World Journal of Diabetes

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.4239/wjd.v6.i1.1

World J Diabetes 2015 February 15; 6(1): 1-7
ISSN 1948-9358 (online)

FIELD OF VISION

One center in Brussels has consistently had the lowest HbA1c values in the 4 studies (1994-2009) by the Hvidoere International Study Group on Childhood Diabetes: What are the "recipes"?

Harry Dorchy

Harry Dorchy, Diabetology Clinic, University Children's Hospital Queen Fabiola, Université Libre de Bruxelles, 1020 Brussels, Belgium
Author contributions: Dorchy H contributed to the manuscript.
Conflict-of-interest: No potential conflicts of interest relevant to this article were reported.

Correspondence to: Harry Dorchy, MD, PhD, DHC, Professor, Diabetology Clinic, University Children's Hospital Queen Fabiola, Avenue JJ Crocq 15, 1020 Brussels, Belgium. hdorchy@ulb.ac.be
Telephone: +32-2-4773185
Fax: +32-2-4773156
Received: August 23, 2014
Peer-review started: August 24, 2014
First decision: October 14, 2014
Revised: November 11, 2014
Accepted: December 16, 2014
Article in press: December 17, 2014
Published online: February 15, 2015

Abstract

The principal aims of therapeutic management of the child, adolescent and adult with type 1 diabetes are to allow good quality of life and to avoid long-term complications (retinopathy, neuropathy, nephropathy, cardiovascular disease, *etc.*) by maintaining blood glucose concentrations close to normal level. Glycated hemoglobin levels (HbA1c) provide a good criterion of overall glycemic control. The Hvidoere Study Group (HSG) on Childhood Diabetes, founded in 1994, is an international group representing about twenty highly experienced pediatric centers from Europe, North America, Japan and Australia. Four international comparisons of metabolic control (1995, 1998, 2005, 2009) have been performed. The one center that has consistently had the lowest HbA1c values (approximate 7.3% or 56.3 mmol/mol) is my center in Brussels. This is more often obtained with a twice-daily free-mixed regimen with additional supplemental fast insulins ad hoc. The so-called "Dorchy's recipes" are summarized. The conclusion is that the number of daily insulin injections, 2 or $\geqslant$ 4, or the use of pumps, by itself does not necessarily give better results. Intensified therapy should not depend upon the number of insulin doses per day, by syringe, pen or pump but rather should be redefined as to intent-to-treat ascertainment (*i.e.*, goals). When there are no mutually agreed upon goals for BG and/or HbA1c, when there is insufficient education and psychosocial support by the medical team or at home, there is likely to be poor outcomes, as shown by the HSG. One of our recipes is not to systematically replace rapid-acting human insulins by fast-acting analogues. Because the multicenter studies of the HSG, performed in developed countries without financial restriction, show that treatment of childhood diabetes is inadequate in general and that levels of HbA1c are very different, diabetes treatment teams should individually explore the reasons for failure, without any prejudice or bias. Any dogmatism must be avoided. Treatment cost *vs* results must also be taken into account.

Key words: Type 1 diabetes mellitus; Insulin regimen; Diabetic children; Glycated hemoglobin; Conventional treatment; Intensive treatment

Core tip: Four international comparisons of the Glycated hemoglobin levels (HbA1c) levels (1995, 1998, 2005, 2009) have been performed by the Hvidoere Study Group on childhood diabetes in about twenty pediatric diabetology centers from about twenty industrialized countries in Europe, North America, Japan and Australia. The one center that has consistently had the lowest HbA1c values (approximate 7.3% or 56.3 mmol/mol) is my center in Brussels. This is more often obtained with a twice-daily free-mixed insulin regimen. The so-called "Dorchy's recipes" are summarized.

