

## MASTER CLASS

## Complications of Obesity in Pregnancy



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Obesity is one of the world's fastest growing and most insidious pandemics. At least 400 million adults worldwide, and one-third of adult Americans fit the criteria for obesity (JAMA 2010;303:235-41). Indeed, obesity is increasingly being diagnosed at earlier ages; it is estimated that between 16% and 33% of U.S. children and adolescents are obese.

It is particularly distressing when obesity impacts women of child-bearing age because they, along with their offspring, are the populations most vulnerable to the consequences of obesity. There are many long-term, downstream consequences of obesity for pregnant women, including a significantly higher risk of developing type 2 diabetes, hypertension, and cardiovascular dis-

ease. Additionally, the offspring of these women face significant health consequences in utero, during birth, as well as for many years afterward. Children born to obese women are more likely to be large for gestational age, delivered by cesarean section, or have birth defects and are at significantly greater risk of becoming obese and developing obesity-related complications, such as type 2 diabetes, in adolescence and adulthood.

Because obesity is so prevalent among women of child-bearing age, we have decided to devote a Master Class to discussing the potential complications of obesity during pregnancy and how best to manage and/or prevent those complications. The goal is to give practitioners the basic knowledge they need to identify those at-risk obese patients so they can institute appropriate preventive and therapeutic measures.

Patrick Catalano, M.D., professor and chair of the department of reproductive biology at Case Western Reserve University, is one of the world's leading experts on

the short- and long-term consequences of obesity for pregnant women and their offspring. He served on the Institute of Medicine committee that in 2009 reexamined guidelines on weight gain during pregnancy. He also is leading the effort to inform physicians and the public about the costly complications of obesity in pregnancy and in finding ways to prevent these complications from occurring in the first place. Dr. Catalano's research focus is on insulin resistance and glucose metabolism in pregnancy and the role of placental cytokines in the regulation of fetal growth and adiposity. ■

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## Managing Obesity During Pregnancy

Obesity is a worldwide epidemic with management implications that are more urgent than ever for obstetrics. The latest data from the Centers for Disease Control and Prevention show a prevalence of obesity that surpasses 35% in U.S. women of reproductive age.

## Implications of Obesity

The potential maternal, fetal, peripartum, and neonatal complications in our obese pregnant patients are numerous. Studies have shown that the obese woman has a significantly increased risk of early miscarriage (an odds ratio of 1.2) and recurrent miscarriage (OR of 3.5), compared with a normal-weight woman after natural conception (Hum. Reprod. 2004;19:1644-6). The risk of congenital anomalies also rises in obese women. In a recent meta-analysis, obese mothers were at significantly increased risk of having a child affected by a neural tube defect (OR 1.9), spina bifida (OR 2.2), cardiovascular anomalies (OR 1.3), and other anomalies, compared with body mass index (BMI)-appropriate mothers (JAMA 2009;301:636-50). In a prospective, multicenter study of more than 16,000 women, obese women and morbidly obese women were 2.5 and 3.2 times, respectively, more likely to develop gestational hypertension than nonobese women. They also were 1.6 and 3.3 times more likely, respectively, to develop preeclampsia. Gestational diabetes was 2.6 and 4 times more likely to occur in obese and morbidly obese women, compared with normal-weight pregnant women (Am. J. Obstet. Gynecol. 2004;190:1091-7).

Obesity also increases the risk of indicated preterm delivery, caused by complications such as preeclampsia and diabetes. The risk of cesarean delivery and associated morbidities increases as well,

as does the risk of macrosomia and fetal overgrowth (an increase in adipose tissue rather than lean body mass).

Macrosomia then perpetuates the problem of obesity in the offspring. Evidence clearly points toward an increase in adolescent and adult obesity in infants

who are born either large for gestational age or who are macrosomic.

Excess maternal weight gain, particularly in average-weight women, is also a risk factor for excess birth weight (Obstet. Gynecol. 2008;112:999-1006).

