The geography of spina bifida in England and Wales

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ABSTRACT

Spina bifida is a generic term describing malformations of the central nervous system in infants. Over 1000 cases of spina bifida were notified in England and Wales in 1971, but this had declined to 360 in 1985, partly due to maternal screening and the acceptance of therapeutic abortion. This paper reviews hypotheses about the causes of spina bifida and uses Poisson probabilities and regression techniques to examine spatial variations in the prevalence of spina bifida between 1983 and 1985. Differences in the maternal screening policies of health authorities are highlighted as an important factor, indicating that the study of 'geographical epidemiology' cannot he divorced from issues of health care.

KEY WORDS: Medical geography, Congenital malformations, Spina bifida, England and Wales, Maternal screening, Poisson regression

INTRODUCTION

Spina bifida is a malformation of the central nervous system in which one or more of the vertebrae are separated and the spinal cord protrudes beyond its normal limits. It occurs during the first 25 days of pregnancy when the neural tube that forms the spinal cord fails to develop properly. In its most common form a sac containing part of the spinal cord protrudes from the back and there is paralysis below the damaged vertebrae.

Despite considerable research the precise causes of spina bifida remain uncertain. The consensus is, nevertheless, that both genetic and environmental factors are involved. This study seeks to examine the influence of these factors upon the contemporary geography of spina bifida in England and Wales. Attation is also focused on the impact of differences in the maternal screning policies operated by health authorities, in the section below the existing literature on the aetiology of spina bifida is reviewed and this is followed by a brief discussion of data sources for geographical analyses of congenital malformations An analysis of spatial variations in the prevalence of spina bifida in England and Wales between 1983 and 1985 is then presented and the paper concludes with an assessment of the findings together with some proposals for future research.

SPINA BIFIDA: DESCRIPTION AND AETIOLOGY

The term 'spina bifida' embraces a variety of central nervous system malformations which occur in the embryo when the neural tube fails to dose. In one of these, *spina bifida* occulta, there is only a minor gap in the vertebrae and no permanent disability. This malformation can often only be detected by X-ray and so is unlikely to be recognized at, or before, birth. More obvious deformities are the two types of *spina bifida cystica,* which manifest themselves as a cyst or sac protruding from the back. In meningocele, a condition which occurs in about 10 per cent of cystic cases, the spinal cord is undamaged and the sac contains cerebrospinal fluid which protects the nerve cells. There is little or no permanent disability in these cases. Much more serious is myelomeningocele, a condition which characterizes approximately 90 per cent of cystic cases, and in which the sac contains not only the fluid but also the spinal cord itself. Cases of myelomeningocele can be further subdivided into *open* and *closed* lesions (Stark, 1977; Wald and Cuckle, 1984).

TABLE I. *Incidence of neural tube defects in England and Wales 1977-1985*

	Rate peer 10 000 birth				
	1977	*1979*	*1981*	*1983*	*1985*
Spina bifida	15·3	13·1	10·4	6·7	5·5
Anencephaly	9·9	7·1	3·9	1·8	0·9

Source: congenital malformations, 1985, OPCS Monitor Series MB3 86/2, office of Population Censuses and Surveys, 1986

Neural tissue is completely uncovered in open cases, but covered by shin or a thick membrane in closed lesions. The distinction is important in that only open lesions (some 80 per cent of myelomeningocele cases) can be detected by biochemical means before birth. Due to damage of the spinal cord infants born with myelomeningocele (whether open or closed lesions) invariably suffer from paralysis of the legs, incontinence and in many cases mental retardation (Stark, 1977).

Another important type of central nervous system malformation is *anencephaly,* in which the bones of the skull do not join at the back of the head and the brain fails to develop properly. Stillbirth or death within a few hours of birth is inevitable in these cases- Taken together, anencephaly and spina bifida are usually referred to as *neural tube defects* and since evidence suggests (Lawrence *et al.,* 1967) that they are aetiologically similar some reference will be made to anencephaly below.

'Data recently published by the Office of Population Censuses and Surveys (OPCS, 1983; OPCS, 1986a) clearly indicate that there has been a decline in the prevalence of babies born with spina bifida and anencephaly since the early 1970s (see Table I). It should be noted that approximately one-fifth of babies born with spina bifida are stillborn and that the malformation rate is approximately 25 per cent higher for females than males (OPCS, 1983). As noted in a later section the data are imperfect (Knox *et al.,* 1984) and are based on a system of voluntary notifications by District Medical Officers. Furthermore, it must be emphasized that the figures are thought to grossly understate overall incidence since many malformed foetuses will have been detected during screening tests and aborted therapeutically, whilst among those not identified, up to four-fifths of mothers may miscarry at an early stage (Leck, 1974). In what follows, the term 'prevalence' is used to denote cases recognized at birth, while 'incidence' refers to the condition as it occurs during embryogenesis,

Screening for spina bifida and anencephaly became possible in the mid 1970s and has undoubtedly been a factor in the decline in the number of babies born with these malformations (OPCS, 1985a). District Health Authorities do differ, however, in the extent to which they routinely screen pregnant women for naural tube defects. Those which do offer routine screening usually begin with an alphafetoprotein (AFP) test on a sample of the mother's blood at between 16 and 18 weeks into the pregnancy. This test is relatively cheap [approximately £5 Per woman screened at 1980 prices), but has been found to detect only 70 per cent of spina bifida cases and produce some positive results when there is no malformation present (Wald and Cuckle, 1984). If the blood test is positive it is therefore common practice to undertake a second analysis. This often consists of an amniocentesis in which a sample of the amniotic fluid surrounding the foetus is dram and examined for high AFP levels. Amniocentesis is a reliable means of diagnosing open myefomeningocele, but is less effective with other forms of spina bifida. In some health authorities it is now accompanied, or has been replaced, by high resolution ultrasound scanning which can detect all forms of neural tube defects. Ultrasound scanning is a technique which is still being developed, but it clearly has considerable potential (Harris and Read 1981) and is cheaper than amniocentesis (£20 rather than £40 peg woman screened at 1980 prices). At present, if the results of an amniocentesis or ultrasound scan suggest spina bifida or anencephaly then the mother is commonly offered a therapeutic abortion.

