

Short reports

Schizophrenia: increased risk associated with winter and city birth - a case-control study in 12 regions within England and Wales

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In a recent Swedish study, Lewis *et al*¹ found that the risk of schizophrenia was greater in people brought up in cities than in those brought up in rural areas. The factors responsible for this effect are uncertain but a winter birth excess has been consistently reported in schizophrenia.² We suggest that the same factors are responsible for both the urban/rural difference in risk and the winter birth excess. We predict (a) winter birth and urban birth are each associated with an increased risk of schizophrenia; and (b) the effects of winter birth and urban birth potentiate each other.

Methods: We obtained from 12 regional health authorities (RHAs) information on the sex, age, date of birth, and place of birth of first admission psychiatric patients born between 1938 and 1963 in England or Wales, and discharged between 1976 and 1986, who received a diagnosis of schizophrenia (ICD 295). Similar data on patients with a diagnosis of affective psychosis (ICD 296), personality (ICD 300), or neurotic disorder (ICD 297) were obtained and used as controls for the schizophrenic patients.

To classify the patients according to place of birth, we used data from OPCS to identify 65 districts in England and Wales as "cities". These districts were conurbation areas with high population density throughout the period 1938-63. The rest of England and Wales was

considered as "non-cities". Season of birth was defined as a categorical variable: winter (December-February), spring (March-May), summer (June-August), and autumn (September-November). To allow for potential confounding, we identified the sex, birth period (five, 5 year periods), and age of admission (under or over 26 years) of each subject.

To compare the schizophrenic and the control groups in respect of the exposure variables, we used linear logistic regression. Diagnostic status (schizophrenia *v* control) was defined as the response variable. Models were fitted with different combinations of predictor variables. The statistical significance of a predictor variable was assessed by the reduction in deviance (G^2) with its inclusion into the model.

Results: The inclusion of possible confounders into the logistic regression model resulted in significant reductions in G^2 for sex and birth period, but not for age of onset. However, all three variables were retained so as to allow for them. When place of birth was entered into the model, G^2 was reduced by 14.25 ($df=1$), implicating a significant ($p=0.0002$) influence of place of birth on the diagnosis of schizophrenia in adult life. The inclusion of season of birth into the model, with or without the inclusion of place of birth, resulted in no significant improvement in goodness of fit. However, adding the interaction of season of birth and place of birth into the model, reduced G^2 by 8.43 ($df=3$), indicating that the effect of place of birth was significantly influenced ($p=0.038$) by the season of birth.

The final model therefore includes the five main effects (sex, birth period, age of onset, place of birth and season of birth) and the interaction between place of birth and season of birth. The odds ratio (OR) in the final model for the association between "city birth" and schizophrenia, allowing for potential confounders, was 1.12 (95% CI 1.057, 1.189). The ORs obtained from the final model are given in the table, which shows that city birth was associated with an increased risk of schizophrenia in those born in autumn (OR 1.19) and winter (OR 1.21), while those born in summer showed no city birth effect (OR 1.01).

Parameter estimates of the best logistic regression model allowing for confounding factors

| Place of birth | Season of birth | No of cases | No of controls | OR* | |
|----------------|-----------------|-------------|----------------|----------|----------------|
| | | | | Estimate | (95% CI) |
| City | Autumn | 606 | 1499 | 1.193 | (1.057, 1.347) |
| | Winter | 679 | 1636 | 1.213 | (1.079, 1.364) |
| | Spring | 700 | 1872 | 1.082 | (0.964, 1.213) |
| | Summer | 582 | 1678 | 1.009 | (0.894, 1.139) |
| Non-city | Autumn | 901 | 2691 | 0.978 | (0.880, 1.088) |
| | Winter | 952 | 2814 | 0.985 | (0.886, 1.096) |
| | Spring | 1127 | 3222 | 1.029 | (0.878, 1.075) |
| | Summer† | 986 | 2893 | 1 | — |

* In the logistic regression, sex, birth period, and age of onset were controlled for as potential confounders.

† Reference category: non-city summer birth

Cases = schizophrenics ($n=6533$);
controls = comprised by three diagnostic groups; (affective disorders $n=4398$, personality disorders $n=4298$, neurotic disorders $n=9609$).
These parameter estimates were obtained by reparameterising the final model for ease of interpretation.

