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## Chapter Objectives

1. Identify some of the pathophysiological factors present in morbid obesity that increase susceptibility to polycystic ovarian syndrome.
2. Gain an understanding of the current evidence available describing the effect of bariatric surgical procedures on fertility in morbidly obese women.

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## Introduction

Women are twice as likely to be morbidly obese as men. Approximately 80–85 % of women undergoing bariatric surgery are of childbearing age. Polycystic ovarian syndrome (PCOS) has a prevalence of 6–10 % in women of reproductive age. Over 50 % of women with PCOS are overweight or obese. Obese women with PCOS have higher rates of anovulation than their leaner counterparts with the same diagnosis. The American Society for Reproductive Medicine criteria for PCOS requires two of the following symptoms: oligomenorrhea and/or anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries. There also has to be exclusion of other hyperandrogenic causing states.

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## Pathophysiology of Obesity and Polycystic Ovarian Syndrome

The pathophysiology of PCOS is complex, multifactorial, and incompletely understood. Excess adipose tissue in an obese individual can lead to insulin resistance and a hyperin-

sulinemic state. Insulin in turn stimulates androgen production via the ovarian theca cells and also inhibits hepatic synthesis of sex hormone-binding globulin. This results in a functional hyperandrogenic state that inhibits normal follicular maturation (Fig. 38.1) [1, 2].

Obesity is independently associated with anovulation in women trying to conceive. Women with obesity and/or the diagnosis of PCOS should be strongly encouraged to lose weight prior to conception. Studies evaluating the impact of lifestyle modification in obese PCOS women have shown that weight loss of 5–10 % of total body weight can result in improvements in insulin sensitivity and return of ovulation [1].

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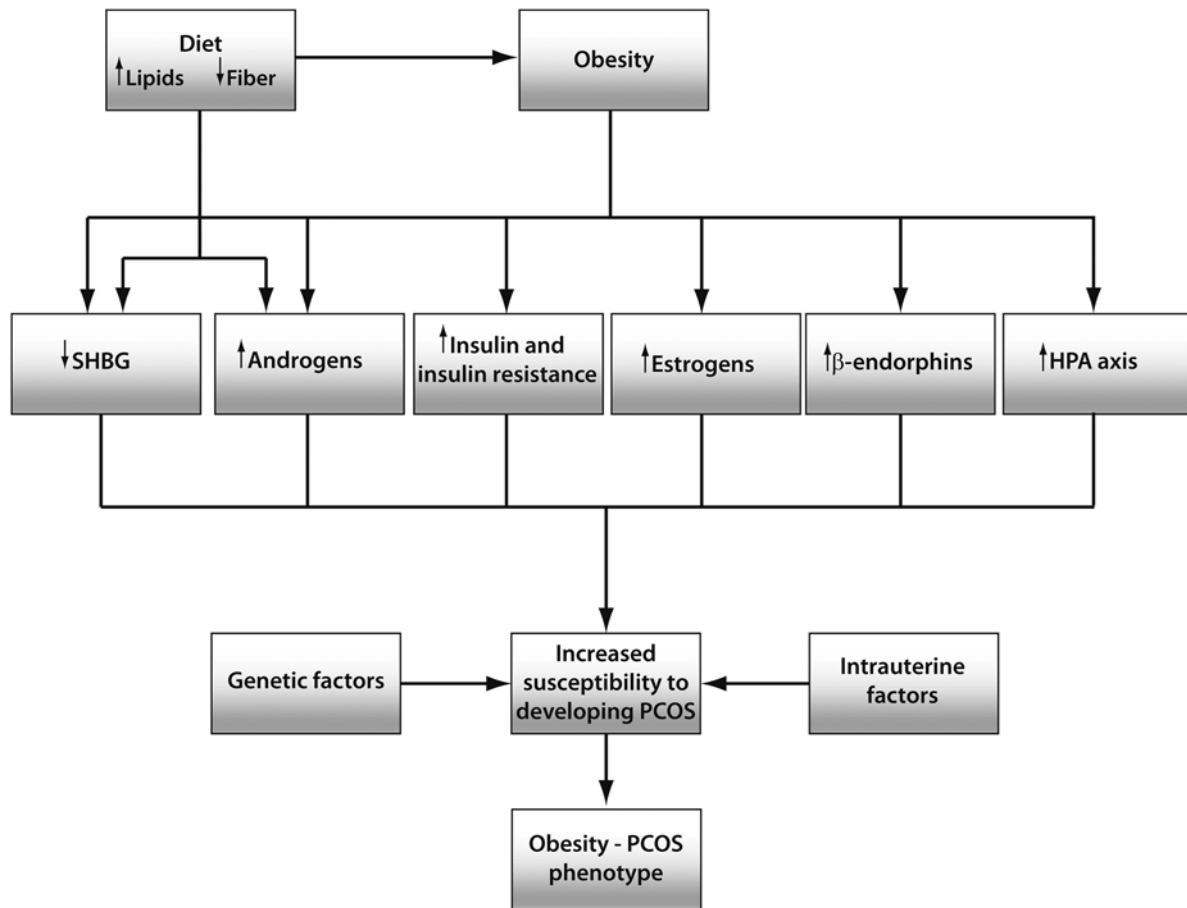
## Impact of Bariatric Surgery on Fertility: Current Evidence

Patients who fail conventional weight loss measures often seek bariatric surgery. To date, there are no prospective randomized trials assessing the impact of bariatric surgery on PCOS and fertility rates.

