Effects of obesity on women's reproduction and complications during pregnancy

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Received 10 March 2004; revised 24 May 2004; accepted 2 June 2004

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Summary

Obesity is increasing rapidly among women all over the world, and more women in fertile ages become overweight and obese. Among all other problems, women who are obese have higher rates of amenorrhoea and infertility. Obese women have a higher risk of complications during pregnancy such as hypertensive diagnoses and gestational diabetes, and delivery complications such as higher rates of caesarean sections and prolonged time of delivery. The aim of this article is to review the consequences of being obese during the reproductive life of a woman.

Keywords: Obesity, pregnancy, weight gain.

obesity reviews (2004) **5**, 137–143

Introduction

Obesity is increasing rapidly among women all over the world (1–5), and more women in fertile ages are becoming overweight and obese. In USA the prevalence of overweight and obese women in the age group of 18–49 was 44% and a study from the United Arab Emirates reported that nearly 40% of married women are obese (6,7). In Sweden the percentage of overweight women has increased from 9% in 1980/1981 to 12% in 1996/1997 (7). In the Swedish sample the largest proportional change was for women aged 16–44 years, among whom the prevalence of overweight doubled. Overweight women also have similar comorbidity and stigmata as men (8,9), but also have some problems related to their gender. These gender-specific problems start in puberty with amenorrhoea and dysovulation and continue until after menopause with higher incidence of endometrial cancer and breast cancer, as listed in Table 1 (10–12).

Among all other problems, women who are obese have higher rates of amenorrhoea and infertility (13–15). Obese women have a higher risk of complications during pregnancy such as hypertensive diagnoses and gestational diabetes and also have delivery complications such as higher rates of caesarean sections and prolonged delivery. Their obesity may also affect the health of their child in a negative way (4,16).

The aim of this article is to review the consequences of being obese during the reproductive life of a woman.

Infertility

Obese women have a higher prevalence of amenorrhoea and infertility (15,17–20). In the Nurses Health Study, women with a BMI > 30 had a 2.7 times higher risk of infertility problems compared with normal weight women. It was also clear that obesity in combination with smoking had a negative impact on fertility (19).

Obesity alone was not a cause of delayed conception. The same association was found in underweight women (15).

The risk of miscarriage in obese women was also found to be higher (14,21,22). Hamilton-Fairley *et al.* found that the risk of miscarriage before the first living born child was 25–37% higher in obese women (23).

Unfortunately, obesity has a negative impact on the treatment of infertility. Obese women who are treated for their infertility problems at infertility clinics are less likely to get pregnant and if they do become pregnant after *in vitro* fertilization (IVF) treatment, their risk of early pregnancy loss is greater (19,24–26).

On the other hand, weight loss has a very positive effect on the likelihood of women conceiving (13,27–29). In an Australian study, women attended a weekly programme

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Table 1 Diseases and conditions associated with overweight and obesity

General
Choice of contraceptive pills
Hyperandrogonadism
Amenorrhoea
Dysovualation
Infertility
Hyperinsulinaemia
Polycystic ovary syndrome
Depression
Endometrial cancer
Breast cancer
During pregnancy
Gestational diabetes
Hypertension
Preeclampcia
Dyslipidaemia
Impaired endothelial function
Back pain
Preterm delivery
More induced deliveries
Prolonged delivery
Vulval or perineal tears
Caesarean section and its complications
Thromboembolism
Effects on baby
Spina bifida
Microsomia
Head trauma
Shoulder dystocia
Brachial plexus lesion
Fracture of the clavicle
Increased perinatal mortality
Haemorrhage after delivery
Menopause
Choice of hormone replacement therapy

aimed at lifestyle changes in relation to exercise and diet for 6 months. These women had from the beginning a mean BMI of 37.4 ± 6.9 and lost an average of 10.2 ± 4.3 kg. Sixty of the 67 anovulatory subjects resumed spontaneous ovulation, 52 conceived (18 spontaneously) and 45 of the women delivered a baby. The cost savings of the programme were considerable. Prior to the programme, the 67 women had had treatment costing a total of A $550 000 to achieve a total of two live births, a cost of A $275 000 per baby. After the programme, the same women required treatment costing a total of A $210 000 for 45 babies, a cost of A $4600 per baby (27).

Polycystic ovary syndrome (PCOS)

PCOS is a common endocrine disorder in pre-menopausal women and it is estimated that between 5% and 20% of all women suffer from PCOS (30,31). Fifty per cent of women who have PCOS are overweight (32), but the interaction between obesity and PCOS is not fully understood. PCOS is a syndrome characterized by overweight, insulin resistance, infertility, irregular menstruation, hirsutism, acne, male-pattern hair loss, as well as polycystic ovaries.

