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INSIDE

Oral Contraceptive Mortality

ABSTRACT & COMMENTARY

VESSEY, PAINTER, AND YEATES FROM THE UNIVERSITY OF Oxford used the prospective cohort of women enrolled in the Oxford Family Planning Association Study to assess mortality in users and nonusers of oral contraceptives. By the end of the year 2000, 889 deaths had occurred in 17,032 women in England and Scotland enrolled in the study. There was no increase in breast cancer associated with oral contraceptives in either smokers or nonsmokers. However, death from cervical cancer was increased with oral contraceptive use (although the confidence intervals were very wide because of small numbers). Mortality from endometrial cancer and ovarian cancer were reduced in the oral contraceptive users, a result consistent with many previous reports. Comparing never users and users, there was an 80% overall reduction in endometrial cancer deaths and a 60% reduction in ovarian cancer deaths. The risk of deaths from all causes was significantly increased only in smokers (especially with 15 or more cigarettes daily), and the risk increased with increasing age (Vessey M, Painter R, Yeates D. *Lancet*. 2003;362:185-191).

COMMENT BY LEON SPEROFF, MD

The conclusions of this prospective cohort study are limited by the small numbers of deaths in the various categories, as indicated by the wide confidence intervals. However, the results are consistent with a very large literature and further strengthened because they are derived from a single cohort of women. It is important to point out that the data are derived largely from the use of products containing 50 µg ethinyl estradiol, a dose that is now considered to be high. For this reason, the overall safety of oral contraceptives in this report is reassuring, and we would expect even better results with modern, low-dose formulations.

This report confirms previous reports (especially the publications from the World Health Organization and the Nurses' Health Study) that the risk of cardiovascular mortality associated with oral contraceptives is confined to smokers. It is very likely that this risk is present only in current users, an observation that could not be documented in the Oxford study because of the design.

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Table

Death from Ischemic Heart Disease, Stroke, and VTE

Users compared with nonusers	RR, 1.4 (CI, 0.8-2.5)
Heavy smokers for 48 mos	2.4 (0.4-16.3)
For 49-96 mos	4.8 (1.3-26.2)
97 mos or more	2.8 (0.8-15.8)
Hemorrhagic stroke, heavy smoker	5.8 (2.2-16.5)
Venous thromboembolism	no increase

The accumulated literature over many years has consistently established an increased risk of venous thrombosis associated with oral contraceptives. The Oxford report identified no deaths from venous thromboembolism that could be attributed to oral contraceptive use. Most deaths from this condition are linked to trauma, surgery, or a major illness.

The experience with oral contraceptives, in my view, emphasizes the importance of good patient screening. The occurrence of arterial thrombosis is essentially limited to older women who smoke or have other cardiovascular risk factors, especially hypertension. Avoiding the use of oral contraceptives in older smokers and hypertensive women requires effective interaction between the patient and a clinician (not necessarily a physician). Providing oral contraceptives over the counter would bypass this vital interaction, and undoubtedly there would be deaths that could have been avoided. ■

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Management of Port-Site Metastasis After Laparoscopic Surgery for Ovarian Cancer

ABSTRACT & COMMENTARY

Synopsis: *Port-site metastasis after laparoscopic surgery during chemotherapy, or when adequate chemotherapy has been given, is usually associated with poor outcome.*

Source: Huang K-G et al. *Am J Obstet Gynecol*. 2003; 189:16-21.

