Dancing With Many Different Ghosts

Treatment of youth with type 2 diabetes

My training in the treatment of type 2 diabetes in children began when my father recounted stories of his experience in northern Canada as a fur trader with the Hudson's Bay Company (HBC) in the 1930s. The Cree people lived in tents in the winter months and took them down in the summer and fall to go out on the land to hunt. The HBC store traded fur pelts for flour, lard, and saccharine (sugar was much too expensive). Later, in the 1970s, as a medical student on an elective in northern communities, the itinerant dentist talked of the frustration at having to do so many dental extractions in young children with rotten teeth. My early “diabetes” training was continuing with the stories told by the pregnant women who sat for hours together carving soapstone behind the hospital. The women had “come out” from their communities to wait until after delivery before returning home. They talked of their hardships and sorrows, their children and families, and living off the land.

I’ve also learned from our northern outreach clinics. We fly in small planes to small communities surrounded by rock, lakes, rivers, and boreal forest. After our afternoon clinics, we walk to the store along the frozen barren roads in winter or the potholed, dust-covered roads shared with pickup trucks in spring. Several youth from our clinic show up. We walk around the aisles together as a group—the teens, doctor, dietitian, nurse, and social worker. We read labels of snack foods and compare prices of fresh, frozen, and canned products. Elders express their concern about diabetes in their community and especially about the fate of the children. We scrutinize the checkout counter to see how many cartons of soda pop and chips are going through. We learn that two of the teens with us are responsible for buying groceries every week for their family of seven. The dietitian assesses and makes a mental note of their arithmetic skills, reading skills, knowledge of nutrition, and food preparation. The event is spontaneous and fun.

It feels as if we have accomplished more in 1 h at the store than the 4 h in the clinic at the health center. Grocery store tours are not a new idea, but they are a vital component of our education and work with the youth with type 2 diabetes. Appearances on unscheduled phone-in programs on the community television network and visits to the community recreation center and school are also revealing.

Other important lessons about type 2 diabetes care are learned at summer camp. With careful supervision and the high physical activity of camp, the children demonstrate that daily average pre-meal blood glucose levels can decrease from 20 to 6 mmol/l in <2 weeks (1)! They also teach us about the challenges of food access, their experience with food preparation, their opportunities for recreation, their fears about diabetes and its treatments, their personal perspective on the losses, horrors, and tragedies related to diabetes complications in their families, and the experience of their family with residential schools, substance abuse, and relocation (2). To these experiences, I add my observations from visits to the schools and community clubs in the inner city.

The relevance of our experience in northern remote communities in Canada to youth living in large urban centers in other parts of Canada, the U.S., and other countries in the world may not be readily apparent. But observation and feedback from many colleagues indicate remarkable similarities in our youth with type 2 diabetes. I am sure that the face of disenfranchisement and child poverty is international.

The treatment of type 2 diabetes in children and adolescents is a huge challenge because of the diverse linguistic, geographic, cultural, social, economic, and political barriers that influence the access to, acceptance of, and outcome of treatment (3). The consequences of NOT achieving therapeutic goals in childhood will be devastating in young adult life.

The failure of “standard diet and exercise” treatment and conventional education approaches in this group has accelerated the demand for clinical trials in children of oral agents that have previously been approved and used widely for adults with type 2 diabetes. Through the International Conference on Harmonization (ICH), the international community has endorsed the importance of studying the efficacy and safety of drugs in children to discourage the use of drugs that have not been approved for use in children.

As reported in this issue of Diabetes Care, Dr. Ken Jones et al. (4) have championed this process in five countries (the U.S., Russia, Belarus, Poland, and the Ukraine) by completing the first study of efficacy and safety of an oral drug in children with type 2 diabetes. They enrolled 82 youth with type 2 diabetes aged 10–16 years in a 16-week, randomized, placebo-controlled study of the effect of metformin on fasting blood glucose (FBG) levels. The subjects were “counseled on dietary and exercise practices provided at each study visit.” The mean decrease in FBG from baseline was 2.4 mmol/l in the study group. The drug was well tolerated. Short-term safety markers were normal.

