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Incidence and Mortality Data from the Women's Health Initiative

ABSTRACT & COMMENTARY

By Jeffrey T. Jensen, MD, MPH, Editor

Synopsis: New results from the WHI show that women exposed to combined conjugated estrogens and medroxyprogesterone acetate HRT have an increase in both breast cancer diagnosis and mortality.

Source: Chlebowski RT, et al. Estrogen plus progestin and breast cancer incidence and mortality in postmenopausal women. *JAMA* 2010;304:1684-1692.

THE AUTHORS INVESTIGATED INVASIVE BREAST CANCER INCIDENCE AND mortality after a total follow-up of 11 years among the 16,608 postmenopausal women aged 50-79 years with no prior hysterectomy who were randomized to combined oral conjugated equine estrogens (0.625 mg/day) plus medroxyprogesterone acetate (2.5 mg/day) or placebo in the Women's Health Initiative (WHI) HRT study. In the initial reports from the WHI HRT study, breast cancer incidence was increased (hazard rate [HR], 1.26; 95% confidence interval [CI], 1.00-1.59). After the original trial completion date (March 31, 2005), re-consent was required for continued follow-up for breast cancer incidence, and was obtained from 12,788 (83%) of the surviving participants, with roughly equal participation in the treated and placebo cohorts.

The authors used an intention-to-treat analysis that included all randomized participants, censoring those not consenting to additional follow-up. Compared to the placebo cohort, women that used HRT had more invasive breast cancers (385 cases [0.42% per year] vs 293 cases [0.34% per year]; HR, 1.25; 95% CI, 1.07-1.46). While breast cancers in the HRT estrogen-plus-progestin group were similar in histology and grade to breast cancers in the placebo group, they were slightly more likely to be node-positive (24% vs 16%; HR, 1.78; 95% CI, 1.23-2.58). Overall, there were more deaths directly attributed to breast cancer (25 deaths [0.03% per year] vs 12 deaths [0.01%

EDITOR

Jeffrey T. Jensen, MD, MPH
Leon Speroff Professor and
Vice Chair for Research
Department of Obstetrics
and Gynecology
Oregon Health &
Science University
Portland

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per year]; HR, 1.96; 95% CI, 1.00-4.04) as well as more deaths from all causes occurring after a breast cancer diagnosis among women in the HRT group. The authors concluded that combined estrogen plus progestin HRT was associated with greater incidence of breast cancer, and that the cancers that occur are more commonly node-positive and associated with higher mortality.

■ COMMENTARY

The Women's Health Initiative study continues to produce headlines (and calls from patients), but the results from this study are not shocking. First, to recap the original WHI publications, an increase in the incidence of breast cancer was noted in the combined (Prempro®) HRT group, but not in the estrogen-only (Premarin®) study. However, the increase in breast cancer incidence in the original combined HRT study was not statistically significant after adjustment for multiple comparisons (HR, 1.26; 95% CI, 0.83-1.92).¹ Since the present study did not focus on multiple outcomes, an adjusted HR was not calculated. The 25% increase in breast cancer diagnosis seen with HRT comes as no surprise as this is a consistent number seen across multiple studies, including the large Nurses Health Study in the United States and the Million Women's Study in the United Kingdom.

The new information about mortality reported in this paper is important to consider. First, most observational studies have suggested that breast cancers associated with combined hormone therapy use generally have more favorable histology and receptor status, lower stage, and lon-

ger survival than those diagnosed in non-users of HRT.²⁻⁴ Since the WHI findings come from a prospective randomized study, they suggest that the optimistic findings from observational studies may have resulted from screening bias. However, it is important to note that the results of an RCT with restrictive inclusion/exclusion criteria may also not be generalizable to the entire population at risk. Most notably, the WHI enrolled an asymptomatic group that was overall older, more obese, and more high-risk than most healthy young menopausal women that initiate hormone therapy shortly after the onset of symptoms.

The findings of the new report support that the risk of breast cancer is slightly increased among women that used combined oral HRT, and that the risk of mortality from breast cancer was also higher. This will reinforce the entrenched position of some providers who have adopted a "do no harm" approach to the management of menopause. In my opinion this overlooks the possibility of "doing good" for our patients, and does not fulfill our obligation to balance potential risks with potential benefits.