There are no published data on the number of abortions due specifically to suspected spinal bifida, but recent OPCS Monitors (OPCS, 1985b; OPCS, 1986b) indicate that in England and Wales there were 536 abortions due to all types of central nervous system malformations in 1984 and 517 in 1985. For these two years there are also data on reported therapeutic abortions by Regional Health Authorities and these are shown in Table II. The data indicate that most regions are close to the national trend, but that South West Thames has a lower rate of therapeutic abortions and both Oxford and Wales rather high ones. Whether this reflects differences in attitudes to termination is not known, but it certainly suggests that care needs to be taken when using data on births to examine variations in the incidence of spina bifida. This points is returned to in the concluding section of the paper.

TABLE II. *The regional distribution in 1984 and 1985 of abortions due to central nervous system malformations in the foetus*

Regional Health Authority	*Abortions due to CNS malformations in 1984-85*	*Babies born with CNS malformations in 1984-85*	*Abortions as a % of total abortions and births*
Northern	81	116	41·1
Yorkshire	70	122	36·4
Trent	99	157	38·7
East Anglian	46	55	45·5
N.W. Thames	51	91	35·9
N.E. Thames	75	80	48·4
S.E. Thames	54	104	34·2
S.W. Thames	33	75	30·6
Wessex	62	86	41·9
Oxford	56	56	50·0
South Western	49	95	34·0
West Midlands	124	205	38·0
Mersey	63	85	42·6
North Western	102	124	45·1
Wales	88	83	51·5
England and Wales	1053	1534	40·7

Sources: Abortion statistics 1984, Monitor Series AE No. 11, OPCS, 1985
Abortion statistics 1985, Monitor Series AB No. 12, OPCS, 1986
Congenital malformations 1984, Monitor Series MB3 85/2, OPCS, 1985
Congenital malformations 1985, Monitor Series MB3 86/2, OPCS, 1986

Some medical professionals dispute the value of nationwide routine screening (e.g., Standing *et al.,* 1981; Hibbard *et al.,* 1985). On the basis of cost-benefit analyses it has been suggested that AFP testing should be discouraged in areas with a prevalence of neural tube defects (including terminations as well as births} below 2·5 per 1000 pregnancies (Hibbard *et al.,* 1985). Fewer than a quarter of the District Health Authorities in England and Wales currently have prevalence rates above this limit and restricting routine AFP testing to such areas might well be a most cost effective policy (see however Spencer and Carpenter, 1985; Henderson, 1985). As Hibbard *et al.* note, however, such economic analyses ignore the intangible costs of suffering. The Maternity Alliance (1982) has called instead for a national policy of routine screening and has pointed to inequalities in the availability of AFP tests. In a survey of the 201 District Health Authorities in England and Wales in 1982 it was found that only 101 provided routine screening, 65 did not have such a policy and the remaining 35 either did not reply or had no consistent policy within the district (Maternity Alliance, 1982). Figure 1 shows the distribution of health authorities with different screening policies and it is evident that many of those which did not provide routine screening in 1982 are concentrated in more rural parts of the country. It might be expected that the screening policy of a health authority would have some impact on the notifications of spina bifida in that district and this relationship is examined in a later section of the Paper

As far as the causes of spina bifida are concerned some researchers postulate a genetic origin, the argument being that ethnic groups differ in their predisposition to such malformations. At the global scale, for instance, rates for people of British and Irish descent are amongst the highest in the world. Rates for people from the Indian subcontinent are also high, while those for West Indians are relatively low (Lawrence *et al.,* 1967; Stark, 1977). Hewitt (1963) suggested an inbreeding hypothesis to account for high rates among certain ethnic groups and, more recently, Balarajan and McDowell (1985) have offered a similar explanation of differences in congenital malformation rates among infants born to mothers who were themselves born outside the United Kingdom. In the absence of suitable data on inbreeding Hewitt (1963) used data on low birthweight since evidence suggests that intense

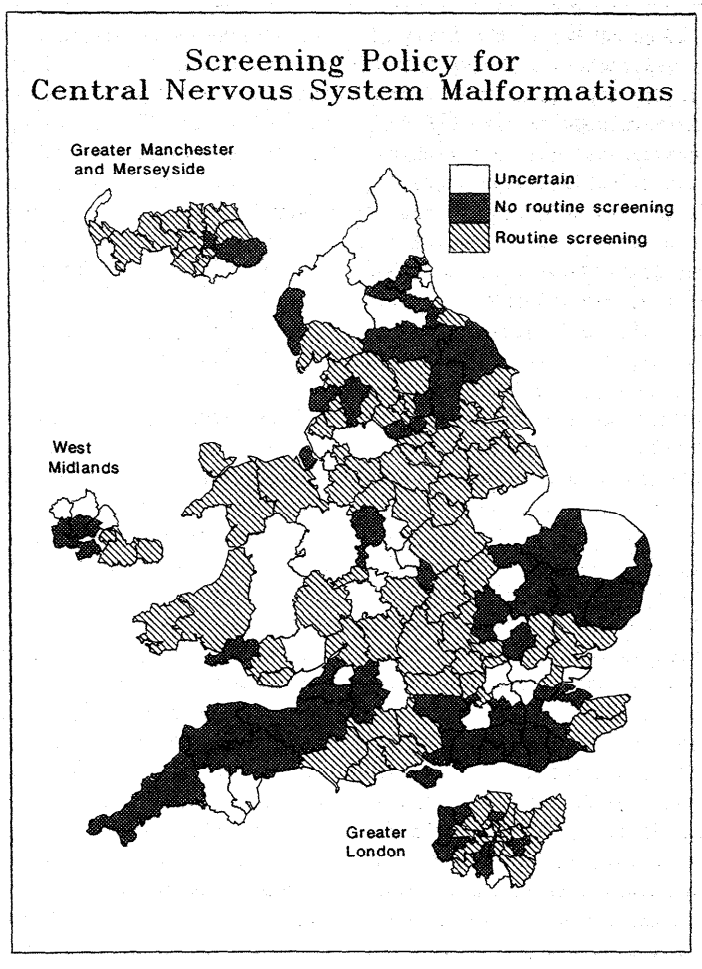

FIGURE 1. Screening policies of District Health Authorities in 1982 (based on data in Maternity Alliance, 1982)

inbreeding lowers mean birthweight. He found a significant positive correlation between low birthweight and spina bifida mortality in the USA

