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Confinement of Winter Birth Excess in Schizophrenia to the Urban-born and its Gender Specificity

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Background. The season of birth phenomenon in schizophrenia was reexamined in relation to place of birth, in order to test the hypothesis that a seasonal factor might operate preferentially among those who were urban-born.
Method. The seasonal distribution of births was examined among 3253 patients in two case registers having an ICD–9 diagnosis of schizophrenia and compared with the distribution of births among the normal population born in those catchment areas over the same period; those subjects born in population centres greater than 50 000 were defined as urban-born.
Results. Patients who were urban-born showed an excess of winter births relative to controls that was absent among their rural-born counterparts. On comparing patient groups, those who were urban-born were more likely to be born in the winter, while those who were rural-born were more likely to be born in the spring; this urban–rural distinction was confined essentially to female patients.
Conclusions. These findings might be accommodated most readily in terms of a spatially as well as seasonally varying environmental factor that is associated with urbanicity and to which female offspring are more vulnerable.

A principal epidemiological finding in schizophrenia studies is the excess of winter/early spring births among patients with schizophrenia relative to the general population (Bradbury & Miller, 1985; Boyd *et al*, 1986; Hare, 1988). While some studies have not noted any relationship between season of birth and inferred genetic risk (Baron & Gruen, 1988; Pulver *et al*, 1992), another suggests that the 'season-of-birth' effect may be most evident among patients without a family history of the disorder (O'Callaghan *et al*, 1991*a*).

These findings suggest the action of a seasonally-varying environmental factor. Significant associations between season-of-birth and the prevalence of diphtheria, pneumonia and influenza were reported by Watson *et al* (1984), while Torrey *et al* (1988) reported similar associations with measles, polio and herpes zoster. While there have been some negative reports (Kendell & Kemp, 1989; Torrey *et al*, 1991; Crowe & Done, 1992), several studies have described an increased risk for schizophrenia in the offspring of mothers who were exposed to influenza in mid-gestation, both during the 1957 A2 pandemic in particular (Mednick *et al*, 1988; O'Callaghan *et al*, 1991*b*; Kunugi *et al*, 1992; Adams *et al*, 1993) and during periodic epidemics in general (Barr *et al*, 1990; Sham *et al*, 1992; Takei *et al*, 1994).

A further epidemiological clue lies in the finding that urban birth (Takei *et al*, 1992) and upbringing (Lewis *et al*, 1992) appear to be associated with an increased risk for subsequent schizophrenia. As infections, including influenza, are more communicable in urban relative to rural environments (Horne, 1957; McNeil, 1976), one could hypothesise that there might be a greater prominence of the season-of-birth phenomenon in an urban environment.

Method

Computerised information was obtained from the Dublin Case Register (DCR) and from the Three Counties Case Register (TCCR). The DCR encompasses approximately 280 000 inhabitants of a Dublin psychiatric hospital catchment area (O'Hare & Walsh, 1987). It contains data on all psychiatric admissions from 1971 onwards; information is collected by specific interview on each contact with the psychiatric service, and only those patients fulfilling ICD–9 criteria (World Health Organization, 1978) for schizophrenia are considered in the present study. The TCCR encompasses approximately 150 000 inhabitants of three predominantly rural Irish counties (Walsh *et al*, 1980), specifically selected so as to be representative of the normal socioeconomic distribution in Ireland, with the register containing data on all psychiatric in-patients in 1973 and on all subsequent contacts; information collection and diagnostic criteria were as for the DCR.

Using methods described previously (O'Callaghan *et al*, 1991*a*), the quarterly (January–March, April–June, July–September, October–December) distribution of births for the general population of Dublin and the three counties for each year were used to

calculate the expected quarterly distribution of patients born in that year; these control values were subsequently summed across the years 1921–1960 to give the overall expected sample distribution. The two databases were searched to establish the following characteristics: sex; date of birth; educational attainment defined as years in the educational system; marital status; age at first presentation or admission; duration of hospitalisation on admission; family history, defined in terms of any first or second degree relative with a psychiatric disorder requiring treatment; place of birth, defined as urban if that birth occurred in either Dublin or Cork cities, with all other births being defined as rural. Statistical analysis was performed using the one or two sample χ^2 test as appropriate. For the one sample χ^2, adjusted standardised residuals (ASRs) were calculated to identify the categories responsible for a significant χ^2 value (Haberman, 1973). Seasonal excesses and deficits are expressed as the percentage difference between the observed and the expected values.

Results

The seasonal distribution of births in the control population was remarkably stable over the 40-year period considered; in each year there was a 2–5% excess in the second quarter. For the total patient population ($n=3253$), there was only a trend ($P=0.13$) for births not to be evenly distributed by quarter relative to the general population, with a 5% excess in the first quarter. However, when taking place of birth into account, there was a significant ($P=0.04$) difference in quarterly distribution of births between urban-born patients ($n=1362$) and urban-born controls; patients who were urban-born were more likely (+13%) than controls to be born in the winter. There was a trend for an excess (+8%, $P=0.14$) of spring births among rural-born patients ($n=1799$) relative to rural-born controls (Table 1). Control data relating to gender were not available.

On further analysis of place of birth, there was a significant ($P=0.03$) difference in the quarterly distributions of births between urban- and rural-born patients: those who were urban-born were significantly (ASR = 2.3, $P<0.05$) more likely to be born in the winter; conversely, rural-born patients were significantly (ASR = 2.2, $P<0.05$) more likely to be born in the spring (Table 2). This urban–rural distinction in season of birth was most marked among female patients ($P=0.03$): women who were urban-born were significantly more likely (ASR = 2.0, $P=0.03$) than their rural-born counterparts to be winter-born, while rural-born women were significantly more likely (ASR = 2.4, $P=0.03$) to be spring-born than their urban-born counterparts; no comparable phenomena were evident among male patients.