Dorchy H. One center in Brussels has consistently had the lowest HbA1c values in the 4 studies (1994-2009) by the Hvidoere International Study Group on Childhood Diabetes: What are the "recipes"? *World J Diabetes* 2015; 6(1): 1-7 Available from: URL: http://www.wjgnet.com/1948-9358/full/v6/i1/1.htm DOI: http://dx.doi.org/10.4239/wjd.v6.i1.1

COMMENTARY ON HOT TOPICS

Diabetes Control and Complications Trial research group

The principal aims of therapeutic management of the child, adolescent and adult with type 1 diabetes are to allow good quality of life[1,2] and to avoid long-term complications (retinopathy, neuropathy, nephropathy, cardiovascular disease, *etc.*) by maintaining blood glucose concentrations close to the normal level[3,4] while always minimizing hypoglycemia. Glycated hemoglobin levels (HbA1c) provide a good criterion of overall glycemic control. According to the diabetes control and complications trial research group (DCCT), they must be, in adults, under 7% (53 mmol/mol), if the upper normal limit is about 6% (42 mmol/mol)[3]. The DCCT obtained such results utilizing targeted blood glucose (BG) treatment decisions usually with multidose insulin (MDI) (≥ 4 shots/d) and/or insulin pump treatment compared to a relatively fixed insulin dose schedule in the control group[3]. Such MDI and continuous subcutaneous insulin infusion (CSII) treatment was subsequently known as intensive treatment when it really should have been defined as the targeted BG intent to reach BG goals and HbA1c goals safely that was "intensive treatment". However, in our experience, this is possible even in diabetic children and adolescents with the twice-daily free mixing insulin regimen as well as with the basal-bolus regimen, as we have shown since the 90 s[5-7].

Hvidoere Study Group on childhood diabetes

After the publication of the conclusions of the DCCT and of my own results, causing some debate about "Dorchy's recipes"[6], The Hvidoere Study Group on childhood diabetes (HSG) evolved in 1994, during a workshop, to discuss strategies that could be important in improving quality of pediatric and adolescent diabetes care and, therefore good HbA1c levels. Four international comparisons of metabolic control (1995, 1998, 2005, 2009) have been performed in about twenty pediatric diabetology centers from about twenty industrialized countries in Europe, North America, Japan and Australia[2,8-10]. A capillary blood sample was provided by participants and analyzed centrally at the Steno Diabetes Center in Denmark. HbA1c was DCCT aligned: normal range 4.4%-6.3% or 25-45 mmol/mol, mean 5.4% or 35.5 mmol/mol. The mean is 0.3% higher than the DCCT laboratory level: normal range 4.05%-6.05%, mean 5.05%.

Cameron *et al*[11] have reviewed the major studies of the HSG, both cross-sectional and longitudinal, and summarized the body of work published in 28 peer reviewed medical and scientific journals (Table 1). The authors note that "The one center that has consistently had the lowest HbA1c values from 1995 to 2009" is my center in Brussels. They comment: "The Hvidoere member in question is highly charismatic and has a very prescriptive, 'recipe'-based approach to managing diabetes in his clinic. He prescribes mostly twice-daily free mixing injections of insulin and eschews, a flexible approach to dietary intake. This does not appear to be at the expense of either hypoglycemia or QOL in his patient group. Although many aspects of his practice are shared by other Hvidoere members, it has proved very difficult to translate this total approach into other contexts for a variety of reasons. However, this experience is emblematic that consistently excellent outcomes can be achieved by simple, 'non-intensive' insulin regimens that are underpinned by a strong philosophy of care"[11].

Cameron *et al*[11] conclude in their review: "Therapeutic strategies in and of themselves are not enough to obtained desired clinical outcomes. While all clinical regimens have some clinical utility, it is the underlying therapeutic philosophy based on a qualified common training for all team members delivering diabetes care and education to the families that drives improvement. The clinical aphorism of 'Ask for mediocrity and you will receive' holds true. Thus, it appears that the best results will be obtained by physicians who are target-driven and teams and families that have unanimity of purpose. Perhaps the conclusions relating the best clinical practice drawn from the entire body of work of the Hvidoere studies can be best summarized as -be dogmatic about outcome but flexible in approach".

In the studies of the HSG, the different insulin regimens were: "conventional" twice daily (CT), CTpremix, CTfreemix, CTfreemix + (used only in center number one, *i.e.*, in my center in Brussels), basal-bolus injections (MDI), CSII. In the 4th study[10], there was confusion between CTfreemix and CTfreemix +, fortunately corrected by an erratum[10]. The lowest HbA1c levels were found in the CTfreemix+ group, 7.3% ± 0.5% (56.3 mmol/mol); approximately the same values were obtained in the three preceding studies by the Brussels team. In 2007, after three HSG studies, de Beaufort *et al*[9] noted:

Table 1 HbA1c comparisons in the 4 studies by the Hvidoere international study group on childhood diabetes (1995-2009)