Such ethnic or regional differences could indeed be due to genetic predisposition or inbreeding. Nevertheless, many studies (for instance Lawrence *et al.,* 1967; Kallen and Lofqvist, 1984) have clearly indicated that there are marked local variations in prevalence that do not seem capable of explanation in terms of gene Pool differences. Shifts in areas of high prevalence, as in Sweden between 1950 and 1967 (Kallen and Lofqvist, 1984), are also hard to account for in terms of sudden genetic changes. In the absence of adequate genetic explanations several researchers have investigated possible influences on the prenatal environment such as parental social class and diet. A major project carried out by OPCS using data for 1974-79 identified a strong tendency for cases of spina bifida to be more frequent in the lower social classes, especially Social Class V (OPCS, 1983). This finding could reflect the concentration of particular occupations or ethnic groups in the lowest social class, but another possible explanation is that dietary factors may increase the risk of congenital malformations such as spina bifida.

Rogers and Weatherall (1976) described the results of studies on the link between diet and the incidence of spina bifida as inconclusive, but greater progress has recently been made. Research reported in Dobbing (1983) clearly suggests that spina bifida is linked to vitamin, folic acid and zinc deficiency among mothers. It is argued that vitamin deficiencies, acting together, may interfere with the closure of the neural tube or that such deficiencies may allow some

unknown teratogen (an agent causing malformations) to have an influence. There are, however, still difficulties in evaluating the relationship between diet and congenital malformations since, as Baird (1974) argues, it may not be diet during early pregnancy that is aetiologically sign&ant but rather conditions during the mother's childhood. This interpretation, along with improvements in the nutritional status of women during the post-war years, may help to explain the recent decline in the prevalence of central nervous system malformations. Together, these findings certainly suggest that environmental factors have an important role, although it has been argued that they are essentially a 'trigger' which only acts on genetically susceptible sub-sections of the population (Rogers and Morris, 1971).

An environmental factor which has been the subject of considerable investigation is water quality. Two studies in South Wales have produced conflicting results. Lawrence *et al.* (1967) concluded that there was no relationship between the prevalence of neural tube defects and water hardness, whereas Lowe *et al.* (1971) found a significant negative correlation which persisted even when a control was made fur social class. Using data for towns in the UK, Fedrick (1970) identified a negative correlation between anencephaly rates and water hardness (calcium content) and similar results were reported by Crawford *et al.* (1972). Fedrick (197O) suggested that one reason for the relationship was that softer, acidic waters might dissolve the lead from aid pipes and that this agent could contribute to foetal malformations.

In addition to ecological analysis at the national or regional scale Lowe *et al.* (1971.) suggested that it was also important to compare samples of tap water from houses of women who had delivered malformed infants with those from the homes of a control group who had given birth to normal infants. One such study by Morten *et al.* (1976) found that congenital malformation rates were positively correlated with aluminium content and negatively associated with calcium, copper and barium levels. These findings were not, however, confirmed by the more extensive research of St Leger *et al.,* (1980). In this analysis the only significant difference identified was for zinc, the concentration being lower for the cases of malformations than the controls.

One of the most persuasive arguments yet presented for an association between central nervous system malformations and water quality is the study by Dorsch *et al.* (1984 based on 218 case-control pairs in Southn Australia. They compared women who had consumed only rainwater during their pregnancy with women whose source of water was principally groundwater and found that the latter group had a statistically significant increase in the risk of bearing a malformed child. The authors then analysed the water for nitrate concentration and found substantially higher concentrations in the groundwater. Of particular interest is the finding that:

> ... the distribution of water containing high concentrations of nitrate in this aquifer coincides with the areas where large amounts of waste have been disposed of directly underground within a confined area. (Dorsch *et al.,* 1984, p. 475).

This point suggests that it may be important to consider the potential teratogenic effects of poor domestic and industrial waste disposal. There is certainly some evidence of higher rates of congenital malformations in areas around major waste disposal sites. One of the most notorious examples is Love Canal, a suburb of Niagara City in New York State, where a housing estate was built in the 1950s on top of a recently closed chemical dump. During the 1970s it became apparent that chemicals were leaking from the dump and in 1978 a large part of the estate was evacuated and has now been fenced off. Considerable controversy surrounds some of the medical research subsequently carried out at Love Canal (Landy, 1986), but one study quoted by Hildyard (1983) calculated that in the worst affected areas between 1974 and 1978 a fifth-of the children born had congenital malformations, compared to a ratio of 1 in 14 for the immediate surrounding area. There has been nothing on the scale of Love Canal in the United Kingdom, but given the doubts expressed by the Hazardous Waste Inspectorate (HWI, 1985) about some waste disposal practices there would seem to be a case for an investigation of the links between malformations and groundwater pollution in this country. There are, however, many difficulties in such research, particularly since regulation of hazardous waste disposal commenced only 15 years ago and it is possible to do little more than speculate about contamination of water supplies by disused waste dumps whose locations are unrecorded.

THE AVAILABILITY AND QUALITY OF DATA ON CONGENITAL MALFORMATIONS

A national scheme for the monitoring of all congenital malformations was established in 1964 and is now

operated by the Office of Population Censuses and Surveys. In the wake of the thalidomide tragedy the need was 'to detect sudden increases in the incidence of any particular malformation or group of malformations' (OPCS, 1983, p. iv}. The precise manner in which malformation data are assembled varies between District Health Authorities, but District Medical Officers are formally responsible for collecting data from either midwives, doctors delivering a baby or hospital administrators. The data are then forwarded to OPCS using a notification form (Rogers and Weatherall, 1976). Two points need to be made about this notification procedure. First, only n&formations identified during the first week of life are included on the notification form. Secondly, the system is voluntary, so that if the District Medical Officer is not informed the data forwarded to OPCS will be incomplete.