There has been increasing awareness over the past decade, moreover, of the role that maternal obesity may play in unexplained antepartum fetal death. At least two studies—one in a Canadian population and one in a Danish National Birth Cohort—have shown that maternal pregravid weight increased the risk of unexplained fetal death, even in women without medical or obstetric complications (Obstet. Gynecol. 2000;95:215-21, and Obstet. Gynecol. 2005;106:250-9).

## Managing the Obese Patient

Vigilant management of the obese pregnant woman is critical not only for the woman and her baby, but for future generations as well. We must increase our attentiveness to and surveillance for all the risks that obesity poses during pregnancy, and must think preventively during comprehensive preconceptional and postpartum care, with the goal of breaking the vicious cycle of obesity.

Until we gain a better understanding of underlying genetic predispositions, physiology, and mechanisms relating to maternal and fetoplacental interactions that affect fetal growth and development, all treatments in obese pregnant women must be empiric. However, we need to build upon the information we currently possess because waiting may not be an option.

Here are some of the key components of effective obesity management in pregnancy:

► **Appreciate that obesity is treatable.** Certainly, women should aim to conceive while at a normal body mass index (BMI). Our ability to manage obesity preconceptionally is constrained by the fact that many pregnancies are unplanned. However, when given the opportunity, we must encourage and help facilitate weight loss before pregnancy.

With proper counseling, some obese women can indeed achieve meaningful weight loss before conception. We know that lifestyle measures involving both nutritional counseling and exercise are more beneficial than either approach alone. The American College of Obstetricians and Gynecologists has practical guidelines on how to assess and manage obesity in the nonpregnant woman ("The Role of the Obstetrician Gynecologist in the Assessment and Management of Obesity," Committee Opinion Number 319, October 2005).

We also must treat obesity as a problem itself, with an individualized, patient-centered approach. This point was stressed in the report on weight gain in pregnancy issued last year by the Institute of Medicine and National Research Council (www.nap.edu, "Weight Gain During Pregnancy: Reexamining the Guidelines").

As obstetricians we tend to home in during pregnancy on the complications of obesity while overlooking the underlying problem. We also are less likely to think about individualized, patient-centered treatment for a woman who is overweight or obese as we would for a woman with a more straightforward problem like gestational diabetes. We need a change of mind set.

If a woman enters pregnancy obese, limiting her weight gain to recommended levels will help lower her risk of various complications and reduce postpartum weight retention. Exercise and other lifestyle changes will also improve insulin

use in women with diabetes.

In the postpartum period, we must help women meet the important goal of returning to their prepregnancy weight, and then encourage them to lower their weight before the next pregnancy, referring them to specialists if necessary to break the cycle of obesity.

Breastfeeding is an important tool to reducing postpartum weight retention—it increases caloric utilization by 500-800 calories per day and has short- and long-term benefits for both the mother and the baby. We must appreciate, however, that it is technically more difficult for an obese woman to breastfeed, compared to a nonobese woman. The obese patient may need special help from a lactation consultant.

► **Think inflammation and insulin resistance.** In the pregravid state, an obese woman has increased inflammation and more insulin resistance to begin with. Her inflammatory profile and level of insulin resistance then only increases in pregnancy. (There are significant 50%-60% decreases in maternal insulin sensitivity by the end of the third trimester.)

Increased insulin resistance in pregnancy, studies show, can drive an excess flow of nutrients to the fetus and lead to macrosomia. Insulin resistance also may increase the risk of preeclampsia and gestational diabetes.

Although insulin sensitizers such as metformin or thiazolidinediones theoretically may be useful for increasing insulin sensitivity, these agents cross the placenta and their fetal safety has not been documented. This brings us back to lifestyle interventions to improve insulin resistance—a calorie-appropriate diet that is low in saturated fat and high in complex carbohydrates, for instance, along with exercise that uses large skeletal muscles, such as walking and swimming.

