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A monthly update of developments in female reproductive medicine

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An Analysis of Two vs. Three Grades for Endometrial Cancer

ABSTRACT & COMMENTARY

Taylor and associates retrospectively reviewed endometrial biopsy and uterine histology specimens, quantifying the percentage amount of nonsquamous solid tumor by intervals of 10. They then compared these percentage values to other histopathologic prognostic variables. The current grading of uterine endometrioid adenocarcinoma uses a three-grade system based on the amount of nonsquamous solid histologic architecture. Of these three grades, Taylor et al questioned the practical clinical utility of the intermediate grade. Eighty-five stage I and II endometrioid adenocarcinoma patients had their preoperative endometrial curettings and operative hysterectomy pathology specimens reviewed independently by two gynecologic pathologists for surgical staging and outcome with mean follow-up time of six years.

A two-tiered system for assessing uterine tumors found less interobserver variation (k = 0.966) compared to the current three-tiered grading system (k = 0.526). There were no differences between the two- and three-tiered grading systems regarding myometrial invasion, lymph vascular space invasion, and survival. In the diagnosis of endometrial biopsies, the two-tiered system also improved the prediction of uterine histology grade over the three-tiered system, (90% and 63% respectively). Taylor et al concluded that a two-grade architecture system with a delineation value of 20% would be more reliable and less cumbersome and would have the same or better prognostic significance as the currently used three-grade system. (Taylor RR, et al. *Gynecol Oncol* 1999;74:3-6.)

COMMENT BY DAVID M. GERSHENSON, MD

Endometrial cancer is the most common gynecologic malignancy and afflicts approximately 40,000 women in the United States annually. Several prognostic factors are associated with outcome, the most important of which are FIGO stage, histopathologic grade, myometrial invasion, and histologic subtype. The most common histologic subtype of endometrial cancer is endometrioid. The current FIGO grading system includes three levels—well differentiated, moderately differentiated, and poorly differentiated. In the pre-

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sent study, Taylor et al suggest that a two-grade system would be more reproducible than a three-grade system. In this small study of 85 early-stage patients, they produce data to support their hypothesis. Seemingly, this type of simplification of the grading system flies in the face of the current trends in oncology. Particularly with the explosion of information about the molecular biology and genetics of gynecologic neoplasms, the current push is to individualize treatment based on the patient's unique clinicopathologic and molecular profile. However, I personally support the efforts of Taylor et al and happen to agree with their findings. A simpler, more reproducible grading system would not, in my opinion, compromise our efforts toward individualization of treatment; in fact, it might enhance them. Our group at M.D. Anderson Cancer Center has unofficially adopted a similar system for the grading of epithelial ovarian cancer. Clearly, a broader study of this area is necessary, with several participating pathologists and institutions, before the scientific community can embrace such a change. ❖

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Maternal and Child Health After Forceps or Vacuum Delivery

ABSTRACT & COMMENTARY

Synopsis: *There is no evidence to suggest that the use of either a vacuum extractor or forceps is more or less likely to be associated with adverse outcomes for the mother or her child five years after delivery.*

Source: Johanson RB, et al. *Br J Obstet Gynaecol* 1999;106:544-549.

To determine whether there were differences in maternal or pediatric outcomes in women delivered by forceps or vacuum extraction, Johanson and associates performed a five-year follow-up study of a cohort of women who had been delivered in a randomized controlled trial performed in England. Most were low or outlet deliveries with the fetus in the occiput anterior position. Questionnaires were sent to women asking about bowel and urinary dysfunction and child development, including the child's vision. Nearly 75% of the questionnaires were returned (228/306), including 113 women who had been delivered by vacuum extraction and 115 who had been delivered by forceps. In response to questions about loss of bowel or bladder control, no significant differences were noted between the groups. However, adverse symptoms were relatively common with 47% of the women reporting urinary incontinence of varying severity, 44% describing bowel urgency, and 20% noting loss of bowel control "sometimes" or "frequently." Overall, the incidence of childhood developmental problems was low, with no significant differences between the groups. Thirteen percent of the 158 children who had had eye examinations had visual problems. Most of these were refraction errors, far sightedness, or amblyopia, and all but a few were associated with a positive family history for this problem.

Johanson et al conclude there is no evidence to suggest that the use of either a vacuum extractor or forceps is more or less likely to be associated with adverse outcomes for the mother or her child five years after delivery .