The first point is only a slight problem in the case of spina bifida (especially cystic farms), since the severity of the malformation is such that it should be detectable at birth. The second caveat is, however, more significant and may explain same of the imperfections in the data to which Knox *et al.* (1984 *have* drawn attention. They compared notifications made to OPCS of several classes of malformations with those recorded independently by the Department of Social Medicine at Birmingham University. The Birmingham register is widely regarded as reliable and the results of the comparison suggested that for 'neural tube defects the accuracy of reporting (to OPCS) was poor' (Knox *et al.,* 1984, p. 303). Between 1972 and 1978 only about half of the cases of central nervous system malformations recognized by the Birmingham register were entered on the OPCS records. The situation in Birmingham may be exceptional since there is evidence that fewer malformations may be reported to OPCS in those areas where a separate local register exists (Batting, 1987; Macfarlane, 1987). Nevertheless it needs to be recognized that there are problems of under-reporting within the OPCS system and it should also be stressed that the QPCS data cover only births and exclude miscarriages or terminations due to neural tube defects. The 'true' incidence. of spina bifida is consequently underestimated in several important respects.

These limitations mean that some caution is required when using the OPCS data to examine the geography of spina bifida in England and Wales. There are, however, no better data at a national scale and an ecological analysis would at least seem to provide a starting paint far any assessment of the role of genetic and environmental factors. In any area-based study there is nevertheless a need to be aware of the 'ecological fallacy' (Langbein and Lichtman, 1978) and in the analysis described below a particular problem is the lack of information on mobility. The interpretation of the results assumes that cases of spina bifida notified within a health authority were born to mothers who had spent their pregnancy as residents of the district. It is, however, quite possible that an apparent excess of spina bifida in one authority may simply reflect the in-migration of two or three mothers during the course of pregnancy. The problems concerning the scale of the analysis (such as the size of the District Health Authorities) and the need far individual-level data and case-control studies are assessed in the concluding section.

THE CONTEMPORARY GEOGRAPHY OF SPINA BIFIDA IN ENGLAND AND WALES

In order to examine the contemporary distribution of spina bifida in England and Wales the OPCS notification data for the period 1983-85 were mapped (see Fig. 2). Many of the higher rates occurred in coastal districts whilst central England and the London conurbation were characterized by lower values. Two contrasts with the 1971-80 pattern described in OPCS (1983) should also be noted. These are the emergence of relatively high rates in parts of southern England and the less prominent position of the East Midlands and North West.

One cautionary point which should be made about the interpretation of Figure 2 is that the number of cases in each District Health Authority is relatively small. Only 31 districts had 10 or more cases and 116 had 5 or less. This characteristic means that apparently large variations in prevalence may be due to only one or two additional cases. In such situations it is more appropriate to examine spatial variations in prevalence using Poisson probabilities (White, 1972). Figure 3 shows the districts where cases of spina bifida significantly exceeded the number expected if national trends had been followed. On a purely random basis, given 201 health authorities and a 0·10 confidence level, 20 districts with significant probabilities might have been expected, but there are actually 31. There appears to be a slight clustering of these authorities In Wales, the West Midlands and northern England, but others are scattered throughout the country. Figure 4 shows those health authorities which had significantly fewer cases of spina bifida

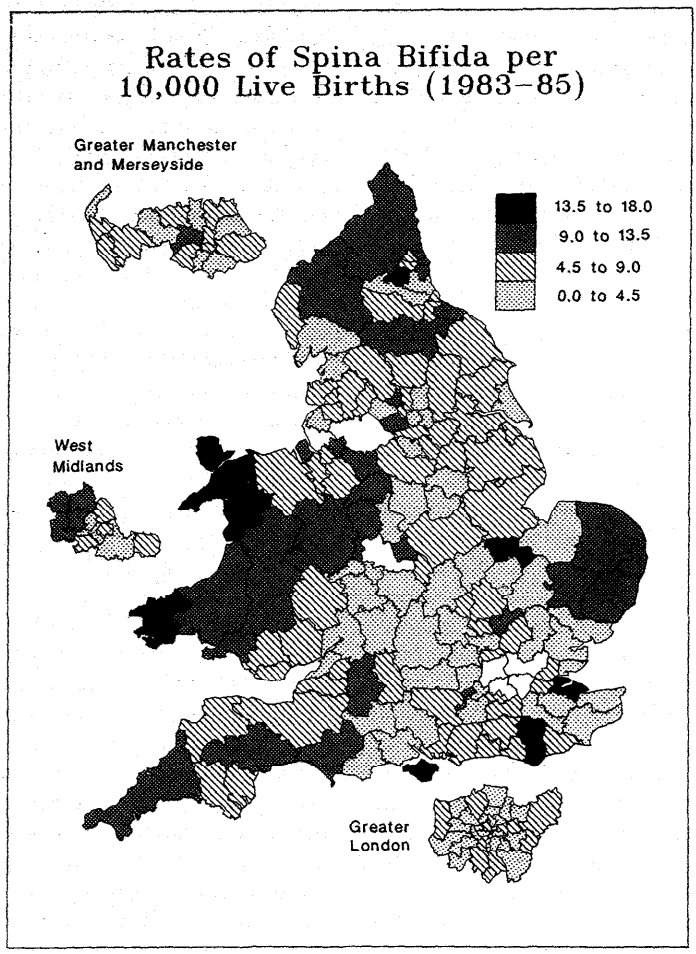

FIGURE 2. The prevalence of spina bifida in England and Wales 1983-85

than expected and, in contrast to Figure 3, these are largely concentrated in southern England,

Fifteen districts had significantly fewer cases of spina bifida than expected at the 0·05 confidence level. Another 10 health authorities can be added to this if the confidence level is relaxed to 0·10. The screening policies of the two sets of districts with significantly higher or lower levels of spina bifida can be compared by means of an x^2 test. Table III shows the results of such a comparison and indicates that those health authorities where the prevalence of spina bifida was significantly greater than expected were much less likely to carry out routine AFP testing than those districts where the prevalence was significantly lower than expected. A similar relationship is apparent if all 201 District Health Authorities are classified in terms of their screening policy and the average rate of spina bifida per 10 000 births is calculated for each of the three categories. Table IV indicates that the average rate was lowest in districts where screening was routine and highest in those where it was not. The third category of districts where the policy was uncertain occupy an intermediate position. An Analysis of Variance on the rates confirmed that there was a significant difference in prevalence between the three categories at the 0·05 confidence level.