The role of dietary supplements such as fish oil and vitamin D in decreasing inflammation and improving metabolic function are currently under investiga-

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tion. While we do not believe either causes any harm, it is too early to make official recommendations. At this point, we must focus on lifestyle interventions as our primary management approach.

► **Pursue early glucose testing, and tight glucose control in patients with gestational diabetes mellitus (GDM).** Women who are obese should be considered for early glucose screening rather than waiting until the 24- to 28-week standard screening period. Such early screening enables the detection of undiagnosed type 2 diabetes, or overt diabetes, and is the new recommendation of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) for the diagnosis of GDM (Diabetes Care 2010;33:676-82).

When results from early screening are normal, testing should be repeated later. If either pregestational diabetes or gestational diabetes is detected, tight glucose control should be the goal.

A recent paper from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study suggests there are strong independent associations of fasting C-peptide (an index of insulin sensitivity) and BMI with preeclampsia. Maternal glucose levels in this study (levels below those found in diabetes mellitus) had weaker associations with preeclampsia (Am. J. Obstet. Gynecol. 2010;202:255.e1-7).

Other data show that tight glucose control in obese women with diabetes may decrease the risk of preeclampsia and other complications.

► **Limit weight gain in pregnancy.** Although pregravid weight, rather than weight gain during pregnancy, has the strongest correlation with the complications of maternal obesity in pregnancy and with birth weight, maternal weight gain during gestation still is positively correlated with excess birth weight and with various complications.

At minimum, we can work with women on limiting weight gain in pregnancy and following the new guidelines published last year by the Institute of Medicine and National Research Council. The report, which updates the previously published guidelines from 1990, specifies a new weight gain range for obese women, limiting their gain to 11-

20 pounds during pregnancy.

Studies published after the previous guidelines were released in 1990 have consistently shown that women who gain weight within the recommended amounts have better outcomes. Women who do not gain excess weight also are less likely to retain extra pounds after birth.

Research also has shown, however, that a high proportion of women report that they were either given no advice on how much weight to gain or were advised to gain outside of their recommended range.

Indeed, an increasingly large proportion of women has gained in excess of the recommendations: From 1993 to 2003, the proportion of overweight women gaining in excess of the 1990 IOM recommendations increased to approximately 63%; approximately 46% of obese women gained excess weight.

Given the IOM's lower weight gain recommendation for obese women, such proportions will likely rise unless we increase the counseling we give patients on weight, diet, and exercise, and unless we routinely record and discuss patients' weight, height, and BMI.

More recent studies have focused on interventions to help women limit their weight gain during pregnancy. Although none of the four trials conducted in North American populations and reviewed by the IOM was completely successful in helping women limit their gestational weight gain and adhere to the 1990 guidelines, two European studies demonstrate that it's possible to motivate obese pregnant women to limit their weight gain during pregnancy to 6-7 kg. The interventions involved individual dietary or motivational counseling, and in one of the studies, the provision of specially designed aqua aerobics classes.

In general, interventions described in the literature have included counseling, the provision of unique physical activity classes, dietary prescription, and even daily recording of dietary intake.

► **But do not encourage weight loss.** Some investigators have recently proposed that obese women should consider weight loss during pregnancy in order to decrease adverse perinatal outcomes. It is my opinion that while women should avoid excessive weight gain, they should not be advised to lose weight un-

### Weight Gain Recommendations

Prepregnancy BMI	BMI (kg/m <sup>2</sup> )	Total weight gain (lb)
Underweight	<18.5	28-40
Normal weight	18.5-25	25-35
Overweight	25-30	15-25
Obese	>30	11-20

Source: Institute of Medicine

til additional investigation shows that there are benefits and no adverse consequences to the mother and/or fetus.