First, let's run the numbers. While the risk of death was almost two-fold higher among users of Prempro (HR, 1.96; 95% CI, 1.0-4.04) this translates to absolute risks of 2.6 vs 1.3 deaths per 10,000 women per year in the HRT and placebo groups, respectively. According to the American Cancer Society, the overall mortality rate for breast cancer for women of all ages in 2006 was about 2.3/10,000.^{5,6} This suggests that the unusual findings of the original and subsequent WHI results are not the slightly higher incidence and mortality figures for breast cancer among the HRT cohort, but the unusually low rates in the placebo group. While we expect that a large randomized study will be free of bias, recall that with adjustment, the breast cancer increase in the original publication was no longer statistically significant. Although the authors of the present study performed a number of subgroup analyses that demonstrated that the trend toward increased mortality was the same regardless of age, BMI, risk factors, prior HRT use, or years from menopause, this is not the same as performing a multivariate adjustment that simultaneously corrects for the effect of multiple confounders. Moreover, since this study required consent, the resulting analysis group effectively becomes a cohort study unprotected by the magic touch of randomization. Therefore, adjusting the hazard ratios for important baseline confounders would have been appropriate.

Even if we accept the results as presented, we should understand the limitations and communicate the absolute risks rather than relative risks to patients. The data demonstrate that there will be about 1 additional breast cancer death per year among 10,000 women meeting the inclusion/exclusion criteria of WHI treated with oral conjugated estrogens and medroxyprogesterone acetate. Obviously in caring for our individual patients we recognize that the

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Questions & Comments

Call **Paula Cousins**, Senior Managing Editor,
at (404) 262-5468.



numbers don't matter if you are the one facing a diagnosis of breast cancer, but they put this risk into perspective. Early diagnosis and aggressive treatment remain our most important allies in reducing breast cancer mortality. As previously discussed in *OB/GYN Clinical Alert* (see *January 2010 issue*), the 2009 U.S. Preventive Services Task Force released revised recommendations on breast cancer screening. The panel recommended against routine mammography for women in their 40s to prevent unnecessary morbidity due to screening. However, starting annual mammograms at age 40 instead of age 50 and continued to age 69 will prevent 1 additional cancer death (8.3 vs 7.3) for every 1000 women screened at the expense of 63 unnecessary biopsies. Reducing the screening interval to every other year results in 70 fewer biopsies/1000 women, but 2 additional women will die from breast cancer.⁷ This is excess mortality of 10-20/10,000 women screened.

I continue to believe that the positive health aspects of ERT/HRT outweigh potential risks among young otherwise healthy menopausal women. The WHI demonstrates that starting therapy in asymptomatic women remote from menopause is associated with more risks and fewer benefits. The risk of breast cancer mortality may be one consideration. While we need to counsel our patients that the present study suggests that breast cancer prognosis is not better among women that develop disease while using HRT, otherwise healthy young menopausal women looking to prevent future problems due to hormone deficiency will still benefit from treatment that is initiated shortly after the onset of menopause. And while on HRT, women should receive mammograms every year. ■

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Prenatal Care: Is Earlier Better?

ABSTRACT & COMMENTARY

By John C. Hobbins, MD

Professor, Department of Obstetrics and Gynecology,
University of Colorado Health Sciences Center, Denver

Dr. Hobbins reports no financial relationship to this field of study.

Synopsis: Despite the standard admonition that patients should be scheduled for prenatal care as early as possible in pregnancy, this study shows that often this does not occur.

Source: Nettleman MD, et al. Scheduling the first prenatal visit: Office-based delays. *Am J Obstet Gynecol* 2010;203:207.e1-3.

FOR MANY YEARS WE HAVE BEEN PUSHING THE CONCEPT THAT the earlier that prenatal care is initiated, the better will be the outcome. Since there are certainly data proving that late enrollment makes for worse outcomes, this "the-earlier-the-better" mantra has almost attained bumper sticker status.

To see if we back up our recommendations with action, a group of investigators from Michigan State University went undercover. A research assistant attempted to call all OB/GYN offices in Michigan and got through to 239. Posing as a prospective patient who, 2 days past her missed period, had just found that she was pregnant via a home pregnancy test, she asked when she could come in for her first visit.