These results suggest that differences in the screening policies of health authorities have been an important influence on the distribution of babies born with spina bifida. The existence of comparatively high

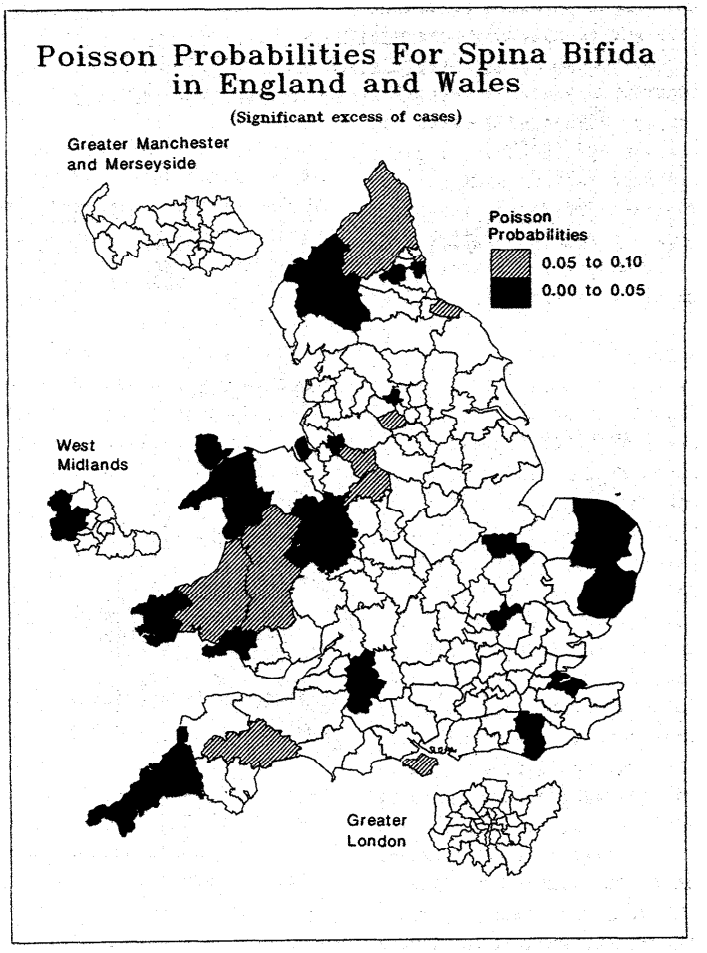

FIGURE 3. District Health Authorities where the prevalence of spina bifida was significantly higher than expected

rates in many districts which lack routine AFP testing requires some comment, particularly since the majority of these districts were in relatively low prevalence regions in the 1970s (OPCS, 1983). One explanation is that the decline in the prevalence of spina bifida has been much greater in those districts that introduced routine AFP testing in the mid-1970s than those that did not. Consequently, some previously low incidence areas where routine testing was not felt to be worthwhile now have higher levels of malformations than districts which fifteen years ago had around twice their rate.

The introduction of AFP testing has not, however, produced a total change in the distribution of spina bifida since, for example, Wales remains a region with high rates despite the widespread adoption of routine screening. It is also important to recognize that the districts which did not provide routine testing in 1982 are clustered in several, largely rural, parts of the country. The decline in spina bifida rates in districts with routine testing might therefore be due more to particular socio-economic or environmental characteristics rather than screening policy. These two points imply that it is important to examine the influence of other factors such as social class composition or environmental pollution and to assess the impact of maternal screening policies once such variables have been controlled for. This can best be achieved by means of a multiple regression analysis in which a number of variables (including screening

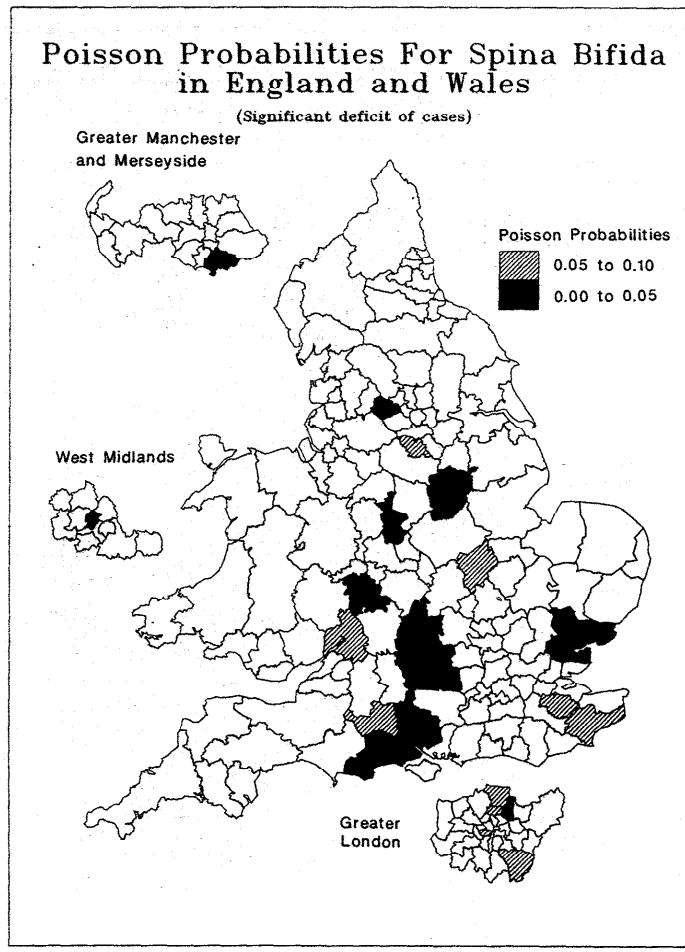

FIGURE 4. District Health Authorities where the prevalence of spina bifida was significantly lower than expected