It is still unclear if obesity leads to PCOS or if the opposite is true. It has been reported that women with PCOS seem to have difficulty dealing with energy balance and have a self-reported strong hunger, increased tendency to gain weight, and to suffer from eating disorders, particularly bulimia (33–35). This would suggest that PCOS is the primary event, leading to BMI increase.

PCOS is often associated with high levels of cholesterol and blood sugar, which in turn lead to cardiovascular disease and type 2 diabetes and the metabolic syndrome (13,36–38). Therefore women with PCOS should be treated as a high risk group for the metabolic syndrome (39). Also in women with PCOS the benefit of weight loss is great (40,41). A weight loss of more than 10% leads to an increased frequency of spontaneous ovulation, increased rate of conception and fewer miscarriages (13,41).

Recently, metformin, a drug primarily used in the treatment of type 2 diabetes, has been used to treat women with PCOS. Metformin is first choice therapy in the treatment of overweight and obese type 2 diabetics, because it has a weight-reducing effect of unclear genesis. As women with PCOS often have high insulin resistance, the effect of metformin on PCOS has been studied and today, many gynaecologists and endocrinologists prescribe it for this group of patients with a reported good effect (42). The problem is that the studies are small and often uncontrolled. To date, no large study has been published. Harborne *et al.* concluded in a recently published review that sufficient evidence for treating PCOS with metformin is lacking and more research is needed before any recommendation can be made (43).

Normal weight gain during pregnancy

Weight gain during pregnancy, because of the weight of the foetus, placenta, breast growth and expanded blood-volume, has been calculated to be around 9.1 kg (44). Any additional gestational weight gain is an energy reserve for the mother to nourish her child. During pregnancy, women's appetites increase and increased body fat becomes a buffer of over 30 000 kcal against the possibility of nutrition deprivation in late pregnancy, when foetal demands increase rapidly. This mechanism may have evolved and have been of great protective value at a time when food supplies were uncertain and there was a need for pregnant women to perform hard physical work, as is still the case in many developing countries today.

The actual total pregnancy weight gain has varied over time. In 1944 Chesley (45) reviewed the literature from the 1800s until 1943 and reported an average weight gain

during pregnancy of 10.9 kg. In the 1980s several studies reported a mean weight gain of 13–15 kg (10,23–27).

Recommendations of weight gain during pregnancy

The recommendations of weight gain during pregnancy have changed considerably over time. In the 1950s the recommended total weight gain during pregnancy was 7–8 kg. The rationale for this recommendation was to prevent macrosomia and complicated deliveries (46). But when caesarean section became common clinically and alleviated these problems, the recommendations became more liberal and women were allowed to gain more weight. However, in the beginning of the 1990s the Institute of medicine (IOM) recognized high weight gain during pregnancy and obesity as an obstetric problem (47). However, the IOM recommendations only focus on the well-being of the foetus. The recommendations are based on prepregnancy weight and range from 6.8 kg for overweight women to an upper limit of 18 kg for underweight women (Table 2).

Overweight and weight gain during pregnancy

As overweight women already have a weight problem from a clinical perspective, there is a fear that overweight women will gain additional weigh during pregnancy. A number of studies have investigated the relationship between pre-pregnant weight or BMI and weight gain during pregnancy (48–53). Some found no consistent relationship between pre-pregnant weight and weight gain during pregnancy (50,51,54) whereas others did (52,55,56).

Abrams & Laros (54) evaluated 4674 women with 'good' pregnancy outcomes. Pre-pregnancy BMI groups were constructed as underweight (BMI < 19.2), normal weight (BMI 19.2–25.6), overweight (BMI 25.6–28.9) and obese (BMI > 28.9). Compared to the normal weight group, the underweight group gained on average 0.65 kg less, while the very obese group gained 2 kg less. However, the variation in weight increase was much higher in the very obese group.

Table 2 Weight recommendations from the Institute of Medicine (IOM)

Pre-pregnancy BMI	Recommended weight gain
Low pre-pregnancy weight (BMI under 19.8 kg m^{-2})	12.5–18.0 kg
Normal pre-pregnancy weight (BMI 19.8–26.0 kg m^{-2})	11.5–16.0 kg
High pre-pregnancy weight (BMI 26.0–29.0 kg m^{-2})	7.0–11.5 kg
Very high pre-pregnancy weight (BMI over 29.0 kg m^{-2})	6.8 kg*

*Recommended minimum weight gain.