Analyses of the urban–rural dichotomy taking into account family history, marital status and educational attainment revealed no significant differences.

Discussion

An overall analysis of our data revealed a trend for an excess of winter births in patients with schizophrenia. A number of studies have reported a more robust seasonality effect (Bradbury & Miller, 1985), while two previous studies in Ireland have reported a spring birth excess (O'Hare *et al*, 1980) or an overall trend towards a winter birth excess (O'Callaghan *et al*, 1991*a*) similar to that noted here. However, categorisation of patients according to place of birth revealed a significant excess of winter births among those born in urban areas; no such effect was apparent in those who were born in rural areas and, rather, some excess of spring births was apparent. Our categorisation is in accordance with the established census practice that a city population greater than 50 000 is defined as urban; furthermore, the urban–rural divide in Ireland is considerably more apparent than in many other European countries, providing a more favourable basis for such studies.

Our findings can be considered in the context of previous studies in an Irish setting. O'Hare *et al* (1980) found a shift in the seasonality of schizophrenic

Table 1
Comparison of seasonal distributions (quarterly) of births for urban- and rural-born patients with controls (1921–1960)

	January–March	April–June	July–September	October–December	χ^2 (3 d.f.)	*P*
Normal (control) population (1921–1960) ($n=787\,285$)	191 833	211 028	203 668	180 756		
Total patient population ($n=3253$)	839(+5%)	888	808	718	5.57	0.13
Urban-born controls ($n=613\,211$)	149 659	164 902	158 651	139 999		
Urban-born patients ($n=1362$)	381(+13%)	344	326	311	8.12	0.04
Rural-born controls ($n=174\,074$)	42 174	46 126	45 017	40 757		
Rural-born patients ($n=1799$)	438	518(+8%)	457	386	5.45	0.14

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Table 2
Comparison of seasonal distributions (quarterly) of births for urban- and rural-born patients

	January–March	April–June	July–September	October–December	χ^2 (3 d.f.)	*P*
Urban-born (*n* = 1362)	381	344	326	311		
Rural-born (*n* = 1799)	438	518	457	386	8.8	0.03
Women: urban-born (*n* = 637)	174	159	153	151		
rural-born (*n* = 789)	179	243	201	166	8.7	0.03
Men: urban-born (*n* = 684)	196	176	161	151		
rural-born (*n* = 1007)	259	275	255	218	2.2	0.5

births from spring to winter over the 35 birth years of their sample. Their population was drawn from patients born between 1921 and 1955 (years of increasing urbanisation in Ireland) who were first admissions to Irish psychiatric hospitals between 1972–1975. Those patients born between 1921 and 1940 exhibited a spring birth excess and would have been predominantly rural-born, whereas those born after 1940 exhibited a winter birth excess and would have included a greater number of urban births. A comparable investigation by Hare (1978) which was based on an English and Welsh, more urbanised, population demonstrated an overall winter birth excess. Secular changes in the birth patterns of individuals who later develop schizophrenia have also been reported by Hare (1978) and Shimura & Muira (1980). These studies would suggest that a changing demographic pattern such as increasing urbanisation could be a factor related to the seasonal rate of occurrence of schizophrenia. Our overall finding of only a modest and not statistically significant trend toward a winter birth excess might be explained by the distribution of our sample (57% rural), and may become more pronounced with continuing urbanisation.

Support for a detrimental effect on health of urban living comes partly from the finding that mortality rates are increased in urban over neighbouring rural areas (Chilvers, 1978). Furthermore, a recent study demonstrated that health, as estimated from data on birth weight and childhood height, was poorer in urban than rural areas independent of extent of deprivation (Reading *et al*, 1993) and led the authors to conclude that living in an urban environment constitutes a substantial biological disadvantage unrelated to material circumstances.

A number of communicable diseases have a primary effect in urban areas (McNeil, 1976) and this might give rise to an associated effect in outlying, rural regions only after some interval had elapsed; the present excess of spring births among rural-born patients, occurring after the winter birth excess among their urban-born counterparts, would be compatible with such a process.

The availability of control data only by quarter rather than by month makes it difficult to determine more precisely the relative timings of the seasonality peaks in the urban and rural populations. However, inspection of the data on schizophrenic births by month indicated that the urban winter excess appeared most prominent in January and March, with the rural spring excess peaking in April and declining through to June. A more extensive database would be needed to clarify this further.

The present winter birth excess among those born in urban areas appeared to be a phenomenon essentially of urban-born women. This finding is complemented by findings concerning a number of factors that may influence the rate of occurrence of schizophrenia. These indicate female offspring are at greater risk from maternal influenza (Mednick *et al*, 1990; O'Callaghan *et al*, 1991*b*; Takei *et al*, 1994) and maternal dietary insufficiency (Susser & Lin, 1992). Furthermore, women appear more likely to show both geographical (Youssef *et al*, 1993) and temporal (Waddington & Youssef, 1994) variations in rate of occurrence of schizophrenia.

In a male (conscript) population, Lewis *et al* (1992) reported that persons with an urban upbringing were at significantly greater risk for schizophrenia than their rural-reared counterparts; data from a comparable population of women would be necessary to clarify how the results of this approach might relate to the present gender-specific seasonality findings.

The differing patterns in season-of-birth between urban- and rural-born schizophrenic patients are accommodated most readily in terms of a spatially varying environmental factor. The present preponderance of women showing this phenomenon extends a number of other recent epidemiological findings which also indicate a greater vulnerability of women to such factors.

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