There are obligatory physiological changes that for most women result in a "net maternal weight gain": on average, 4-5 kg of weight at term represents the fetus, the placenta, and amniotic fluid.

For reasons that we don't fully understand, some obese women do not gain weight during pregnancy, or may actually lose weight, and still have a healthy baby. These women may have a decrease in energy expenditure in pregnancy and a subsequent decrease in intake, and/or there may be other physiologic issues at work.

As long as such a patient is eating well, seeing a nutritionist, and does not have ketonemia/ketonuria, and her baby is growing well, I would not encourage excessive intake in order to meet a particular weight gain target. I would just monitor her carefully.

The bottom line: Until we learn more about the safety of intentional weight loss during pregnancy, we face a delicate balancing task. On one hand, we need to appreciate that some women do not gain weight during pregnancy and should not necessarily be urged to gain an arbitrary amount while, on the other hand, we should not encourage these women to lose weight.

► **Consider bariatric surgery to be a tool in your armamentarium.** Population studies and reports of long-term outcomes from the United States and Scandinavia suggest that bariatric surgery has potential long-term benefits—in terms of weight loss and improvement in metabolic function—for women of reproductive age who do not have success with lifestyle measures and medical treatments.

In our practice, we often refer women after delivery to see our obesity specialist, who institutes medical therapy and will move on to consideration of bariatric surgery if the medical therapy is not successful. Experts have determined that bariatric surgery may be considered in women with a BMI greater than 35 (class II obesity) who have significant medical problems such as hypertension or diabetes, or in women who have a BMI greater than 40 (class III obesity) and no obvious medical complications.

ACOG's committee opinion No. 315 from 2005 includes various recommendations about how long to delay pregnancy after surgery (12-18 months after laparoscopic adjustable gastric banding, for example), and what vitamin supplementation is necessary. Women who have laparoscopic adjustable gastric banding should be monitored by both their obstetrician and bariatric surgeon during pregnancy, according to the

ACOG committee's recommendations (Obstet. Gynecol. 2005;106:671-5).

► **Don't "miss the forest for the trees."** When encountering various complaints and problems during pregnancy, think of the underlying obesity and not only the effects of pregnancy. Because obese women have an increased risk of developing or having manifestations of the metabolic syndrome—hypertension, proteinuria, dyslipidemia, and diabetes—we are seeing an increase in medical problems that in the past have been diagnosed primarily in older nonpregnant patients. Sleep apnea and nonalcoholic fatty liver disease are examples.

A woman who has shortness of breath or declining levels of oxygen saturation post partum, particularly after a cesarean delivery, may actually have sleep apnea, for instance, rather than a pulmonary embolism or pregnancy-related changes in tidal volume.

Similarly, elevated liver function tests may be an indication of nonalcoholic fatty liver disease rather than a manifestation of severe preeclampsia or the HELLP syndrome. Non-alcoholic fatty liver disease is actually the most common reason today for a woman of reproductive age to have elevated liver function tests. Increasingly, it is becoming a more common diagnosis in the obese patient. Obesity, increased estrogen concentrations, elevated lipids, and increased insulin resistance have all been recognized as factors contributing to the development of non-alcoholic fatty liver disease.

► **Up the ante on kick counts.** Because the risk of stillbirth is significantly increased in the obese pregnant woman (even the patients without hypertensive disorders or other complications), fetal monitoring with kick counts is all the more important.

The cost/potential benefit of more extensive evaluation is unclear for the obese woman without any medical or obstetric complications (and fetal assessment is more difficult in the obese patient), but certainly a lower threshold for more formal testing should be considered for women who do have complications and for women in whom a "red flag" is raised.

A patient whose baby appears to be very large on ultrasound or in the clinical exam, for instance, or a patient whose baby is well above the 90th percentile too early in gestation might benefit from more formal evaluation of fetal well-being, even if glucose and blood pressure tests are normal.

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### Prevalence of Obesity Among U.S. Adults, 2008