The response from the office staff varied from "immediately" (4 weeks) to 11 weeks, with a mean of 6.4 weeks. Fifty percent recommended a first appointment to be at < 6 weeks, 66% at < 7 weeks, and 75% at < 8 weeks. Of the 118 offices offering visits at > 6 weeks, only once was a request honored for an earlier visit. During 27% of the interactions, the staff did not ask about last menstrual period (LMP), and only 14% of the time the research assistant was asked whether this was her first pregnancy. Not surprisingly, 91% of offices asked the woman about

her insurance status. However, information regarding inter-current conditions, medications, or smoking was requested during only 5% of the calls.

The authors' major point was that patients, especially in their first pregnancies, need to receive some guidance regarding their individual needs as early as possible during the vulnerable first trimester. In lieu of an immediately scheduled office visit, they make a pitch for some type of easily accessed, updated, evidence-based resource to be available on-line that would provide advice about smoking cessation, vitamins, medications to avoid, etc.

■ COMMENTARY

One can agree to a point with the authors' perspective. However, I guess one has to weigh delving too deeply into a patient's life during the first telephone contact with the need to obtain important information regarding who needs to be seen immediately. In a companion editorial in the same issue of the *American Journal of Obstetrics & Gynecology*, Arnold Cohen, MD, laid out some suggestions that a trained individual could ask¹:

1. When was your last menstrual period?
2. Have you had any problems in the previous pregnancy?
3. Do you have diabetes?
4. Do you take any medicines other than prenatal vitamins?
5. Do you have any chronic medical problems?
6. Are you taking prenatal vitamins with folic acid?
7. Are you drinking alcohol now that you know that you are pregnant?
8. Do you think there is any reason that the doctor/midwife should see you as soon as possible?

While pushing for a selective approach toward very early appointments, Cohen addressed another important issue concerning how often low-risk patients should be seen during their pregnancies. The standard timetable generally involves office visits being scheduled at 8, 12, 16, 20, 24, 28, 30, 32, 34, 36, 37, 38, 39, and 40 weeks. In a Kaiser system study it was found that, using a more pragmatic and cost-efficient schedule of 8, 12, 16, 24, 28, 32, 36, 38, 40 weeks for low-risk patients, resulted in equivalent outcomes.² From a public health standpoint skipping five visits per patient translates into substantial cost-savings and an approach that leans far more toward enhanced patient convenience. ■

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Misoprostol Is Not for Everyone

ABSTRACT & COMMENTARY

By Alison Edelman, MD, MPH

Associate Professor, Assistant Director of the Family Planning Fellowship, Department of Obstetrics & Gynecology, Oregon Health & Sciences University, Portland

Dr. Edelman reports no financial relationship to this field of study.

Synopsis: The routine use of misoprostol for intrauterine device insertion did not "ease" insertion for patients or providers.

Source: Heikinheimo O, et al. Double-blind, randomized, placebo-controlled study on the effect of misoprostol on ease of consecutive insertion of the levonorgestrel-releasing intrauterine system. *Contraception* 2010;81:481-486.

THIS TRIAL WAS A RANDOMIZED DOUBLE-BLIND CONTROL trial of 89 women undergoing consecutive removal and replacement of a levonorgestrel-releasing intrauterine device (LNG-IUD). Of note, this study was part of a larger multicenter trial evaluating the bleeding profile and safety with repeat use of a LNG-IUD in women who had used their first device for close to 5 years. Women were randomized to 400 µg of sublingual misoprostol or placebo 3 hours prior to their procedure. The main goal of the study was to assess the ease of insertion for providers and then also side effects and adverse events. The majority of the women enrolled were parous, with nulliparous rates of only 9% and 2% in the misoprostol and placebo groups, respectively. Ease of removal and insertion for providers was no different between the groups with more than 90% reporting both were easy. "Ease" or pain of removal and insertion reported by the women undergoing these procedures was worse in the misoprostol group (severe pain reported with removal 14% vs 2% and insertion 23% vs 11%). Rates of adverse events were also significantly higher in the misoprostol group, 51% vs 11%.

■ COMMENTARY

Misoprostol or PGE1 is the wonder drug of the 21st century for many of us in obstetrics and gynecology and it seems we use it for everything these days including labor induction, miscarriage management, cervical priming for

hysteroscopy, and abortion care. In fact, I am surprised that we have not trialed it as a sweetener for our morning coffee (don't try this, it does not taste very good). However, this and several other published trials studying the routine use of misoprostol for intrauterine device insertions^{1,2} are a good reminder that in our effort to do better, we often do harm. Remember bloodletting — that didn't work out so well for the field of medicine either.

