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Seasonality of birth of patients with childhood diabetes in Britain

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Indirect evidence suggests that early environment is important in the causation of insulin dependent diabetes mellitus.¹ Viral infection is thought to be the most likely trigger. Although biochemical and immunological abnormalities develop several years before the clinical onset of insulin dependent diabetes, the age at which exposure to infection might induce the disease is unclear. The high prevalence of diabetes mellitus in patients with the congenital rubella syndrome shows that the process may be initiated in utero.¹ As most viral infections are seasonal, the pattern of dates of birth of people with diabetes should differ from that of the general population if a significant proportion of cases was caused by intrauterine or perinatal viral infection. We therefore examined seasonality of birth in three large independent populations of children with insulin dependent diabetes in Britain.

Patients, methods, and results

The details of the three registers have been reported previously.²⁻⁴ To ensure that the populations were independent, cases incident in Yorkshire² and Scotland³ were excluded from the population in the British Paediatric Association's study.⁴ The analysis was restricted to births during the time common to all three populations—that is, 1974-88. The method of Walter and Elwood was used for analysis of seasonality of month of birth.⁵ We adjusted for the seasonality of live births in the general population by constructing pseudocohorts of births on the basis of the number of births during each month of the study. The numbers of live births in England and Wales published by the Office of Population Censuses and Surveys were used for analysis of the data from Yorkshire and the British Paediatric Association's study.^{2,4} The numbers of live births obtained from the registrar general for Scotland were used for analysis of the Scottish data.³

The Scottish, Yorkshire, and British Paediatric Association registers contained respectively 2258, 1142, and 1265 patients with diabetes born during 1974-88. For each register the monthly pattern of births differed significantly from that in the general population

Fig 1—Observed divided by expected number of births each month in three populations with diabetes compared with respective general populations. Numbers are births each month in each diabetic population

(Scotland, $\chi^2 = 9.7$, $P = 0.002$; Yorkshire, $\chi^2 = 8.7$, $P = 0.005$; England and Wales, $\chi^2 = 3.5$, $P = 0.04$). For each register more patients were born during the spring and early summer and fewer during the winter months compared with the general population (fig 1).

Comment

The seasonal pattern of birth of patients with diabetes mellitus has not, to our knowledge, been reported to differ from that of the general population. Our study has shown abnormal seasonality of birth in three large independent populations with childhood onset diabetes. This is unlikely to be due to chance, and it is difficult to conceive of a bias that might account for the results.

Several important conclusions can be drawn from our observation. Firstly, as seasonality of birth cannot be accounted for by genetic mechanisms, environmental factors must be important in the aetiology of diabetes. Secondly, to induce seasonality of birth these environmental factors must exert their influence in utero or in the first year of life. Thirdly, these environmental factors must, of course, be seasonal in nature.

Our observations are consistent with the hypothesis that the disease process resulting in childhood diabetes is initiated by viral infection early in life. Further studies

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of diabetic patients' environmental exposures during intrauterine and early life, together with differences in the pattern of seasonality of birth with place and time, may identify environmental exposures specific to the initiation of the diabetogenic process.

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Rate of bone loss from lumbar spine in women with distal forearm fracture

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Fig 1—Annual rate of change of lumbar spine bone mineral density in 86 cases (women with distal forearm fracture) and 297 controls. Results shown as box and whisker plots in which height of the boxes represents interquartile range, horizontal line shows the median, cross shows mean, and vertical lines show the range of the data apart from outliers ($>1.5 \times$ interquartile range above or below interquartile range), which are shown as individual data points

Women who sustain a distal forearm fracture are at increased risk of vertebral osteoporosis, particularly if it occurs before the age of 60.¹ The aim of this study was to determine the mechanism for low bone mineral density in the lumbar spine of these women by prospectively evaluating the rate of bone loss from the spine.

Subjects, methods, and results

From our previous study population,¹ we studied 86 (69%) of the women (aged 50-81) who had sustained a distal forearm fracture between six months and three years before baseline and 297 women from an age matched, population based cohort. These women did not differ from those lost to follow up in their age, weight, height, years after menopause, or baseline bone mass of the lumbar spine. We measured bone mineral density by dual energy x ray absorptiometry (Lunar DPX, Lunar Corporation, Madison, WI, USA) at baseline and after two years. We examined the effect of age on bone mineral density by linear regression analysis and compared regression lines by a multiple linear regression technique. We compared normally distributed variables by unpaired *t* tests.

The cases did not differ from the population based controls with respect to age, weight, height, or years after menopause. Of the controls, 35 (12%) took hormone replacement therapy during the study, compared with 13 (15%) of the cases (95% confidence interval of difference -5% to 12%).

The baseline mean Z score for lumbar spine bone mineral density (the standard deviation from the mean bone mineral density of the controls after normalisation for age and weight) was decreased in the cases (-0.37 (-0.58 to -0.16)). Baseline lumbar spine bone mineral density decreased with age in the controls ($r = -0.29$, $P < 0.0001$) but not in the cases ($r = 0.08$, $P > 0.05$). The slopes and intercepts of this relation differed significantly between the two groups ($P = 0.009$ and $P = 0.003$ respectively). The controls lost bone from the lumbar spine at a rate of -0.59% a year ($P < 0.0001$), but the cases showed no bone loss (fig 1), and this difference was significant (0.59% (0.08% to 1.1%) a year, $P = 0.02$). In the controls the rate of change of lumbar spine bone mineral density was related to age ($r = 0.14$, $P = 0.02$) and years after menopause ($r = 0.12$, $P = 0.05$). There was no such relation in the cases, but the rate of change in these women was related to the time from distal forearm fracture ($r = 0.24$, $P = 0.03$). Exclusion of women who had

taken hormone replacement therapy during the study did not alter the results.

Comment

Distal forearm fracture is a typical manifestation of postmenopausal osteoporosis.² Propensity to fracture is thought to relate to decreased bone mass resulting from increased bone turnover after the menopause.³ We found that women with distal forearm fracture were at increased risk of vertebral osteoporosis: their decrease in lumbar spine bone mass was consistent with a doubling of the risk of vertebral fracture.⁴ Furthermore, these women had decreased rates of bone loss from the lumbar spine. The differences between the groups did not seem to be related to the use of hormone replacement therapy.

We suggest that the mechanism of decreased lumbar spine bone mass in women with distal forearm fracture may differ from that in other fracture syndromes. The decreased lumbar spine bone mass may result from low peak bone mass or a phase of accelerated bone loss in the early postmenopausal years, with subsequent decreased rates of loss. Both explanations would be consistent with our finding that the younger women had the lowest Z scores of lumbar spine bone mineral density. The explanations would also be consistent with an increased incidence of distal forearm fractures in women at the time of the menopause followed by a plateau in later years, as has been demonstrated in many epidemiological studies.^{2,5} We postulate that the excess fractures occur at the time of increased bone turnover, when reversible bone loss in the form of increased resorption is maximal. The finding of greater bone loss in those women with more recent fracture favours the concept of an earlier phase of accelerated bone loss as the cause of low lumbar spine bone mass.

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