CME ACTIVITY

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CME Objectives

After completing this CME activity, the psychiatrist should be able to:

- Examine the effect of anorexia nervosa on a woman's ability to both conceive and carry a pregnancy to term
- Consider the effect of maternal body weight on both maternal and fetal complications of pregnancy
- Determine what additional prenatal care needs should be appropriate for women with a history of anorexia nervosa

Statement of Need and Purpose

Physicians responding to articles in *The Journal of Clinical Psychiatry* and its related CME activities have indicated a need to know more about the diagnosis and management of patients who have eating disorders. This CME enduring material provides clinically relevant information about patterns of fertility and reproduction in women with a history of anorexia nervosa. There are no prerequisites for participating in this CME activity.

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Fertility and Reproduction in Women With Anorexia Nervosa: A Controlled Study

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Background: Women who have anorexia nervosa may experience difficulties with fertility and reproduction.

Method: We examined fertility and reproductive history in 66 women who had a history of anorexia nervosa (DSM-III-R) and 98 randomly selected community controls as part of a follow-up investigation examining the course of anorexia nervosa.

Results: Although women with a history of anorexia nervosa and controls did not differ on rate of pregnancy, mean number of pregnancies per woman, or age at first pregnancy, women with anorexia nervosa had significantly more miscarriages and cesarean deliveries, and the offspring of women with anorexia nervosa were significantly more likely to be born prematurely and were of lower birth weight than offspring of controls. There were no differences between women with active versus remitted anorexia nervosa on any of these measures; however, offspring of anorexic women with no history of bulimia nervosa had significantly lower body weight than offspring of anorexic women with a lifetime history of bulimia nervosa.

Conclusion: Our results argue for intensive prenatal care for women with both active and remitted anorexia nervosa to ensure adequate prenatal nutrition and fetal development.

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It was previously believed that pregnancy in women with anorexia nervosa was quite rare, secondary to the endocrinologic, psychologic, and psychosocial features of the disorder.[1,2] Supporting these beliefs, caloric restriction and undernutrition have been identified as contributing factors to infertility in women—not just those with anorexia nervosa.[3,4] With recent advances in fertility technology, women with anorexia nervosa who are at low body weight and amenorrheic may now successfully conceive.[5] The induction of pregnancy in women with active anorexia nervosa has raised important questions regarding pregnancy complications and mothering patterns in these women.[6–9]

Examining the effects of maternal body mass index (BMI, kg/m^2) on pregnancy outcome in the general population provides a context for the examination of the effects of eating disorders on reproduction. A higher incidence of birth complications arises at both the low and high end of the maternal BMI spectrum. Population-based data reveal that offspring of mothers with a BMI > 30 have the highest infant mortality rate.[10] In addition, underweight mothers (BMI < 19) are at significantly greater risk of delivering infants who weigh below the 10th centile.[11] Although neither of these studies controlled for the presence of eating disorder, they reveal the importance of maternal weight on pregnancy outcome.

Studies that have directly addressed pregnancy in women with eating disorders have yielded conflicting results. Low birth weight has been cited in a number of studies of women who were underweight or endorsed eating disorder symptoms.[8,12] Treasure and Russell[13] noted that the fetuses of women with anorexia nervosa experience a rate of abdominal circumference growth that is diminished during the third trimester and below the 3rd centile at birth. In addition, markedly higher perinatal mortality (greater than 6 times the expected rate) was observed in offspring of women with anorexia nervosa. These findings have not been universally replicated,[14] and there is some evidence that complications may be greater

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in women with current rather than remitted eating disorders.[15]

The above studies have provided preliminary evidence on potential problems with fertility and reproduction faced by women with eating disorders. Unfortunately, many of the studies relied on questionnaires and failed to provide clear diagnostic information about the mothers, and none had a control group without eating disorders. The purpose of the present study was to examine patterns of fertility and reproduction in women with a history of anorexia nervosa in comparison to a randomly selected sample of controls.

METHOD

Overview

Complete details of the methods used in this study have been presented elsewhere.[16] The purpose of this portion of the study was to assess fertility and reproduction in women with a history of anorexia nervosa in comparison with randomly selected controls. The design comprised a historical observational cohort study in which women with anorexia nervosa who were assessed or treated over a decade earlier were located and followed up, paired with a case-control study. The study was reviewed and approved by the local ethics committee, and all subjects provided written informed consent.