Kleiman (52) analysed a subsample of the 1980 National Survey data (NNS). The sample was divided into groups according to body mass: low (BMI < 19.8), moderate (BMI 19.8–26.0) and high (BMI > 26.0). For some analyses, a fourth group labelled 'very high' with a BMI > 29 was included.

Results of multiple regression analyses showed that there was a very small difference in mean weight gain between low and moderate BMI groups, but women in the high BMI group gained 2.7 kg less than the two lower groups.

Öhlin & Rössner followed a group of 1423 women up to 1 year after delivery (57–59). The weight retention was not correlated with prepregnancy body weight or parity. However, the degree of weight retention up to 1 year after delivery varied more in overweight and obese women compared to normal weight women (57–59) (Fig. 1).

Complications during pregnancy

Gestational diabetes

Obesity and gestational diabetes are closely linked (60,61). It is clear that women with gestational diabetes (GDM) have a higher risk of developing type 2 diabetes mellitus (DM) later in life (62–65). Although it is generally stated that 1–3% of women develop GDM during pregnancy, obese women have a higher risk of about 17% (66,67). Even overweight women with a BMI of 25–30 have 1.8–6.5 times greater risk of developing GDM (3,4,65,68).

In a study by Lu *et al.* almost 30% of the cases of gestational diabetes seen in their clinic attributed to obesity (69).

Other factors related to the risk to develop GDM are ethnicity, prepregnancy weight, previus occurrence of GDM, age, parity, family history of diabetes and degree of hyperglycaemia in pregnancy (4,63,66,67,70–73).

In earlier studies, women with GDM have been reported to be heavier than matched pregnant women with a normal

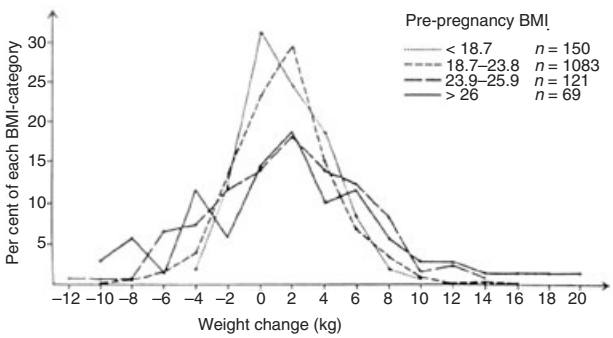

Figure 1 Distribution of weight change 1 year post partum compared with pre-pregnancy body weight in groups with different pre-pregnancy BMI.

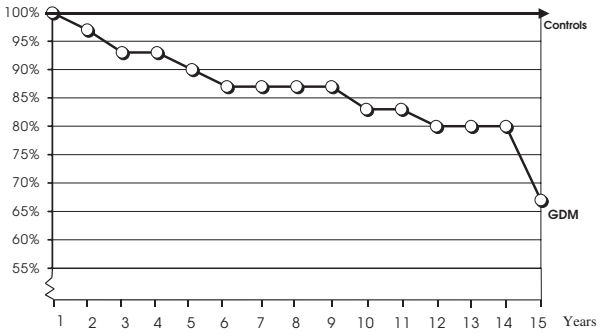

Figure 2 Cumulative frequency of gestational diabetes (GDM) women who remain free from type 2 diabetes mellitus during 15 years ($P < 0.001$), Kaplan-Meier plot.

glucose tolerance (72). Weight gain during pregnancy has on the other hand been found to be about 1.5–2 kg less in women with GDM than in controls (72).

In a study by Linné *et al.* 28 women diagnosed with GDM in 1984–85, and a control group ($n = 52$) who gave birth at the same time performed an 2-h oral glucose tolerance test (OGTT) 15 years later. The result showed that 35% of the women with prior GDM were diagnosed with type 2 DM 15 years later and none in the control group (Fig. 2). Mean BMI in the diabetic group was 27.4 kg m^{-2} and in the non-diabetic GDM group 24.6 kg m^{-2}. There were no significant differences in the mean weight gain since the first child between the GDM group and the control group (8.4 kg vs. 8.1 kg). The women with GDM who developed type 2 DM, however, gained significantly more (15.1 kg) since the birth of their first child compared to both women without GDM and women with GDM how did not developed type 2 DM.

As this group of women with GDM is at a very high risk for type 2 DM, it is pertinent also to monitor long-term weight development in parallel to the natural history of type 2 DM (62).

Hypertensive disorders

Maternal haemodynamic changes in obese mothers include higher arterial blood pressure, haemoconcentration and altered cardiac function (74). The prevalence of hypertensive disorder and pre-eclampsia is higher in obese women (75,76). Especially in severely obese patients, obesity is an independent factor for high blood pressure, independent of other factors such as diabetes and age (4,77–79).