Recruitment of subjects for the study was difficult. Most were recruited by screening children at high risk for type 2 diabetes. They were offered immediate recruitment to the study. There were 10 dropouts, with only 4 of these from adverse events. The rescue criteria were stringent, with the subjects requiring rescue to metformin if FBG was >12.8 mmol/l at 2 weeks, >10 mmol/l at 4 weeks, and >7.8 mmol/l at 6 weeks. Success of standard diet and exercise counseling in the placebo group was low, with 26 of 36 subjects requiring rescue. Only 4 of the 36 subjects in the study group required rescue. In addition, on the basis of the results of an interim analysis at the point when 50% of the subjects had completed 8 weeks of the study, the data safety monitoring board recommended that the study be terminated early. The
results were based on an analysis of the change in FBG from baseline to the last visit of the double-blind portion of the study for each subject, even if that last visit was after only 2 weeks of the study. An unfortunate occurrence in this study was that the two study groups differed in their baseline FBG, despite randomization by permuted block design. A greater number of youth (20/40 = 50%) randomized to the placebo group had a baseline FBG $>11.1$ mmol/l compared with the metformin group (9/42 = 21%). It is impossible to evaluate whether more youth in the metformin group had passed the rescue criteria simply because their baseline FBG was lower, and also whether more subjects in the metformin group had passed the 8-week point when the study was terminated. In the final analysis, only 3 subjects in the placebo group and 19 subjects in the metformin group completed the 16-week study. The rescue with study drug precluded an intent-to-treat analysis at 16 weeks.

This study is an important first step in our understanding of the pharmacologic treatment of type 2 diabetes in youth. Which children would benefit most from metformin? Are there subgroups of youth who would benefit more from short-term insulin or another oral agent as first line of therapy? According to the protocol used in the Jones study, a youth with an FBG of 18 mmol/l at diagnosis who achieves an FBG of 9 mmol/l after 6 weeks of intense effort to modify their lifestyle would be a candidate for “rescue” with metformin. Is the potential benefit of adding metformin at this point justified over enthusiastic and supportive encouragement in lifestyle changes? What is the impact of adding metformin versus continued counseling on the youth’s self-esteem? On glycemic control at 1 year? On family dynamics, the adolescent-parent relationship, and family economics?

What is the chance that the youths will take the drug on a daily long-term basis? In a recent study of metformin in obese adolescents for 6 months, only three subjects withdrew (5). We know that adolescents with renal transplants and type 1 diabetes miss their medications even if it means losing their transplant or life-threatening diabetic ketoacidosis. Teens with type 2 diabetes, in addition to adolescent risk-taking and defiant behaviors, have other reasons to refuse medications. These reasons include lack of symptoms, fear that the complications of diabetes are caused by pills and insulin, fear of pills or needles, a feeling of hopelessness, a lack of empowerment, and low self-esteem.

Is there a way to create more effective diabetes education programs that will address lifestyle factors in a more therapeutic manner for this age group? There are many parallels in the justice systems in Canada and the U.S. In his 1992 book entitled Dancing With a Ghost, Rupert Ross wrote that in order for courts to deal effectively with young offenders, court personnel must understand the reasons why conventional systems fail these young people (6).

Our diabetes personnel must understand the reasons why conventional diet and exercise systems fail youth with type 2 diabetes. We need to improve our communication and cross-cultural skills. We need to understand the impact of systemic elements and determinants of health on diabetes care for youth. We need to accept the central importance of decision making around the goals of the teen and family. It is not negligent to wait a few more weeks or months before considering pills or insulin in a youth who is making progress. We need to be able to accept unique, individual time frames for achieving therapeutic goals.

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H. J. D. has received honoraria/consulting fees from Pfizer and Eli Lilly for the clinical trials of products used in the treatment of diabetes.

Acknowledgments — I am indebted to my colleagues, Drs. Elizabeth Sellers and Mike Moffatt, for sharing my passion to help this group of youth and discussing the content of this editorial. I also appreciate the help of Jake MacDonald and Rupert Ross in expressing that passion in words.

References