Case Definition and Ascertainment

Potential cases were drawn from the records of the Eating Disorders Service at The Princess Margaret Hospital in Christchurch, New Zealand. Any woman assessed or treated by the Eating Disorders Service for the first time from January 1, 1981, to December 31, 1984, was eligible for inclusion in this study.

The hospital record of every new referral seen during 1981–1984 was independently reviewed and abstracted by 2 trained medical students under the close supervision of P.F.S. Following a consensus conference between the 2 raters and P.F.S., potential cases were defined as any woman first seen by the Eating Disorders Service in 1981–1984 who met DSM-III or DSM-III-R criteria for definite or probable anorexia nervosa.

Case Finding

To locate potential cases, we used a variety of methods including (1) a computerized search of the New Zealand mortality database to identify any women among the potential cases who may have died; (2) the addresses listed in the hospital case notes (e.g., for the person, parents, and general practitioner); (3) searches of all New Zealand telephone directories; and (4) searches of the electoral roll directories. For the women not located through these means, we arranged for a search of the New Zealand Register of Births, Deaths, and Marriages to identify the names of any women who might have changed names through marriage. Finally, we also checked the telephone directories and electoral rolls for the major metropolitan areas in Australia.

Control Definition and Ascertainment

To obtain a community sample of adult women, we randomly selected individuals from the 1993 Christchurch electoral rolls. All adults are required by New Zealand law to register for the electoral roll, and 95.5% of the adult population was in fact registered.[17] These women were matched to women with anorexia nervosa by gender and age banding (i.e., current age = 23–45 years).

Subjects

A chart review identified 89 individuals who were thought to have had definite or probable anorexia nervosa. Of these 89 potential cases, 1 had died by suicide, 3 could not be located, 8 did not give full consent, and, upon interview and diagnostic review, 7 clearly had never met criteria for anorexia nervosa. Personal interviews were thus obtained with 70 women who met lifetime DSM-III-R criteria for anorexia nervosa. The participation rate for cases was thus 86.4% (70/[89–1–7]). For controls, 111 women were approached, 10 refused and 3 were excluded because of the presence of subthreshold anorexic symptoms. Personal interviews were obtained with 98 women, none of whom met lifetime DSM-III-R criteria for anorexia nervosa. The participation rate for controls was 91.7% (101/111). The participation rates of cases and controls were not statistically different ($p = .32$) and were somewhat greater than the rate in a large community survey using the Christchurch electoral rolls.[17] Four cases granted only truncated interviews that did not include questions on fertility and reproduction. Thus, the effective sample size for this study was 66 case subjects and 98 control subjects.

Data Collection Protocol

The interview was performed face-to-face for 91.4% of the cases, and the remainder were interviewed by telephone where geographic distance was prohibitive (i.e., residence in Australia, England, or North America). Information on fertility, reproductive history, and obstetric complications was obtained by patient report as part of a

Table 1. Clinical Characteristics and Obstetric History in Women With Anorexia Nervosa and Controls

Variable	Anorexic Group (N = 66)		Controls (N = 98)		Analysis	
	Mean	SD	Mean	SD	t	p
Age at interview, y	32.4	8.0	35.5	6.2	–2.83	.005
Current BMI, kg/m^2	20.1	2.1	25.6	6.4	41.9	< .0001
Ideal BMI	19.7	1.9	22.6	2.6	57.2	< .0001
Lowest past BMI	14.7	1.7	20.8	3.1	200.9	< .0001
Highest past BMI	22.8	3.0	27.3	6.7	23.5	< .0001
Mean number of pregnancies	1.8	2.3	1.9	1.4	0.17	NS
Age at first pregnancy, y	24.5	4.7	23.7	4.7	0.92	NS
Mean gestational weight, g	3139	617	3337	535	6.40	.01
	N	%	N	%	χ^2	p
Infertility treatment	3	5	11	11	FET[b]	NS
Ever pregnant	45	68	76	78	0.66	NS
Abortions[a]	12	27	10	13	3.47	.06
Miscarriages[a]	17	38	12	16	7.50	.006

[a]Indicates the number of women who experienced abortions and miscarriages, not the total number of each event reported. The denominator is the number of women who had ever been pregnant.
[b]FET = Fisher exact test.

