# Birth prevalence and recurrence rates of neural tube defects in southern Alberta in 1970-81

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**Given the observed variation in birth prevalence and recurrence rates of neural tube defects, it is important to obtain such data specific to a given locality for research and genetic counselling purposes. A review of hospital medical charts, the patient lists of the Medical Genetics and Myelomeningocele clinics at Alberta Children's Hospital and data from the Canadian Congenital Anomalies Surveillance System revealed the annual birth prevalence rate of neural tube defects in southern Alberta in 1970-81 to be 1.62/1000 total births. This figure suggests southern Alberta to be a low-frequency area. There was no significant variation in the annual rates of spina bifida, encephalocele or all neural tube defects combined over the study period. A significant linear decline in the frequency of births of anencephalic infants, however, was noted (p = 0.025). Information on the total reproductive history of the mothers revealed that the empiric risk of recurrence of a neural tube defect was 2.2%, and the risk to all siblings was estimated to be 2.3%. In future prevalence studies multiple sources of case ascertainment should be used, including data on pregnancies terminated because of a fetal neural tube defect.**

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**Vu les variations observées de la fréquence des anomalies du tube neural à la naissance et de leur survenue lors de grossesses ultérieures, il importe d'établir les taux propres à chaque région pour la recherche clinique et pour le conseil génétique. À partir des dossiers hospitaliers, des listes de sujets suivis aux consultations de génétique médicale et de myéloméningocèle à l'Alberta Children's Hospital et du Réseau canadien de surveillance des malformations congénitales, nous trouvons pour le sud de l'Alberta de 1970 à 1981 un taux annuel de 1,62 pour 1000 naissances. Ce chiffre suggère que le sud de l'Alberta est une région de basse fréquence. Le taux varie très peu d'une année à l'autre, ni pour le spina bifida, ni pour l'encéphalocèle, ni pour l'ensemble des anomalies du tube neural. Mais on note un net abaissement linéaire de la fréquence des naissances anencéphales (p = 0,025). L'anamnèse complète de la procréation chez les mères montre que le risque de survenue d'une anomalie du tube neural lors d'une grossesse ultérieure est de 2,2%; dans la fratrie hormis le sujet il serait de 2,3%. Toute enquête devra désormais pour la reconnaissance des cas recourir à plusieurs sources de renseignements, y compris ceux concernant les interruptions de grossesse motivées par une anomalie du tube neural.**

Spina bifida cystica, anencephaly and encephalocele occur when the neural tube fails to close properly. These conditions, collectively known as neural tube defects, are among the most

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striking of the common congenital anomalies. Depending on the location and size of the defect as well as the presence of other congenital anomalies, the effects of a neural tube defect may range from negligible or no handicap to paralysis and early death.

The epidemiologic features of neural tube defects are complex. The birth prevalence and recurrence rates vary considerably according to geographic region, ethnic population, season of birth and period of observation. Recently several centres around the world have reported a decline in birth prevalence rates over the last 10 to 20 years.[1-5] In Canada it has been reported that the birth prevalence rate of neural tube defects is higher in the eastern provinces, the rate progressively declining in the west.[6-8]

Baseline epidemiologic data on neural tube defects are needed for hypotheses about causal factors. Because of the observed variation in birth prevalence and recurrence rates, it is equally important to obtain such data specific to a given locality for research and genetic counselling.

We carried out a study to determine the birth prevalence rate of neural tube defects in southern Alberta using several sources of case ascertainment and to estimate the risks of recurrence to siblings of the affected child.

## Methods

The study group comprised all families who had a liveborn or stillborn child with a neural tube defect (index case) born between 1970 and 1981 inclusive in southern Alberta, which for the purposes of this study was defined as the 11 southern health units in the province: Banff National Park, Red Deer, Mountview, Drumheller, Big Country, City of Calgary, Foothills, Chinook, City of Lethbridge, Barons-Eureka-Warner and Medicine Hat.

The index cases were ascertained from four sources: the medical charts at acute care hospitals, the patient lists of the Medical Genetics and Myelomeningocele clinics at Alberta Children's Hospital, and the Canadian Congenital Anomalies Surveillance System. The Medical Genetics Clinic list includes patients seen at the Antenatal Genetics Clinic, where some affected pregnancies were terminated. The Canadian Congenital Anomalies Surveillance System screens the following Alberta vital statistics documents for the presence of a congenital anomaly: physician's notice of a live birth or stillbirth, medical certificate of death for an infant under 1 year of age, medical certificate of stillbirth and the hospital-based congenital anomaly reporting form.