The regional distribution of fat may modulate the risk of cardiovascular diseases in pregnant women. In a study involving 22 patients with pre-eclampsia and a control group of 126 women, the ratio of upper-body to lower-body fat was more accurately associated with the development of pre-eclampsia than was the total body fat (80).

Duration of pregnancy and delivery complications

The duration of the pregnancy is generally not significantly different in obese women compared to normal weight women (79), nor is the incidence of preterm delivery (4,65,79). Some studies have shown no effect of obesity status on the duration of the delivery (78,79) while Jonson *et al.* reported that the delivery time was longer in obese women (77). However, obese women also have a higher frequency of induction of labour (78,79). Furthermore, obese women have a higher rate of both planned and acute caesarean sections (4,65,68,78,81). According to Gross *et al.*, the most frequent indications are incomplete dilation of the cervix, foetal distress and induction failure (78). However, the higher rate of caesarean sections seems to be related to the higher rate of complications in the obese women rather than the obesity itself (65). Also other sorts of assisted delivery are more common among obese women (82).

Obese patients have overall a higher risk of complications attributed to surgery. With the higher frequency of caesarean sections comes the general risks of surgery in obese patients, that is, thromboses, infections and massive bleeding (65,79).

With vaginal delivery the risk for perineal tears is higher in obese women compared to normal weight women. This could be because of the higher weight of the child (83).

Other complications and possible positive effect of being obese during pregnancy

Pregnancy and obesity also affect the airways (84,85). In a study by Maasilta *et al.* an increased rate of snoring and sleep-related apnoea and hypo-apnoea was found (85). However, the study was not large enough to determine whether the sleep-related disorders had any effect on the pregnancy outcome.

There are very few positive effects of being obese during pregnancy. However, anaemia appears to occur less often in obese women than normal weight women (4,68). Maternal obesity is also a predicting factor against delivering a small-for-delivery child (6,86).

Discussion

Overweight and obesity have negative effects on the health of both mother and child. Obstetric costs will rise enormously as more women become overweight and obese (1–5).

Most studies are retrospective and some of the studies have not been corrected for other factors such as obesity-related co-morbidities to show the direct effect of obesity as an independent risk factor.

The classification of obesity is not always consistent, which makes a comparison between studies difficult. However, there is strong evidence that obesity is indeed an independent cause of pregnancy and delivery complications (4,6,16,78,79,87).

Little data are available on the extra cost induced by pregnancy of obese women. One of the few studies on the extra cost for treating obese women during pregnancy is a report by Galtier-Dereure *et al*. where 435 pregnant women were followed during and after pregnancy and the duration of night-time and daytime hospitalization was recorded (79). The cost for the obese mothers was five times higher than for the normal weight mothers.

Prevention of obesity at an early age would always be preferable, but very hard to achieve in practice. In reality, obese women planning to become pregnant should be informed about the potential complications of obesity and their pregnancy.

However, for obese women with infertility problems, weight loss programmes should be the first choice of treatment to achieve conception. The economic and health benefits of weight loss programmes compared to induced pregnancy attempts are enormous (29,79). Results from weight loss programmes today are not very promising regarding the chance for obese women to reach normal weight, but as in many other obesity-related diseases, a weight loss of 10% can make a great difference (27,29).

The mother's obesity thus not just affect herself but her children. Children of obese mothers have a higher risk for intrauterine foetal death (3,4,16), congenital abnormalities (3), head trauma, shoulder dystocia, brachial plexus lesions, fractures of the clavicle (88) and increased risk of death within the first year (11,87,89).

There is a need for more worldwide systematic recording of weight gain during pregnancy. The American IOM recommendations focus on the foetus, but also prevent high weight retention after delivery (47). Some authors have concluded that the effect of obesity can be modified with a lower rate of weight gain (86). On the other hand it is not the obese women who gain most during pregnancy but the variation in these group is large (50,51,54). Some women retain weight after pregnancy and many women enter the second pregnancy heavier (90).

It should be pointed out that obesity also affects male reproduction in a negative way but this research area is still in its infancy (91–93).