This study originated in the homeland of the levonorgestrel-releasing intrauterine device (LNG-IUD), Finland. In Finland's vast experience with this device, there are anecdotal reports of second insertions being more difficult, thought perhaps to be due to the atrophic effect of progestin on the uterus and cervix. Interestingly, across the pond in the United States, there appears to be worries regarding a different population with difficult insertions, the nulliparous woman. There is increasing anecdotal reports of routine misoprostol use prior to IUD insertion in these patients, in hopes of making the insertion easier. However, the evidence is consistent and growing that the use of misoprostol routinely for both multiparous or nulliparous does not ease placement for the provider or the patient.^{1,2} What has been found is that the majority of IUD placements are easy in both multiparous and nulliparous women and that routine use of misoprostol increases the discomfort a woman experiences prior to and during her IUD removal and insertion.^{1,2} In other words, more harm than good. Studies have not followed women after their IUD placement to document if they experience more discomfort once they leave the clinic and no study has been powered to determine if there is a difference in expulsion rate. Finally, what about using misoprostol only in patients who have had a failed first attempt? A very small case series (8 women) demonstrated that it might be helpful, but stay tuned, as more work in this area is needed.³

So how can we make IUD insertion easier? Since the majority of providers (more than 90%) reported that IUD insertion was easy with or without misoprostol — we are hard pressed to find an agent to increase our ease. For patients, making insertion easier is best done by avoiding routine use of misoprostol prior to IUD insertion. ■

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Amniotic Sheets — A Sheet Is Not a Band

ABSTRACT & COMMENTARY

By *John C. Hobbins, MD*

Professor, Department of Obstetrics and Gynecology, University of Colorado Health Sciences Center, Denver

Dr. Hobbins reports no financial relationship to this field of study.

Synopsis: *A new study challenges the concept that the ultrasound finding of a “sheet” is innocuous.*

Source: Nelson LD, Grobman WA. Obstetric morbidity associated with amniotic sheets. *Ultrasound Obstet Gynecol* 2010;36:324-327.

IT SEEMS THAT AT LEAST TWICE A WEEK WE EITHER INADVERTENTLY find, or have a pregnant patient referred with a band-like structure that runs north-to-south between the uterine walls. In a non-pregnant uterus this would be called a synechium, but the most common label assigned to this finding in pregnancy is a “sheet.”

The usual take on this finding, based on anecdotal experience, is that it is generally innocuous. However, two authors from Chicago recently accumulated data from 122 women noted to have amniotic sheets, and compared their outcomes with 244 matched control patients without sheets. In both groups, pregnancies with structural or chromosome abnormalities were excluded from the analysis.

Maternal outcomes included cesarean section rates, preterm birth, premature rupture of membranes, abruption, chorioamnionitis, and preeclampsia. Neonatal outcomes evaluated were birth weights < 2500 g, prematurity, and NICU admissions.

Although there was a trend toward better outcome without sheets in many of the subcategories, none of them reached statistical significance individually. Therefore, the authors lumped them together and found “composite obstetric morbidity” to be higher in those with sheets (21.3% vs 8.2%) with a relative risk of 2.6 (95% confidence interval [CI], 1.5-4.5). The cesarean section rate was significantly higher in the sheet group (38.5% vs 24.6%; 95% CI, 1.1-2.1). Neonatally, there was an increase in low birth weight (18% vs 5.3%; relative risk [RR], 3.3; 95% CI, 1.5-4.3) and admissions to the NICU (16.45 vs 7%; RR, 2.3; 95% CI, 1.3-4.3). There were no stillbirths in the study groups and there were no differences in Apgar scores between groups.

■ COMMENTARY

The results of this study surprised me. Perhaps the largest surprise was the fact that only 35% of those with sheets had had a previous dilation and curettage. This brings up the possibility that, as the authors point out, it may not be the sheet per se that is responsible for the somewhat increased morbidity, but the patient herself who may simply represent the source of increased risk. We have followed many of these patients with serial ultrasound exams and found that the sheets, while seemingly dramatic when noted at 16-24 weeks, virtually always get pushed to the side, and in late pregnancy give way to the fetus to a point where they can no longer be seen. Interestingly, the authors did not address the incidence of malpresentations or difficult deliveries.