Table 2. Clinical Characteristics and Obstetric History in Anorexic (AN) Women With and Without Lifetime Bulimia Nervosa (BN)

Variable	AN + BN (N = 37)		AN Only (N = 29)		Analysis	
	Mean	SD	Mean	SD	t	p
Age, y	31.6	6.5	33.5	9.6	0.97	NS
Current BMI, kg/m^2	20.3	2.4	19.9	1.7	0.64	NS
Mean number of pregnancies	1.8	2.7	1.7	1.6	–0.32	NS
Age at first pregnancy, y	25.2	5.4	23.8	3.6	–1.01	NS
Mean gestational weight, g	3327	622	2993	579	–2.3	.02
	N	%	N	%	χ^2	p
Ever pregnant	25	68	20	69	0.02	NS
Abortions[a]	10	40	12	60	1.78	NS
Miscarriages[a]	8	32	12	60	3.53	.06

[a]Indicates the number of women who experienced abortions and miscarriages, not the total number of each event reported. The denominator for the ratios is the number of women who had ever been pregnant.

more extensive structured psychiatric interview using the Diagnostic Interview for Genetic Studies.[18]

Statistical Analysis

Continuous variables were compared between groups with Student t tests and categorical variables with chi-square or the Fisher exact test. Given that there was a significant difference in age between cases and controls, age was included as a covariate in nominal logistic and standard least squares regression procedures. All analyses were performed with JMP[19] or SAS.[20]

RESULTS

Cases Versus Controls

A complete description of the nature of the case and control samples including comorbidity and psychometric profiles has been reported elsewhere.[16] Table 1 presents demographic and obstetric history for cases and controls. BMI data indicate that women with anorexia nervosa were at a significantly lower body weight at the time of interview than controls (this difference remained even after controlling for the presence of current anorexia nervosa). By definition, cases had also had significantly lower minimum past BMIs than controls, and controls reported significantly higher maximum past BMIs. There was no difference across groups in the percentage of women who received treatment for infertility. Sixty-eight percent of cases and 78% of controls reported ever having been pregnant (a nonsignificant difference).

As indicated in Table 1, there were no differences in the mean number of pregnancies per woman across groups nor in age at first pregnancy. Significantly more women in the anorexia group than the control group had miscarriages, and there was a statistical trend for more women in the anorexia nervosa group to have had an abortion. The mean gestational weight for live births was significantly lower for the offspring of women with anorexia nervosa than the offspring of controls.

Effect of Current Anorexia Nervosa on Reproduction

We then compared obstetric history in those women determined to have been actively anorexic at the time of pregnancy to that in women who either had recovered from anorexia nervosa prior to conception or first met criteria for anorexia nervosa after childbirth. There were no significant differences in the percentage of women in each group who had ever been pregnant, the percentage of women who received fertility treatment, the number of pregnancies per woman, or in the percentage of women with miscarriages or abortions (data not shown).

Effect of Lifetime Bulimia Nervosa on Reproduction

Table 2 presents the next series of analyses in which we compared anorexic women with (N = 37) and without (N = 29) a lifetime diagnosis of bulimia nervosa. There

Table 3. Maternal Obstetric Complications in Women With Anorexia and Controls[a]

	Anorexic Group (N = 45)		Controls (N = 76)		χ^2	
Complication	N	%	N	%	or FET	p
No complication	23	51	57	75	7.2	.007
Confined to bed	1	2	0	0	FET	NS
Preeclampsia	5	11	8	10	.04	NS
Severe vomiting	1	2	3	4	FET	NS
Premature labor	0	0	1	1	FET	NS
Induced labor	3	7	7	9	FET	NS
Cesarean delivery	7	16	2	3	FET	.01
Forceps delivery	4	9	11	15	FET	NS
Breech presentation	0	0	4	5	FET	NS
Posterior presentation	1	2	3	4	FET	NS
Retained placenta	0	0	4	5	FET	NS
Postpartum hemorrhage	1	2	3	4	FET	NS
Postpartum infection	0	0	1	1	FET	NS
Other	2	4	1	1	FET	NS

[a] The 45 women with anorexia gave birth to 69 offspring and the 76 control subjects gave birth to 153 offspring. The values indicate the number of women who experienced each of the complications, not the total number of complications reported; that is, if a woman had 2 cesarean sections, it is reported as 1 individual rather than 2 procedures. In addition to the numbers reported, 4 anorexic women and 7 controls experienced more than 1 complication on at least 1 occasion, and 1 anorexic mother experienced 3 complications.

