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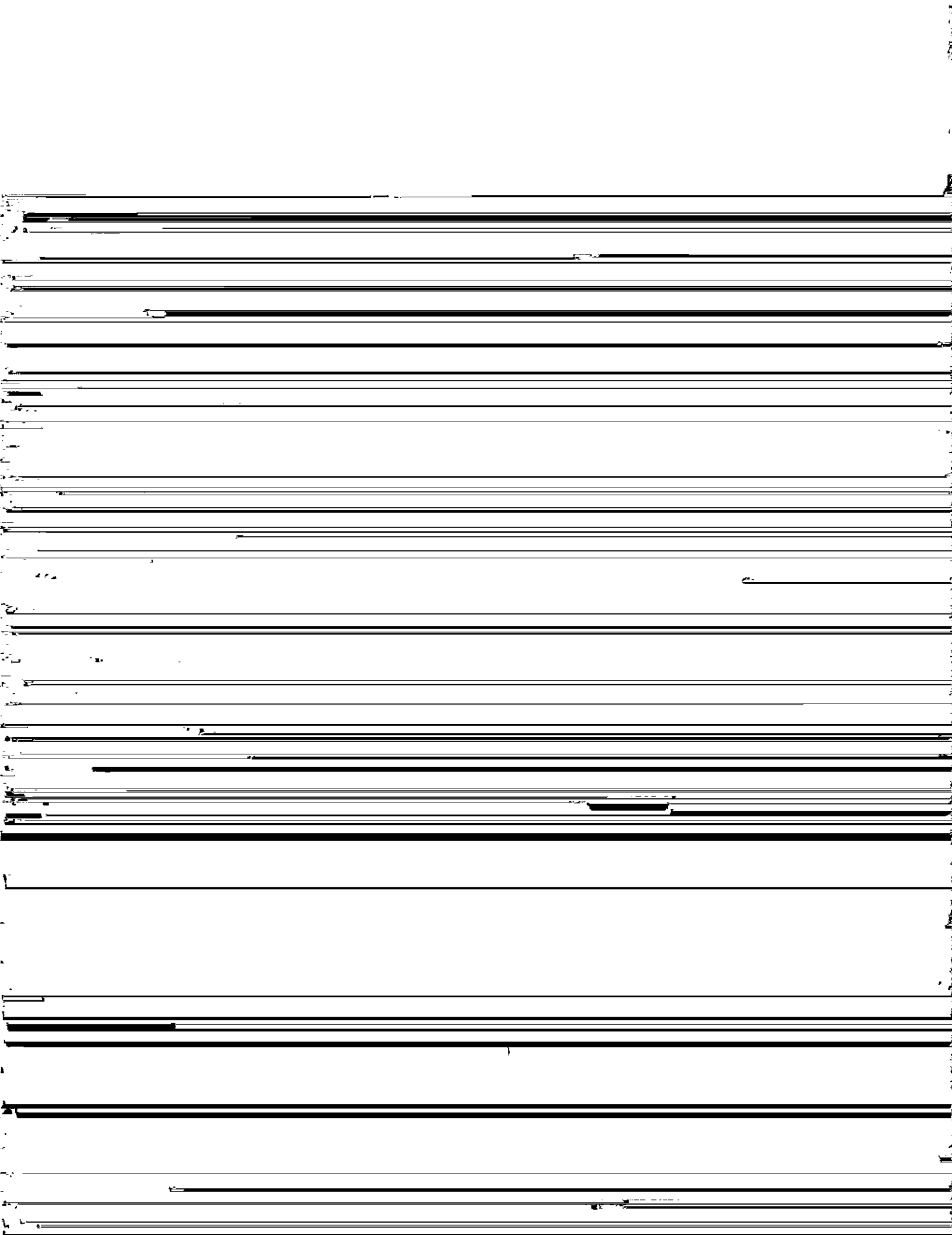
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**Table 1**  
Criteria to diagnose PCOS

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Primarily a clinical diagnosis; the patient must be:

- Anovulatory (no menses >3 months of the previous year)
- Hirsute

Normal plasma concentrations of:

- 17-hydroxyprogesterone
- Prolactin
- Thyroid hormones
- Growth hormone
- Cortisol
- FSH

Patient must not have been taking any of the following medications for six months prior to diagnosis