Discussion: Individuals born in cities and winter are at increased risk of schizophrenia. Moreover, the city birth effect seems to be modified by the season of birth. City birth did not increase the risk of schizophrenia among those born in summer, but was associated with a 21% increase among the winter born. The confirmation of our predictions suggests that adverse events at or before birth are at least partly responsible for the association between urban upbringing and increased risk of schizo-

phrenia found in the recent Swedish cohort study.¹

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- 1 Lewis D, David A, Andréasson S, Allebeck P. Schizophrenia and city life. *Lancet* 1992;340:137-40.
- 2 Hare E. Temporal factors and trends, including birth seasonality and the viral hypothesis. In: Nasrallah HA, ed. *Handbook of schizophrenia*, Vol 3. Amsterdam: Elsevier, 1988.

Insulin dependent diabetes mellitus: incidence in childhood in Belgrade 1982-92

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A retrospective technique was used to register all newly diagnosed cases of insulin dependent diabetes mellitus (IDDM) in Belgrade children 0-14 years of age, between 1982 and 1992. Two independent sources of data were used: patients' records from hospitals where the disease was diagnosed (according to WHO criteria¹) and the population based register. To establish the completeness of ascertainment the capture/recapture method was used.²

For calculation of yearly incidence rates, the population denominator data were obtained from the 1981 and 1991 national census data with interpolation. The incidence was standardised by the direct method using the world population as the standard. The 95% confidence intervals were calculated assuming a Poisson distribution. The significance of seasonal variation was analysed by an ordinary χ^2 test.

Results: The ascertainment probability for the whole study period was 90.05%, ranging from 74.04% to 98.74%. Between 1982 and 1992, the mean, annual, age adjusted incidence rates of IDDM (per 100 000) were 7.3 for boys, 8.1

for girls, and 7.7 for both sexes. The highest incidence was in the age group 10-14 years. The overall male:female ratio was 0.90 (table).

There was a year to year fluctuation in both crude incidence and estimated incidence (crude rate/completeness of ascertainment), with two peaks, one in 1985 and the other surrounding the year 1991.

The largest numbers of new cases were identified in the months of January and September, and the smallest numbers in April, May, and June. The seasonal pattern in the total material was significantly different from a uniform distribution of new cases throughout the year ($p < 0.01$). The mean number of new cases in the winter months, December, January and February, was significantly different from the yearly mean ($p < 0.05$).

Discussion: The IDDM incidence rate of 7.7 per 100 000 in Belgrade compares with rates in European countries with low-medium incidence. This rate is comparable to those in France, Hungary, Austria, and northern Italy; is higher than that in Israel; and is lower than rates in Nordic countries, in Denmark, and the United Kingdom.³ In Belgrade, however, the IDDM incidence is higher than that during the years 1989 and 1990 in Bucharest,³ which is on a latitude close to that of Belgrade. It is also higher than the rates in Slovenia and Poland,³ which are further north. There are other examples which are inconsistent with a north to south gradient.³ Taking into account year to year fluctuation and epidemic type variation in IDDM incidence, however, a north to south gradient can not be discussed on the basis of one or two year incidence rates, especially when small variations in latitude and rates of incidence are concerned. The rates in Sardinia and Iceland³ could be regarded as exceptions.

Our data confirm earlier findings that there is often a slight female preponderance in low incidence populations.

A trend of increasing incidence for childhood

Incidence rates (95% confidence interval(CI)) (per 100 000) of insulin dependent diabetes mellitus in Belgrade children 0-14 years in relation to sex, average for 1982-92

| | Age group (y) | | | Crude rate 0-14 | Age adjusted rate 0-14 |
|----------------|---------------|------------|------------|--------------------|---------------------------|
| | 0-4 | 5-9 | 10-14 | | |
| Boys | | | | | |
| Cases (no) | 24 | 43 | 59 | 126 | |
| Population | 47-574 | 51-594 | 50-870 | 150-038 | |
| Incidence rate | 4.6 | 7.6 | 10.5 | 7.6 | 7.3 |
| (95% CI) | (2.9,6.8) | (5.5,10.2) | (8.1,13.7) | (6.4,9.1) | (6.1,8.8) |
| Girls | | | | | |
| Cases (no) | 16 | 55 | 62 | 133 | |
| Population | 44-610 | 48-477 | 47-500 | 140-587 | |
| Incidence rate | 3.3 | 10.3 | 11.9 | 8.6 | 8.1 |
| (95% CI) | 1.9,5.3 | 7.8,13.5 | 9.2,15.4 | 7.2,10.2 | (6.8,9.7) |
| Total | | | | | |
| Cases (no) | 40 | 98 | 121 | 259 | |
| Population | 92-184 | 100-071 | 98-370 | 290-625 | |
| Incidence rate | 3.9 | 8.9 | 11.2 | 8.1 | 7.7 |
| (95% CI) | 2.8,5.3 | 7.3,10.9 | 9.3,13.4 | 7.1,9.2 | 6.8,8.7 |