COMMENT BY STEVEN G. GABBE, MD

When considering whether to use forceps or a vacuum extractor for an assisted vaginal delivery, the

obstetrician is most likely to use the instrument with which he or she is most comfortable. It has been assumed that the vacuum extractor, while less traumatic for the mother, may be associated with more neonatal risk including cephalohematomas and retinal hemorrhages.

Maternal bladder and bowel function after a normal or assisted vaginal delivery have not been well studied. Johanson et al now present data from a large prospective randomized controlled trial of vacuum extraction and forceps. At the time of delivery, significant maternal injuries including third-degree perineal tears or lacerations of the upper vagina were more common in women delivered with forceps (12/115, 10%) when compared to vacuum extraction (6/113, 5%). However, at five years of follow-up, there were no significant differences between the study groups.

Regardless of the method of delivery, women frequently reported bowel or urinary bladder dysfunction. Johanson et al do emphasize that some of these problems may be related to factors other than birth trauma and note that they have observed a high incidence of similar problems in women having a spontaneous vaginal delivery. Certainly, the information on pediatric outcome is reassuring. ❖

Postmenopausal Hormone Therapy Reduces the Risk of Colorectal Cancer

ABSTRACT & COMMENTARY

Synopsis: *Current use of postmenopausal hormone therapy provides substantial protection against colorectal cancer.*

Source: Grodstein F, et al. *Am J Med* 1999;106: 574-582.

Grodstein and associates performed a meta-analysis of the 18 published epidemiologic reports that have examined the association between postmenopausal hormone therapy and the risk of colorectal cancer. Overall, there was a 20% reduction in the risk of colon cancer and a 19% decrease in the risk of rectal cancer whenever users of postmenopausal hormone therapy were compared with never users. Nine studies indicated a similar benefit for both proximal and distal colon cancers. Greater protection was associated with current use compared with ever use. A summary of 10 studies with information on timing of hormone use indicated a 34% reduced risk of colorectal cancer in current users. The protection was substantially lost within several years after discontinuing hormone use, and by five years a benefit was no longer apparent. Surprisingly, there was no indication that protection was affected by duration of use. Although data were limited, there was no indication that the effect was influenced by the addition of a progestational agent to treatment regimens. These estimates were unaffected by various adjustments to correct for possible differences between hormone users and nonusers (such as body mass index, aspirin use, and smoking).

COMMENT BY LEON SPEROFF, MD

In the latest cancer statistics for U.S. women, colorectal cancer accounts for 11.2% of all cancers, third in prevalence after breast (29.7%) and lung cancers (13.3%), and 9.8% of cancer deaths, compared with 24.8% from lung cancer and 16.1% from breast cancer.[1] In both prevalence and mortality, colorectal cancer outranks the more familiar reproductive cancers (endometrial, ovarian, and cervical).

One can only speculate regarding the biologic mechanism for this protective effect of estrogen. Estrogen causes a decrease in bile acids, substances associated with promotion of colorectal cancer. Estrogen may maintain tumor suppression, either directly or indirectly by reducing mitogens such as insulin like growth factor.

An anti-estrogen can be expected to have opposite effects, and there is some evidence that tamoxifen is associated with a slight increase in the risk of colorectal cancer, raising concerns regarding the long-term effects of the selective estrogen receptor modulators (like raloxifene).

Although the results of the ongoing long-term randomized clinical trials will be necessary to confirm this effect of estrogen, the uniformity and agreement among the many observational studies make it legitimate to provide this information to our patients. Indeed, this is a little-publicized effect of estrogen even among healthcare providers. I believe it is appropriate and important to include this possible benefit in our discussions regarding the use of postmenopausal hormones. This is especially important to elderly women considering hormone therapy for the first time. ❖

Reference

1. American Cancer Society, http://www.cancer.org/statistics.html.

Severity of Osteopenia in Estrogen-Deficient Women with Anorexia Nervosa and Hypothalmic Amenorrhea

ABSTRACT & COMMENTARY

Synopsis: *Women with anorexia nervosa had lower bone density of the lumbar spine and hip than women with functional hypothalamic amenorrhea, despite the presence of comparable duration of amenorrhea in both groups. Both women with AN and FHA had lower bone density than eumenorrheic women.*

Source: Grinspoon S, et al. *J Clin Endocrinol Metab* 1999;84:2049-2055.