Hvidoere studies	Number of countries of pediatric centers	Number of subjects	Age (yr)	Mean HbA1c (%) ± SD (mean DCCT aligned)	Spread in center mean HbA1C (%) (DCCT aligned)	Conclusions
1995[8]	18 (Europe, North America, Japan) 22	2873	0-18	8.6 ± 1.7 (8.3)	7.6-10.2 (7.3-9.9)	No difference in glycemic control was found among adolescents treated with two, three, and four or more daily injections. Girls on 4 injections had higher BMI
1998[2]	17 (Europe, North America, Japan) 21	2101	11-18	8.7 ± 1.7 (8.4)	7.7-10.1 (7.4-9.8)	The differences between centers were not explicable by differences in insulin regimens. The centers with the lowest mean HbA1c also had lowest rates of severe hypoglycemia and reported better QOL
2005[9]	19 (Europe, North America, Japan, Australia) 21	2093	11-18	8.6 ± 1.7 (8.2)	7.7-9.5 (7.4-9.2)	Intensified insulin regimens (MDI and CSII) showed no lower HbA1c compared with twice daily free-mixing (lowest HbA1c)
2009[10]	17 (Europe, North America, Japan, Australia) 18	1113	< 11	8.3 ± 1.3 (8.0)	7.6-9.2 (7.3-8.9)	despite major changes in management (> 99% on analog insulins and 33% with CSII), the lowest HbA1c levels were found in the twice daily free-mixing insulin regimen in Brussels (7.3% ± 0.5%)

MDI: Multidose insulin; CSII: Continuous subcutaneous insulin infusion.

"The management of children and adolescents with type 1 diabetes has undergone many changes over the past decade, aiming to improve glycemic control and reduce risks of vascular complications, without sacrificing quality of life. These have included increased usage of insulin analogues, basal-bolus regimens, and CSII. Despite these substantial changes, it has been difficult to demonstrate significant improvements in metabolic outcome. This study in 21 international centers was initiated to investigate the impact of treatment changes on glycemic control and to establish whether the previously reported differences between centers were diminishing. The results confirm that there has been no improvement in glycemic control over a decade, with mean A1c levels of 8.6% or 70.5 mmol/mol (1995), 8.7% or 71.6 mmol/mol (1998), and 8.6% or 70.5 mmol/mol (2005), and the substantial differences between centers have remained stable." That means that more expensive and technically complicated treatments have nearly no impact on HbA1c. Only two centers showed a significant reduction (≥ 0.5%) in A1c from 1998 to 2005 and one center had a significant increase in A1c. The conclusion is that, in countries unable to afford a sophisticated and expensive treatment, it is possible to obtain good results without necessarily using expensive insulins and pumps.

As my team has consistently had the lowest HbA1c values during the comparisons of the HSG from 1995 to 2009, I think that I am allowed to summarize the so-called "Dorchy's recipes..."[6,12-15].

Dorchy's recipes

Two daily insulin free-mixed regimen in children or even teenagers: Two daily insulin free-mixed regimen with an human rapid-acting insulin or a fast-acting analogue and NPH (*i.e.,* 4 insulins per day as in the basal-bolus regimen) in children < 15-16 years is easy and effective in countries where the meal schedule allows correct allocation of diet. The first injection (and insulin dose alteration) is done before going to school and the second injection (and insulin dose alteration) after returning from school, before dinner, with the facultative help of the parents. Diabetic children have to eat a snack in the middle of the morning and afternoon periods with their friends, without the need to give an additional insulin injection or to measure blood glucose. This reduces the risk of insulin omission. The doses of the 4 insulins are adjusted according to the results of 4 daily blood glucose measurements of the preceding days (retroactive analysis) and not only to the present glycemia (reactive responsitivity). A third injection with a fast-acting analogue may be done to allow a greater snack or to correct hyperglycemia (= CTfreemix +).

