Seasonality of Birth in Patients With Childhood Diabetes in The Netherlands

In the three birth registers from Scotland, Yorkshire, and England and Wales, the seasonal pattern of birth of patients with childhood-onset diabetes differed from that of the general population (1). We examined the birth distribution in two nationwide diabetes incidence studies in The Netherlands (2), 1978–1980 (n = 1,308) and 1988–1990 (n = 1,325), together with the total birth distribution. The ascertainment percentages were estimated to be 88 and 81%, respectively. Data regarding day, month, and year of birth and sex were available for all patients (age 0–19 years; 1,394 males and 1,239 females [sex ratio = 113]). The patients were born between 1959 and 1979 and between 1968 and 1990. We adjusted the aggregated data per month for live births in the general population on the basis of the weighted number of births (1959–1990) per month as published by the Central Bureau for Statistics, The Hague (Fig. 1).

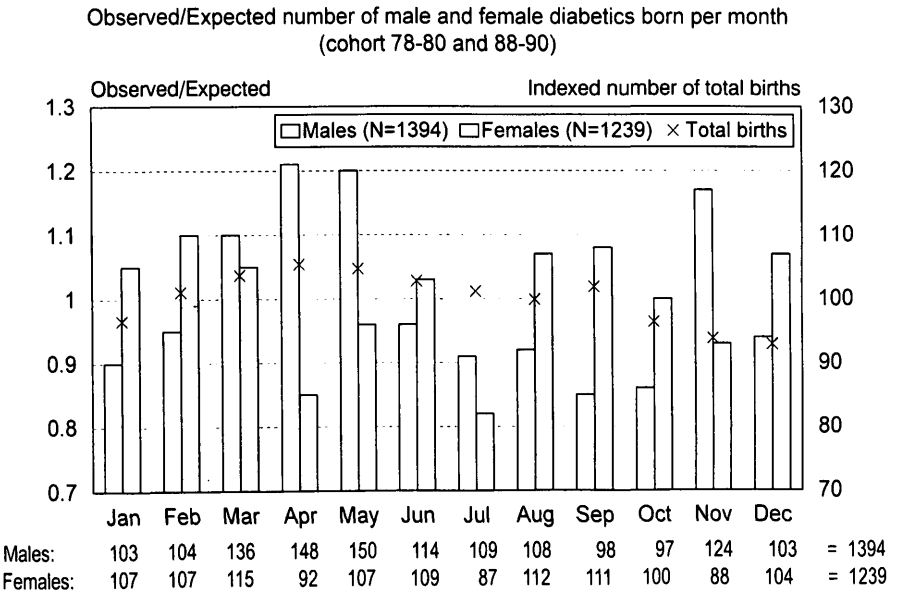

Figure 1—*Observed divided by expected number of births per month of 1,394 male and 1,239 female individuals with childhood diabetes (left axis) compared with the total number of births in The Netherlands (right axis) as indicated by asterisks (weighted for number of births per year and indexed: average = 100).*

The monthly pattern of births differed from that in the general population only in boys: χ^2 = 23.33, 11 df: P = 0.02 (girls: χ^2 = 9.94, 11 df: P = 0.54; total: χ^2 = 10.19, 11 df: P = 0.51). Using logistic regression to test for a sinusoidal pattern (3) we obtained the following: males: χ^2 = 8.66, 2 df: P = 0.01; females: χ^2 = 1.68, 2 df: P = 0.43; and for the pooled data: χ^2 = 3.9, 2 df: P = 0.14.

A similar excess in winter/spring births in childhood diabetes that differs from that of the general population was found in Britain (1) and earlier in The Netherlands (4) and Japan (5). This excess always coincides with the physiological increase of total births, which suggests that a common agent at the very early onset in utero is responsible for the distribution of both the normal and the pathological births, with higher intensity, however, for the latter. This "amplified deviation" (6) of pathological winter/spring births has also been found in congenital anomalies of the central nervous system (7) and in constitutional diseases becoming apparent in adolescence or even in adulthood such as schizophrenia (8) and menstrual disorders (9). This amplified deviation is in line with the seasonal preovulatory overripeness ovopathy (SPrOO) hypothesis (10), which presumes in humans inherent ovulatory and anovulatory seasons and some relics of those heat periods present in almost all mammals. The disproportional increase of pathological conceptions is predicted to occur particularly at the transitional stage between anovulatory cycles in winter and ovulatory cycles in spring. This increase, of course, occurs synchronously with the physiological increase of total conceptions and renders this excess of pathological births in winter/spring.