References

1. Hyattsville M. National Center for Health Statistics: United States, 1996.
2. WHO. *Obesity: Preventing and Managing the Global Epidemic*. Report of a WHO Consultaton on Obesity, 3–5 June. WHO: Geniva, 1997.
3. Naeye R. Weight gain and the outcome of pregnancy. *Am J Obstet Gynecol* 1979; **135**: 3–9.
4. Garbaciak JA Jr, Richter M, Miller S, Barton JJ. Maternal weight and pregnancy complications. *Am J Obstet Gynecol* 1985; **152**: 238–245.
5. Taffel SM. *Maternal Weight Gain and the Outcome of Pregnancy: United States 1980*. Vital Health Statistics Series 21, No. 44. DHHS Publication Number (PHS): 86–1922.
6. Kumari A. Pregnancy outcome in women with morbid obesity. *Int J Gynaecol Obstet* 2001; **73**: 101–107.
7. Lissner L, Johansson SE, Qvist J, Rossner S, Wolk A. Social mapping of the obesity epidemic in Sweden. *Int J Obes Relat Metab Disord* 2000; **24**: 801–805.
8. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults. findings from the third National Health and Nutrition Examination Survey. *JAMA* 2002; **287**: 356–359.
9. Latner JD, Stunkard AJ. Getting worse: the stigmatization of obese children. *Obes Res* 2003; **11**: 452–456.
10. Bongain A. Obesity in obstetrics and gynaecology. *European J Obestetrics Gynecol Reprod Biol* 1998; **77**: 217–228.
11. Baeten J, Bukusi E, Lambe M. Pregnancy complications and outcomes among overweight and obese nulliparous women. *Am J Public Health* 2001; **91**: 436–440.
12. Ramsay J, Ferrell W, Crawford L, Wallance A, Greer I, Sattar N. Maternal obesity in associated with dysregulation of metabolic, vascular, and inflammatory pathways. *Clin Endocrinol Metab* 2002; **87**: 4231–4237.
13. Moran LJ, Norman RJ. The obese patient with infertility: a practical approach to diagnosis and treatment. *Nutr Clin Care* 2002; **5**: 290–297.
14. Wang JX, Davies MJ, Norman RJ. Obesity increases the risk of spontaneous abortion during infertility treatment. *Obes Res* 2002; **10**: 551–554.
15. Bolumar F, Olsen J, Rebagliato M, Saez-Lloret I, Bisanti L. Body mass index and delayed conception: a European multicenter study on infertility and subfecundity. *Am J Epidemiol* 2000; **151**: 1072–1079.
16. Cnattingius S, Lambe M. Trends in smoking and overweight during pregnancy: prevalence, risks of pregnancy complications, and adverse pregnancy outcomes. *Semin Perinatol* 2002; **26**: 286–295.
17. Grodstein F, Goldman MB, Cramer DW. Body mass index and ovulatory infertility. *Epidemiology* 1994; **5**: 247–250.
18. Lake JK, Power C, Cole TJ. Women's reproductive health: the role of body mass index in early and adult life. *Int J Obes Relat Metab Disord* 1997; **21**: 432–438.
19. Rich-Edwards JW, Goldman MB, Willett WC, Hunter DJ, Stampfer MJ, Colditz GA, Manson JE. Adolescent body mass index and infertility caused by ovulatory disorder. *Am J Obstet Gynecol* 1994; **171**: 171–177.
20. Rowland AS, Baird DD, Long S, Wegienka G, Harlow SD, Alavanja M, Sandler DP. Influence of medical conditions and lifestyle factors on the menstrual cycle. *Epidemiology* 2002; **13**: 668–674.
21. Wang JX, Davies MJ, Norman RJ. Polycystic ovarian syndrome and the risk of spontaneous abortion following assisted reproductive technology treatment. *Hum Reprod* 2001; **16**: 2606–2609.
22. al-Ansary LA, Babay ZA. Risk factors for spontaneous abortion: a preliminary study on Saudi women. *J R Soc Health* 1994; **114**: 188–193.
23. Hamilton-Fairley D, Kiddy D, Watson H, Paterson C, Franks S. Association of moderate obesity with a poor pregnancy outcome

