



**Article:**

D. Sacks.

*Diagnosis of Gestational Diabetes Mellitus: It Is Time for  
International Consensus*

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**Guest:**

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Bob Barrett:

This is the podcast from *Clinical Chemistry*. I am Bob  
Barrett.

Gestational diabetes mellitus is often defined as any degree  
of glucose intolerance during pregnancy. Fetal complications  
and adverse outcomes for both the fetus and the mother are  
important concerns in gestational diabetes.

The January 2014 issue of *Clinical Chemistry* is devoted to  
the area of Women's Health, and in that issue Dr. David  
Sacks published an opinion article on the need for  
international consensus on the diagnosis of gestational  
diabetes mellitus.

Dr. Sacks is Chief, Clinical Chemistry Service at the  
Department of Laboratory Medicine, National Institutes of  
Health, Bethesda, Maryland, and he is our guest in today's  
podcast.

Welcome back Dr. Sacks. What exactly is gestational  
diabetes and why does it need to be identified?

Dr. David Sacks:

Gestational diabetes is defined as any degree of glucose  
intolerance that has its onset or its first recognition during  
pregnancy.

So this is distinct from the other forms of diabetes which are  
termed Type 1 or Type 2, which are the most common  
forms.

So a woman who already has diabetes prior to becoming  
pregnant is not deemed to have gestational diabetes.

The need to identify gestational diabetes is because it's  
associated with complications to both the mother and the  
baby.

For the baby these complications include macrosomia which  
is, just means a large baby, but as you can imagine if the  
baby is very large, it can result in birth injuries during its

passage through the birth canal. And of course this results in an increased prevalence of cesarian sections for the mother because of the potential problems of normal birth.

The babies also have hypoglycemia or low glucose, frequently, soon after they're born because of the high insulin in the mother.

The mothers' risks, in addition to the cesarian section, include complications of pregnancy, hypertension during pregnancy, and a condition called preeclampsia which can be potentially life-threatening.

The other potential complication for the mother is that the mothers are at significantly increased risk of developing Type 2 diabetes after the pregnancy.

In terms of the prevalence of the condition, the published literature ranges from less than 1% of the pregnant women have gestational diabetes to as high as 28%, and I'll return to this point later in this podcast.

Bob Barrett: How is the diagnosis of gestational diabetes mellitus made in practice?

Dr. David Sacks: Well, it's generally agreed that it should be done in pregnant women between 24 and 28 weeks of gestation, but there is a problem as to how exactly it should be diagnosed.

Although pregnant women have been evaluated for gestational diabetes for more than 50 years and there have been five international workshops held since 1979, there is no consensus regarding the best method to identify patients.

The criteria for screening for gestational diabetes and for diagnosing gestational diabetes vary widely among countries, and often between different organizations in a single country.

So, in some countries the diabetes organization has one set of criteria and the obstetric organizations have another set of criteria.

In terms of screening, the recommendations range from none, so patients should not be screened; some countries have selective screening where you screen only those at high risk; and some organizations advocate universal screening. Screening can be done either by a fasting glucose, random glucose or a glucose challenge.

Now, the diagnosis is made with an oral glucose tolerance test. In 1964, O'Sullivan and Mahan derived criteria that are the basis for the majority of diagnostic approaches used.

It's important to know a little bit about this study since this is so fundamental to diagnosis of gestational diabetes.

What they did was they took 752 unselected asymptomatic pregnant women, and all of them had a 3-hour oral glucose tolerance test. They defined gestational diabetes as two or more values that were more than two standard deviations above the mean.

So these arbitrary criteria were actually established to predict the subsequent development of diabetes after the pregnancy and they were not designed to identify pregnancies with adverse outcomes such as complications to the mother or to the baby.

Now while the oral glucose tolerance test is universally used for diagnosis, there again is no agreement.

For example, the glucose load can be either 100 gm of glucose or 75 gm. The test duration varies widely ranging from two hours to three hours and the number of high values that are accepted for diagnosis range between 1 and 2.

So you can see that a large number of different combinations are possible regarding the diagnosis.

Bob Barrett: Talk a bit about the Hyperglycemia and Adverse Pregnancy Outcome study or the HAPO study.

Dr. David Sacks: So the HAPO study was designed because of the flaw in the diagnostic criteria. As I mentioned these were based on the risk of future hyperglycemia not on outcomes of the pregnancy.

The HAPO study which was published in 2008 is a remarkable study. The objective was to determine the relationship between the concentration of glucose in the mother's blood and adverse pregnancy outcomes.

It was a perspective randomized multi-national study that included remarkably 23,316 women. As you can imagine, the logistics to carry this out were phenomenal.

All of these women underwent an oral glucose tolerance test which was performed by giving 75 gm of glucose, somewhere between 24 and 32 weeks of gestation.

And then they looked at the outcomes in terms of the complications to the baby, as I mentioned macrosomia neonatal hyperglycemia and also the mother for example cesarian section.

