Gestational Diabetes

State of the Union

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In November 1990 investigators and clinicians from around the world met in Chicago to participate in the Third International Workshop-Conference on Gestational Diabetes Mellitus. Representatives of various interested organizations, including the American Diabetes Association, American College of Obstetricians and Gynecologists, American Academy of Pediatrics, National Diabetes Advisory Board, Centers for Disease Control, and Diabetic Pregnancy Study Group of the European Association for the Study of Diabetes, were active participants. The proceedings were published as a supplement to *Diabetes* in the December 1991 issue. It would be impossible to review each of the 41 published articles in this brief commentary, but anyone interested in the current issues and controversies surrounding gestational diabetes should have a copy because it is a major source of information for years to come. A review of the highlights of the summary and recommendations, which comprise the last article in the supplement, should convey a sense of the issues that were dealt with.

The proceedings were dedicated to the memories of two very significant contributors to these meetings, and to our understanding of diabetic pregnancy in general. Dr. Norbert Freinkel, who had planned the first two International Workshop-Conferences, died ~1 yr before this most recent meeting. His death was a tragic loss for the medical and scientific communities, and a Memorial Symposium was held in his memory at the conference. Dr. Ronald Kalkhoff, cochairman of the workshop-conference, died shortly after the meeting was completed.

Four panels were formed to consider possible recommendations in the areas of *1*) diagnosis and prevalence, *2*) perinatal implications, *3*) long-range implications, and *4*) management strategies. Once the panels had reached consensus, their reports were presented to the entire group of >250 attendees. Somewhat lively discussions ensued, which led to a number of revisions.

With regard to screening and diagnosis of gestational diabetes, the group reaffirmed its support of universal screening with a 50-g 1-h glucose challenge at 24–28 wk, but acknowledged that the 7.8-mM (140-mg/dl) threshold for further testing was arrived at by consensus and may miss a proportion of individuals with gestational diabetes. Lowering the threshold to detect these additional cases would, however, entail a substantial increase in the number of full glucose tolerance tests to be performed, therefore the group did not alter the threshold recommendation. Similarly, the group acknowledged that the diagnostic thresholds for the 100-g 3-h oral glucose tolerance test (OGTT), converted from the O'Sullivan and Mahan (1) criteria, which were recommended at previous conferences, probably overcorrected for method changes. Because, as described herein, there was a consensus favoring the collection of data leading to the formulation of new criteria for gestational diabetes, the group decided not to recommend lowering the current criteria at the present time.

The panel made some practical recommendations, including the suggestion that a plasma glucose value ≥11.1 mM (200 mg/dl) in a situation that is not a formal OGTT or a truly fasting plasma glucose ≥7.8 mM (140 mg/dl) suggests the diabetic state and warrants further investigation. This investigation might consist of fasting and postprandial glucose measurements. If such tests are normal, then a formal OGTT may be in order. Furthermore, the panel recognized that the recommendation for screening at 24–28 wk should not preclude earlier testing if there is a strong index of suspicion. As in the previous set of recommendations, the use of test strips and reflectance meters for screening and diagnostic testing was discouraged because of insufficient precision and accuracy.

The panel devoted most of its time to outlining the need for prospective carefully controlled studies, with well-defined outcome criteria, to derive thresholds for the 75-g OGTT to diagnose gestational diabetes. It is hoped that international use of the same glucose challenge will allow for comparability of data between the pregnant and nonpregnant state, and among different populations. Most importantly, those in attendance strongly believed that future diagnostic criteria should be based on objective measures of pregnancy outcome.

The panel on Perinatal Implications noted that with the current approaches to management fetal death rates in gestational diabetic pregnancies appear to be no higher than those in the general population. They devoted most of their discussions to perinatal morbidity, in particular macrosomia. They cited increasing

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evidence, including that presented at the conference, that glucose is not the only important variable governing fetal growth, and suggested a potential role for lipids and amino acids. They identified as important areas for future research the development of better animal models for the morbidity of gestational diabetic pregnancy, identification of the most efficient markers for morbidity, development of a better understanding of the interactions of factors such as maternal obesity and metabolism in producing macrosomia, and an elucidation of the mechanisms and importance of placental fuel transfer. Clinically, more information is needed about the best way to select the mode of delivery in women with gestational diabetes.