in women with polycystic ovary syndrome treated with low dose gonadotrophin. *Br J Obstet Gynaecol* 1992; **99**: 128–131.
24. Orvieto R, Ben-Rafael Z, Ashkenazi J, Yoeli R, Messing B, Perri T, Shalev Y, Bar-Hava I. Outcome of pregnancies derived from assisted reproductive technologies: IVF versus ICSI. *J Assist Reprod Genet* 2000; **17**: 385–387.
25. Bellver J, Rossal LP, Bosch E, Zuniga A, Corona JT, Melendez F, Gomez E, Simon C, Remohi J, Pellicer A. Obesity and the risk of spontaneous abortion after oocyte donation. *Fertil Steril* 2003; **79**: 1136–1140.
26. Fedorcsak P, Storeng R, Dale PO, Tanbo T, Abyholm T. Obesity is a risk factor for early pregnancy loss after IVF or ICSI. *Acta Obstet Gynecol Scand* 2000; **79**: 43–48.
27. Clark AM, Thornley B, Tomlinson L, Galletley C, Norman RJ. Weight loss in obese infertile women results in improvement in reproductive outcome for all forms of fertility treatment. *Hum Reprod* 1998; **13**: 1502–1505.
28. Silva PD, Cool JL, Olson KL. Impact of lifestyle choices on female infertility. *J Reprod Med* 1999; **44**: 288–296.
29. Clark AM, Ledger W, Galletly C, Tomlinson L, Blaney F, Wang X, Norman RJ. Weight loss results in significant improvement in pregnancy and ovulation rates in anovulatory obese women. *Hum Reprod* 1995; **10**: 2705–2712.
30. Hoeger K. Obesity and weight loss in polycystic ovary syndrome. *Obstet Gynecol Clin North Am* 2001; **28**: 85–97, vi–vii.
31. Hill KM. Update: the pathogenesis and treatment of PCOS. *Nurse Pract* 2003; **28**: 8–17, 22–23, table of contents; quiz 23–5.
32. Gambineri A, Pelusi C, Vicennati V, Pagotto U, Pasquali R. Obesity and the polycystic ovary syndrome. *Int J Obes Relat Metab Disord* 2002; **26**: 883–896.
33. Eggers S, Kirchengast S. The polycystic ovary syndrome – a medical condition but also an important psychosocial problem. *Coll Antropol* 2001; **25**: 673–685.
34. Hung IH, Shing Lee TD, Cheung LP, Chung WS, Wing KL, Haines CJ. Psychiatric morbidity amongst infertile chinese women undergoing treatment with assissted reproductive technology and the impact of treatment failure. *Gynecol Obstet Invest* 2002; **53**: 195–199.
35. Trent ME, Rich M, Austin SB, Gordon CM. Quality of life in adolescent girls with polycystic ovary syndrome. *Arch Pediatr Adolesc Med* 2002; **156**: 556–560.
36. Jayagopal V, Kilpatrick ES, Holding S, Jennings PE, Atkin SL. The biological variation of insulin resistance in polycystic ovarian syndrome. *J Clin Endocrinol Metab* 2002; **87**: 1560–1562.
37. Dahlgren E, Johansson S, Lindstedt G, Knutsson F, Oden A, Janson PO, Mattson LA, Crona N, Lundberg PA. Women with polycystic ovary syndrome wedge resected in 1956 to 1965: a long-term follow-up focusing on natural history and circulating hormones. *Fertil Steril* 1992; **57**: 505–513.
38. Korhonen S, Hippelainen M, Niskanen L, Vanhala M, Saarikoski S. Relationship of the metabolic syndrome and obesity to polycystic ovary syndrome: a controlled, population-based study. *Am J Obstet Gynecol* 2001; **184**: 289–296.
39. Macut D, Micic D, Cvijovic G, Sumarac M, Kendereski A, Zoric S, Pejkovic D. Cardiovascular risk in adolescent and young adult obese females with polycystic ovary syndrome (PCOS). *J Pediatr Endocrinol Metab* 2001; **14**(Suppl. 5): 1353–1359; discussion 1365.
40. Wahrenberg H, Ek I, Reynisdottir S, Carlstrom K, Bergqvist A, Arner P. Divergent effects of weight reduction and oral anticonception treatment on adrenergic lipolysis regulation in obese women with the polycystic ovary syndrome. *J Clin Endocrinol Metab* 1999; **84**: 2182–2187.