TABLE III. *Screening policies of District Health Authorities with significant Poisson probabilities*

Poisson probabilities	*Screening policy of health authority*		
	Routine testing	*No routine testing*	*Policy uncertain*
Obs. > Exp. at 0·1 level	8·00 (14·95)	14·00 (8·86)	9·00 (7·20)
Obs. < Exp. at 0·1 level	19·00 (12·05)	2·00 (7·14)	4·00 (5·80)

Notes: 1. Values in parentheses are expected frequencies
2. Calculated $X^2 = 14{\cdot}93$ with 2 df. Critical value at 0·05 significance = 5·94

TABLE IV. *Average spina bifida rates for District Health Authorities classified by screening Policy*

Screening policy	*Number of districts*	*Average spina bifida rate per 10 000 births*	*Standard deviation*
Routine testing	101	4·99	3·09
No routine testing	65	7·45	3·42
Policy uncertain	35	6·60	3·58

Note: calculated F statistic = 11·59. Critical value at 0·05 significance = 3·05

policy) are used to try to account for spatial variations in the prevalence of spina bifida.

THE MULTIPLE REGRESSION ANALYSIS

Given the small number of cases in each health authority it was felt inappropriate to use the spina bifida rate per 10 000 births as the dependent variable in the multiple regression analysis. If, however, a count of the number of babies born with spina bifida is used then many of the assumptions of conventional Ordinary Least Squares regression are untenable (Flowerdew and Aitkin, 1982). In particular the discrete nature of the dependent variable must be taken into account and this can best be done by using a Poisson regression model. Poisson regression techniques have been described in detail by several geographers (e.g., Flowerdew and Aitken, 1982; Lovett *et al.,* 1986) and so only a brief outline will be given here.

The main characteristics of Poisson regression can be most easily described by means of a comparison with conventional Ordinary Least Squares regression. In Ordinary Least Squares regression the predicted values of the dependent variable are given by a linear combination of the independent variables. The predicted value $\acute{y}_i$ can also be regarded as the estimated mean of a normally distributed random variable Y_i, one possible realization of which is the observed value y_i of the dependent variable. The difference between the observed and predicted values of the dependent variable can therefore be evaluated in terms of the probability of a value of Y_i being equal to y_i. Poisson regression differs from Ordinary Least Squares in that the random variable Y_i is regarded as having a Poisson distribution, an assumption which is much more appropriate when the dependent variable consists of counts. In addition, the predicted value $\acute{y}_i$ is not identical to a linear combination of the independent variables, but logarithmically linked. The equation for a Poisson regression model can therefore be presented as:

$$\ln \hat{y}_i = \beta_0 + \sum_{j=1}^{K} \beta_j x_{ij} \qquad (1)$$

or

$$\hat{y}_i = \exp(\beta_0 + \sum_{j=1}^{K} \beta_j x_{ij}) \qquad (2)$$

where K is the number of independent variables; x_{ij} is the value of the ith observation on the jth independent variable; $\beta_0 is$ the intercept, the value of $\acute{y}$ when each independent variable equals zero; and β_j is the amount by which $\acute{y}$ changes when the value of the jth independent variable increases by one unit and those of the others are held constant.

Maximum likelihood estimates for the parameters of a Poisson regression model can be obtained by using an iteratively reweighted least squares procedure such as that available in the GLIM computer package (O'Brien, 1983). In GLIM the goodness of fit for a Poisson regression model is measured by the log-likelihood ratio statistic, also known as the deviance. This is given by the equation:

$$d = 2[\sum_{i=1}^{N} y_i \ln (y_i/\hat{y}_i)] \qquad (3)$$

where d is the deviance. A small deviance value indicates a good fit and it is possible to test whether the regression model could have produced the observed data by comparing the deviance with the critical value of x^2 fur the appropriate significance level and number of degrees of freedom. If the deviance is less than the critical value the model can be regarded as a satisfactory fit at the chosen significance level. Apart from this test of overall fit it is also possible to evaluate the significance of individual variables as they are added to the regression model. This is done by comparing the reduction in deviance that occurs with the critical value of x^2 for the corresponding loss of degrees of freedom. If the decline in deviance is greater, then the variable can be considered significant at the chosen confidence level.

The main sources of variables for the multiple regression analysis were the 1981 census and OPCS Monitors. Table V lists the variables used and their mnemonics. Census variables were 'selected on the basis of previous findings about the aetiology of spina bifida, and the SASPAC package (Rhind, 1983) was used to obtain data for the 201 District Health Authorities in England and Wales. In addition data on the number of births and cases of spina bifida in each health authority were taken from the OPCS Monitor Series MB3 (OPCS, 1984, 1985a, 1986a). Details of the percentage of babies with low birth weight were derived from the OPCS Monitor Series DH3 (OPCS, 1985c) and the screening variable was obtained from the previously discussed Maternity Alliance survey (Maternity Alliance, 1982). It would have been desirable to include data on water quality and hazardours waste disposal in each District Health Authority, but such details essentially refer to points (e.g., landfill sites, incinerators, or water sampling stations) and overall figures for areas may not be

TABLE V. *Variables used in the multiple regression analysis*

Mnemonic	*Variable description*
SB	Number of cases of spina bifida 1983-85
B	Total number of live and still births 1983-85
SC	Screening policy of health authority in 1982
LBW	Percentage of total births weighing under 2500 gms in1984
I	Percentage of female residents born in Eire
CAB	Percentage of female residents born in the Caribbean
lND	Percentage of female residents born in India
PAK	Percentage Of female residents born in Pakistan
U	Percentage of the economically active population unemployed
LA	Percentage of residents living in council housing
LC	Percentage of residents in households lacking a car
Cl2	Percentage of residents in households with a head classified as Social Class 1 or 2
AG	Percentage of economically active residents employed in agriculture