- Synthetic glucocorticoids
- Adrenocorticotrophic hormone
- Metyrapone
- Anabolic steroids
- Levonorgestrel-containing oral contraceptive pills
- Maternal use of synthetic progestational agents

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tios, and hyperinsulinemia. The diagnosis of PCOS is not based primarily on pathologic changes in the ovaries or plasma hormone disturbances, but is instead a clinical diagnosis based on the coexistence of chronic anovulation and varying degrees of hirsutism [3]. PCOS is not only a disease of infertility, but is also associated with an increased risk of type II diabetes, gestational diabetes, stroke, hyperlipidemia, coronary artery disease, and endometrial carcinoma [4–6]. The etiology of PCOS is unclear. Proposed hypotheses of the pathogenesis of PCOS include a central-primary defect in the hypothalamic/ pituitary axis; an ovarian-primary abnormality of steroidogenesis; and insulin resistance.

Since 1935, when Stein and Leventhal [7] first described the syndrome, obesity has been recognized as a major factor in the pathogenesis of PCOS. Estimates of the prevalence of obesity in women with PCOS vary from 35% to 60% [8,9]. Weight loss has been recognized as an important treatment for women with obesity and PCOS, but nonsurgical weight loss is often temporary and has not resulted in complete resolution of the symptoms [10].

In an attempt to determine the effect of sustained weight loss on PCOS, we reviewed the clinical outcomes of laparoscopic Roux-en-Y gastric bypass in women with PCOS.

## Methods

This was a retrospective study. The patients were identified from a prospectively maintained database. A chart review was performed of all women with the diagnosis of PCOS seen between July 1997 and November 2001 at the University of Pittsburgh Medical Center who had undergone laparoscopic Roux-en-Y gastric bypass and had at least 1 year of follow-up. All women in the study were diagnosed with PCOS by their endocrinologist using established criteria (Table 1) [3]. All patients underwent laparoscopic Roux-en-Y gastric bypass. In brief, the surgical ap-

proach involves construction of an isolated small gastric pouch (15-cm<sup>3</sup>) with an antecolic, antegastric Roux limb (75 cm) and stapled gastrojejunostomy and jejunojunostomy. We extend the Roux limb length to 150–250 cm for the superobese (body mass index [BMI]  $\geq 60$ ).

Postoperatively, all women were followed up in our clinical center. Information about the patient's current weight, medical comorbidities, medications used, hirsutism, acne, fertility status, and any current menstrual cycle irregularities were gathered. All descriptive statistical analysis was done using Sigma Stat Software.

The diagnosis of hypertension was made when the average of two or more diastolic blood pressure measurements on at least two subsequent visits was  $\geq 90$  mm Hg or when the average of multiple systolic blood pressure readings on two or more subsequent visits was consistently  $>140$  mm Hg. Type II diabetes mellitus was defined as a fasting plasma glucose measurement from venous blood of  $\geq 140$  mg/dL combined with the need for medication. Amenorrhea was defined as absence of menses for  $>3$  months of the previous year. Infertility was defined as the inability of a couple to achieve a pregnancy after 1 year of regular unprotected sexual relations or the inability of a woman to carry a pregnancy to a live birth.

## Results

A total of 30 patients with PCOS were identified from the pool of patients who had undergone weight loss surgery between July 1997 and November 2001. Of these, 24 patients were included for analysis; 6 patients were excluded owing to incomplete follow-up data or the use of medications (steroids, oral contraceptive pills). Preoperatively, these patients had a mean age of  $34 \pm 9.7$  years (range 22–48) and a mean BMI of  $50 \pm 7.5$  (range 36–66). In addition to PCOS, 21 of the 24 patients had at least three other weight-related comorbid conditions, including dyslipidemia. The mean number of medications per patient was 2.5, with 11 patients having three or more prescriptions. All patients were oligomenorrheic. Of the 24 patients, 23 (96%) had hirsutism, 5 (20%) had acne, and 12 (50%) had undergone preoperative ultrasonography of their ovaries that showed multiple cysts.