Basal-bolus regimen in adolescents but more complicated: Basal-bolus regimen in adolescents: increased flexibility in daily life and dietary freedom, but more complicated; no simplistic sliding scales according to the present glycemia; insulin dose alteration must be triple: (1) retrospective, according to previous BG analysis, trial and error experiments, in order to enjoy more freedom for meals, sports, *etc*; (2) prospective according to programmed changes in meals and sports (*i.e.,* add more insulin if overeating or temporarily reduce insulin dose to prevent activity-related expected hypoglycemia); and (3) with only a "touch" of compensatory adaptation (reactive dose changes) according to the present glycemia. This needs psychological maturity and ongoing education support and teaching of child, adolescent and family

members, otherwise the multiple injection system lead to anarchy, "cheating" and obesity, especially but not only in adolescent girls. Before or after the meals, there is an injection of rapid human insulin or fast-acting analogue, and before sleeping, an injection of a stable long-acting analogue[16]. The doses of the 4 insulin injections are adjusted according to analysis of the results of at least 4 daily blood glucose measurements (if three meals; otherwise more blood glucose determinations and injections) of the preceding days and not only to the present BG level.

CSII is very rarely recommended: In our experience, CSII is very rarely recommended and used in about 1% of our patients at their request. We do not promote use of expensive insulin pump regimens and believe that patients and their family members can do as well with pens and syringes. Pumps in children and adolescents have not been associated with significant improvements in daily BG results or in A1c according to results of the HSG[11] and also by the PedPump study in 30 centers of 17 countries[17]. In that study, the use of less than 6.7 daily boluses was a significant predictor of an HbA1c level > 7.5% or 58.5 mmol/mol, despite increasing blood glucose measurements and the added expense that this entails. We suspect this reflects insufficient education and motivation and inconsistent team target goal setting as the explanation. In a Belgian retrospective cross-sectional study among 12 pediatric centers, A1c actually was higher among patients with insulin pump therapy[18].

No rejection of non-analogue older human insulins: No systematic (automatic or dogmatic) replacement of rapid-acting human insulins by fast-acting analogues such as more expensive aspart, lispro or glulisine[14]. In the two daily insulin free-mixed regimen as well as in the basal-bolus regimen, the choice of a fast-acting analogue is made if the time period between the injection and the following glycemia, allowing to judge the insulin injected before, is less than 3 or 4 h, *i.e.,* the duration of action of the fast-acting analogue. Otherwise, we use a human rapid-acting insulin whose duration of action reaches 6 to 8 h rather than the newer and more expensive fast-acting analogues.

No carbohydrate counting: The dietician never gives rigid meal plans or exchange lists. "Diet" is never prescribed. No carbohydrate counting is recommended because there is no linear correlation between the metabolization of X grams of glucose by Y units of insulin[12,13,15]. The dietician builds up a picture of the family's and child or teen's usual habits and life style. When possible, the family is encouraged to adopt a similar and normal eating pattern so that the child and adolescent with diabetes does not have to eat specially prepared meals. The main problem with the twice-daily insulin regimen is the allocation of carbohydrates in 6 meals according to the cumulated action of the insulins. The dietician must know perfectly the actions of the insulins and their adjustment. While being criticized for this being too difficult, our glycemic control and A1c results certainly prove that this is feasible to accomplish with large numbers of children, adolescents and young adults. In addition, all members of the professional diabetes team must have the same treatment philosophy, as promulgated by the DCCT, to provide the same message and same target BG and A1c goals[19].

Screening for subclinical complications: Screening for subclinical and asymptomatic complications by sensitive methods from puberty in order to increase the motivation of both the patient and the doctor[20]. After age 13 and/or 3 years of diabetes duration, we perform every year: retinal fluorescein angiography (rather than just direct ophthalmoscopy), measurement of motor and sensitive conduction velocities (which is different from a painful electromyography), sympathetic cutaneous response or heart rate variability and dosage of microalbuminuria. It is important to do a diagnosis at the stage of functional and reversible abnormalities before the installation of irreversible lesions. It is important to be able to say to the patient, for example, "you have no complaint, but as you can see on this photograph, there are two leakages of fluorescein in your left eye; it is reversible if you improve your HbA1c; otherwise, that will become an irreversible lesion leading later to overt complications". The same message for the slowing of conduction velocity or the presence of abnormal microalbuminuria. Every year, we also perform lipid analyses, thyroid and celiac screenings, measurement of blood pressure, *etc.,*[21,22]. Early identification of such abnormalities allows potential early treatment, *i.e.,* medication to control hypertension or early nephropathy, lower lipids, *etc.*

Knowledge of HbA1c target: One hundred percent of our patients and/or their parents as well as the members of the multidisciplinary team know the HbA1c target, *i.e.,* less than 7% or 53 mmol/mol, and one hundred percent of our patients and/or their families know the result of their HbA1c results obtained, on average, every two months before the consultation. This is strongly associated with HbA1c outcome as shown by the HSG[23].

