

as this group appears to be similar to women without diabetes with respect to infant feeding decisions.

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References

1. American Academy of Pediatrics: Breast-feeding and the use of human milk. *Pediatrics* 115:496–506, 2005
2. Arora S, McJunkin C, Weher J, Kuhn P: Major factors influencing breastfeeding rates: mother's perception of father's attitude on milk supply. *Pediatrics* 106:e67, 2000
3. Freed GL, Towes TM, Schendler RJ: Prenatal determination of demographic and attitudinal factors regarding feeding practice in an indigent population. *Am J Perinatol* 5:420–424, 1992
4. Scott J, Shaker I: Parental attitudes toward breastfeeding: their association with feeding outcome at hospital discharge. *Birth* 31:125–131, 2004

Treatment of Hyperglycemia in a 7-Year-Old Child Diagnosed With Neonatal Diabetes

Permanent neonatal diabetes is persistent, insulin-requiring hyperglycemia occurring before 1 month of life. Recent studies have identified activating mutations in *KCNJ11* encoding the Kir6.2 subunit of the ATP-sensitive K^+ channel as a common cause of neonatal diabetes (1–5). These patients can be successfully managed with oral sulfonylureas rather than insulin (2,4,6,7). We describe our experience with a 7-year-old Mexican-American girl diagnosed with insulin-dependent diabetes at 2 weeks of age when she presented with a respiratory infection. Her blood glucose level was 442

mg/dl, C-peptide 0.33 ng/ml (ref. 0.8–4), insulin 3.1 uU/ml (ref. 0–22), and HbA_{1c} (A1C) 7.7% (ref. <6.4), and she had negative diabetes autoantibodies. Her mother was diagnosed with insulin-dependent diabetes at 6 months of age. The prognosis was evaluated at the pediatric diabetes center at Loma Linda University at the age of 6 years, and DNA testing revealed the presence of the permanent neonatal diabetes-associated mutation Arg201His in *KCNJ11* in both her and her mother (2). Glucagon and mixed-meal glucose tolerance testing did not show an increment in C-peptide from the baseline value. Insulin was weaned and discontinued over 2 weeks, with a starting glyburide dose of 1.25 mg b.i.d. ($0.05 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$) and incremental increase to the current dose of 3.5 mg glyburide b.i.d. Previously, the patient's A1C on insulin ranged from 7.1 to 11.5%. Off insulin, and over the past 24 months, her quarterly A1C range was 5.1–6.3%, with no record or symptoms suggestive of hypoglycemia. Our results were consistent with other reports in the literature (2,4,6,7). The patient and her family were overwhelmingly pleased with the discontinuation of insulin, which they referred to as “a miracle.”

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References

1. Gloyn AL, Pearson ER, Antcliff JF, Proks P, Bruining GJ, Slingerland AS, Howard N, Srinivasan S, Silva JM, Molnes J, Edghill EL, Frayling TM, Temple IK, Mackay D, Shield JP, Sumnik Z, van Rhijn A, Wales JK, Clark P, Gorman S, Aisenberg J, Ellard S, Njolstad PR, Ashcroft FM, Hattersley AT: Activating mutations in the gene encoding the ATP-sensitive potassium-channel subunit Kir6.2 and permanent neonatal diabetes. *N Engl J Med* 350:1838–1849, 2004

2. Sagen JV, Raeder H, Hathout E, Shehadeh N, Gudmundsson K, Baevre H, Abuelo D, Phornphutkul C, Molnes J, Bell GL, Gloyn AL, Hattersley AT, Molven A, Sovik O, Njolstad PR: Permanent neonatal diabetes due to mutations in *KCNJ11* encoding Kir6.2: patient characteristics and initial response to sulfonylurea therapy. *Diabetes* 53:2713–2718, 2004
3. Vaxillaire M, Populaire C, Busiah K, Cave H, Gloyn AL, Hattersley AT, Czernichow P, Froguel P, Polak M: Kir6.2 mutations are a common cause of permanent neonatal diabetes in a large cohort of French patients. *Diabetes* 53:2719–2722, 2004
4. Zung A, Glaser B, Nimri R, Zadik Z: Glibenclamide treatment in permanent neonatal diabetes mellitus due to an activating mutation in Kir6.2. *J Clin Endocrinol Metab* 89:5504–5507, 2004
5. Massa O, Iafusco D, D'Amato E, Gloyn AL, Hattersley AT, Pasquino B, Tonini G, Dammacco F, Zanette G, Meschi F, Porzio O, Bottazzo G, Crino A, Lorini R, Cerutti F, Vanelli M, Barbetti F, Early Onset Diabetes Study Group of the Italian Society of Pediatric Endocrinology and Diabetology: *KCNJ11* activating mutations in Italian patients with permanent neonatal diabetes. *Hum Mutat* 25:22–27, 2005
6. Codner E, Flanagan S, Ellard S, Garcia H, Hattersley AT: High-dose glibenclamide can replace insulin therapy despite transitory diarrhea in early-onset diabetes caused by a novel R201L Kir6.2 mutation (Letter). *Diabetes Care* 28:758–759, 2005
7. Klupa T, Edghill EL, Nazim J, Sieradzki J, Ellard S, Hattersley AT, Malecki MT: The identification of a R201H mutation in *KCNJ11*, which encodes Kir6.2, and successful transfer to sustained-release sulfonylurea therapy in a subject with neonatal diabetes: evidence for heterogeneity of beta cell function among carriers of the R201H mutation (Letter). *Diabetologia* 48:1029–1031, 2005

Circulating Vitamin D Concentrations in Two Neighboring Populations With Markedly Different Incidence of Type 1 Diabetes

Recent studies have suggested that vitamin D deficiency may increase the risk of type 1 diabetes (1). In Finland, the incidence of type 1 diabetes is the highest in the world, while in the neighboring Karelian Republic of Russia, the incidence is approximately one-sixth

that in Finland, despite no difference in HLA-conferred susceptibility (2). Thus, the reason(s) must be linked to environmental factors.