Grinspoon and associates undertook the present study to determine if factors other than estrogen deficiency contribute significantly to the osteopenia seen in amenorrheic women. To do this, they compared bone densities and other biochemical parameters in women with anorexia nervosa (AN) whose amenorrhea is due largely to undernutrition to those with amenorrhea and normal body weight, i.e., women with functional hypothalmic amenorrhea (FHA). A control group of eumenorrheic women was included. A total of 79 women were enrolled. Nineteen had FHA, 30 had AN, and 30 were eumenorrheic. Women with FHA were between 90 to 110% of ideal body weight, whereas those with AN weighed less than 85%. Physical activity was comparable in FHA and AN. Total calcium and vitamin D intakes did not differ between the three groups. Lifetime duration of amenorrhea, age of menarche, estradiol level, testosterone level, and prior use of estrogen also did not differ between the AN and FHA groups. Body mass index, lean body mass, calorie intake, fat intake, and IGF-I were lower in AN compared to FHA and control women. Bone density was lowest in AN and highest in the controls. At the lumbar spine, 40% of AN and 16% of FHA demonstrated spinal bone density more than 2.0 SD below the expected outcome. Likewise, at the hip, 40% of AN and only 5% of FHA had bone density more than 2.0 SD below the expected outcome.

COMMENT BY SARAH L. BERGA, MD

Bone accretion in women depends on several factors, including estrogen exposure, adequate calcium and mineral intake, sufficient vitamin D exposure, appropriate amounts of exercise, and overall good nutrition. Excess cortisol blocks and androgens increase osteoblastic activity. Osteoblasts build bone, so too much cortisol of either endogenous or exogenous origin can prevent bone formation. In contrast, estrogens decrease osteoclast activity, thereby slowing bone resorption. Bone accrues when osteoblast activity exceeds that of the osteoclasts. One might think that women with anorexia nervosa, who are thought to have cortisol levels much higher than those of women with "garden variety" FHA would have lower bone mass than women with FHA because of reduced osteoblastic activity. This study shows that women with AN do indeed have lower bone mass, but not because they have higher cortisol levels. Interestingly, women with FHA had elevated 24-h urinary free cortisol levels more often (50%) than women with AN (30%). Rather than having decreased osteoblastic activity and decreased bone formation, women with AN had lower bone mass largely due to increased bone resorption. This differentially increased bone resorption seen in AN and less so in FHA was attributed not to differences in estrogen exposure but, rather, the impact of undernutrition. The important take-home point, and one not mentioned by Grinspoon et al, is that this biochemical picture suggests that women with AN might respond better to bisphosphonates or exogenously given sex steroids, which slow bone resorption, than women with FHA.

This paper raises a related point. I have often been asked if FHA is not just a milder version of AN. Certainly, in some aspects, FHA and AN are similar. Both are accompanied by amenorrhea due to decreased GnRH drive. But this paper supports the view that they are different in some important ways. One is that the genesis of the disorders differs. Women with AN eat significantly less and weigh significantly less than women with FHA. The primary cause of AN is undernutrition and a distorted body image that creates a huge drive for thinness. Women with FHA may lose weight and not eat properly, but they do not starve themselves to the same extent. Our research supports the notion that women with FHA are stressed rather than seriously undernourished. This contention is supported by the somewhat higher cortisol levels observed in FHA as compared to AN in this study. Further, in my experience, women with FHA do not later become anorectics. This is not to say that anorectics are not sometimes misdiagnosed as having "garden variety" FHA. Because the genesis of AN and FHA differ, both the sequelae and treatment differ too. While anorexia is much less common (about 1% of reproductive-age women) than FHA (5-15% of reproductive-age women), only AN carries a risk of death. While it is important to recognize both disorders, if the diagnosis is

felt to be AN, it is imperative that prompt psychiatric consultation be instituted. Women with FHA, on the other hand, have a good chance of recovering ovulatory function if a compassionate clinician can guide them in the art of stress management and a healthier lifestyle. ❖

Prior Stillbirth and Depression in the Next Pregnancy

ABSTRACT & COMMENTARY

Synopsis: *Women who have had a prior stillbirth are significantly more likely to be depressed and anxious in the third trimester of their next pregnancy and at one year after delivery.*

Source: Hughes PM, et al. *BMJ* 1999;318:1721-1724.