Table 4. Fetal Complications in Offspring of Women With Anorexia and Controls[a]

	Anorexic Group (N = 45)		Controls (N = 76)		χ^2	
Complication	N	%	N	%	or FET	p
No fetal complication	28	67	59	78	3.3	.07
Resuscitated	2	4	2	2	FET	NS
Small for gestational age	1	2	1	1	FET	NS
Premature	9	20	6	8	3.8	.05
Jaundice	0	0	5	6	FET	NS
Rh incompatible	0	0	8	11	FET	NS
Congenital anomaly	1	2	2	2	FET	NS
Cord around neck	1	2	0	0	FET	NS

[a]Indicates the number of women who had at least 1 child who experienced each of the complications, not the total number of complications reported; that is, if a woman had 2 offspring who were small for gestational age, it is reported as 1 individual rather than 2 occurrences.

were no significant differences across subgroups in the percentage of women who had ever been pregnant nor in the mean number of pregnancies per woman. There was a trend for more women in the anorexia-only group to have miscarriages. The mean gestational weight for the offspring of women with anorexia only was significantly lower than for the offspring of anorexic women with lifetime bulimia nervosa.

Obstetric Complications Associated With Live Births

Examining live births only, we then compared obstetric complications in women with anorexia nervosa and in controls. Table 3 indicates that significantly more controls experienced uncomplicated deliveries than did women with anorexia nervosa. Examining the nature of the complications, significantly more women with anorexia nervosa had cesarean deliveries than did controls. There were no differences between groups in rates of any of the other maternal complications noted.

Fetal Complications Associated With Live Births

Again, examining live births only, the offspring of significantly fewer control women experienced fetal complications at birth than offspring of anorexic women (Table 4). Examining the nature of the fetal complications, significantly more offspring of the women with anorexia nervosa were born prematurely than offspring of controls.

Effect of Current Anorexia Nervosa on Obstetric Complications

We then attempted to determine whether the observed effects were due primarily to the presence of anorexia nervosa at the time of pregnancy. Of all of the live births among women with anorexia nervosa, 10 children were born prior to the first onset of anorexia nervosa, 78 were born after recovery from anorexia nervosa, and 30 were born prior to recovery from anorexia nervosa. Although statistical power was insufficient to detect a significant difference (power analyses indicated that over 500 births would be required to detect a difference at the $p < .05$ level), the mean ± SD birth weight of children born prior to the first onset of anorexia nervosa (3317 ± 869 g) was greater than the mean birth weights of the children born either after recovery from the disorder (3104 ± 654 g) or during an active phase of the illness (3130 ± 386 g). None of the children born to mothers who had not yet developed anorexia nervosa were delivered by cesarean section, whereas 6% of children born after recovery and 13% of children born during the acute phase of the illness were delivered in this manner.

DISCUSSION

In this controlled investigation of fertility and reproduction in women with a history of anorexia nervosa and

controls, several parameters emerged as significantly different, suggesting that a history of anorexia nervosa may be associated with more frequent obstetric complications.

Contrary to expectations, there were no apparent differences in the number of cases and controls who received fertility treatment, nor in the percentage of cases and controls who had ever been pregnant, the total number of pregnancies per woman, nor the age at first pregnancy. Thus, at least in this sample, having a history of anorexia nervosa that necessitated referral to a specialist service did not appear to affect the ability to conceive.

In terms of the outcome of the pregnancies, however, differences between groups did emerge. Of the women who had been pregnant, approximately twice as many women with anorexia (30%) than controls (16%) experienced miscarriages. Therefore, it appears that a history of anorexia nervosa is associated with difficulties in carrying an infant to term. There was no difference in the rate of miscarriage between those women who were actively anorexic during pregnancy and those who were remitted. This could suggest either that anorexia nervosa at any time in life has an adverse effect on reproduction or that women who have had anorexia nervosa in the past continue to engage in some of the behaviors (i.e., restrictive eating or dieting) during pregnancy that could theoretically affect pregnancy outcome. It is important to view these results as tentative, because the timing of pregnancy in relation to episodes of the disorder is unlikely to be precise. Although the difference was not significant, women who had anorexia nervosa alone (i.e., did not report a lifetime history of bulimia nervosa) were twice as likely as those with such a history to miscarry.