Escobar-Morreale and colleagues [3] performed a prospective review of 36 premenopausal patients who presented for bariatric surgery at their institution for a 3½-year period. All patients were diagnosed with PCOS as defined by the National Institute of Child Health and Human Development Conference criteria. All patients underwent biliopancreatic diversion or laparoscopic gastric bypass at the discretion of the surgeon. Seventeen of these 36 patients were diagnosed with PCOS. Another five patients had increased levels of total and or free testosterone levels. However, they had regular menstrual cycles precluding the diagnosis of PCOS. Of the 17 women diagnosed with PCOS, 12 were available for reevaluation at a mean of 12 months after their surgical procedure. The mean weight loss was 41 kg. In addition to this weight loss, there was marked improvement in hyperandrogenism in 11 of these 12 patients. Regular menstrual cycles were restored in all 12 patients following

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**Fig. 38.1** Factors contributing to polycystic ovarian syndrome in obese women. *SHBG* sex hormone-binding globulin, *HPA* hypothalamic-pituitary-adrenal, *PCOS* polycystic ovarian syndrome

weight loss. Ten of these 12 had luteal phase serum progesterone concentrations available with values of 4 ng/mL, suggesting ovulation was restored in the hyperandrogenic patients in addition to restoration in menstrual regularity. They concluded that their data strongly suggests that the sustained and marked weight loss achieved after bariatric surgery leads to the almost complete resolution of PCOS.

Eid and colleagues [4] performed a retrospective analysis of 24 patients—all of whom were oligomenorrheic. They had a mean age of 34 years and a mean body mass index (BMI) of 50 kg/m<sup>2</sup>. They all underwent Roux-en-Y laparoscopic gastric bypass, and a mean follow-up of 27.5 months had 56.7 % excess weight loss and a mean postoperative BMI of 30 kg/m<sup>2</sup>. In addition to significant resolution of a multitude of other comorbidities, all patients had complete resolution of their menstrual abnormalities and five patients who desired to conceive were able to do so following surgery without the use of clomiphene.

In 2008, Maggard and colleagues [5] published a systematic review of literature looking at pregnancy and fertility following bariatric surgery. They screened 260 articles, of which 75 were included in the review. Specifically with regard to bariatric surgery and fertility, six studies addressed fertility outcomes in patients following a variety of bariatric surgical procedures. Three studies showed improvements in fertility rates and one study noted no change. The other two studies focused on the impact of fertility rates and gestational diabetes. One noted 6.7 % of patients that required fertility treatment following bariatric surgery versus 2.3 % in the general population ( $P < 0.001$ ). Another showed 21.4 % of patients following bariatric surgery who had gestational diabetes required fertility treatment versus 5.5 % in the general population who had gestational diabetes ( $P < 0.001$ ). The authors noted that there are no prospective randomized trials focusing on the impact of bariatric surgery and fertility, which limits the strengths of the evidence. There is also a

variety of bariatric surgical procedures that were involved in these studies, some of which are currently performed on an infrequent basis.

Jamal and colleagues recently published a retrospective review of 31 morbidly obese female patients with a history of PCOS documented before undergoing an elective Roux-en-Y gastric bypass [6]. Twenty of these had sufficient data for inclusion in their follow-up analysis. The mean age was 32 years and the mean preoperative BMI was 52.8 kg/m<sup>2</sup>. Mean duration of obesity was 20 years and the mean duration of PCOS prior to the surgery was 8.6 years. Mean postoperative follow-up was 46.7 months with a percentage of excess weight loss of 64 %. After surgical weight loss 82 % had a return of regular menstrual cycles and 29 % had complete resolution of hirsutism. Six patients desired a child, but were infertile prior to surgical intervention; all had a live birth within 3 years of Roux-en-Y gastric bypass. Five of these conceived without hormonal treatment and one conceived with intrauterine insemination. The authors concluded that surgical weight loss following Roux-en-Y gastric bypass significantly improves the clinical symptoms of PCOS and results in an exceptional fertility rate in patients who were previously infertile and desiring pregnancy.

There are several methodological weaknesses in the current body of literature evaluating the impact of bariatric surgery on fertility. Many suffer from small sample sizes, do not report the number of women desiring to conceive, and do not record the ovulatory status of the patients.

## Conclusion

Currently the American College of Gynecologists (ACOG) does not recommend bariatric surgery for the treatment of fertility [7]. Despite these limitations, there does seem to be evidence that bariatric surgery can possibly impact fertility rates following surgical weight loss. Further study is necessary to determine the optimal bariatric surgical procedure, timing of pregnancy after surgery, and fertility success rates in the future.

## Question Section

### Questions

- Increases in all of the following are contributing factors to the development of polycystic ovarian syndrome except:
  - Androgens
  - Insulin
  - Lipids
  - Sex hormone-binding globulin (SHBG)
- How many prospective, randomized trials have been completed to assess the impact of bariatric surgery on fertility?
  - 0
  - 1
  - 5
  - 20

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