To determine the likelihood of depression and anxiety during the next pregnancy in women who have had an intrauterine fetal death after 18 weeks gestation, Hughes and associates performed a cohort study of 60 women who have had a stillbirth and 60 matched controls. Women in both groups had no living children, were at least 20 years of age, had a partner, and were matched for socioeconomic group and ethnic origin. Patients in both groups were progressing normally in the present pregnancy. Depression and anxiety were evaluated in the third trimester and at six weeks, six months, and 12 months after delivery. Women who had a prior stillbirth were significantly more likely to be depressed and anxious in the third trimester of their pregnancy and at one year after delivery. Depression in the third trimester was highly correlated with depression one year later. These differences were due to a significantly higher rate of depression in women who conceived less than 12 months after their prior stillbirth. In contrast, women who had waited at least 12 months after their prior stillbirth were no different from controls on follow-up. Hughes et al conclude that the likelihood of depression and anxiety in a pregnancy following a stillbirth is related to the time since the fetal death with those who undertake a pregnancy within 12 months at greatest risk. Because increased maternal anxiety and depression may compromise pregnancy outcome and maternal-neonatal interactions after delivery, Hughes et al suggest that, if a patient has had a prior stillbirth, there may be an advantage in waiting 12 months before conception.

COMMENT BY STEVEN G. GABBE, MD

Women and their partners are often anxious to undertake a pregnancy after a fetal death in hopes of easing their grief by replacing their lost child. However, obstetricians have recognized that it may take 12 to 18 months or even longer to mourn for the fetal death. In addition, a prolonged grief response appears to be more common in women who become pregnant soon after their loss. These observations are confirmed in this carefully conducted cohort study by Hughes et al. Women who had had a prior fetal death, but who went on to a successful pregnancy, were more likely to be depressed and anxious if they undertook the subsequent pregnancy within 12 months of the stillbirth. Women who waited at least one year before becoming pregnant were found to be no different from controls. Hughes et al do not comment on the influence of an early (20-28 weeks gestation) or late (> 28 weeks gestation) fetal death on the likelihood of depression and anxiety in a subsequent pregnancy. ❖

Postmenopausal Hormone Therapy and Benign Breast Disease

ABSTRACT & COMMENTARY

Synopsis: *Postmenopausal hormone therapy does not increase the risk of invasive breast cancer in women with biopsy-proved benign breast disease.*

Source: Dupont WD, et al. *Cancer* 1999;85:1277-1283.

Dupont and associates from vanderbilt university reported a retrospective cohort study of women who underwent breast biopsies that proved to be benign between 1952-1978. The median duration of follow-up was 20 years. During this period of time, there were 444 cases of invasive breast cancer. Women who took estrogen and who had biopsy proven atypical hyperplasia had an increased risk of breast cancer, relative risk 2.87 (CI = 1.3-6.3), but this did not differ significantly from the relative risk in those who did not take postmenopausal estrogen therapy, relative risk 2.53 (CI = 1.0-6.3). Similarly, the relative risk did not differ in women with complex fibroadenoma, comparing users and nonusers. Women who had proliferative disease without atypia did not have a statistically significant increased risk of breast cancer whether they used estrogen or not. Dupont et al concluded that postmenopausal estrogen therapy does not increase the risk of invasive breast cancer in women with true benign breast disease, and that hormone therapy should be contraindicated in these women.

■ **COMMENT BY LEON SPEROFF, MD**

Approximately 5% of breast cancer patients have a history of benign breast disease. Statistical accuracy requires histological characterization and definition. The most important variable in biopsy specimens is the degree and character of epithelial proliferation, and only 4-10% of benign biopsies have atypical hyperplasia. For these reasons, this publication from Vanderbilt is unique and especially helpful. It is the only report with a substantial number (9494 women) followed after a consecutive series of biopsies and analyzed according to histologic types of benign breast disease. The results indicate that estrogen use does not increase the risk of breast cancer in women with surgically proven benign breast disease, even with atypia.