We then narrowed our focus to examine the frequency and nature of maternal and fetal complications in those infants who were carried to term. The most striking difference was that significantly more women with anorexia nervosa delivered via cesarean section than controls. As we did not have data on the precise reason for the cesarean delivery, we are unable to determine the cause of this higher rate. These results are consistent with Fahy and O'Donoghue[6] and Stewart et al.[15] who showed that women with anorexia nervosa were more likely to experience difficult labors that required medical intervention. Likewise, Lemberg and Phillips[14] reported that women with anorexia nervosa are often viewed as high-risk by their obstetricians—an additional factor that may increase the likelihood of having a cesarean delivery.

In terms of fetal complications, the only significant difference that emerged was the greater likelihood of women with anorexia nervosa to give birth to premature infants than controls. Again, the precise mechanism for prematurity is unknown.

Perhaps the most concerning finding of this study is significantly lower average gestational weight of offspring of women with a lifetime history of anorexia nervosa in comparison to offspring of controls. These data are consistent with the findings of Stewart et al.[15] and Brinch et al.[8] and with the findings of our prior study of older offspring of women with eating disorders.[21] Although statistical power was limited, there was no apparent difference in mean birth weight between offspring born to recovered versus actively anorexic mothers. This may reflect the fact that even when recovered, women with a history of anorexia nervosa tend to maintain a comparatively low BMI[16] and may continue to exhibit restrictive eating patterns.

It is possible that women with current or past anorexia nervosa fail to consume adequate calories during their pregnancy, leading to lower birth weight infants. In addition, it appears that those women with a restrictive pattern of anorexia produce even lighter infants than those women who also display bulimic eating patterns. Although preliminary data suggest that these early deficits in birth weight are equalized within the first 3 months postpartum,[21] the long-term effects of lower birth weight in the offspring of women with anorexia nervosa are unknown. Given the inadequacy of the diets of women with anorexia nervosa, it is conceivable that their diet during pregnancy is depleted in both quantity and nutritional quality, which could lead to more subtle developmental deficiencies in their offspring.

Although it has been suggested that women with active anorexia nervosa require especially intensive prenatal care, the present findings suggest that this recommendation may be relevant for women with a history of anorexia nervosa as well. It is possible that the weight gain associated with pregnancy rekindles concerns about shape and weight in women with a history of anorexia nervosa and may contribute to inadequate prenatal nutrition contributing to miscarriage, low birth weight, prematurity, and birth complications. In terms of management, it is important to emphasize to the mother that her attempts at caloric restriction could directly affect her child. Thus, we recommend adequate prenatal care including nutritional counseling and support during prenatal weight gain, as well as clear and accurate information about the nature and timing of weight gain and postpartum weight loss for women with a history of anorexia nervosa.

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Psychiatrists may receive 1 hour of Category 1 credit toward the American Medical Association Physician's Recognition Award by reading the article starting on page 130 and correctly answering at least 70% of the questions in the posttest that follows.

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1. Population-based data suggest a higher incidence of birth complications in mothers who are:

a. At the low end of the BMI spectrum (i.e., BMI < 19 kg/m^2)
b. At the high end of the BMI spectrum (i.e., BMI > 30 kg/m^2)
c. Of normal weight
d. At both the low and high end of the BMI spectrum
e. None of the above—maternal weight is not related to birth complications

2. Which of the following statements is true?

a. Women with anorexia nervosa have marked difficulty conceiving.
b. In this sample, significantly more women with anorexia nervosa sought infertility treatment than controls.
c. Women with anorexia nervosa reported significantly more miscarriages than control women.
d. Control women reported a greater number of abortions than women with anorexia.
e. There was no difference in pregnancy outcome between women with anorexia nervosa and controls.