So what the study observed was that the risk of adverse outcomes to the mother, the fetus, and the baby increased continuously as the mother's glucose increased.

Unfortunately, there were no thresholds at which the risk increased considerably so there are no convenient cutoffs.

Another factor that's very important is that each of the three values in the oral glucose tolerance test had an independent contribution to adverse outcome. So that is the fasting, the one hour, and the two hour values in glucose, each contributed independently to adverse outcome.

Now to translate the results of the HAPO study into clinical practice, the International Association of Diabetes and Pregnancy Study Groups, termed IADPSG, sponsored a workshop to develop recommendations for the diagnosis of gestational diabetes.

And on the basis of the HAPO study, the panel suggested that a 75 gm oral glucose tolerance test be performed, and that gestational diabetes be diagnosed if any one of the values for fasting glucose, one hour glucose, or two hour glucose, equaled or exceeded the diagnostic threshold. And these thresholds are 92 mg per deciliter for fasting, 180 for the one hour sample and 153 for the two hour sample. In SI units, these would be 5.1 for fasting, 10.0 for one hour, and 8.5 for two hours.

The IADPSG guidelines had been adapted by the World Health Organization and are in use in several countries, for example Germany, Italy and Australia.

In United States they have been adapted by the American Diabetes Association and the National Association for Clinical Biochemistry. They have not been adapted by the American College of Obstetricians and Gynecologists.

Bob Barrett: And there appears to be some controversy about that. Why is there controversy surrounding the adaption of the criteria to diagnose gestational diabetes mellitus?

Dr. David Sacks: The thresholds actually differ very little from the thresholds that we used previously in the oral glucose tolerance test.

However, the prevalence of gestational diabetes in the United States would increase from approximately 7% to

18%, that is from about 250,000 women to 640,000 per year.

The reason for this is that the prior criteria during the oral glucose tolerance test required at least two of the values to be increased, so that is the fasting plus the one hour or the two hour, or just the one hour and the two hour. The IADPSG criteria require only one of the values to increase.

So because of this, there will be a large increase in the number of patients with gestational diabetes which will result in a considerable increase in the cost to society.

Another reason for the controversy is that some people say, and this is true, that there are -- no perspective study has documented that the additional pregnant women who are identified by the HAPO criteria will benefit from therapy. So no perspective study has actually used the HAPO criteria to look at long-term outcomes. The HAPO study itself was merely an observational study.

However, a large study was published in 2009 in the *New England Journal [of Medicine]*, there were 950 or so patients, which was a multi-center randomized trial that looked at treatment for mild gestational diabetes, that is women who would not have been diagnosed with the standard criteria at the time, and it showed that treatment actually reduced some of the complications to the baby and to the mother.

I think that the big advantage of the IADPSG recommendations is that they are the first large scale evidence based guidelines for gestational diabetes that correlates the glucose concentrations in the mother to outcomes, as opposed to the prior guidelines which as I mentioned were based on the risk of the mother developing diabetes after the pregnancy.

Bob Barrett: Finally doctor, the title of your opinion piece in *Clinical Chemistry* is insistent that we need consensus now. Could you tell us why, what's the rush?

Dr. David Sacks: So I think the current situation for gestational diabetes reminds me of the large number of diagnostic criteria that existed for diabetes in non-pregnant individuals in the 1960s and 1970s and there was, at that time, considerable confusion regarding who had diabetes, and a large number of different criteria were in use.

The National Diabetes Data Group or NDDG developed recommendations which were published in 1979 for diagnosis, and this sort of unified the diagnostic criteria.

So the situation for gestational diabetes that exists currently makes it very difficult for clinicians to manage the condition. They can't determine the prevalence because the diagnosis varies.

As I mentioned earlier the prevalence in the published literature ranges very widely. Now part of that is due to differences in different countries, but obviously if you have different diagnostic criteria, you are not identifying the same people with the disease.

And this results in a potential problem for an individual patient where if they see one doctor who uses one set of diagnostic criteria, the doctor says you have gestational diabetes, whereas if that same patient with the same results goes to another doctor, the other doctor will say no you do not have the condition. So obviously this is a serious problem.

Consensus is also needed because it is difficult currently to establish the risk of progression to diabetes after delivery or to do any studies that look at possible variations among different ethnic groups and in fact it's very difficult to even compare published studies because of the different criteria used to establish diagnosis which makes it very difficult for clinicians to decide exactly how to manage the patients.

I think the reason why it is so important to have consensus is that a rational approach to define cutoffs for diagnosis, I think, should be based on the correlation of the blood glucose concentrations in the mother, and the risk of subsequent complications to the fetus, the baby, and the mother.

And I think having such an approach would enable clinicians to reduce both the morbidity and the mortality associated with gestational diabetes.

Bob Barrett:

Dr. David Sacks is Chief, Clinical Chemistry Service at the Department of Laboratory Medicine, National Institutes of Health, Bethesda, Maryland and he has been our guest on this podcast on gestational diabetes from *Clinical Chemistry*.

I am Bob Barrett, thanks for listening!