41. Norman RJ, Davies MJ, Lord J, Moran LJ. The role of lifestyle modification in polycystic ovary syndrome. *Trends Endocrinol Metab* 2002; **13**: 251–257.
42. Velazquez EM, Mendoza S, Hamer T, Sosa F, Glueck CJ. Metformin therapy in polycystic ovary syndrome reduces hyperinsulinemia, insulin resistance, hyperandrogenemia, and systolic blood pressure, while facilitating normal menses and pregnancy. *Metabolism* 1994; **43**: 647–654.
43. Harborne L, Fleming R, Lyall H, Norman J, Sattar N. Descriptive review of the evidence for the use of metformin in polycystic ovary syndrome. *Lancet* 2003; **361**: 1894–1901.
44. Hytten F, Chamberlerlein G. *Clinical Psysiology in Obstertics*. Blackwell Scientific Publications: Oxford, 1980.
45. Chesley L. Weight changes and water balance in normal and toxic pregnancy. *AM J Obstet Gynecol* 1944; **48**: 565–593.
46. Dieckman W. *The Toxemias of Pregnancy*. Mosby: St Louise, 1952.
47. Institute of Medicine. *Nutritional Status During Pregnancy, Weight Gain and Nutrient Supplement*. National Academy Press: Washington DC, 1990.
48. Abrams B, Parker J. Maternal weight gain in women with good pregnancy outcome. *Obstet Gynecol* 1990; **76**: 1–7.
49. Ash S, Fisher C, Truswell A, Allen J, Irwig L. Maternal weight gain, smoking and other factors in pregnancy as predictors of infant birth-weight in Sydney women. *Aust NZ J Obstet Gynsecol* 1989; **29**: 212–219.
50. Mitchell M, Lerner E. A comparison of pregnancy outcome in overweight and normal weight women. *J Am Coll Nutr* 1989; **8**: 617–624.
51. Brown J, Jacobson H, Askue L, Peick M. Influence of pregnancy weight gain an the size of infants born to underweight women. *Obstet Gynecol* 1981; **57**: 13–17.
52. Kleinman J. *Maternal weight gain during pregnancy: determinants and consequences*. NCHS Working Paper Seires No. 33. National Center for Health Statistics, Public Health Service, US Department of Health and Human Services.
53. Theron G, Thompson M. A centile chart for weight gain in pregnancy for the urban population of the Western Cape, South Africa. *Int J Gynaecol Obstet* 1990; **33**: 127–133.
54. Abrams B, Laros R. Prepregnancy weight, weight gain, and birth weight. *Am J Obstet Gynecol* 1986; **154**: 503–509.
55. Gunderson E, Abrams B, Selvin S. Does the pattern of postpartum weight change differ according to pregravida body size? *Int J Obes* 2002; **25**: 853–862.
56. Harris HE, Ellison GT, Richter LM, de Wet T, Levin J. Are overweight women at increased risk of obesity following pregnancy? *Br J Nutr* 1998; **79**: 489–494.
57. Öhlin A, Rössner S. Maternal body weight development after pregnancy. *Int J Obes* 1990; **14**: 159–173.
58. Öhlin A, Rössner S. Trends in eating patterns, physical activity and socio-demographic factors in relation to postpartum body weight development. *Br J Nutr* 1994; **71**: 457–470.
59. Öhlin A, Rössner S. Factors related to body weight changes during and after pregnancy: the Stockholm pregnancy and weight development study. *Obes Res* 1996; **4**: 271–276.
60. Glowinska B, Urban M, Koput A. Cardiovascular risk factors in children with obesity, hypertension and diabetes: lipoprotei (a) levels and body mass index correlate with family history of cardiovascular disease. *Eur J Pediatr* 2002; **161**: 511–518.
61. Meigs J. Epidemioligy of the metabolic syndrome, 2002. *Am J Manag Care* 2002; **8**(Suppl. 11): S283–S292.
62. Linne Y, Barkeling B, Rossner S. Natural course of gestational diabetes mellitus: long term follow up of women in the SPAWN study. *BJOG* 2002; **109**: 1227–1231.