Perhaps the greatest danger of a sheet is it being mislabeled as a “band,” which then morphs into the possibility of amniotic band syndrome — something that certainly gets the attention of couples going on-line for more information. These patients look like deer in headlights when they reach our door, and it often takes more than a few minutes to peel them off the ceiling while explaining that the sheet is not a band.

This study brings up important information, but, unfortunately, it leaves us with nothing preemptive that we can do to reverse the trend in possible increased morbidity. It is heartening that there were no neonatal deaths or poorer 5-minute Apgar scores in the sheet group. ■

Early Detection and Treatment of Ovarian Cancer Improves Outcome: Right?

ABSTRACT & COMMENTARY

By Robert L. Coleman, MD

Professor, University of Texas;
M.D. Anderson Cancer Center, Houston

Dr. Coleman reports no financial relationship to this field of study.

Synopsis: *In this randomized phase III trial of early vs delayed treatment based on CA125 surveillance, no benefit to overall survival was observed for early treatment. Further, patients undergoing early initiation of therapy had more rapid deterioration in global health quality-of-life measures.*

Source: Rustin GJS, et al. Early vs delayed treatment of relapsed ovarian cancer (MRC OV05/EORTC 55955): A randomised trial. *Lancet* 2010;376:1155-1163.

PATIENTS WITH ADVANCED OVARIAN CANCER FREQUENTLY have corresponding CA125 values that pace tumor response and progression during therapy. This has supported the common practice of monitoring patients with serial CA125 in complete remission following primary chemotherapy. The supposition is that earlier identification of recurrent disease can be better controlled by earlier initiation of therapy. To formally address this hypothesis, the EORTC conducted a randomized phase III trial in which women in complete clinical remission following primary surgery and chemotherapy were enrolled into a blind surveillance program. Follow-up visits were scheduled every 3 months during which an exam was performed and blood was taken for CA125 assessment. All registrants were blind to their CA125 values during this time. However, when an individual's CA125 rose to twice the upper limit of normal, they were randomized 1:1 to unblinding of the result (early) or continued blinded surveillance (delayed). In this latter group, intervention was determined by the development of clinical or symptomatic relapse. Post-progression therapy was determined by local standards of care. The primary endpoint of the study was overall survival. In all, 1442 patients were registered, of whom 529 were randomly assigned to the treatment groups. Patients unblinded and made aware of their rising CA125 values generally started treatment immediately, and on the median, 4.8 months before those in the delayed group. After a median follow-up of nearly 57 months from randomization and 370 deaths, there was no difference in overall survival between the arms (hazard rate, 0.98; 95% confidence interval, 0.8-1.2). Median survival in the early treatment group was 25.7 months compared to 27.1 months in the delayed group. For patients receiving third-line therapy, the time differential to initiation was nearly the same as the time differential to initiation of second-line therapy (median, 4.6 months). Interestingly, first deterioration in Global Health score occurred significantly sooner in the early treatment group. The authors conclude no benefit in survival is gained by treatment dictated solely by asymptomatic rise in CA125 and challenge the practice of routine biomarkers surveillance in this setting.

■ COMMENTARY

This extremely provocative study was no doubt as difficult to conduct as the results are to accept. It is remarkable that such a large cohort of patients accepted follow-up care without one of the staples of reassurance — their CA125. However, the investigators are to be congratulated in tackling a mantra of care that is absolutely pervasive in clinical management. Patients and clinicians alike are “addicted” to CA125, particularly in those where the biomarker follows clinical disease regression. Since it's usually obtained with every course of therapy during primary management, it frequently serves as a surrogate for the

unseen and positive reinforcement to endure the unpleasantness of chemotherapy. However, the results suggest our dependence on, and clinical response to, the biomarker does not help our patients live longer.