Thus far, there are insufficient data to evaluate the effect of adding a progestin to postmenopausal estrogen regimens. However, it is increasingly apparent that breast tenderness and discomfort are a reflection of the progestational agent, not estrogen (see the data from the PEPI trial).[1] Nevertheless, clinicians repeatedly receive complaints of mastalgia from elderly women beginning estrogen therapy for the first time. Although mastalgia by itself is not a risk factor for breast cancer, its presence often creates apprehension and affects compliance with hormone therapy. For these reasons, I recommend trying alternative progestational agents in younger women who report mastalgia, and beginning treatment in elderly women with lower doses of estrogen, either orally or transdermally. Recent studies have indicated that half the usual doses of oral estrogen can maintain bone. However, long-term data are not yet available (the impact on fracture rate and the number of nonresponders are not known). Therefore, after six months to one year, I recommend an increase to standard doses to maximize the bone, cardiovascular, and central nervous system effects. ❖

Reference

1. Greendale GA, et al. *Obstet Gynecol* 1998;92:982-988.

Special Feature

Tubal Sterilization Techniques

By Kenneth Noller, MD

Several months ago, one of our readers wrote the editorial staff and asked a question that I can paraphrase: "Which technique of tubal sterilization should we use in our practices?" Obviously, this physician is aware of the recent information that has been published from the Centers for Disease Control and Prevention (CDC). That information has changed the way many of us have approached our patients when discussing tubal sterilization.

The history of tubal sterilization is quite interesting. The first widely accepted method of tubal occlusion was the Pomeroy technique, devised by Ralph Pomeroy, but not reported during his lifetime. This simple procedure should be counted as one of the most important techniques ever developed in the field of gynecologic surgery. Although many other techniques of open sterilization have been developed, this simple, safe occlusion of the fallopian tubes using absorbable suture may be our best overall choice.

For many years, for many societal reasons (including religious, ethical, sexist, and racist) sterilization was frowned upon by the medical community. I well remember the years when a physician might not be allowed to perform a sterilization procedure without consultation from another physician, agreement in writing by the patient's husband, and classification of the patient according to some mixture of her age and parity. Fortunately, those days are behind us. Sterilization is currently the most widely practiced method of contraception in the United States.

Although laparoscopy was first introduced as a diagnostic procedure, it rapidly became the method of choice for the performance of tubal sterilization. Several different techniques were developed, unipolar cautery being the first. When significant problems with unipolar cautery were identified, bipolar cautery, silastic bands, and interlocking clips were (and are) widely used. Nonetheless, Pomeroy tubal sterilization remains a common procedure in the immediate postpartum.

As a resident in obstetrics and gynecology, I was taught that postpartum tubal sterilization was the method most likely to fail. Reviewing published data from that era, it is clear that: 1) there were no good data; and 2) postpartum tubal sterilization was no better or worse than other techniques.

However, by the 1980s information was beginning to emerge that suggested that postpartum tubal sterilization was as good as laparoscopy, and all were extremely successful.[1,2] But the data from these early reports of the "sterilization era" were flawed. Most represented short follow-up, inconsistent reporting, and poor study design.

Fortunately, the CDC accepted a proposal by Peterson and associates to perform a prospective study of

women undergoing tubal sterilization at several medical centers. As would be expected from this preeminent epidemiologic study group, the methodology and study execution are impeccable. Their publication,which came out in April 1996, provides us with information we can use directly when discussing tubal sterilization with our patients.[3]

The study identified several important outcomes. First, while tubal sterilization is effective overall (approximately 2 failures per 100 procedures after 10 years), it is less effective than most of us had expected, and there are considerable differences among the techniques. Based on the information from the early 1980s, most women have been quoted a risk of pregnancy following any type of tubal sterilization of approximately 3-4 per 1000 procedures. The CDC report clearly shows that the failure rate is substantially higher. The main reason for the high rate of failure was the discovery that pregnancies continue to occur for many years after the sterilization procedure. Previous studies usually only counted pregnancies within the first 12 months. When followed for 10 years the overall failure rate is nearly 2%. Likewise, the CDC was able to show that there were significant differences in success rates among the various procedures. In contrast to widely held beliefs, postpartum tubal sterilization (usually using the Pomeroy technique) and unipolar coagulation resulted in the lowest rate of pregnancy, with less than 1% of procedures resulting in pregnancy. Silicone rubber band application was the next best technique, but resulted in more than twice the number of failures. Bipolar cautery and spring clips were the least effective methods.

Peterson et al also identified the fact that women who were sterilized at an earlier age (younger than 28 years) were more likely to have a subsequent pregnancy than those women who were sterilized at age 34 or older.[3] Finally, when pregnancies did occur nearly one-third were ectopic.

Further examination of the data suggests that bipolar coagulation is probably as good as the silicone band technique when the operator is thoroughly familiar with the technology. The CDC study was performed at a time when bipolar cautery was just being introduced into some of the medical centers in the project, and thus, it is possible that the poor performance of bipolar cauterization might be due to relatively inexperienced operators.