Note: All census variables are for 1981

TABLE VI. *Results of the Poisson regression analysis*

Model	*Deviance*	*Degrees of freedom*	*Critical value of x^2 at 0·05 significance*
Null	554·11	200	240·6
LOGB	349·28	199	239·5
+SC	305·32	197	237·3
+ CAB	285·04	196	236·2
+ U	266·88	195	235-I
+ AG	256·03	194	234-O
+ SC.U	249·02	192	231·8

particularly meaningful. There are, in any case, no readily available data on these variables for all District Health Authorities in England and Wales and so in what follows they are considered largely in terms of accounting for regression residuals.

The first step in the Poisson regression analysis was to check whether any of the independent variables needed to be transformed As a result of a series of plots it was decided to use the natural log transformation of number of births (LOGB) and retain the other variables in their original form. A Poisson regression model containing only an intercept term was then fitted in order to provide a measure of the variation in the dependent variable around its mean. Once this benchmark had been established a stepwise method was used in which each independent variable was separately added to the existing model and the one which produced the largest reduction in deviance was incorporated into the model if a X^2. test on the decline in deviance was significant. This stepwise procedure was repeated until no further significant reductions in deviance could be obtained

Table VI summarizes the results of the regression analysis. The first independent variable to be included was the log transformation of number of births (LOGB) and the addition of the screening variable (SC) as a three category factor produced a further large drop in deviance to 305·3. This model (LOGB + SC) can be thought of as a set of three regression lines with difference intercepts but a common slope. The highest intercept value was for districts where there was no routine screening whilst the lowest was for those health authorities where AFP testing was standard practice. Such a result supports the hypothesis that the absence of routine AFP testing in a health authority contributed to a higher prevalence of babies born with spina bifida.

The next independent variable to be included in the regression analysis was the percentage of female residents born in the Caribbean (CAB). This had a negative parameter estimate which may reflect genetic factors since previous studies have suggested that people of Caribbean origin are less vulnerable to spina bifida than those of European descent (Hewitt, 1963). Given the small size of the Caribbean born population (no more than 9 per cent of female residents in any health authority) this interpretation should, however, be treated with a degree of caution. Et could also be argued that the negative parameter estimate for females of Caribbean origin simply reflects the low prevalence of spina bifida in some of the major conurbations (particularly London) and the high levels of some rural areas. This pattern is in almost direct contrast to the distribution of the Caribbean born population (Peach, 1982).

Further cycles through the stepwise procedure led to two more variables being included in the regression model. The first of these was percentage unemployment (U) and the second was the percentage of the economically active population employed in agriculture (AG). Both of these variables had positive parameter estimates. In the case of unemployment this result can be regarded as a reflection of the known social class gradient in the incidence of spina bifida, with babies born to mothers in the lower classes being at a greater risk due to possible deficiencies in the maternal diet (Baird, 1974; Robbing, 1983), The positive parameter for agricultural

TABLE VII. *Parameter estimates for the Poisson regression model*

Variable	*Regression coefficient*	*Standard error*
LOGB	1·06	0·07
CAB	−0·11	0·03
U	0·046	0·009
AG	0·039	0·011
intercept r.s.	−8·61	0·68
intercept n.r.s.	−8·18	0·67
intercept p.u.	−8·43	0·68

Notes: For list of variables see Table V
r.s. = routine screening
n.r.s. = no routine screening
p.u. = policy urcertain

employment is less straightforward to interpret, but it is known that the intensity of agricultural activity is a major influence on nitrate concentrations in streams (Walling and Webb, 1981) and since nitrates are potentially teratogenic (Knox, 1972) it is possible that there could be a link between certain types of agricultural activity and the prevalence of spina bifida. in Britain the highest background concentrations of nitrates occur in eastern England (Walling and Webb, 1981; Beresford, 1985), but as Figure 2 indicates some of the health authorities in this area have relatively high rates of spina bifida and others very low ones. The available evidence is therefore inconclusive and more disaggregated data is clearly necessary to make any proper assessment of the relationship between nitrate levels in water supplies and congenital malformations.

Following the inclusion of agricultural employment in the regression model no further variables were found to produce a significant reduction in deviance. A significant interaction between the screening variable and unemployment was, however, identified. Including this interaction term in the regression model was equivalent to allowing the parameter for unemployment to vary between health authorities according to their screening policy. The *t* values of the parameter estimates indicated that while unemployment was a significant predictor of the incidence of spina bifida in districts where there was routine screening, it was insignificant in other circumstances. This result is difficult to interpret since, if anything it might have been expected that routine screening would have reduced social class variations in incidence. The significance of the interaction could have reflected the influence of an unmeasured variable and, for reasons of intelligibility, attention was therefore focused on the interpretation of the regression model without the interaction term.

The parameter estimates and standard errors for the regression model LOGB + SC + CAB + U + AG are shown in Table VII. All of the parameter estimates have *t* ratios which are significantly different from zero at the 0·05 level, but it should be noted that the model is not an entirely satisfactory predictor of the observed data since the deviance value of 256·03 is greater than the appropriate critical value of x^2 (234-O). This suggests that the analysis could be beneficially extended to include other, currently unmeasured, variables such as water quality, but it does not invalidate any interpretation of the parameter estimates for the five independent variables which have been included. One particularly important feature of the model is that the screening variable remains a significant predictor of prevalence even when differences in the socio-economic characteristics of health authorities are taken into account. The intercept values in Table VII indicate that the highest levels of malformations are predicted in those districts which lack routine AFP testing and this result again supports the hypothesis that screening has had a real influence on the distribution of babies born with spina bifida.