Friendly and personal contacts: Friendly and personal contacts with a large dose of psychological support are indispensable in the long-term relationship of a patient with a chronic disease and diabetes is perhaps the best example because of the multitude of daily behavioral decisions that must be acknowledged and accomplished. The diabetologist must know the whole story of the life of his or her patient, and must adapt his or her psychology to the psychology of the patients and of their families, and not the reverse. The diabetologist is not interchangeable as it can be the case for some other pediatric specialties or practices and this too may help explain our consistent excellent A1c results compared to

others in Hvidoere.

Observers are not allowed during consultations: In the office of the diabetologist, at the outpatient clinic, we do not allow observers: temporary assistants or students. This is most important especially with adolescents, in an effort not to disrupt the mutual trust and to preserve privacy. Patients are not undressed (except to search for lipodystrophies)... They are not ill... It is important on a psychological point of view, mainly with adolescents and with Muslims.

Education is made-to-measure: Nearly 50% of our patients are immigrants and mainly of Moghrabin origin (especially from Morocco). Because of the such cultural, economic and social differences, the education we offer must be adapted to the family and their food choices with individualized teaching modules and concepts but with the same overall glycemic goals in mind. Education must be made-to-measure.

High frequency of long-duration consultations: The duration of the medical consultation varies between 30 to 60 min and is preceded by a consultation with a nurse specialized in pediatrics as well as in diabetology. If necessary further consultation takes place with the dietician, the psychologist or the social worker.

Treatment is nearly costless; the nurses are allowed to go to schools: Care is provided in a specialized pediatric and adolescent/young adult diabetology clinic of a high ranking Belgian university public hospital, recognized by the Belgian Social Security ministry in an official manner. Medical and paramedical (nurse, dietician, psychologist, social worker) "consultations" and material necessary for treatment are nearly costless. Nurses are also allowed and compensated for time to do home and school visits and this is especially helpful for those in poor financial, psychological or immigrant circumstances where more teaching time is required to reach goals and sustain them. We believe that such multidisciplinary ongoing care helps explain our good results even among otherwise potentially more problematic patient populations.

We follow our patients into adulthood: We follow our patients into adulthood and do not automatically suggest their transition to adult physicians after an arbitrary age of 18 years. We believe this allows us to assist with transition through adolescence and into better self-care behaviors as young adults. We also believe that this allows our professional team to be better aware of the actual complications that may only occur after longer duration of diabetes. At the onset of 2014, we followed 527 children and adolescents with diabetes aged < 18 year and 495 aged ≥ 18 year.

Influence of family characteristics and alexithymia on HbA1c: The HSG has shown that family factors, particularly dynamic and communication factors such as parental over-involvement and adolescent-parent concordance on responsibility for diabetes care appear be important determinants of metabolic outcomes in adolescents with diabetes[24]. We tried to determine the family characteristics and the psychological factors influencing A1c. The maternal perception of family cohesiveness and maternal alexithymia predict on glycemic control in children and adolescents with diabetes[25]. We showed, for the first time, that children who have difficulties in expressing their feelings to others are more at risk of poor glycemic control. In future, it will be useful to identify the diabetic young people who have such difficulties and to consider interventions designed specifically for them[26].

