Area differences in the incidence of neural tube defects and the rate of spontaneous abortion

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Fedrick, J. and Adelstein, P. (1976). *British Journal of Preventive and Social Medicine*, 30, 32-35. **Area differences in the incidence of neural tube defect and the rate of spontaneous abortion.** In an attempt to corroborate the finding of Roberts and Lloyd (1973) of increased incidence of previous abortions in women living in those areas of South Wales with relatively low incidences of malformations of the central nervous system, we examined the data of the 1958 *British Perinatal Mortality Survey*. We also found evidence that the history of preceding abortion among all mothers in this survey was slightly more prevalent in areas where the rates of stillbirth and neonatal death from anencephalus or spina bifida were low, but the order of magnitude was much less than in the Welsh study.

It has frequently been noted that women who have been delivered of infants with either spina bifida or anencephalus are more likely to have reported having had one or more previous abortions than a series of control women. (Böök, 1951; Coffey and Jessop, 1957; Smilkstein, 1962; Smithells, Chinn, and Franklin, 1964; Smithells and Chinn, 1965). Fetuses with neural tube defects have been shown to be relatively common in series of spontaneous abortions: in Belfast, Stevenson, Dudgeon, and McClure (1959) found six of 87 (7%) spontaneously aborted fetuses to have dysraphic defects and in London, Alberman, Creasy, and Polani (1973) reported 2% of their larger series to have malformations of the central nervous system.

It is therefore inferred that many of the previous abortuses of the women who subsequently give birth to infants with these defects, are themselves likely to have had malformations of the central nervous system (CNS).

Roberts and Lloyd (1973) examined the data from South Wales with a view to explaining the differences in the rates of CNS malformations in different parts of their region. They considered two areas: area A comprising the mining valleys with a high incidence, and area B (the rest of the region) with a much lower incidence. They showed that the proportion of women reporting previous abortions was consistently and substantially higher in area B

(Table I). They then made the suggestion that the results support the hypothesis that there is little or no difference between the two areas in the incidence of CNS defects shortly after conception: the observed difference in the third trimester arising only because the conceptus is more likely to abort if the mother resides in a low incidence area.

It is the purpose of the present study to test this hypothesis using the data of the 1958 *British Perinatal Mortality Survey*.

TABLE I
PROPORTION OF WOMEN REPORTING PREVIOUS SPONTANEOUS ABORTION BY AREA OF BIRTH IN SOUTH WALES*

Parity of Index Pregnancy					Area A %	Area B %
Singletons with CNS defects						
0	..	..	..	..	5.2	10.1
1	..	..	..	..	14.3	20.0
2+	..	..	..	..	26.0	30.8
All	..	..	..	..	13.9	19.6
Singletons without CNS defects						
0	..	..	..	..	6.9	7.3
1	..	..	..	..	11.2	13.4
2+	..	..	..	..	18.3	22.7
All	..	..	..	..	13.0	14.9

*From Roberts and Lloyd

MATERIAL AND METHODS

In 1958 the first *British Perinatal Mortality Survey* set out to study two sets of data in depth (Butler and Bonham, 1963; Butler and Alberman, 1969). The first survey attempted to collect information on all deliveries occurring in the whole of England, Scotland, and Wales during the first week of March in that year. In the event some 98.5% of all births were included. This population will be known as the 'control week population'.

The second part of the survey attempted to study all stillbirths and neonatal deaths (that is, deaths up to 28 days) occurring in England, Scotland, and Wales in the three-month period March to May 1958. Some 94% of all cases were included in the study, and are known as the 'three months' deaths'.

For both populations detailed questionnaires were filled in by the midwives after delivery. Among the information requested was a detailed list of all previous pregnancies with dates and outcome. Parity is defined as the number of previous pregnancies exceeding 27 weeks' gestation, or resulting in a livebirth.

Areas of residence of the mothers were classified into the regions defined by the Registrar General. We have considered two areas: area II comprising the east of England, London, and the south-east (that is, regions of comparatively low incidence of CNS defects); and area I including Scotland, Wales, and the rest of England.

For purposes of simplicity, the present study analyses only index pregnancies resulting in the delivery of a singleton. In calculating the incidence of the stillbirths and neonatal deaths we have, in conformity with other analyses of these data (Butler and Alberman, 1969), taken the population at risk to be twelve times the control week population.