Apart from highlighting the role of maternal screening the regression model suggests that prevalence was positively related to the number of births, unemployment and agricultural employment and negatively correlated with the percentage of female residents born in the Caribbean. In general the results suggest that both genetic and environmental factors are important predictors but, given the ecological nature of the analysis, some caution is required when assigning particular causal roles to variables.

Since the regression model was not an entirely satisfactory fit and there were problems in interpreting one interaction term it was felt important to examine the spatial pattern of the residuals. Figure 5 highlights those health authorities which had standardized residuals larger than + 1·5 and it is evident that there is no obvious clustering of either the positive or negative residuals. Indeed, in several instances, a district with a high positive residual adjoins one with a substantial negative residual. Some districts with high positive residuals such as Medway, the Black Country and parts of Cheshire are also areas where large amounts of hazardous industrial waste have been deposited (Gatrell and Lovett, 1986). Consequently these might be localities where more

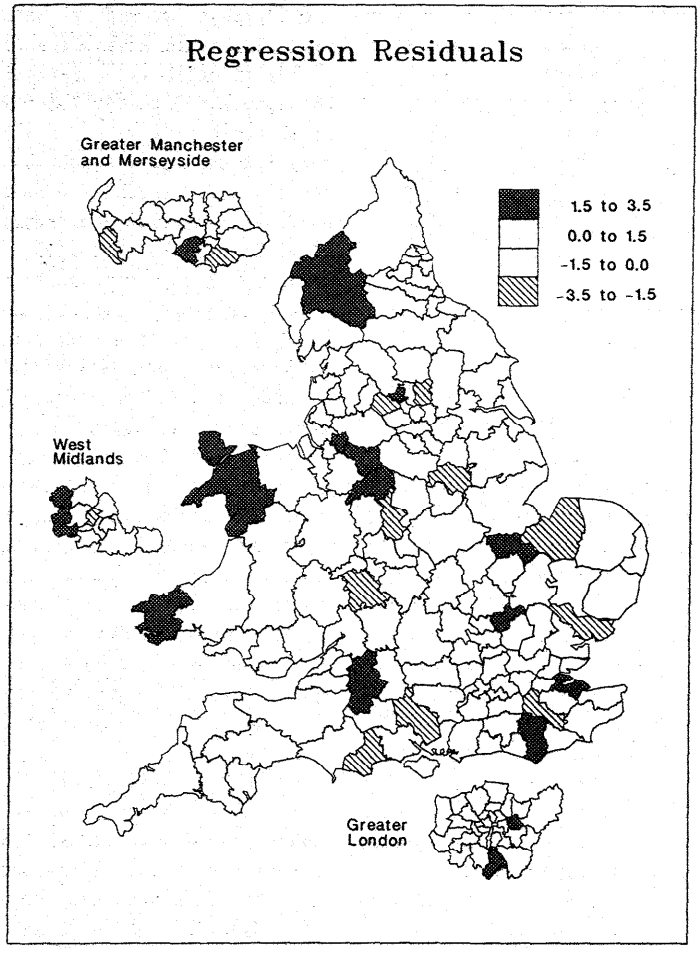

FIGURE 5. Standardized residuals from the Poisson regression model LOGB + SC + CAB + AG

detailed investigation of the links between environmental pollution and congenital malformations would be merited.

CONCLUSIONS

it should be clear from the above that there is no simple explanation of the distribution of spina bifida in England and Wales. The Poisson regression analysis nevertheless implies that variations in social class and ethnic composition are important factors and suggests that the role of water quality (and hazardous waste disposal) needs to be investigated in more detail. An additional feature of the analysis was that the maternal screening policy adopted by a health authority was found to be a significant predictor of the number of babies born with spina bifida in that district. There would seem to be little doubt that regional differences in the implementation of AFP testing have been responsible for significant changes in the prevalence and distribution of spina bifida in England and Wales since the mid 1970s. Implementing routine AFP testing throughout the country might not be particularly cost-effective (Hibbard *et al.,* 1985), but it is surely inconsistent if many of the districts with the highest prevalence do not provide such a service. The results reported in this paper certainly suggest that those health authorities which do not offer routine AFP testing should, at least, review their policies.

Two limitations of the work described in this paper must be noted. The first concerns the scale of analysis.

Although it has been possible to identify those districts in which the prevalence of spina bifida was significantly different from national trends there is no information on where, within the health authorities, the malformations actually occurred. This, for example, means that any assessment of the links between a point source of environmental pollution and the distribution of congenital malformations can be little more than speculation. The cases notified to OPCS are currently being postcoded and it is anticipated that information on malformations by postcode sector will be available in the near future (McDowall, 1985). This would allow more detailed epidemiological analysis, but the restrictions of an ecological approach would still exist.

The second limitation concerns the coverage and reliability of the OPCS notification data, particularly the problems posed by suspected differences in reporting levels between districts. It is unlikely that these deficiencies are sufficiently severe to invalidate the analysis reported here, but better quality data would be desirable. For some parts of the country such as Birmingham (Knox *et al.,* 1984) and Glasgow {Stone and Hamilton, 1987) there are independent registers of congenital malformations, some of which predate the OPCS system. Like the OPCS records these do not include miscarriages or therapeutic abortions, but they do contain data on individual cases of malformations and, fur their own registration area, invariably have better coverage and more reliable diagnosis than OPCS. If the records in such registers were gee-coded it would be feasible to undertake a much more satisfactory epidemiological investigation of congenital malformations. Ideally, such a study would use a case-control approach (Kelsey *et al.,* 1986) to examine the role of factors such as parental occupation, diet, water quality and proximity to waste disposal sites. There would still be the problem of examining only prevalence at birth rather than overall incidence, but it is hard to see how this could be overcome without widespread access to medical records and the attendant difficulties which this would entail. The present study, with its focus on factors influencing the geography of spina bifida at a national scale, has provided a context in which such intensive local research can be set. In highlighting the role of maternal screening, it also provides an apposite example in support of Mayer's (1982) call for a removal of the artificial barriers between the epidemiological and health care traditions in medical geography.

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