That the deviation of births is much stronger in male than in female diabetic children is very well in line with the SPrOO hypothesis, because the incidences of male and female births are different at the slopes and zenith of the seasonally bound conception peaks (11). Gradually increasing incidences of childhood diabetes according to higher latitude are in line as well because seasonality of total births gradually increases with latitude (12).

In the search for etiological factors of childhood diabetes, there are additional arguments for conceptopathology: first, the low concordance rates (up to 50–70%) in monozygotic twins, because experimental overripeness of the egg in animals results in a "tendency of axial duplications, taking the form of twins, either of equal size and normal appearance, or of unequal dimensions" (13); second, the higher prevalence of diabetes in children with nonspecific chromosomal aberrations (14); and third, the relation with early and advanced maternal age and/or parity (15), which is strongly related to menstrual irregularities.

The more usual explanation for childhood diabetes is a disease process initiated by viral infection early in life (1,5). Viruses, however, are not ubiquitous, and their persistence varies from season to season and year after year. Nonoptimal maturation of the oocyte, superimposed on any genetically determined familial risk, appears to be a more appropriate explanation for the epidemiology of this disease.

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Response to Akhter

We read with interest the letter from Jaweed Akhter, MD in the June issue of *Diabetes Care* entitled "The American Diabetes Association's Clinical Practice Recommendations and the Developing World" (1).

Dr. Akhter clearly has an intimate familiarity with the real situation in the developing world. We think it is most timely and appropriate to bring to his attention, as well as that of your readers, the intent of the Declaration of the Americas on Diabetes, which happens to appear in the same issue (2).

This Declaration expresses the recognition of difficulties being faced by the 30 million people with diabetes in the Western hemisphere. It has involved both governmental and nongovernmental organizations (NGOs), rallying them in a concerted effort to tackle problems related to diabetes from a policy direction at the governmental level as well as through an intensification of outreach programs from the NGO perspective. The countries involved in this effort span the spectrum from developed to developing.

In ensuring that the plan outlined in the Declaration happens, components of the International Diabetes Federation (IDF), including the North American and South and Central American Regions in conjunction with the Pan American Health Organization, as well as industry partners, have come together to monitor the progress of the Declaration, which has been endorsed by the Ministers of Health in the Western hemisphere and has an increasing commitment from the health-related NGOs in the region. The Executive Committee on the Declaration of the Americas on Diabetes (DOTA) welcomes inquiries and comments to the undersigned.

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Infection of Continuous Subcutaneous Insulin Infusion Site With *Mycobacterium peregrinum*

Toth et al. (1) reported the case of a patient with recurrent infection of continuous subcutaneous insulin infusion (CSII) sites with *Mycobacterium fortuitum.* We report a similar case in which a subcutaneous infection with *M. peregrinum* occurred 2 months after withdrawal of pump therapy.

A 30-year-old woman with IDDM of 21 years' duration was referred because of a thigh abscess. Glycemic control had been poor (HbA_{1c} 9–10%, normal values 4.2–5.6%) for several years, and CSII had been instituted. The patient changed the injection site every 24–48 h after swabbing with alcohol. Because she tolerated the subcutaneous needle poorly, she decided to discontinue CSII and resumed administration of three daily insulin injections. A small erythematous nodular lesion developed on the right thigh (a previous site of infusion) 8 weeks after stopping CSII therapy. There was no fever and there were no general symptoms. Blood cell counts and sedimentation rate were normal. Despite several antibiotic courses, including oxacillin, josamycin, and pristinamycin, 2 months later the lesion had progressed to a large (10 × 5 cm) warm tender erythematous abscess. Surgical drainage was performed, but the abscess did not resolve completely. Culture returned positive for *M. peregrinum* 3 weeks later, sensitive to amikacin, ciprofloxacin, imipenem, and clarithromycin. Treatment with ciprofloxacin (200 mg i.v., b.i.d.), imipenem (500 mg i.v., t.i.d.), and amikacin (500 mg i.v., b.i.d.) for 4 weeks, then with ciprofloxacin 750 mg orally b.i.d. for 2 months, led to a complete cure of the lesion.

M. Peregrinum belongs to the Mycobacterium fortuitum complex, which now includes four distinct species (*M. fortuitum, M. chelonae, M. peregrinum, M. abscessus*)