In an attempt to define the clinical features and long-term prognosis of port-site metastasis after primary laparoscopic surgery for ovarian cancer, Huang and associates reviewed all patients with ovarian cancer who had undergone primary laparoscopic surgery at their institution. They then analyzed the clinicopathologic factors, presentation of port-site implants, management of the individual patient, long-term outcome, and several molecular biomarkers (flow cytometry, p53, p27, bax, HER-2/neu, and bcl-2). Of the 31 patients with epithelial ovarian cancer or borderline malignancy who underwent primary laparoscopic surgery over an 8-year period, 6 (19.4%) had port-site metastasis. Another 2 patients were referred after port-site metastasis. Those patients who had port-site metastasis develop during chemotherapy (n = 2) or after adequate chemotherapy treatment was given (n = 2) all died of cancer. Two patients were alive without disease; the tumors of these latter 2 patients were p27-positive and p53-negative, HER-2/neu-negative, and bcl-2-negative. Huang et al concluded that port-site metastasis after laparoscopic surgery during chemotherapy, or when adequate chemotherapy had been given, is usually associated with poor outcome. They also concluded that further investigations are necessary to define the mechanisms and effective management to prevent and treat this serious complication.

COMMENT BY DAVID M. GERSHENSON, MD

Minimally invasive surgery has clearly experienced a major resurgence in popularity among gynecologists over the past decade or so. This transformation has principally related to improvements in technology, including optics. Gynecologic oncology has not been immune from this change, and certain groups of oncologists have not only embraced these advances but have rapidly expanded indications for the use of operative laparoscopy. Minimally invasive surgery has been used extensively for surgical staging and restaging for various malignancies, primary surgical treatment of endometrial cancer, radical surgical techniques for cervical cancer, and for pelvic and paraaortic lymphadenectomy. While these procedures have been advocated by some groups for treatment of ovarian cancer, most gynecologic oncologists believe that there is no role for such in this malignancy. One of the major objections for its use in ovarian cancer has been the incidence of port-site metastases, although this complication has been reported in virtually all gynecologic cancers. However, laparoscopy has been used very effectively in the resection of benign adnexal masses; the problem lies in inability to accurately distinguish benign from malignant disease using currently available studies (ultrasound, serum CA 125, etc). The precise mechanism of port-site metastasis remains unclear, but pressure gradients and oxygen content have been implicated in its etiology. The present study simply relates this phenomenon to prognosis in patients treated with postoperative chemotherapy. Several strategies have been suggested to avoid this complication, including using gasless techniques, wound irrigation with saline or heparin, various topical agents, or immediate chemotherapy. The bottom line—laparoscopy should not be used in any patient with known ovarian cancer.

Accuracy of Laparoscopic Diagnosis of PID

ABSTRACT & COMMENTARY

Synopsis: *Compared to histopathology, visual diagnosis of PID is neither accurate nor reproducible.*

Source: Molander P, et al. *Obstet Gynecol*. 2003;101: 875-880.

Molander and colleagues evaluated the ability of 3 obstetrician/gynecologists (12 years average length of time in practice) and 3 third-year OB/GYN residents to accurately diagnose pelvic inflammatory disease (PID) by viewing laparoscopic images from each of 40 patients. The process was repeated 2 days later with the same images presented in a different order. Using histologically proven PID as the reference, overall diagnostic accuracy was 78%. Intra-observer reliability was only fair, although better for practitioners than for residents. Inter-observer reproducibility was poor to fair, again, better among practitioners. Using interpretation of photographic images to diagnose pelvic inflammatory disease appears to be unsatisfactory when compared to histologically proven diagnoses.

COMMENT BY FRANK W. LING, MD

Chalk up another defeat for the "gold standard" concept. Visualization of PID via laparoscopy has generally been considered the definitive way to make the diagnosis. Unfortunately, "seeing" does not seem to be what it's cracked up to be. Not only was the accuracy not as high as would be anticipated, but the ability for individuals to agree with themselves was only moderately good. Although the results are somewhat disappointing, they should not really surprise us. Haven't we been told the same thing when standard colposcopic slides are shown to clinicians, ie, accuracy as well as both inter- and intrarater reliability are suspect? Ditto for laparoscopic diagnosis of endometriosis, particularly the atypical presentations such as the vesicles white lesions and flare lesions. The same holds true for ultrasound images.