Only index cases of the multifactorial type of neural tube defect were included. Cases in which there was a recognized cause (i.e., single gene disorder, chromosomal abnormality, amniotic band syndrome or exposure to a known teratogen) were excluded from study.

Children born with a meningocele or meningomyelocele were classified as having spina bifida, those with craniorachischisis or acrania as having anencephaly, those with anencephaly plus spina bifida as having anencephaly, and those with encephalocele plus spina bifida as having spina bifida.

Data on the annual number of total births (live births and stillbirths) over the study period were obtained from the annual reports of each health unit. The annual birth prevalence rates of neural tube defects were calculated, and the secular trends of the rates were analysed by means of linear trend analysis.[9] Results were considered significant at the 5% level.

Information on the total reproductive history of the mother was obtained in one of two ways. Families who were ethically accessible because they had received services and counselling at the Medical Genetics and Myelomeningocele clinics or the Antenatal Genetics Clinic received a questionnaire directly from us asking for information on all pregnancies and outcomes. The remaining families, who were identified by means of the review of hospital charts or by the Canadian Congenital Anomalies Surveillance System, were not considered to be ethically accessible. The current reproductive history and the name of the family doctor (if available) were abstracted from the hospital chart, and a letter was sent to the physician requesting an update on subsequent pregnancies. If the identified physician was not the family doctor, he or she was asked to provide the name of the current family doctor, if known.

The reproductive histories were reviewed, and the risk of recurrence of a neural tube defect as well as the risk to all siblings were calculated. Assuming a Poisson distribution, we determined confidence levels for the birth prevalence and recurrence rates.[10] We also determined the proportion of cases that each ascertainment source contributed to the total number of cases and the response rates of the physicians.

## Results

Over the study period 280 index cases of a neural tube defect were ascertained in southern Alberta. The overall average birth prevalence rate was 1.62/1000 total births (95% confidence limits [CL] 1.43 and 1.82). Table I shows the number of cases by type of defect and year of birth. Between 1970 and 1981 there was no statistically significant upward or downward trend in the annual birth prevalence rate of all neural tube defects combined ($\chi^2$ for linear trend = 3.51, $p = 0.062$) (Table II). Linear trend analysis by specific defect showed no significant annual variation in the birth prevalence rate except for anencephaly: a significant linear decline was noted over the study period ($\chi^2 = 5.01$, $p = 0.025$).

Of the 85 mothers who were traced either

directly or through their family physician for an update on their reproductive history 28 did not have another pregnancy. The remaining 57 women had one or more pregnancies of at least 20 weeks' gestation after the birth of their affected child, resulting in 90 liveborn infants, 2 of whom had neural tube defects. Therefore, the rate of recurrence of neural tube defects was calculated to be 2.2% (95% CL 0.3 and 7.6) (Table III). In one additional family there was also an affected older sibling. The overall risk of a neural tube defect to siblings was thus calculated to be 2.3% (95% CL 0.5 and 6.6) (Table III).

No single source of ascertainment identified all the cases. The most important contributing sources were the review of hospital medical charts, which identified 83% of the cases, and the Canadian Congenital Anomalies Surveillance System, which identified 74%. The chart review did not necessarily ascertain the same affected infants as the national surveillance system. About 20% of the cases were identified from the patient list of the Medical Genetics Clinic and 18% from the Myelomeningocele Clinic roster. About 36% of the cases were ascertained from a single source, 45% from two sources, 12% from three sources and 7% from four or more sources.

Of the 180 physicians who received a request for information on the pregnancies of the mothers 80 returned the questionnaire with data detailed

**Table I — Birth prevalence rates of neural tube defects in southern Alberta between 1970 and 1981, per 1000 total births**