We assessed vitamin D status in the Russian Karelian and Finnish populations to determine whether vitamin D could play a role in the huge difference observed in diabetes incidence. The geographical location in terms of daily sunlight exposure is approximately the same in both populations (~ 62 – 66°N). Circulating concentrations of 25-hydroxy (25-OH) vitamin D were analyzed using a commercial enzyme immunoassay kit (Immuno-diagnostic Systems Limited, Boldon, U.K.) in cohorts representing the background population (schoolchildren and pregnant women). The schoolchildren series included 100 subjects from Finland and 100 subjects from Russian Karelia matched for age, sex, and month of sampling (mean age \pm SD, 10.9 ± 1.7 years, 52% male subjects). Serum samples were collected during the years 1994–2000, and 86% were drawn during March–April. The series of pregnant women included 103 female subjects from Russian Karelia and 172 women from Finland matched for age and date of sampling (mean age 26.7 ± 5.3 years). Samples were collected at the end of the first trimester of pregnancy as a part of the routine prenatal follow-up during the year 2000, and 81% of them were drawn during October–December. The study was approved by the local ethical committees and the Finnish Maternity Cohort steering group. The study was carried out in accordance with the Declaration of Helsinki.

The median serum concentrations of 25-OH vitamin D were approximately the same in both countries among schoolchildren (35.0 in Karelia vs. 39.3 nmol/l in Finland, $P = \text{NS}$ Wilcoxon test) and pregnant women (28.4 vs. 28.9 nmol/l, $P = \text{NS}$ by conditional logistic regression test). Sex had no effect on vitamin D status among the schoolchildren. According to the previously suggested cutoff limit for vitamin D deficiency (serum 25-OH vitamin D < 25 nmol/l) (3,4), the proportion of vitamin D–deficient subjects was not higher in Finland compared with Karelia (16 vs. 27% in schoolchildren, $P = 0.091$; 38 vs. 41% in pregnant women, $P = \text{NS}$, respectively).

The results suggest that circulating vitamin D concentrations do not differ markedly between Finland and Russian Karelia. Accordingly, vitamin D status may not contribute to the marked differ-

ence in the incidence of type 1 diabetes between the countries, and there must be other factors protecting the Karelian children from developing type 1 diabetes.

Nevertheless, vitamin D substitution remains an important issue in these countries, even beyond infancy, and regular substitution has long been recommended in both countries (5–7), especially during pregnancy, infancy, and the dark months of the year.

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References

- Mathieu C, Badohoop K: Vitamin D and type 1 diabetes mellitus: state of art. *Trends Endocrinol Metab* 16:261–266, 2005
- Kondrashova A, Reunanen A, Romanov A, Karvonen A, Viskari H, Vesikari T, Ilonen J, Knip M, Hyöty H: A six-fold gradient in the incidence of type 1 diabetes at the eastern border of Finland. *Ann Med* 37:67–72, 2005
- Roth DE, Martz P, Yeo R, Prosser C, Bell M, Jones AB: Are national vitamin D guidelines sufficient to maintain adequate blood levels in children? *Can J Public Health* 96:443–449, 2005
- Schroth RJ, Lavelle CL, Moffatt ME: Review of vitamin D deficiency during pregnancy: who is affected? *Int J Circumpolar Health* 64:112–120, 2005
- Hasunen K, Kalavainen M, Keinonen H, Lagström H, Lyytikäinen A, Nurtila A, Peltola T, Tälviä S: *Nutrition Recommendations for Infants and Young Children as well as Pregnant and Breastfeeding Mothers*. Vol. 11. Helsinki, Ministry of Social Affairs and Health, 2004 [in Finnish]
- Korovina NA, Zakharova IN, Cheburkin AV: A new view on D vitamins. *Russian Medical Journal* 8:46–50, 2000 [in Russian]
- Prophylaxis and treatment of rickets in young age children. In *Methodical Recommendations of the Ministry of Health of the Russian Federation*, Moscow, Ministry of Health, 1990 [in Russian]
- Viskari H, Ludvigsson J, Uibo R, Salur L, Marciulionyte D, Hermann R, Soltesz G, Fuchtenbusch M, Ziegler AG, Kondrashova A, Romanov A, Kaplan B, Laron Z, Koskela P, Vesikari T, Huhtala H, Knip M, Hyöty H: Relationship between the incidence of type 1 diabetes and maternal enterovirus antibodies: time trends and geographical variation. *Diabetologia* 48:1280–1287, 2005

Soluble Tumor Necrosis Factor Receptor 2 Is Independently Associated With Brachial-Ankle Pulse-Wave Velocity in Nonobese Japanese Type 2 Diabetic Patients

Type 2 diabetes is associated with high mortality and morbidity due to atherosclerosis. Biermen (1) estimated that typical risk factors, including blood pressure, cholesterol, and smoking, can account for no more than 30% of excess cardiovascular risk factor in diabetic patients. Thus, other factors seem to play a role in the progression of atherosclerosis in diabetes.

Aortic stiffness measured by pulse-wave velocity (PWV) is shown to be highly predictive of cardiovascular mortality in type 2 diabetic patients (2). While age and blood pressure are shown to be associated with PWV, age and blood pressure alone do not completely account for the abnormalities of aortic stiffness in type 2 diabetic patients.

Tumor necrosis factor (TNF) system activity seems to be associated with the progression of atherosclerosis in type 2 diabetes. Shai et al. (3) demonstrated that soluble TNF receptor 2 (sTNF-R2) is