

Introduction to the 4th World Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy)

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The first CODHy Congress was held in Berlin in 2006. The acronym CODHy originally stood for “Controversies in Obesity, Diabetes and Hypertension.” It was, however, soon realized that controversies needed to be overcome in an attempt to achieve as much consensus as possible. Would this represent a compromise between two opposite points of view or simply the agreement on identifying areas of knowledge still requiring more investigations and data collection? The final goal was to allow participants to appreciate the process of evaluating in a critical manner all information, even the one appearing, at first sight, contradictory if not at variance with the current knowledge. Because of these considerations, the Congress slightly, though substantially, changed its definition to “Controversies to Consensus in Diabetes, Obesity and Hypertension” while keeping the already well-established acronym CODHy. Discussions, opinions, potential ways to reconcile different positions, and proposals for gaining consensus have been traditionally translated into articles that have always been published in a Supplement of *Diabetes Care*. The 4th CODHy Congress was held last November in Barcelona much in line with the spirit illustrated above, and this renovated Supplement collects the highlights of that Congress that saw internationally renowned experts

interacting with diabetologists, endocrinologists, hypertension specialists, and general practitioners.

The overall scenario in diabetes, obesity, and hypertension has changed little, if any, since the time of the previous edition of CODHy. The growing prevalence of these conditions has not abated, and it continues to raise medical and societal concerns (1). The American Diabetes Association has recently released the data of diabetes-related costs in the U.S. (2): in just 5 years, costs have increased by 40%. This alarming increase in the costs was not attributable to more expensive drugs or procedures. Interestingly, the growing number of individuals affected by the disease largely accounted for it. Obesity and hypertension follow the same pattern (3,4), and together with diabetes they drive a continuous cardiovascular risk. In light of such a panorama, the search for effective preventative measures becomes imperative. In the meantime, however, we must exert more effort and invest further resources to reduce the risk of long-term complications.

For diabetic subjects, this requires careful control of multiple cardiovascular risk factors along with awareness that we still are far from reaching the degree of control that may effectively reduce such a risk. The recent analysis of the data generated by the National Health and Nutrition

Examination Survey and the Behavioral Risk Factor Surveillance System has well documented how partial the results are in controlling cardiovascular risk. Though some improvements in risk-factor control and adherence to preventive practices were apparent in the period 1999–2010, almost half of U.S. adults with diabetes do not meet the recommended goals for diabetes care including HbA_{1c}, lipid, and blood pressure levels (5).

The reasons for the limited efficacy of our interventional maneuvers are many and quite different in nature. Genetic predisposition, different phenotypes, treatment strategies, appropriateness of therapies, efficacy and limitation of available antidiabetic drugs, and many more can all concur, in a complex interaction, in reducing our capacity to achieve more significant results in the fight against chronic metabolic diseases and related complications. In summary, many clinical and scientific questions remain unanswered, and many are the challenges that both the investigators and the physicians still have to face. Some of these issues have been the matter of discussion in the occasion of the 4th CODHy meeting. This Supplement collects the most relevant contributions, selected by the peer-review process, from the 4th CODHy meeting.

We have already mentioned the growing prevalence of chronic disease, and an extensive view on the molecular mechanisms accounting for such a worrisome phenomenon is provided. This article sets the background for the discussion of all other specific topics. In particular, the reader will find great emphasis on multiple aspects of diabetes. Genetic studies, for instance, have shed light on the predisposition to develop diabetes, but whether this could turn into a clinically useful tool for prevention of the disease requires more thought and direct assessment.

From prevention, the reader will be able to move to pathophysiologic aspects such as the nature of the β -cell defect (mass vs. function). Moreover, diabetes

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pathophysiology is carefully discussed to establish to what extent it may provide a rational guideline for appropriate treatment of type 2 diabetes. Should we tackle insulin resistance or insulin secretion at the time of diagnosis? Or should we try to consider the complex pathophysiology of type 2 diabetes by addressing simultaneously more than one mechanism? Upon selection of the initial form of treatment, the question remains how we should intensify treatment in order to ensure sustained glycemic control, keeping in mind the need to minimize weight gain and hypoglycemia along with reasonable safety and cost. Are the new guidelines to be more efficient than the old ones? How can we translate into clinical practice the concept of treatment individualization? Should the individualization process be limited to glycemic target or other cardiovascular factors (for instance, hypertension) or must it be addressed in a personalized manner as well? Will treatment personalization result in more appropriate glycemic control with glucose levels closer to normal with low risk of hypoglycemia and, therefore, avoiding excessive glucose fluctuations? But which one of the three, i.e., hypoglycemia, hyperglycemia, or glucose fluctuation, contributes more to the risk of complications?

Along with targets and strategies, various aspects of treatment are discussed including the role of physical activity and old and new forms of therapy. The role of peroxisome proliferator-activated receptor- γ in present and future diabetes therapy is presented as well as the pros and cons of incretin versus insulin as second- or third-line therapy. GPR40, a future novel drug as possible therapy, is also described in this section. However, it is insulin treatment that has been debated in great detail. A number of articles discuss the use of insulin in the very early stages of diabetes, the opportunities provided by different formulations, the opportunities offered by new long-acting insulin analogs, the use of continuous subcutaneous insulin infusion in type 2 diabetes, and the combination of insulin with incretin-based therapies along with updates on the relationship between insulin and incretin therapy and the risk of

cancer. Altogether, these articles can offer quite an updated and critical analysis of the role of insulin therapy in type 2 diabetes. They should also help the clinician to appreciate the challenges and the opportunities that this therapeutic approach generates and, hopefully, provide him or her with more elements for a balanced therapeutic decision. Finally, with respect to treatment, the more recent data on the mechanisms through which metabolic surgery may favor remission of diabetes are also discussed.

Cardiovascular risk remains a major burden in type 2 diabetes. A strong association between plasma glucose concentration and vascular death has recently been reconfirmed by the results of the survey performed by the Emerging Risk Factors Collaboration (6). Because of the relevance of this complication, still the main cause of mortality among type 2 diabetic patients, a large section of this Supplement has been dedicated to this topic. Different aspects of the relationship between diabetes and cardiovascular risk are critically analyzed including a further analysis of the potential effect of glycemic control on cardiovascular risk, safety of insulin therapy, role of concomitant obesity with specific reference to the recently proposed “obesity paradox,” potential cardiovascular protection of novel anti-diabetes agents, and finally, the pros and cons of multifactorial intervention in elderly diabetic patients.

The last section of the Supplement focuses on the role of personalized therapy for both hypertension and dyslipidemia. Additional articles describe the prognostic value of blood pressure variability, the importance of ambulatory blood pressure monitoring, and ways to overcome statin intolerance.

It has always been the spirit of CODHy to throw on the table those questions that most likely many physicians keep asking themselves. A solid answer may not necessarily be at hand. In all of these cases, a critical review of the available information may be the best way to go: weigh the evidence, highlight the elements that have not yet been sufficiently investigated, compare approaches and

interpretations, critically assess results, and add in any new information. It may not be easy, but we are afraid it is not going to get easier. This Supplement may help us to appreciate that type 2 diabetes is not a mild condition and it is not a simple disease; rather, it is a complex condition.

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