The panel on Long-Range Implications of Gestational Diabetes observed that the association of gestational diabetes mellitus with increased risk of later overt diabetes in the mother has now been established without doubt and emphasized the responsibility of caregivers to educate women with gestational diabetes about this risk and the need for follow-up at regular intervals to detect developing diabetes, particularly in preparation for any future pregnancy. The panel also noted studies, including those presented at the conference, showing a link between gestational diabetes and macrosomia in the neonate and obesity in adolescence. A greater likelihood of glucose intolerance developing in the offspring was also supported. Particularly intriguing were the data presented at the conference suggesting that alterations of maternal fuel metabolism during pregnancy may have adverse effects on neurobehavioral development at birth and in early childhood. These issues clearly require greater amplification before our understanding can be considered complete, and the panel made many recommendations for the directions future research ought to take.

The final panel was charged with considering Management Strategies. There was some disagreement whether self-monitoring of blood glucose should be recommended as standard for women with gestational diabetes. After consideration of the fact that 2–3% of pregnant women in the U.S. have this condition, and of the cost in both dollars and human resources of implementing such a strategy for all such patients, the following compromise was reached:

> "In addition to the use of venous plasma, the self-monitoring of capillary blood glucose (SMBG) has been useful in allowing the woman to participate in her own management. SMBG may contribute to behavior modification in management. It was noted that the utility of SMBG in the patient with mild GDM not requiring insulin, although reasonable and logical, has not been formally proved and its costs and benefits require study."

With regard to nutritional therapy, the conference acknowledged recent revisions in the recommendations for nutrition during pregnancy promulgated by the National Academy of Science/Nutrition Research Council, specifically the prescription of a diet based on body mass index, and the recommendation that routine nutritional supplementation consist of elemental iron (i.e., routine multivitamin supplementation is not recommended). The need for more data regarding the safety and efficacy of hypocaloric diets for obese women with gestational diabetes was emphasized, and the consideration of other aspects of diet beside caloric requirements was suggested.

Current recommendations for the institution of insulin therapy when fasting plasma glucose exceeds 5.8 mM (105 mg/dl) and/or 2-h postprandial values exceed 6.7 mM (120 mg/dl) were cited, but data supporting the upper limit of normal for fasting plasma glucose being <5.8 mM, and data suggesting a salutary effect of insulin treatment on birthweight and the frequency of macrosomia were acknowledged. More research regarding the optimal method of selecting individual patients for insulin therapy was recommended. Exciting new developments in the use of exercise as a possible substitute or adjunct to insulin were reported, but again a note of caution was sounded in the suggestion that more data are needed before this becomes standard care. The urgent need for national and international cooperative clinical trials of various means of intervention was the primary recommendation of this panel.

The summary and recommendations ended with a call for timely and effective implementation of the recommendations made. The need for support, including funding, for the many studies that are needed was underlined, and it was suggested that various national and international bodies, listed in the summary, be approached.

It may be disappointing to some readers that more definitive recommendations and conclusions were not made. However, a perusal of the reports contained in the supplement to *Diabetes* and a comparison with the results of the First International Workshop-Conference in 1979 (*Diabetes Care* 3:499–501, 1980), should reassure the reader that much progress has been made in the last 10 yr. Evidence has accumulated from both animal models and clinical studies that gestational diabetes has both immediate and long-term effects on the progeny. New approaches to therapy have been developed and are now being evaluated. Diagnostic criteria are in the process of refinement. We should anticipate the Fourth International Workshop-Conference (not yet even in the planning stages, but certain to take place) with excitement and enthusiasm.

References

1. O'Sullivan JB, Mahan CM: Criteria for the oral glucose tolerance test in pregnancy. *Diabetes* 13:278–85, 1964