Admittedly, this study is artificial and somewhat removed from real-life clinical medicine. The physicians were viewing enlargements of pictures taken at the time of surgery. They did not have access to the physical examination findings, or laboratory results. They also could not manipulate the pelvic structures as they would if truly evaluating a real patient in real time. Without the context of the clinical presentation, one can argue that their ability to make an accurate diagnosis was compromised. It should be recognized, however, that such standard findings as edema, tubal erythema, adhesions, and cul-de-sac fluid should be reproducible.

The good news is that the practicing clinicians were more accurate and more reproducible than the residents. Thank goodness! At least the value of experience was supported. As we tell our residents now, "That's why it's a 4-year program." The take-home message of findings such as these addresses the very nature of PID. It remains a condition which, in many cases, is still commonly over- or underdiagnosed. We should still use all the appropriate tools we have to be as accurate as we can. We should certainly not expect laparoscopy to answer the question for us.

Prevention of Breast Cancer with Tamoxifen

ABSTRACT & COMMENTARY

Synopsis: *Only 5% of white women and 0.6% of black women are potential candidates for tamoxifen chemoprevention.*

Source: Freedman AN, et al. *J Natl Cancer Inst*. 2003; 95:526-532.

Freedman and colleagues from the National Cancer Institute estimated the total number of US women in the year 2000 eligible for tamoxifen treatment to prevent or defer breast cancer. Of this number, applying a benefit/risk ratio substantially reduced the number of women who could expect a benefit from treatment (*see Tables 1 & 2*).

COMMENT BY LEON SPEROFF, MD

I reviewed the combined results of breast cancer prevention trials in the April 2003 issue of *OB/GYN Clinical Alert*. The important numbers include the following: Tamoxifen 20 mg daily for 5 years produced a 48% reduction in estrogen receptor-positive cancers, no effect on estrogen receptor-negative cancers, an increase in the relative risk of endometrial cancer to 2.4, and an increase in the relative risk of venous thrombosis to 1.9. There is still insufficient follow-up to answer 2 important questions: 1) will tamoxifen treatment yield a difference in breast cancer mortality and; 2) does tamoxifen treatment prevent or defer the diagnosis of breast cancers. It is estimated that treatment of 1000 high-risk women would produce an 18% reduction in breast cancer mortality over the ensuing 10 years.

This recent report from the National Cancer Institute serves to emphasize that because of the side effects, only a small percentage of eligible US women stand to benefit from this treatment. However, this still adds up to about 2 million women per year.

The decision to take 5 years of tamoxifen chemoprevention, therefore, is not easy. The individual patient that can anticipate an expected benefit must be carefully chosen. The patient has to balance potential benefit against the side effects and cost. Ultimately, this difficulty means that we need a better method for prophylactic treatment, and we must continue to emphasize early detection by exam and mammography. Whether raloxifene will provide a better benefit/risk ratio than tamoxifen awaits the outcome of the STAR (Study of Tamoxifen and Roloxifene) clinical trial. The problem with aromatase inhibitors is an increase in fractures and possibly coronary heart disease. The best chemoprevention method awaits future development. ■

Table 1

Women in the United States Eligible for Tamoxifen Treatment

Total No.	Percentage
Women without breast cancer per year (10,232,816)	15.5%
White women	18.7%
Black women	5.7%
Hispanic women	2.9%

Table 2

Women with a Positive Benefit/Risk Ratio

Total No.	Percentage
White women per year (2,431,911)	4.9%
Black women (42,768)	0.6%
Hispanic women	unable to estimate

Intraperitoneal Radioactive Phosphorus (32P) vs Observation After Negative Second-Look Laparotomy for Stage III Ovarian Carcinoma

ABSTRACT & COMMENTARY

Synopsis: *Intraperitoneal chromic phosphate did not decrease the risk of relapse or improve survival for patients with stage III epithelial ovarian cancer after a negative second-look surgery.*

Source: Varia MA, et al. *J Clin Oncol*. 2003;21: 2849-2855.