Confusion between conventional and intensive therapy

The team that I have created in Brussels believes it is inappropriate to automatically designate the term "intensive treatment" only to imply insulin pumps or multidose insulin regimens when, in fact, it is the goals of glycemic control and A1c achievement that should define intensified treatment not the manner or number of insulin doses each day. It is inadequate to systematically assign the multiple injection regimen, or the pump therapy, to "intensive" treatment, and some forms of the twice-daily injection regimen abusively called "conventional" (there are different strategies as shown by the HSG, premix insulins giving the worst results and the CTfreemix + obtaining the best HbA1c levels) to a non-intensified therapeutic category of insulin therapy. Indeed, a multiple injection regimen, or the use of pumps, not associated with a good intensified and complete education, as well with the application of the consecutive knowledge, may have deleterious effects on HbA1c, as shown by the HSG. The confusion between "conventional therapy" and "intensive therapy" was born from misinterpretation of how the DCCT was structured in 1993[3]. In their "conventional group" with one or two daily injections, there was no insulin adjustment except in order to avoid clinical symptoms such as polyuria and polydipsia with hyperglycemia or symptoms and signs reflecting excessive hypoglycemia and there were very few consultation visits except for every three months follow-up assessments for overall monitoring and lab work. There was no blood glucose target established for the conventional treatment group, no specific amount of monitoring and minimal education sessions that took place; all of this was designed to mimic the type of "non-intensive" usual treatment at that time[3]. Bolli[27] wrote: "One concept should be clear. The difference between intensive and non-intensive therapy is limited to the glycemic targets (mean glycemia < 150 mg/dL which gives an HbA1c < 7%). Non-intensive therapy is defined as a model of insulin treatment (2 or ≥ 4 injections, CSII, diet, HBGM, education, *etc.*) giving a mean blood glucose concentration and % of HbA1c above the values indicated by the DCCT".

General conclusion

Because recent multicenter studies, even those performed in developed countries without financial restriction, show that treatment of childhood, adolescent and young adults diabetes is inadequate in general and that levels of HbA1c are very different, diabetes treatment teams should individually explore the reasons for failure, without any prejudice or bias, in their own centers especially when center average A1c results are over 8%. The number of daily insulin injections, 2 or $\geqslant$ 4 or the use of pumps, by itself does not necessarily give better results. Merely increasing the number of daily insulin injections or encouraging insulin pump treatment does not automatically produce better results although may offer greater flexibility for the patient and family. Key remains unified education by a team of diabetes professionals who know their patient and his/her family, work to educate and re-educate and mutually sets goals known and greed upon by not only the entire team providing such care but also the patient and his or her family. Any dogmatism must be avoided. Treatment cost *vs* results must also be taken into account.

ACKNOWLEDGMENTS

I thank Stuart J Brink (Past President of the International Society for Pediatric and Adolescent Diabetes (ISPAD) and current ISPAD International Education Chair; Senior Endocrinologist, New England Diabetes and Endocrinology Center (NEDEC), Waltham, MA, United States; Associate Clinical Professor of Pediatrics, Tufts University School of Medicine and Clinical Instructor of Pediatrics, Harvard Medical School, Boston, MA, United States) who kindly debated, amended and editorialized my paper. He shares my field of vision and gets average A1c close to mine. He kindly corrected my English.