| | Defect | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Spina bifida | | | Anencephaly | | | Encephalocele | | | Total | | |
| Year | No. of cases | Rate | Fraction | No. of cases | Rate | Fraction | No. of cases | Rate | Fraction | No. of cases | Rate | Fraction |
| 1970 | 11 | 0.79 | 1/1266 | 13 | 0.94 | 1/1064 | 1 | 0.07 | 1/14286 | 25 | 1.80 | 1/556 |
| 1971 | 9 | 0.68 | 1/1471 | 12 | 0.91 | 1/1099 | 1 | 0.08 | 1/12500 | 22 | 1.67 | 1/599 |
| 1972 | 12 | 0.97 | 1/1031 | 9 | 0.73 | 1/1370 | 3 | 0.24 | 1/4167 | 24 | 1.94 | 1/515 |
| 1973 | 10 | 0.80 | 1/1250 | 5 | 0.40 | 1/2500 | 2 | 0.16 | 1/6250 | 17 | 1.37 | 1/730 |
| 1974 | 19 | 1.50 | 1/667 | 9 | 0.71 | 1/1408 | 0 | 0.00 | 0 | 28 | 2.22 | 1/450 |
| 1975 | 13 | 0.97 | 1/1031 | 9 | 0.67 | 1/1492 | 2 | 0.15 | 1/6667 | 24 | 1.80 | 1/556 |
| 1976 | 14 | 1.00 | 1/1000 | 8 | 0.57 | 1/1754 | 3 | 0.21 | 1/4762 | 25 | 1.79 | 1/559 |
| 1977 | 10 | 0.69 | 1/1449 | 10 | 0.69 | 1/1449 | 1 | 0.07 | 1/14286 | 21 | 1.45 | 1/690 |
| 1978 | 18 | 1.20 | 1/833 | 3 | 0.20 | 1/5000 | 1 | 0.07 | 1/14286 | 22 | 1.47 | 1/680 |
| 1979 | 17 | 1.07 | 1/935 | 8 | 0.50 | 1/2000 | 6 | 0.38 | 1/2632 | 31 | 1.95 | 1/513 |
| 1980 | 3 | 0.17 | 1/5882 | 12 | 0.69 | 1/1449 | 5 | 0.29 | 1/3448 | 20 | 1.15 | 1/870 |
| 1981 | 12 | 0.64 | 1/1563 | 7 | 0.38 | 1/2632 | 2 | 0.11 | 1/9091 | 21 | 1.13 | 1/885 |
| Total | 148 | 0.86 | 1/1163 | 105 | 0.61 | 1/1639 | 27 | 0.16 | 1/6250 | 280 | 1.62 | 1/617 |

**Table II — Linear trend analysis of neural tube defects by year of birth***

| | Defect | | | |
|---|---|---|---|---|
| Variable | Spina bifida | Anencephaly | Encephalocele | Total |
| Linear trend $\chi^2$ | 1.60 | 5.01 | 1.08 | 3.51 |
| Degrees of freedom | 1 | 1 | 1 | 1 |
| Probability | 0.206 | 0.025 | 0.313 | 0.062 |

*The independent variable is taken to be the number of years after 1970, and the dependent variable is the birth prevalence rate per 1000 total births.

**Table III — Risk of recurrence of neural tube defects and risk to all siblings**

| | No. of siblings | | No. (and %) of affected siblings (and 95% confidence limits) | |
|---|---|---|---|---|
| Defect in index case | Subsequent | All | Subsequent | All |
| Spina bifida | 62 | 89 | 2 (3.2) | 3 (3.4) |
| Anencephaly | 23 | 30 | 0 (0.0) | 0 (0.0) |
| Encephalocele | 5 | 10 | 0 (0.0) | 0 (0.0) |
| Total | 90 | 129 | 2 (2.2) (0.3, 7.6) | 3 (2.3) (0.5, 6.6) |

enough for analysis. Of the 46 acute care hospitals in southern Alberta 36 cooperated with us in this study. All the large and medium-sized hospitals in the 11 health units were included in the study.

## Discussion

There is no substitute for using multiple sources of ascertainment to calculate birth prevalence rates in a population. Even for a congenital anomaly as obvious and easily diagnosed as a neural tube defect it is still necessary to screen several different documents. The most fruitful sources of ascertainment in our study were the review of hospital medical records and the Canadian Congenital Anomalies Surveillance System. However, only 51% of the cases were correctly identified by both of these sources.

To ensure comparability of data it is important to determine that the methods of case ascertainment used in various studies are similar. Also, because there appears to be a worldwide secular decline in the frequency of neural tube defects it is important to compare our data with those from other studies examining similar periods.