In a gynecologic oncology group study, Varia and colleagues reported that 202 patients with negative second-look surgery were randomized to either intraperitoneal chromic phosphate or no further therapy. With a median follow-up of 63 months in living patients, 68 patients in the treatment group (65%) and 63 patients in the observation group (64%) developed tumor recurrence. The relative risk of recurrence was 0.90 (90%

confidence interval [CI], 0.68-1.19). The 5-year relapse-free survival rate was 42% and 36% for the treatment and observation groups, respectively; the difference was not statistically significant. There was no statistically significant difference in overall survival. The relative risk of death was 0.85. Sixteen patients (8%) experienced grade 3 or 4 adverse effects, with 8 in each group. Varia et al concluded that intraperitoneal chromic phosphate did not decrease the risk of relapse or improve survival for patients with stage III epithelial ovarian cancer after negative second-look surgery. Despite complete pathologic remission at second-look after initial surgery and platinum-based chemotherapy, 61% of stage III ovarian cancer patients had tumor recurrence within 5 years of negative second-look surgery. They further concluded that these findings indicate a need for more effective initial therapy and further studies of consolidation therapy.

COMMENT BY DAVID M. GERSHENSON, MD

One of the greatest challenges facing oncologists is to improve the cure rate of patients with advanced epithelial ovarian cancer. Currently, only about 20% of patients with stage III disease and less than 5% of those with stage IV are cured. Although a very high percentage of patients (60-70%) are clinically disease-free following standard therapy consisting of primary cytoreductive surgery followed by combination chemotherapy with paclitaxel and carboplatin, most of these patients eventually relapse and die of their cancers. Even with negative findings on second-look surgery performed to assess disease status, up to 50% of patients will have false-negative findings and succumb to their disease. In other words, we are able to achieve minimal, microscopic, or surgically undetectable tumor burden in most patients but unable to completely eradicate the malignancy with our current approach. Several strategies have been considered or tested in this most favorable group of patients—those with negative second-look surgery findings—in an attempt to reduce the disappointing relapse rate. Whole abdominal radiotherapy has been investigated, and essentially all studies reveal no improvement in disease-free survival plus a disturbingly high rate of intestinal injury secondary to radiation. Consolidation chemotherapy has thus far been found to prolong progression-free survival but has not been demonstrated to improve overall survival. This randomized trial tests intraperitoneal chromic phosphate—a treatment used for decades in various settings for ovarian cancer—but without evidence of a favorable effect on either relapse-free survival or overall survival. Therefore, the search continues for effective consolidation therapy to achieve a superior outcome. Although second-look surgery has essentially disappeared from the scene, the surrogate group for future trials will be patients who are clinically disease-free at the conclusion of primary treatment. ■

Use of OCP's to Eliminate Withdrawal Bleeding

ABSTRACT & COMMENTARY

Synopsis: *Daily administration of a low dose oral birth control pill results in significantly fewer bleeding days.*

Source: Miller L, Hughes JP. *Obstet Gynecol*. 2003; 101:653-661.

Miller and Hughes from the University of Washington randomized 79 patients to either cyclic or daily oral contraceptives containing 20 micrograms ethinyl estradiol/100 microgram levonorgestrel for 12 cycles. A subset of the patients also had pelvic ultrasound and endometrial biopsy. Among patients taking daily active pills, 49%, 68%, and 88% reported no bleeding during cycles 2, 6, and 12 respectively. Although spotting was increased initially among patients who took daily active pills, this decreased to the point that by month 9, the spotting was even less than in those patients who took the pills cyclically. Of note, adverse events as well as weight gain, blood pressure elevation, and blood count were similar between the groups.

COMMENT BY FRANK W. LING, MD

This article is likely to generate responses such as "I knew that!" or "We've done that for years!" or "Why didn't I think of that study?" Personally, I loved it. (Sounds like a movie review, doesn't it?) The study is very well-designed: baseline data were collected, there was a "run in" month of drug administration to make sure that withdrawal bleeding could/would occur, it was randomized correctly, blinding of the sonographer and pathologist was used, etc.

