



Discussion

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Dr Catalano: Some recent literature has discussed iron supplementation in women during pregnancy and shown an increased risk of gestational diabetes. Another issue is related oxidative stress. Could this be a factor in placental function? Dr Poston, can you comment?

Dr Poston: There is a potential gestational diabetes increase related to the free iron and oxidative stress. Iron supplements should be given only to women who have demonstrated anemia.

Dr Godfrey: Although we tend to concentrate on nutrient preventive effects, which are important, the placenta also has an important role during pregnancy. We know that the placenta offers the fetus the big vascular circuit and that this alters the fetal cardiovascular system. And we know that altering loading of the fetal cardiovascular system has long-term effects on the coronary reserve. I think this is a ripe and important area. However, we need to think about timing when we assess nutritional effects on the placenta because broadly speaking, nutritional influences may be greater early in pregnancy than later in pregnancy.

Dr Christina Sherry [Abbott Nutrition]: Dr Ozanne, you briefly mentioned the role of adenosine monophosphate-activated protein kinase with exercise. What are your thoughts on exercise prescription during pregnancy?

Dr Ozanne: Clearly exercise improves insulin sensitivity, and both animal and human studies suggest that the insulin resistance of obese mothers is important. So targeting that, whether we do it by exercise or by pharmaceuticals, could be an important intervention.

Dr Sherry: What are your thoughts on whether exercise may have epigenetic modifications through a similar or different vein than diet?

Dr Ozanne: Nutrition and exercise may act through common epigenetic pathways to modify insulin sensitivity. We do not know about during pregnancy but we do know from a Swedish study that exercise results in epigenetic modification of one gene, the transcriptional coactivator gene PGC-1 alpha. So there are data that suggest that exercise does modify epigenetic markers, certainly particular genes. What precise range of genes, we do not know.

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Dr Poston: In our intervention, we are promoting exercise because it is one way to improve glucose tolerance without weight loss. I think that is important in the gestational weight-gain side of the story; it is possible to improve glucose homeostasis without necessarily losing a lot of fat mass.

Dr Catalano: A colleague of mine studied exercise in pregnancy longitudinally, looking at women before pregnancy and during pregnancy [Clapp JF et al. *Am J Obstet Gynecol.* 2000;183:1484-1488]. Not surprisingly, he found that those women who continued to exercise through pregnancy had babies that were not as heavy because they were not as obese, ie, they had less fat mass. But an interesting finding was that women who started to exercise and then stopped in the 3rd trimester because of physiological issues had larger placentas and heavier babies. And this was serious exercise as opposed to walking, close to 50% to 60% VO_2 max. My colleague theorized that hypoxia in pregnancy prevents increased growth of the placental vascularization, improving nutrient transport. Therefore, when the women stopped exercising, their placentas were programmed to increase nutrient transport, and those women ended up having heavier, fatter babies.

Dr Yajnik: The particular activity and level of daily physical activity in pregnant women in India is phenomenal. The average pregnant woman weighs 42 kg. They do not exercise in the gym, but they work at home with the animals on the farms. This is very strongly related to growth retardation in their babies, so in one part of the world exercise may have benefits, but in an undernourished population, exercise is detrimental.

Dr Poston: I was referring to women with a good nutritional status and who are obese.

Dr Godfrey: On the flip side of the coin, almost none of the women in the UK have high levels of strenuous exercise during pregnancy. And in the obese population, the pre-intervention levels of exercise are extremely low.

Dr Yajnik: It seems that certain types of activities such as bending are strongly related to growth retardation.

Dr Hanson: Dr Godfrey, did the Southampton Women's Survey not show that the children of women who are able to walk faster, to undertake more vigorous exercise, have lower bone density [Crozier SR et al. *Am J Clin Nutr.* 2010;91:36-43]?

Dr Godfrey: The thought is that if a woman walks fast, she exerts strength through her bones and thus retains calcium rather than allowing it to leach across to the fetus.



Dr Poston: I think we have to go with the guidelines in the United Kingdom and the United States stating that mild-to-moderate activity in pregnancy is safe and should be encouraged. Current evidence indicates that mild-to-moderate exercise in developed countries is good for pregnancy outcome. I would not like for this audience to think that severe exercise can increase miscarriage rate and so on.

Dr Hanson: This was not severe exercise.

Dr Godfrey: These were women who reported walking faster than average.

Dr Marriage: Did the researchers look at their calcium, vitamin D, and nutritional intake?

Dr Godfrey: We used ultrasound to look at the mothers' bones and found that those women who exercised, who walked faster, tended to retain their calcium in their own bones.

Dr Robert Miller [Abbott Nutrition]: Dr Poston, I want to go back to the model you started with in which you were challenged by undernutrition and then overnutrition. Did I hear correctly that there are 30 million undernourished babies?

Dr Poston: Thirty million babies born small for gestational age.

Dr Miller: And there are how many total births worldwide? There are 24 million in India and 16 million in China, so I think the global figure is around 70 million. So 30 million is nearly half. Then around 8 million are obese. So the 32 million in the middle should be optimally nourished. Is there a definition of optimal or ideal in the middle?

Dr Poston: Not by those criteria because they are based on birth weight. I think we have to be careful about that. It would be nice to be able to define optimal nutrition, but that would be enormous work.

Dr Hanson: I am not happy with this overnutrition and undernutrition dichotomy. I think we probably should think in terms of balanced nutrition and unbalanced nutrition. A lot of women in this country and certainly in mine have plenty of food but they still have a poor, unbalanced diet. Another caveat is that we are talking about pregnancy and nutrition, but mostly we have talked about mothers when what we really want to know is what the baby is getting. That is a different story.

Dr Poston: That is right. I hope I made it clear that even in cases of nutritional excess there can be micronutrient deficiency. Teenage girls often have huge calorie

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excesses, but many of them also have marked micronutrient deficiencies. It is hard to define undernutrition and overnutrition.

Dr Miller: Dr Hanson, this relates to what you said about plasticity. Could you map plasticity temporally in conception, gestation, and then birth? Is there any way of knowing what that looks like in a global perspective? If so, we could understand when, over time, we can have the greatest impact.

Dr Hanson: That is a good question. I do not think we know for each tissue, but I suppose we would tend to map it for the whole organism in terms of an exponential or reciprocal decline in plasticity, and accompanying that, an increase in the risk of disease through an inability to respond and be plastic to new challenges. But the timing of that would depend on organs and history that goes back over more than one generation.

Dr Godfrey: Plasticity is generally greater earlier on, but it is tissue-specific. The velocities for maximal growth of the femur bone are different than those of, for instance, the kidney and the placenta. Bones have periods of high velocity between 13 and 19 weeks' gestation, and then again during puberty.