63. Dornhorst A, Rossi M. Risk and prevention of type 2 diabetes in women with gestational diabetes. *Diabetes Care* 1998; **21**: B43–B49.
64. Kritz-Silverstein D, Barrett-Conorr E, Wingard D. The effects of parity on the later development of non-insulin dependent diabetes mellitus or impaired glucose tolerance. *N Engl J Med* 1989; **321**: 1214–1219.
65. Perlow JH, Morgan MA, Montgomery D, Towers CV, Porto M. Perinatal outcome in pregnancy complicated by massive obesity. *Am J Obstet Gynecol* 1992; **167**: 958–962.
66. Gabbe S. Gestational diabetes mellitus. *N Engl J Med* 1986; **315**: 1025–1026.
67. Guttorm E. Practical screening for diabetes millitus in pregnant women. *Acta Endocrinol (Copenhagen)* 1974; **75**: 11–24.
68. Abrams B, Parker J. Overweight and pregnancy complications. *Int J Obes* 1988; **12**: 293–303.
69. Lu GC, Rouse DJ, DuBard M, Cliver S, Kimberlin D, Hauth JC. The effect of the increasing prevalence of maternal obesity on perinatal morbidity. *Am J Obstet Gynecol* 2001; **185**: 845–849.
70. Catalano P, Roman N, Tyzbir E, Merritt A, Driscoll P, Amini S. Weight gain in women with gestational diabetes. *Obstet Gynecol* 1993; **81**: 523–528.
71. Metzger B, Coustan D. Summary and recomendations of the fourth international workshop-conference on gestational diabetes mellitus. *Diabetes Care* 1998; **21**: B161–B167.
72. Sepe S, Connell F, Geiss L, Teutsch S. Gestational diabetes: incidence, maternal characteristics and perinatal outcome. *Diabetes* 1985; **34**: 13–16.
73. Verma A, Boney C, Tucker R, Vohr B. Insulin resistance syndrome in women with prior history of gestational diabetes mellitus. *J Clin Endocrinol Metab* 2002; **87**: 3227–3235.
74. Tomoda S, Tamura T, Sudo Y, Ogita S. Effects of obesity on pregnant women: maternal hemodynamic change. *Am J Perinatol* 1996; **13**: 73–78.
75. Sibai BM, Ramadan MK, Chari RS, Friedman SA. Pregnancies complicated by HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): subsequent pregnancy outcome and long-term prognosis. *Am J Obstet Gynecol* 1995; **172**: 125–129.
76. Sibai BM, Gordon T, Thom E, Caritis SN, Klebanoff M, McNellis D, Paul RH and the National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units, New York. Risk factors for preeclampsia in healthy nulliparous women: a prospective multicenter study. The National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. *Am J Obstet Gynecol* 1995; **172**: 642–648.
77. Johnson SR, Kolberg BH, Varner MW, Railsback LD. Maternal obesity and pregnancy. *Surg Gynecol Obstet* 1987; **164**: 431–437.
78. Gross T, Sokol RJ, King KC. Obesity in pregnancy: risks and outcome. *Obstet Gynecol* 1980; **56**: 446–450.
79. Galtier-Dereure F, Boegner C, Bringer J. Obesity and pregnancy: complications and cost. *Am J Clin Nutr* 2000; **71**(Suppl. 5): 1242S–1248S.
80. Ijuin H, Douchi T, Nakamura S, Oki T, Yamamoto S, Nagata Y. Possible association of body-fat distribution with preeclampsia. *J Obstet Gynaecol Res* 1997; **23**: 45–49.
81. Mancuso A, D'Anna R, Leonardi R. Pregnancy in the obese patient. *Eur J Obstet Gynecol Reprod Biol* 1991; **39**: 83–86.
82. Flamm BL. Vaginal birth after caesarean (VBAC). *Best Pract Res Clin Obstet Gynaecol* 2001; **15**: 81–92.
83. Samuelsson E, Ladfors L, Lindblom BG, Hagberg H. A prospective observational study on tears during vaginal delivery: occurrences and risk factors. *Acta Obstet Gynecol Scand* 2002; **81**: 44–49.
84. Unterborn J. Pulmonary function testing in obesity, pregnancy, and extremes of body habitus. *Clin Chest Med* 2001; **22**: 759–767.
85. Maasilta P, Bachour A, Teramo K, Polo O, Laitinen LA. Sleep-related disordered breathing during pregnancy in obese women. *Chest* 2001; **120**: 1448–1454.
86. Edwards LE, Hellerstedt WL, Alton IR, Story M, Himes JH. Pregnancy complications and birth outcomes in obese and normal-weight women: effects of gestational weight change. *Obstet Gynecol* 1996; **87**: 389–394.
87. Feldman B, Yaron Y, Critchfield G, Leon J, O'Brien JE, Johnson MP, Evans MI. Distribution of neural tube defects as a function of maternal weight: no apparent correlation. *Fetal Diagn Ther* 1999; **14**: 185–189.
88. Spellacy WN, Miller S, Winegar A, Peterson PQ. Macrosomia – maternal characteristics and infant complications. *Obstet Gynecol* 1985; **66**: 158–161.
89. Moore LL, Bradlee ML, Singer MR, Rothman KJ, Milunsky A. Folate intake and the risk of neural tube defects. an estimation of dose-response. *Epidemiology* 2003; **14**: 200–205.
90. Linne Y, Rossner S. Interrelationships between weight development and weight retention in subsequent pregnancies: the SPAWN study. *Acta Obstet Gynecol Scand* 2003; **82**: 318–325.
91. Bray GA. Obesity and reproduction. *Hum Reprod* 1997; **12**(Suppl. 1): 26–32.
92. Baker HW. Reproductive effects of nontesticular illness. *Endocrinol Metab Clin North Am* 1998; **27**: 831–850.
93. Jung A, Schill WB. Male infertility. Current life style could be responsible for infertility. *MMW Fortschr Med* 2000; **142**: 31–33.

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