Postoperatively, these patients were followed up for a mean of  $27.5 \pm 16$  months (range 12–57). Immediate postoperative gastrointestinal bleeding developed in 1 patient but resolved without any surgical intervention. The mean excess weight loss was  $56.7\% \pm 21.2\%$  (range 12–93%) at 1 year, with a mean postoperative BMI of  $30 \pm 4.5$  (range 25–38). This was a decrease from a mean BMI of 50 preoperatively. At follow-up, 20 (83%) of the 24 patients were free of medication. All 11 patients with type II diabetes mellitus preoperatively were normoglycemic at follow-up. Of the 9 patients with a history of hypertension, 7 (78%) became normotensive without the help of antihypertensive

Table 2  
Patient characteristics pre- and post-gastric bypass

	Pre-operative	Post-operative	% change
Age (yr)	34 ± 9.7	N/A	N/A
Weight (lb)	306 ± 44	201 ± 30	
BMI (kg/m <sup>2</sup> )	50 ± 7.5	30 ± 4.5	
HTN	9	2	77
DM	11	0	100
HA1C (%)	8.2	5.14	62*
GERD	12	0	100
Dyslipidemia	12	1	92
Hirsutism	23	5	79
Depression	10	0	100
Menstrual dysfunction	24	0	100
Medications per hypertensive	1.3 (9 patients on 12 medications)	0.67 (2 patients on 3 medications)	N/A
Diabetic medication	1.1 (11 patients on 12 medications)	0	100
Medications per patient	2.5	0.6	75

BMI = body mass index; HTN = hypertension; DM = diabetes mellitus; HA1C = hemoglobin A1C; GERD = gastroesophageal reflux disease.

\* This data based on five patients who had preoperative HA1c levels and postoperative HA1C levels.

medications. Similarly, 11 (92%) of 12 patients with dyslipidemia no longer required medication based on the reported normalization of their cholesterol or triglyceride level. Of the 23 patients with hirsutism, 12 (52%) had complete resolution at a mean follow-up of  $8 \pm 2.3$  months (range 5–12), six (25%) had moderate resolution at a mean of  $21 \pm 18$  months (range 6–46), and 3 had minimal resolution at  $34 \pm 14$  months (range 21–49). Finally, 2 (8.7%) of the 23 patients reported no change in their hirsutism at 27 and 37 months. All patients had complete resolution of their menstrual abnormalities (Table 2). The mean time to normalization of the menstrual cycle postoperatively was  $3.4 \pm 2.1$  months (range 1–10).

All 5 patients who desired to conceive were able to do so postoperatively without the use of clomiphene.

## Discussion

PCOS is a complex endocrine disorder that is associated with, and aggravated by, obesity. Weight loss has been demonstrated to decrease insulin and androgen levels, as well as to improve the clinical manifestations of PCOS [1–18].

Our data support the hypothesis that weight loss results in resolution of the symptoms associated with PCOS. This weight loss, induced by surgical means, was followed by significant improvements in menstrual dysfunction and hirsutism. Our 75% rate of moderate to complete resolution of hirsutism is superior to that of alternate methods of treatment described in the literature [19]. In addition, marked improvement has been achieved in the treatment of comorbid conditions commonly associated with PCOS, including type II diabetes mellitus, hypertension, and dyslipidemia.

The phenomenon of resumed menstruation after surgically induced weight loss was also observed in the era of the jejunoileal bypass, before the abandonment of this surgical

option because of its long-term metabolic consequences [20]. The current mainline surgical options of Roux-en-Y gastric bypass [21] or the adjustable silicone gastric band (Inamed, Santa Barbara, CA) [22] have far fewer metabolic side effects and have been shown to be highly effective in reversing the insulin resistance associated with type II diabetes mellitus [21,23–25]. The metabolic effects of insulin have been implicated as a key mediator in PCOS syndrome [26].

Our experience with patients who conceived after weight loss is not unique [15,27–30]. However, pregnancy following weight loss surgery, among women who have been previously diagnosed with infertility, has only been reported by Doldi et al. [31]. We believe it is noteworthy that all 5 patients who were infertile before surgery were able to conceive without the aid of clomiphene. Surgery in these instances is beneficial, as it is the only durable method of obtaining sustained weight loss [32,33], thereby improving the chances for successful conception and gestation.

Our study had some limitations, including the small size of the group and the retrospective nature of the analysis.

## Conclusion

Our results suggest that obese patients with PCOS who undergo gastric bypass will experience a significant improvement in multiple clinical problems related to the disorder. Larger prospective studies are needed to confirm further the benefit of surgically induced weight loss in the treatment of women with PCOS.

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