RESULTS

The incidence of anencephalus and spina bifida within each area is shown in Table II. Note that the rates are at least 50% higher in area I than in area II.

In Table III, are presented the proportions of women in each area who reported that the pregnancy immediately preceding the index pregnancy had ended in a spontaneous abortion. Note that both for the control week population and the population of 'three months' deaths' the proportion in area I was lower than that in area II, supporting the Roberts and Lloyd hypothesis. Contrary to their findings, however, were the crude data for multiparous mothers whose index pregnancy had

TABLE II
THE RATE OF DEATHS WITH ANENCEPHALUS OR SPINA BIFIDA IN TWO AREAS *

Parity	Area I (High Incidence)	Area II (Low Incidence)
Parity 0		
Death rate from anencephalus	3.08	1.92
spina bifida	2.30	1.54
Parity 1+		
Death rate from anencephalus	2.39	1.59
spina bifida	1.29	0.57

*British Perinatal Mortality Survey, singletons only

TABLE III
WOMEN REPORTING AN ABORTION IMMEDIATELY PRECEDING THE INDEX SINGLETON PREGNANCY*

Parity and Outcome of Index Pregnancy	Area I (High Incidence)	Area II (Low Incidence)
	%	%
Parity 0		
Control week population ..	7.4 (4498)	8.8 (1780)
Three months' deaths ..	8.8 (2083)	10.5 (693)
Deaths with anencephalus ..	10.8 (166)	9.8 (41)
spina bifida ..	4.1 (124)	4.1 (33)
Parity 1+		
Control week population ..	6.2 (7916)	6.4 (2783)
Three months' deaths ..	9.3 (3320)	10.0 (978)
Deaths with anencephalus ..	12.3 (227)	9.4 (53)
spina bifida ..	13.3 (122)	0.0 (19)

*British Perinatal Mortality Survey, singletons only
Number of births is shown in parentheses

resulted in a death from anencephalus or spina bifida, and those for primiparae whose index pregnancy had resulted in the delivery of an anencephalic.

The incidence of abortion varies greatly with maternal age. It is also true that in the Welsh study, all women who had had an abortion at some stage in their previous reproductive history were included, rather than only those with an abortion immediately preceding the index pregnancy. In Table IV the proportion of women who had ever had a previous abortion, within age, social class, and parity groups are compared. Note that in spite of the small numbers, in 11 of the 16 pairs of observations, the proportion of women having had abortions was higher in area II than in area I. It might be relevant to note that the two categories in which this trend is most apparent (the young primiparae and the old

TABLE IV

PROPORTIONS OF WOMEN IN CONTROL WEEK POPULATION WHO REPORTED EVER HAVING HAD A PREVIOUS ABORTION, BY AGE, PARITY, SOCIAL CLASS, AND AREA OF RESIDENCE AT INDEX DELIVERY

Parity and Social Class				Age Under 30 Years				Age Over 30 Years			
				Area I (High Incidence)		Area II (Low Incidence)		Area I (High Incidence)		Area II (Low Incidence)	
Parity 0											
Social class I and II				31/543	(5·7)	27/290	(9·3)	32/179	(17·9)	10/73	(13·7)
III				161/2320	(6·9)	72/854	(8·4)	43/313	(13·7)	18/143	(12·6)
IV and V				47/700	(6·7)	23/245	(9·4)	15/83	(18·1)	6/31	(19·4)
All*				246/3874	(6·4)	126/1530	(8·2)	93/611	(15·2)	34/259	(13·1)
Parity 1+ Social class I and II				65/553	(11·8)	32/283	(11·3)	102/601	(17·0)	65/292	(22·3)
III				257/2544	(10·1)	88/865	(10·2)	375/1994	(18·8)	137/696	(19·7)
IV and V				136/1153	(11·8)	40/312	(12·8)	135/780	(17·3)	46/221	(20·8)
All*				477/4411	(10·8)	161/1532	(10·5)	632/3501	(18·1)	252/1249	(20·2)

*Including unmarried and those whose social class is unknown. Percentages are given in parentheses.

Observed no. of women in area I reporting abortions in social classes I to V=1399, expected no.=1439, standard error of difference=18.11
 $t = -2.26$, $P < 0.025$

multiparae) are the two in which the incidence of anencephalus in this study was found to be high (Fedrick, 1970).