REFERENCES

1 **Dorchy H**, Olinger S. [Well-being of insulin-dependent diabetics. Evaluation of 100 adolescents and young adults in relation to their metabolic control]. *Presse Med* 1997; **26**: 1420-1424 [PMID: 9404353]
2 **Hoey H**, Aanstoot HJ, Chiarelli F, Daneman D, Danne T, Dorchy H, Fitzgerald M, Garandeau P, Greene S, Holl R, Hougaard P, Kaprio E, Kocova M, Lynggaard H, Martul P, Matsuura N, McGee HM, Mortensen HB, Robertson K, Schoenle E, Sovik O, Swift P, Tsou RM, Vanelli M, Aman J. Good metabolic control is associated with better quality of life in 2,101 adolescents with type 1 diabetes. *Diabetes Care* 2001; **24**: 1923-1928 [PMID: 11679458 DOI: 10.2337/diacare.24.11.1923]
3 The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. *N Engl J Med* 1993; **329**: 977-986 [PMID: 8366922 DOI: 10.1056/NEJM199309303291401]
4 **Verougstraete CM**, Libert JA, Dorchy HR. Discordant diabetic retinopathy in homozygous twins: the importance of good metabolic control. *J Pediatr* 1999; **134**: 658 [PMID: 10228306 DOI: 10.1016/S0022-3476(99)70257-X]
5 **Dorchy H**. [What glycemic control can be achieved in young diabetics without residual secretion of endogenous insulin? What is the frequency of severe hypoglycemia and subclinical complications?]. *Arch Pediatr* 1994; **1**: 970-981 [PMID: 7834046]
6 **Dorchy H**. Dorchy's recipes explaining the "Intriguing efficacity of Belgian conventional therapy". *Diabetes Care* 1994; **17**: 458-460 [PMID: 8062621]
7 **Dorchy H**, Roggemans MP, Willems D. Glycated hemoglobin and related factors in diabetic children and adolescents under 18 years of age: a Belgian experience. *Diabetes Care* 1997; **20**: 2-6 [PMID: 9028684 DOI: 10.2337/diacare.20.1.2]
8 **Mortensen HB**, Hougaard P. Comparison of metabolic control in a cross-sectional study of 2,873 children and adolescents with IDDM from 18 countries. The Hvidøre Study Group on Childhood Diabetes. *Diabetes Care* 1997; **20**: 714-720 [PMID: 9135932 DOI: 10.2337/diacare.20.5.714]
9 **de Beaufort CE**, Swift PG, Skinner CT, Aanstoot HJ, Aman J, Cameron F, Martul P, Chiarelli F, Daneman D, Danne T, Dorchy H, Hoey H, Kaprio EA, Kaufman F, Kocova M, Mortensen HB, Njølstad PR, Phillip M, Robertson KJ, Schoenle EJ, Urakami T, Vanelli M. Continuing stability of center differences in pediatric diabetes care: do advances in diabetes treatment improve outcome? The Hvidoere Study Group on Childhood Diabetes. *Diabetes Care* 2007; **30**: 2245-2250 [PMID: 17540955 DOI: 10.2337/dc07-0475]
10 **de Beaufort CE**, Lange K, Swift PG, Aman J, Cameron F, Castano L, Dorchy H, Fisher LK, Hoey H, Kaprio E, Kocova M, Neu A, Njolstad PR, Phillip M, Schoenle E, Robert JJ, Urukami T, Vanelli M, Danne T, Barrett T, Chiarelli F, Aanstoot HJ, Mortensen HB. Metabolic outcomes in young children with type 1 diabetes differ between treatment centers: the Hvidoere Study in Young Children 2009. *Pediatr Diabetes* 2013; **14**: 422-428 [PMID: 22957743 DOI: 10.1111/j.1399-5448.2012.00922.x]
11 **Cameron FJ**, de Beaufort C, Aanstoot HJ, Hoey H, Lange K, Castano L, Mortensen HB. Lessons from the Hvidoere International Study Group on childhood diabetes: be dogmatic about outcome and flexible in approach. *Pediatr Diabetes* 2013; **14**: 473-480 [PMID: 23627895 DOI: 10.1111/pedi.12036]
12 **Dorchy H**. Insulin regimens and insulin adjustments in diabetic children, adolescents and young adults: personal experience. *Diabetes Metab* 2000; **26**: 500-507 [PMID: 11173723]
13 **Dorchy H**. Dietary management for children and adolescents with diabetes mellitus: personal experience and recommendations. *J Pediatr Endocrinol Metab* 2003; **16**: 131-148 [PMID: 12713249 DOI: 10.1515/JPEM.2003.16.2.131]
14 **Dorchy H**. [Rational use of insulin analogues in the treatment of type 1 diabetic children and adolescents: personal experience]. *Arch Pediatr* 2006; **13**: 1275-1282 [PMID: 16920339 DOI: 10.1016/j.arcped.2006.06.015]
15 **Dorchy H**. [Management of type 1 diabetes (insulin, diet, sport): "Dorchy's recipes"]. *Rev Med Brux* 2010; **31**: S37-S53 [PMID: 21812215]
16 **Heise T**, Nosek L, Rønn BB, Endahl L, Heinemann L, Kapitza C, Draeger E. Lower within-subject variability of insulin detemir in comparison to NPH insulin and insulin glargine in people with type 1 diabetes. *Diabetes* 2004; **53**: 1614-1620 [PMID: 15161770 DOI: 10.2337/diabetes.53.6.1614]
17 **Danne T**, Battelino T, Jarosz-Chobot P, Kordonouri O, Pánkowska E, Ludvigsson J, Schober E, Kaprio E, Saukkonen T, Nicolino M, Tubiana-Rufi N, Klinkert C, Haberland H, Vazeou A, Madacsy L, Zangen D, Cherubini V, Rabbone I, Toni S, de Beaufort C, Bakker-van Waarde W, van den Berg N, Volkov I, Barrio R, Hanas R, Zumsteg U, Kuhlmann B, Aebi C, Schumacher U, Gschwend S, Hindmarsh P, Torres M, Shehadeh N, Phillip M. Establishing glycaemic control with continuous subcutaneous insulin infusion in children and adolescents with type 1 diabetes: experience of the PedPump Study in 17 countries. *Diabetologia* 2008; **51**: 1594-1601 [PMID:

18592209 DOI: 10.1007/s00125-008-1072-2]
18 **Doggen K**, Debacker N, Beckers D, Casteels K, Coeckelberghs M, Dooms L, Dorchy H, Lebrethon M, Logghe K, Maes M, Massa G, Mouraux T, Rooman R, Thiry-Counson G, Van Aken S, Vanbesien J, Van Casteren V. Care delivery and outcomes among Belgian children and adolescents with type 1 diabetes. *Eur J Pediatr* 2012; **171**: 1679-1685 [PMID: 22875314 DOI: 10.1007/s00431-012-1809-2]
19 **Brink SJ**, Miller M, Moltz KC. Education and multidisciplinary team care concepts for pediatric and adolescent diabetes mellitus. *J Pediatr Endocrinol Metab* 2002; **15**: 1113-1130 [PMID: 12387509 DOI: 10.1515/JPEM.2002.15.8.1113]
20 **Dorchy H**. Screening for subclinical complications in young type 1 diabetic patients: experience acquired in Brussels. *Pediatr Endocrinol Rev* 2004; **1**: 380-403 [PMID: 16437030]
21 **Messaaoui A,** Tenoutasse S, Van der Auwera B, Mélot C, Dorchy H. Autoimmune thyroid, celiac and Addison's diseases related to HLA-DQ types in young patients with type 1 diabetes in Belgium. *OJEMD* 2012; **2**: 70-73 [DOI: 10.4236/ojemd.2012.24011]
22 **Messaaoui A**, Willems D, Mélot C, Dorchy H. Risk markers for cardiovascular disease in young type 1 diabetic patients: lipoproteins, high-sensitivity C-reactive protein and adiponectin. *Acta Clin Belg* 2012; **67**: 79-82 [PMID: 22712161]
23 **Swift PG**, Skinner TC, de Beaufort CE, Cameron FJ, Aman J, Aanstoot HJ, Castaño L, Chiarelli F, Daneman D, Danne T, Dorchy H, Hoey H, Kaprio EA, Kaufman F, Kocova M, Mortensen HB, Njølstad PR, Phillip M, Robertson KJ, Schoenle EJ, Urakami T, Vanelli M, Ackermann RW, Skovlund SE. Target setting in intensive insulin management is associated with metabolic control: the Hvidoere childhood diabetes study group centre differences study 2005. *Pediatr Diabetes* 2010; **11**: 271-278 [PMID: 19895567 DOI: 10.1111/j.1399-5448.2009.00596.x]
24 **Cameron FJ**, Skinner TC, de Beaufort CE, Hoey H, Swift PG, Aanstoot H, Aman J, Martul P, Chiarelli F, Daneman D, Danne T, Dorchy H, Kaprio EA, Kaufman F, Kocova M, Mortensen HB, Njølstad PR, Phillip M, Robertson KJ, Schoenle EJ, Urakami T, Vanelli M, Ackermann RW, Skovlund SE. Are family factors universally related to metabolic outcomes in adolescents with Type 1 diabetes? *Diabet Med* 2008; **25**: 463-468 [PMID: 18294223 DOI: 10.1111/j.1464-5491.2008.02399.x]
25 **Meunier J**, Dorchy H, Luminet O. Does family cohesiveness and parental alexithymia predict glycaemic control in children and adolescents with diabetes? *Diabetes Metab* 2008; **34**: 473-481 [PMID: 18783976 DOI: 10.1016/j.diabet.2008.03.005]
26 **Housiaux M**, Luminet O, Van Broeck N, Dorchy H. Alexithymia is associated with glycaemic control of children with type 1 diabetes. *Diabetes Metab* 2010; **36**: 455-462 [PMID: 20863735 DOI: 10.1016/j.diabet.2010.06.004]
27 **Bolli GB**. Rational use of insulin analogues in the treatment of type 1 diabetes mellitus. *Pediatr Endocrinol Rev* 2003; **1**: 9-21 [PMID: 16437009]

P- Reviewer: Li JF, Surani S, Wang CC **S- Editor**: Qi Y
L- Editor: A **E- Editor**: Lu YJ

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com