We've all done it in our respective practices, but this study helps to highlight the safety and use of this technique of rendering a patient amenorrheic using daily active pills. For example, it may well be that if a patient takes active pills daily, the chance of a failure is reduced because of greater compliance. Unfortunately, for some patients, the different colors and the onset of menses can be confusing. Also, inhibition of ovulation may be

improved with daily administration of a hormonally active pill. If the spotting is, in fact, less with continuous pills rather than cyclic pills, we will see patients who are more satisfied with their contraceptive choice with a resultant greater likelihood that they will recommend using contraception to friends, family, etc.

Some practical tips in using this technique may be of some help. I use this very often for endometriosis, reasoning that eliminating menstrual flow also eliminates the stimulation for proliferation/sloughing of endometriotic lesions. Is this evidence-based? Unfortunately, it is not, but it certainly helps in the management of some patients with pain suspected to be related to endometriosis. In a more general sense, this technique is very useful anytime a patient relates any significant symptom complex to the menstrual flow, whether it be pain, cramps, headaches, etc. Interestingly, patients commonly ask whether or not it is safe to do this, the concern being that not sloughing the endometrium may result in cancer. Explaining to them that the oral contraceptive is predominantly the hormone that protects the endometrium from hyperplasia usually reassures them adequately. Some will ask about their own personal need to feel cleansed by having a period intermittently. Again, patient education regarding the perceived need as opposed to the real need to pass the menstrual flow helps.

Finally, a practical administrative note: patients on certain insurance plans may need additional documentation to get this covered. Why? Because a pack of pills no longer lasts 28 days, but only 21. Insurance companies see the additional cost and may balk at coverage. Writing the prescription to specify that a daily active pill is being prescribed or that there should be no "pill-free interval" will help.

In summary, this is a very nicely-conducted study that sends us a useful clinical message. ■

Special Feature

Death by a Thousand Indignities: The Saga of HRT

By Sarah L. Berga, MD

This week there were 2 articles in the *New England Journal of Medicine* that explored the link between postmenopausal hormone use and heart disease. The first article was the final analysis of the Prempro® arm of the WHI. The other was an interventional trial that asked if hormone use would reverse or halt the progression of established coronary artery atherosclerosis. The results of these studies can only be put into perspective by logic. Sadly, when it comes to the topic of postmenopausal hormone use, logic seems to have been replaced by hysteria and polarization. Appropriately, new data are reconciled with previous data, with the result that hypothesis and concepts are refined. In contrast, the tendency has been to view the newer data as supplanting previous data and as completely invalidating prior concepts and hypotheses. Some moderation would seem to be in order.

Let's step back from the fray and examine one of the overarching, but often unspoken, issues fueling the current controversies.

It was expected that reproductive hormone use by menopausal women would prevent or reverse most, if not all, of the debilitating conditions of aging. Why? This expectation reveals an element of wishful thinking and the fallacies of directly extrapolating from bench to bedside. There was also an understandable collusion among doctors who wanted to help, women who wanted to do all that they could to stay well and attractive as they aged, and the pharmaceutical industry that had hormonal preparations to sell. There were some data to support the recommendations, but dose-finding studies were not done for each tissue expected to benefit from these actions. It was assumed that the dose needed for bone or for quelling hot flashes was the dose needed for other tissues. To be honest, there was molecular, cellular, and physiological evidence that had accrued over many years to suggest that most, if not all, tissues in the body were targets of hormones. There were reasons to think that the judicious use of reproductive hormones after menopause might retard aging or at least some of its clinical consequences. But we never were clear as to whether postmenopausal hormone use was intended for prophylaxis or whether it might be used as an intervention for established disease processes. The first study by Manson et al[1] reports the results of using HRT as prophylaxis and the latter by Hodis et al[2] using it as an intervention.