Testing the observations in each of the twelve social class/age/parity classes for consistency, one finds that there is a significant dearth of women reporting a history of previous abortion in area I when compared with area II.

Similarly, considering the populations of mothers of the 'three months' deaths' (Table V) and of women who had had stillbirths or neonatal deaths with

anencephalus or spina bifida (Table VI), it can be seen that there is a similar effect only among the former, although failing to reach statistical significance ($0.10 < P < 0.05$).

DISCUSSION

The results presented above offer some evidence to support the hypothesis of Roberts and Lloyd (1973), although the order of magnitude of the effect shown in the present series is considerably less

TABLE V

PROPORTION OF WOMEN IN 'THREE MONTHS' DEATHS WHO REPORTED EVER HAVING HAD A PREVIOUS ABORTION, BY AGE, PARITY, SOCIAL CLASS, AND AREA OF RESIDENCE AT INDEX DELIVERY

Parity and Social Class				Age Under 30 Years				Age Over 30 Years			
				Area I		Area II		Area I		Area II	
Parity 0											
Social class I and II				18/199	(9·1)	8/78	(10·3)	7/62	(11·3)	8/37	(21·6)
III				88/959	(9·2)	23/257	(9·0)	29/210	(13·8)	17/84	(20·2)
IV and V				32/365	(8·8)	8/117	(6·8)	11/57	(19·3)	2/15	(13·3)
All*				142/1709	(8·3)	43/534	(8·1)	48/369	(13·0)	30/155	(19·4)
Parity 1 +											
Social class I and II				17/136	(12·5)	5/46	(10·9)	57/241	(23·7)	37/109	(33·9)
III				137/819	(16·7)	40/239	(16·7)	252/1022	(24·7)	73/274	(26·6)
IV and V				91/440	(20·7)	25/124	(20·2)	117/481	(24·3)	33/114	(29·0)
All*				258/1472	(17·5)	79/442	(17·9)	450/1841	(24·4)	149/533	(28·0)

*Including unmarried and those whose social class is unknown. Percentages are given in parentheses.

Observed no. of women in social classes I to V in Area I reporting previous abortions=856, expected no. = 875.2; standard error of difference = 12.6, $t = -1.52$, $0.10 < P < 0.05$ (one-tailed test)

than in their study. In the data analysed above for the control week population it was shown that out of the 11 683 women resident in area I (the high incidence area), there was a dearth of 40 women (0.34%) who would have been expected to have had a history of previous abortion. This is the sort of magnitude which would fit the Welsh hypothesis, whereas the magnitude of the effect that they demonstrated was too high, as James (1973) pointed out, unless one assumed that the rate of abortion of fetuses not affected by CNS defects was also higher in the areas of low incidence.

Obviously the results of the present analyses cannot be considered to be conclusive. It is still possible that the results demonstrated could be accounted for by differential reporting in the various areas.

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TABLE VI

PROPORTION OF MOTHERS OF STILLBIRTHS OR NEONATAL DEATHS WITH ANENCEPHALUS OR SPINA BIFIDA WHO REPORTED EVER HAVING HAD A PREVIOUS ABORTION BY AGE, PARITY, SOCIAL CLASS, AND AREA OF RESIDENCE AT THE INDEX DELIVERY

Parity and Social Class	Age Under 30 Years				Age Over 30 Years			
	Area I		Area II		Area I		Area II	
Parity 0								
Social class								
I and II	0/16	(0.0)	1/11	(9.1)	2/5		0/0	
III	15/160	(9.4)	5/36	(13.9)	3/18		0/4	
IV and V	4/61	(6.6)	1/12	(8.3)	1/3		0/3	
All*	19/261	(7.3)	7/66	(10.6)	6/28	(21.4)	0/8	(0.0)
Parity 1+								
Social class								
I and II	3/15	(20.0)	0/3	(—)	6/21	(28.6)	1/3	(33.3)
III	24/99	(24.2)	2/13	(15.4)	24/98	(24.5)	8/27	(29.6)
IV and V	9/51	(17.7)	1/7	(14.3)	15/54	(27.8)	2/11	(18.2)
All*	36/167	(21.6)	4/26	(15.4)	47/180	(26.1)	13/45	(28.9)

*Including unmarried and those whose social class is unknown. Percentages are given in parentheses.

Observed no. women in social classes I to V in Area I reporting previous abortions = 106, expected no. = 105.5.