

# Introduction to the Second World Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy)

## Dilemmas in clinical practice

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Successful management of obesity, diabetes, and hypertension is a matter of great urgency in current medical practice because of the soaring prevalence of these three interrelated conditions worldwide. Their complications (first and foremost, cardiovascular disease) result in significant morbidity, which exerts a heavy toll on health care systems everywhere, especially in industrialized countries. Because the causes and effects of obesity, diabetes, and hypertension are closely intertwined, preventing their complications requires a comprehensive approach. Massive research into the etiology and treatment of these three afflictions has recently generated vast amounts of data, which call into question many of the accepted treatment paradigms. They present physicians in clinical practice with the daily challenges of integrating innovative therapies into the treatment protocol, addressing difficult questions and making controversial decisions.

One of the major dilemmas faced by physicians in this field stems from the recent trials that revealed the relatively small benefits of blood glucose control in certain diabetic patients compared with the possible morbidity and mortality risk. On the one hand, follow-ups to the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (DCCT-EDIC) (1) and the U.K. Prospective Diabetes Study (UKPDS) (2) have supported the importance of early diabetes control in preventing later cardiovascular events

and microvascular complications. Moreover, the STENO-2 Follow-Up Study (3) from the Steno Diabetes Center in Copenhagen demonstrated that early treatment of cardiovascular risk factors reduces cardiovascular morbidity and mortality years later. On the other hand, however, the results of several trials—the Action in Diabetes and Vascular Disease Trial (ADVANCE) (4), the Action to Control Cardiovascular Risk in Diabetes Study (ACCORD) (5), the VA Diabetes Trial (VADT) (6), and Heart 2D study (7)—have cast doubt on the benefits of tight glucose control in older patients with longstanding disease (the only exception being the ADVANCE trial, which demonstrated the advantages of such control for blocking the progression of nephropathy). The risks of intensive treatment in patients with longstanding disease included higher mortality in the ACCORD trial and an increased risk of hypoglycemic events and weight gain in the other trials. The findings from these studies (1–7) have provided clinical evidence for the concept of “glucose memory,” long known from basic research (8). This concept calls for revising the currently accepted approach to optimal glucose control: it reinforces the importance of achieving normal glucose levels immediately upon the diagnosis of diabetes for preventing later-onset complications. Early control, aiming at normoglycemia, is easily attained and involves the use of relatively safe drugs (metformin, acarbose), with small risk of major side effects. Physicians who delay achieving

early normoglycemia cause their patients more harm than good, since aiming at glucose control in the later stages of diabetes may put the patients at a greater risk with marginal benefits.

The second World Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy), held in Barcelona at the end of October 2008, brought together leading international experts with the goal of discussing the most pressing controversies in these three disciplines and reaching a consensus on treatment guidelines for the coming 2 years. To achieve this goal, the Congress included state-of-the-art lectures and reports on the latest clinical studies, as well as numerous debates and discussions in which internationally prominent physicians shared their clinical expertise with the meeting participants. The present supplement, divided into six sections, provides highlights from the meeting, including summaries of lectures and the contents of major debates held at the Congress.

The section on diabetes opens with an overview of the pathophysiology of disease progression. It also dwells on ways in which the development of diabetes is affected by two major characteristics: insulin resistance in different target organs and the failure of  $\beta$ -cells to secrete adequate amounts of insulin due to the shortage or defective function of these cells. The combination of these two characteristics, leading to micro- and macrovascular hyperglycemic damage, raises important questions with respect to the targets for glycemic control: Should physicians concentrate on A1C or attempt to prevent postprandial hyperglycemia? Special emphasis was placed at the Congress on the role of nonpharmacological approaches in preventing diabetes and in treating newly diagnosed diabetes. The significance of early pharmacological intervention was also noted. In fact, aiming at establishing normoglycemia in the early stages of diabetes, to prevent the emergence of “glucose memory” in later

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stages, might call for a change in our approach to the treatment of type 2 diabetes. In this context, meeting participants debated the optimal ways of monitoring blood glucose levels, in particular, the role of self-control of blood glucose as opposed to continuous glucose monitoring in the treatment of patients with type 1 and type 2 diabetes.

Several lectures and debates dealt with novel therapies of diabetes—including incretin-based therapy, bile acid metabolic regulation, and an innovative therapy for latent autoimmune diabetes in adults—as well as with potential use of antioxidant and anti-inflammatory treatments in diabetes. Speakers discussed the best ways of incorporating novel therapies into the treatment regimen and debated whether the new approaches had created a need for a new paradigm in the treatment of diabetes. Furthermore, a significant part of this supplement is devoted to insulin therapy for type 2 diabetes: the ideal timing for starting such therapy and ways of administering it in the early and late stages of the disease.

This supplement's second section on hypertension covers the management of hypertension in patients with diabetes. What is the definition of prehypertension in diabetes? Should this borderline condition be treated in diabetic patients? How should the treatment approach differ between diabetic and nondiabetic patients? The need for 24-h monitoring of blood pressure in diabetes is also discussed. Yet another topic in this section relates to the risks of white coat hypertension and the pros and cons of treating it in diabetic patients.

The connection between diabetes and cardiovascular disease forms the content of the third section. Because diabetes disrupts endothelial function and otherwise contributes to the appearance of cardiovascular disease, the control of blood glucose levels can play an important role in preventing cardiovascular disease. However, other cardiovascular risk factors are easier to treat than hyperglycemia, and they can be improved with less deleterious side effects. In light of this, what are the relative advantages and disadvantages of hyperglycemia treatment for the prevention of cardiovascular disease? This

section provides conclusions drawn from large studies aimed at achieving normoglycemia and discusses the advantages or disadvantages of various hyperglycemic drugs in the prevention of cardiovascular events.

The fourth section, on obesity and lipids, deals with weight gain as a health risk factor for people of all ages, as well as with the need to control various components of dyslipidemia other than LDL (particularly HDL and triglycerides) in the management of obese diabetic patients. The section includes a detailed discussion on the recommendations of the American Diabetes Association for the use of statins in patients with diabetes; evidence from clinical trials suggests that these guidelines might have to be broadened to encompass a wider segment of the population. In addition, the section discusses the role of weight control in the treatment of diabetes. Is weight reduction beneficial in the elderly diabetic patient? Should clinicians concentrate on weight control or physical activity in averting the risk of cardiovascular disease? Highlights of the debates on these topics are provided.

Diagnosis and treatment of microvascular disease is discussed in the fifth section. One important issue is the use of single or double renin-angiotensin system blockade in preventing microangiopathy in the eye and kidney. Other common microvascular complications are discussed, including detailed reviews of painful neuropathy and impotence, both affecting ~50% of patients with diabetes.

The topic of the final sixth section of this supplement is smoking. This addictive behavior amplifies the risk of cardiovascular complications in patients with diabetes and hypertension, yet getting patients to quit smoking is frustratingly difficult. Articles in this section outline the psychological and physiological factors contributing to this difficulty and stress the importance of smoking cessation at any age.

Controversies can serve as a major driving force of progress, since they stimulate thought, discussion, and the yearning for more knowledge. In focusing on controversies relevant to clinical practice rather than basic research, the Congress was intended to promote progress in pa-

tient care. Reflecting the design of the meeting, this supplement aims to provide physicians treating people with diabetes, hypertension, and obesity with the most up-to-date information that can help them make the optimal evidence-based decisions in their daily practice.

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