Given the results of the Prempro® arm of the WHI, we now realize that hormone therapy administered in a nonphysiological manner in a dose that is good for bone and hot flashes does not necessarily prevent cardiovascular disease and may have risks. We should not be completely surprised. What if we gave other hormones in the same manner and expected all who got them to benefit? Hormones are just another of the many agents being promoted for amelioration of the aging process in general, and

cardiovascular disease in particular, that have fallen victim to the chasm between molecular promise and clinical application. Further, failure to demonstrate the desired effect may have as much to do with the manner in which the agent was given or other features of the study design as with the biological rationale for and conceptual foundation behind the study. The question to ask about any study is whether or not it provided a judicious test of the fundamental biological hypothesis. Typically, the answer for any one study is that it provided a partial answer. For instance, a clinical study may show us how not to give an agent, but it may not invalidate the biological concept behind giving the agent. There may be room for refinement or complete revision of the clinical approach. All study designs have limitations, and an honest investigator is typically quite circumspect about the increment in knowledge that each study provides. For some reason, we are now being asked to abandon circumspection in favor of the "bandwagon du jour." We were asked to believe first that reproductive hormone use by postmenopausal women was "all good." Now we are being asked to believe that it is "all bad." Neither of these polarized positions seems reasonable in light of the extant knowledge base.

I wonder what would happen if we were to give a set of key manuscripts to some unsuspecting college students with no axe to grind and ask them to interpret the evidence accrued to date? I would contend that there is no way to grasp the overarching concepts fueling these investigations and to put the current evidence in perspective without resorting to analogy (in addition to a formal, regimented analysis). For instance, by way of analogy, what if we gave all older women an insulin modifier such as metformin at a standard dose in perpetuity because we know that aging is associated with a decline in insulin sensitivity? What if we gave all women a standard dose of thyroxine because we know that metabolism declines with aging and we wanted to give it a boost? What if we gave standard doses of growth hormone by injection to all women older than 50 regardless of body size and composition? Would all benefit equally? Would all benefit? The reason to use standard doses is ease of administration, clinical practicality, and the need to manufacture standard preparations. The con is that too much or too little of any agent may lead to untoward or null clinical results. It had been assumed, but not proven, that the window for benefit was wide open for reproductive hormones, but this assumption is unlikely to be true if one considers what is known about dosing and clinical impact for other hormones like thyroxine, cortisol, and insulin. The nuances of the clinical practice of HRT have not been tested in any clinical trials of reproductive hormones. Physiology has never been used as a guide for study design for postmenopausal administration of reproductive hormones, while physiology is the guide in most other contexts.

There are even greater questions about study design when we extrapolate from what is known about the cellular and physiological effects of a hormone to an interventional disease model. For instance, what if we asked if reproductive hormone use could reverse kyphosis in older women because we know that reproductive hormones promote bone accretion in adolescence? I think that we would agree that this expectation is unrealistic, that kyphosis cannot be reversed, and that the inability of reproductive hormones to restore vertebral integrity does not invalidate the idea that reproductive hormones have important tropic effects for bone. The point that I am trying to make is that there are good reasons to suspect that hormones are important to health and that they play a role in aging. There are reasons to suspect that altering the endogenous hormonal milieu that accompanies aging might ameliorate to some extent certain age-related conditions. However, we would be foolish to think that this would be as simple as giving the same hormonal preparation in a one-size-fits-all dose regardless of age and health risks and years since menopause. Would that health promotion and chemoprevention of aging were so simple!

To my way of thinking, we still have more questions than answers. We need to find some middle ground and not get too polarized. We need to acknowledge that the newer studies have revealed limitations in the standard clinical approach of giving all postmenopausal women the same dose of the same product.