3. How can one best describe the differences between the reproductive history of women with anorexia nervosa only and that of women with anorexia nervosa and a lifetime history of bulimia nervosa?

a. Fewer women with anorexia nervosa only had ever been pregnant.
b. Fewer women with a history of bulimia nervosa had every been pregnant.
c. Women with a history of bulimia nervosa were significantly younger at the age of first pregnancy.
d. Significantly more women with anorexia nervosa had abortions.
e. The mean gestational weight for the offspring of women with a history of bulimia was significantly higher than the mean gestational weight of offspring of women with anorexia nervosa only.

4. In comparing the nature of fetal complications in women with anorexia nervosa and controls, we found that:

a. There were no differences in fetal complications between women with anorexia nervosa and controls
b. More women with anorexia nervosa gave birth to premature infants than control women
c. More offspring of women with anorexia nervosa required resuscitation than offspring of controls
d. The prevalence of congenital anomalies was geater in offspring of women with anorexia nervosa than in controls
e. Rh incompatibility was a more frequent complication in women with anorexia nervosa than in controls

5. How can one best describe the relation between a history of anorexia nervosa and mean gestational weight of offspring?

a. The offspring of women with anorexia nervosa, regardless of state of illness at the time of pregnancy, tend to be of lower gestational weight than the offspring of controls.
b. Only the offspring of women who were actively anorexic at the time of pregnancy tend to be of lower mean gestational weight than offspring of controls.
c. There are no clear differences in the mean gestational weights between women with anorexia nervosa and controls.
d. Once a woman has recovered from anorexia nervosa, her offspring do not appear to be at increased risk for lower birth weight than do offspring of controls.
e. Given that women with anorexia nervosa rarely carry an infant to term, it is difficult to draw conclusions about the mean gestational weight of their offspring.

6. The results of the present study argue:

a. For careful prenatal care including nutritional counseling and support during the period of weight gain and postpartum weight regulation for women with active anorexia nervosa only
b. That careful prenatal care including nutritional counseling and support during the period of weight gain and postpartum weight regulation be extended to both women with active anorexia nervosa as well as those with a history of anorexia nervosa
c. That routine prenatal care should be sufficient for women with active and remitted anorexia nervosa provided weight gain is monitored regularly
d. That pregnancy appears to have a beneficial effect on women with anorexia nervosa as it is easier for them to gain weight if they perceive the weight gain to be "for the baby"
e. For recommending the patients with anorexia nervosa delay pregnancy until they have recovered from the eating disorder

7. Other areas worthy of consideration in the prenatal and postnatal care of women with anorexia nervosa include:

a. Evaluating the appropriateness of caloric intake if breastfeeding is undertaken
b. Evaluating attempts at excessive exercise during or after pregnancy
c. Resurgence of restrictive eating patterns after delivery in attempts to restore prepregnancy weight
d. The mother's ability to nourish her offspring appropriately
e. All of the above

Answers to the August 1998 CME posttest

1. c 2. a 3. d 4. e 5. a 6. d 7. c

Circle the one correct answer for each question.

1.	a	b	c	d	e
2.	a	b	c	d	e
3.	a	b	c	d	e
4.	a	b	c	d	e
5.	a	b	c	d	e
6.	a	b	c	d	e
7.	a	b	c	d	e

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1. Was the educational content relevant to the stated educational objectives? ❑ Yes ❑ No

2. Did this activity provide information that is useful in your clinical practice? ❑ Yes ❑ No

3. Was the format of this activity appropriate for the content being presented? ❑ Yes ❑ No

4. Did the method of presentation hold your interest and make the material easy to understand? ❑ Yes ❑ No

5. Achievement of educational objectives:
   A. Enabled me to examine the effect of anorexia nervosa on a woman's ability to both conceive and carry a pregnancy to term. ❑ Yes ❑ No
   B. Enabled me to consider the effect of maternal body weight on both the maternal and the fetal complications of pregnancy. ❑ Yes ❑ No
   C. Enabled me to determine what additional prenatal care needs should be appropriate for women with a history of anorexia nervosa. ❑ Yes ❑ No

6. Did this CME activity provide a balanced, scientifically rigorous presentation of therapeutic options related to the topic, without commercial bias? ❑ Yes ❑ No

7. Does the information you received from this CME activity confirm the way you presently manage your patients? ❑ Yes ❑ No

8. Does the information you received from this CME activity change the way you will manage your patients in the future? ❑ Yes ❑ No

9. Please offer comments and/or suggested topics for future CME activities.

   _____

   _____

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