We calculated the birth prevalence rate of neural tube defects in southern Alberta during 1970–1981 to be 1.62/1000 total births. When compared with the rates in other geographic areas this figure suggests that southern Alberta is a low-frequency area. Our results are similar to the rates obtained by the British Columbia Health Surveillance Registry, which uses over 60 sources of registration: between 1971 and 1980 the birth prevalence rate of spina bifida and anencephaly in British Columbia was determined to be 1.50/1000 total births.[11] Our results, determined for all neural tube defects, are also comparable with the rates of 1.73/1000 total births in eastern Ontario and western Quebec between 1969 and 1981[12] and 1.64/1000 total births (excluding therapeutic abortions) in Nova Scotia in 1980–84.[13] Newfoundland, however, appears to have the highest rate, 3.18/1000 total births between 1976 and 1983.[14]

A decrease in the birth prevalence rate of neural tube defects has been reported from several areas around the world over the last 10 to 20 years.[1-5] A reduction in annual rates of 50% or more has been reported from some areas, including Great Britain[1,2] and Atlanta, Georgia.[5] Several possible explanations of the observed decline in rates have been discussed elsewhere.[2,3]

In southern Alberta there was no statistically significant annual variation in the birth prevalence rate of all neural tube defects. The rate of anencephaly, however, declined significantly over the 12-year study period. Some investigators have noted a similar decline for anencephaly only,[11,15-17] whereas others have noted a more marked decline for anencephaly than for spina bifida.[1] Whether the observed decline in the rate of anencephaly in southern Alberta is a result of some extraneous factor, such as prenatal testing or periconceptional vitamin supplementation,[18] remains to be evaluated. It has been suggested that the declining trend observed elsewhere may be partly attributable to antenatal diagnosis and termination of affected pregnancies, but there is no known explanation for the rest of the current decline in the prevalence rate.[2]

Several investigators have reported a striking east-to-west decrease in the birth prevalence and death rates for neural tube defects in Canada.[6-8] These studies were subject to the limitations of using death certificates and birth notification forms as a source of data on congenital anomalies. According to recently published data[11-14,19] the east-to-west decline does not appear to have been as great in the 1970s and 1980s as in the 1950s and 1960s (Table IV). Newfoundland and New Brunswick are experiencing the highest birth prevalence rates in Canada; the other provinces, including Nova Scotia, have similar low rates. Current Canadian data do not show an east-to-west decline in rates but, rather, high-risk areas in Newfoundland and New Brunswick. Differences in environmental factors that might relate to the causation of neural tube defects may, therefore, be limited to these two provinces. It would be worth while to obtain similarly collected data from Prince Edward Island, Saskatchewan and Manitoba to pursue this hypothesis.

In one Canadian study the rate of therapeu-

**Table IV — Birth prevalence rates of spina bifida and anencephaly in Canada, per 1000 total births***

| Province or area | Year | Defect; rate | | |
|---|---|---|---|---|
| | | Spina bifida | Anencephaly | Total |
| Newfoundland[14] | 1976–83 | 1.72 | 1.46 | 3.18 |
| Nova Scotia[13] | 1980–84 | 1.08 | 0.70 | 1.78 |
| New Brunswick[19] | 1970–79 | 1.78 | 1.24 | 3.02 |
| Western Quebec/ eastern Ontario[12] | 1969–81 | 1.08 | 0.58 | 1.66 |
| Southern Alberta (present study) | 1970–81 | 0.86 | 0.61 | 1.47 |
| British Columbia[20] | 1952–70 | 0.87 | 0.68 | 1.55 |
| British Columbia[11] | 1971–80 | 0.90 | 0.60 | 1.50 |

*The rates for New Brunswick were calculated per 1000 live births, as extrapolated from graphs.

tically aborted pregnancies involving anencephalic fetuses was two-thirds the rate of live birth and stillbirth of anencephalic infants (0.28 v. 0.42 per 1000 total births).[13] Prevalence studies, therefore, that are based on total birth populations and do not include pregnancies terminated because of a neural tube defect may underestimate the frequency rate. Although data on some terminated pregnancies associated with the Antenatal Genetics Clinic were included in our study, we did not systematically survey all southern Alberta hospitals for such terminated pregnancies, and hence our calculated figure may also be an underestimate.

The empiric risk of recurrence of a neural tube defect in our study was 2.2%; the risk to all siblings was estimated to be 2.3%. These results are similar to those from other areas with a similarly low birth prevalence rate.[12,20-23] Because our sample was small it would be useful to obtain reproductive histories from more mothers of affected children to determine whether our calculated recurrence rates prevail.

We thank the families, physicians and hospitals who participated in this study. We also thank the Alberta Children's Hospital Myelomeningocele Clinic, the Spina Bifida Association of Southern Alberta and the staff of the Canadian Congenital Anomalies Surveillance System for their assistance in this study. We thank Terry Harris for clerical assistance.

This study was partially funded by the Alberta Children's Hospital Foundation and by a grant to Brian Medd from the Summer Studentship Program, Alberta Heritage Foundation for Medical Research.

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