Questions that remain include:

1. Are all estrogens the same (ie, does the type, route, or dose matter)?
2. If dose matters, what is the appropriate range?
3. Are all progestins the same?
4. Does progestin use attenuate or augment estrogen's effects?
5. Is the effect of progestin tissue specific?
6. Is there a SERM that confers a more favorable risk:benefit ratio than any of the traditional estrogens?
7. Will some form of HRT synergistically impact the benefits of lifestyle variables (ie, will those with a healthy lifestyle benefit from some form of HRT while those who smoke, lack exercise, or practice poor nutrition will not)?

Sadly, the search for a reductionistic panacea to the vagaries of aging has led again to disappointing results. The only certainty is that the search will con-

tinue, if for no other reason than most of us want to do something to retard the aging process and maintain health as best we can. This quest is an inherent attribute of a healthy individual and not an objective to be lightly dismissed. ■

References

1. Manson JE, et al. *N Engl J Med*. 2003;349:523-534.
2. Hodis HN, et al. *N Engl J Med*. 2003;349:535-545.

Audio Conference

Seasonal: A Revolutionary Contraceptive

Extended hormonal contraception is drawing dramatic attention due to the desire of many women to reduce or eliminate the number of withdrawal bleeds associated with current birth control methods. The first extended-use oral contraceptive, Seasonale, was just approved by the FDA and is expected to have an enormous impact on family planners and OB/GYNs. This new therapy will reduce the number of periods a woman has to four a year. Researchers also are looking at extended use of the NuvaRing contraceptive vaginal ring and the Evra transdermal contraceptive patch.

To bring you up to speed with the exciting changes in this field, Thomson American Health Consultants offers ***Extended-use Contraception: What You Should Know About Seasonal and Other Options***, an audio conference on Oct. 9, from 2-3 p.m., ET. The conference will be replayed continuously for 48 hours following the original airdate to make it as convenient as possible for busy professionals to attend.

"I consider this [Seasonale] to be the most important change in hormonal contraception since birth control pills initially became available," says Robert Hatcher, MD, MPH, editor of Contraceptive Technology Update, and professor of gynecology and obstetrics at Emory University.

Presenters will be Hatcher, who will act as moderator; Lee Shulman, MD, professor of OB/GYN at Northwestern University, Chicago; and Sharon Schnare, RN, FNP, CNM, MSN, a family planning clinician and consultant in Seattle.

After listening to this program, participants will be able to:

- discuss current and future options for extended-use hormonal contraception
- list advantages of extended-use hormonal contraception.
- recognize potential problems with extended-use hormonal contraception.
- identify best candidates for extended use hormonal contraception.

Each participant in the conference can earn FREE CE or CME for one low facility fee. Invite as many participants as you wish to listen to the audio conference for $99, and each person will have the opportunity to earn 1 nursing contact hour or 1 AMA Category 1 CME credit. The conference package also includes handouts, additional reading, a free 48-hour replay of the live conference, and a CD recording of the program.

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CME Questions

10. Effective consolidation therapy—treatment that reduces relapse risk after completion of primary surgery plus chemotherapy—is:

a. whole abdominal radiotherapy.
b. single-agent chemotherapy.
c. combination chemotherapy.
d. intraperitonal chromic phosphate.
e. None of the above

11. The following statements are true of breast cancer chemoprevention with tamoxifen *except*:

a. Tamoxifen treatment is associated with a reduction in all breast cancers.
b. The major side effects of tamoxifen treatment are endometrial cancer and venous thrombosis.
c. No chemoprevention drug is available that affects estrogen receptor-negative cancers.
d. Bone loss is a major side effect of aromatase inhibitors.

12. All of the following statements concerning the laparoscopic diagnosis of PID are correct *except*:

a. Accuracy is improved with experience.
b. A resident's ability to correctly diagnose PID is highly reproducible.
c. Diagnostic accuracy would be improved if more data than photo enlargements were available.
d. The clinical diagnosis of PID should not be replaced by laparoscopic diagnosis as the method of choice.

Answers: 10 (e); 11 (a); 12 (b)