A second publication from the same study group focused on ectopic pregnancy and reported that the overall 10-year cumulative probability of the ectopic pregnancy was 7.3 per 1000 procedures for all techniques combined.[3] However, those women having bipolar tubal coagulation at younger than 30 years of age had an ectopic pregnancy rate 27 times higher than those women who underwent postpartum partial salpingectomy.

How should we answer the question posed by our reader? Unfortunately, like so many things in medicine there is no single answer. While postpartum sterilization using the Pomeroy technique results in the lowest rates of pregnancy and ectopic pregnancy, many women do not make the decision to have sterilization performed at the end of pregnancy (and indeed some information suggests that more women regret postpartum sterilization than interval sterilization). Unipolar coagulation has the lowest failure rate among laparoscopic techniques but is also associated with the highest risk of serious morbidity. While the rubber band and clip techniques fail more often than unipolar cautery, they are more successfully reversed than other techniques.

In summary, there is no one best method of tubal sterilization. However, knowledge of the success rates of the various techniques allows the physician to discuss realistic failure rates with each patient. In addition, the patient can be informed that late failures do occur as long as a decade after the procedure.

I do need to add one other thought. Nowhere in the papers discussed above nor in this piece have I mentioned hysterectomy as a sterilization method. Although

some morbidity may occur following tubal sterilization in rare cases, the rate of morbidity and mortality from hysterectomy far exceeds that of the simpler techniques. Thus, there is no place for hysterectomy as a method of sterilization. ❖

References

1. Romney SL, et al. *Gynecology and Obstetrics, The Health Care of Women*. New York, NY: McGraw-Hill Book Company; 1981:846-849.
2. Jones HW, et al. *Novak's Textbook of Gynecology*, Eleventh ed. Baltimore, Md: Williams & Wilkins; 1988:26-28.
3. Peterson HB, et al. *Am J Obstet Gynecol* 1996;174: 1161-1170.

CME Questions

13. Major prognostic factors in endometrial adenocarcinoma include all the following *except*:
a. uterine size.
b. histologic grade.
c. depth of myometrial invasion.
d. FIGO stage.
e. None of the above

14. Based on the data of Johanson et al, which of the following outcomes is more common in women delivered by forceps?
a. Urinary bladder dysfunction
b. Bowel dysfunction
c. Perineal and vaginal lacerations
d. Childhood visual problems
e. Childhood developmental problems

15. The following statements are true regarding postmenopausal hormone therapy and the risk of colorectal cancer *except*:
a. Although colorectal cancer is more prevalent than cancers of the uterus and ovaries, it is a less common cause of cancer mortality.
b. Protection against colorectal cancer is limited to current and recent use of postmenopausal estrogen therapy.
c. There is no evidence that adding a progestin influences the risk of colorectal cancer.
d. The protective effect of estrogen is apparent throughout the length of the lower GI tract.

16. Which variable differs most between women with anorexia nervosa and those with functional hypothalamic amenorrhea?
a. Extent of ovarian quiescence
b. Exercise quotient
c. Calcium and vitamin D intake
d. Extent of undernutrition
e. Testosterone levels

17. Based on the data of Hughes et al, in women who have had a prior stillbirth, the likelihood of anxiety and depression during and after their subsequent pregnancy is reduced if the interval between the pregnancy loss and the next pregnancy is at least:
a. 3 months.
b. 6 months.
c. 9 months.
d. 12 months.
e. 15 months.

18. All of the following are true *except*:
a. A woman with atypical hyperplasia on a breast biopsy has an increased risk of developing invasive breast cancer.
b. Postmenopausal estrogen therapy does not influence the risk of breast cancer in women with biopsy-proven benign breast disease.
c. Progestins decrease the risk of breast cancer in women with benign breast disease.
d. Mastalgia with postmenopausal hormone therapy is frequently due to the progestin in a combined estrogen-progestin regimen.

19. Which of the following methods of tubal sterilization has the lowest, 10-year cumulative failure rate?
a. Postpartum partial salpingectomy
b. Laparoscopic bipolar coagulation
c. Laparoscopic silicone rubber band application
d. Laparoscopic clip application

Readers Are Invited

Readers are invited to submit questions or comments on material seen in or relevant to *OB/GYN Clinical Alert.*

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In Future Issues:

Effect of 21-Day and 24-Day Oral Contraceptive Regimens On Ovarian Activity