925	1921
808	M 11/41; M 3/43; F 5/53; F(A) 2/55; *F 1/57; F 4/58sb; M(A) 1/61 No. 029	1922	1921

Appendix II Continued

Serial No.	Sibship	Date of Birth	
		Mother	Father
C: HYDROCEPHALUS			
One-child families			
563	*F 10/57	1932	—
692	*F 1/57	1938	—
Two-child families			
585	*M 5/58; M 5/63	1933	1930
653	*M 11/58; M 7/62	1935	1934
666	M 9/50; *F 7/56	1926	1916
686	M 9/55; *F 1/57	1934	1932
693	*F 2/56; F 12/57; m 7/63	1926	1924
740	[*F 4/57; M 4/57]; m 7/61; m -/62	1935	1908
Three-child families			
565	*F 12/59; M 1/61; M 6/62	1942	1939
729	F 4/52; m -/56; *M 9/58; M 5/60	1932	1927
733	F 1/54; M 1/57; *M 9/59	1931	1930
765	F 3/53; *M 5/57; M 6/58	1934	1924
795	F 5/56; M 9/57; *F 10/58; m -/59; m -/60; m -/61	1929	1919
804	*F 8/57; M 8/58; F 10/59	1934	1933
Four-child families			
674	F 9/53; F 2/55; m -/57; M(A) 2/58 No. 673; *F 6/59; m 7/63	1935	1931
Five-child families			
695	F 1/51; F 2/53; F 7/54; M 2/56; *F 7/57	1924	1925
Six-child families			
614	F 6/47; F 10/49; M 3/53; m 7/55; *M 3/59; F 9/60; M 8/62	1926	1923
Seven (+)-child families			
575	M 12/39; M 2/41; M 11/45; M 9/48; M 5/50; M 11/51; F 4/53; M 9/55; m -/55; *M 9/59; F 9/60	1915	1917
687	M 10/34; F 6/38; F 6/39; [M 3/42; F 3/42]; M 12/43; F 8/48; *F 1/56	1915	1915
703	M 6/49; M 7/51; M 4/53; M 4/55; *F 11/56; M 11/57; M 6/59; F 8/63	1928	1923

AREA KEY

Neath 1-14, 817-829; Port Talbot 15-40, 788-816; Mid-Glamorgan 41-82, 720-787, 592; Glamorgan South East, 83-98, 709-719, 835; Pontypridd, 99-133, 684-708; Rhondda 134-218, 834; Aberdare 219-274; Caerphilly 275-367; Merthyr 368-418; Rhymney 419-456, 621-683, 830, 831; Ebbw Vale 457-511, 548-600; East Monmouth 512-547, 601-620, 832, 833.