Since these data became public in 2009, we have struggled with counseling patients who are concerned that complacency in surveillance will harm their chances at lasting survival. In this regard, it is important to synthesize the message the trial brings. First, the analysis follows a cohort of women destined to recur and, in this regard, the results are not that surprising. Nearly every randomized clinical treatment study conducted to date regarding management of recurrent disease has failed to extend overall survival. The difference in detection of disease in this study is likely too short to make a difference even if all the post-progression treatment is the same. Second, patients with early recurrence are good candidates for treatment trials including ones of biomarker-only recurrence. Biological and immunological therapies are hypothesized to be most efficacious in this setting and are under active investigation. So candidate selection would be a reasonable indication to follow CA125 closely. Third, and maybe most importantly, patients can be reassured that they have time to process, contemplate, and initiate therapy when recurrence is suspected or documented. This is particularly important in those with lasting adverse events from their previous treatment.

It would be of great value to repeat this study with tighter regulation of post-progression management strategies, such as higher utilization of platinum-based combination therapies and secondary surgery, and in the context of newer validated biomarkers. However, based on responses from patients aware of this study's findings, I'm not optimistic. ■

Treating Sexual Dysfunction Related to Antidepressant Use

ABSTRACT & COMMENTARY

By *Frank W. Ling, MD*

Clinical Professor, Department of Obstetrics and Gynecology, Vanderbilt University, School of Medicine, Nashville

Dr. Ling reports no financial relationship to this field of study.

Synopsis: *In a prospective, randomized, double-blind, placebo-controlled trial of women taking SRIs, sildenafil treatment resulted in a reduction of sexual side effects.*

Source: Nurnberg HG et al. Sildenafil treatment of women with antidepressant-associated sexual dysfunction. *JAMA* 2008;300:395-404.

A STUDY GROUP OF 98 PATIENTS WERE ENROLLED THROUGH seven centers to evaluate the efficacy of sildenafil in the treatment of sexual dysfunction associated with the use of selective and nonselective serotonin reuptake inhibitors (SRIs). The patients had to be previously sexually functioning, premenopausal, and successfully treated for their depression with an SRI, but with sexual dysfunction at the time of enrollment. Several validated scales of sexual functioning were used to assess outcomes with the primary outcome being changes on the Clinical Global Impression sexual function scale (CGI). In the 8-week parallel group study, patients took either placebo or sildenafil (50-100 mg flexible dosing schedule) prior to activity. The CGI score of women treated with sildenafil was 1.9 (95% confidence interval [CI], 1.6-2.3), while those taking placebo scored on average 1.1 (95% CI, 0.8-1.5). Hormone levels were comparable and the rate of depression remission was also the same.

■ COMMENTARY

How often has a patient asked you, "Why isn't there a Viagra for women?" Well, there is ... sort of. There was a minor blip on the radar screen of the medical news when this first came out in 2008, but the enthusiasm has somewhat died. The antidepressant-associated sexual dysfunction that we all encounter in our daily practices remains a challenge looking for an effective solution. As an editorial aside, I am particularly sensitive to this because of my personal patient population. I see a population of women that is heavily burdened with chronic pelvic pain, antidepressant use, and sexual dysfunction. Particularly disconcerting is the repeated scenario in which patients prematurely discontinue their antidepressant therapy because of the sexual side effects. What are we to do?

We know that the phenomenon is common, i.e., the literature tells us that anywhere from 30%-70% of patients on selective and nonselective serotonin reuptake inhibitors develop symptoms such as decrease in libido, vaginal lubrication, and sexual sensitivity. In addition, women are also troubled by orgasmic dysfunction, dyspareunia, reduced sexual activity, and reduced satisfaction.

The relevance of the problem and the data in this article should be placed in proper perspective within the landscape of sexual dysfunction which currently consists of four categories: sexual desire disorders (including hypoactive desire and aversion), sexual arousal disorders, sexual orgasmic disorders, and sexual pain disorders (dyspareunia and vaginismus). Whereas sildenafil is FDA-approved for arousal disorders in men, SRI-induced dysfunction is typically of the desire or orgasm type. To complicate the

picture further, desire dysfunction (loss of libido) is the most common type of sexual dysfunction in females. If sildenafil works in women as it does in men, it should not directly affect libido, but should improve blood flow to the pelvic region. In men, this results in erection whereas in women, it would lead to more vasocongestion and vaginal lubrication, thereby simulating the normal physiologic response of arousal. The increase in lubrication should reduce dyspareunia that might otherwise result in dyspareunia.

Even though the literature is not totally consistent in identifying a benefit for the use of sildenafil, it should be noted that in this group of patients, the medicine does show potential efficacy. Since we all see patients that might benefit from its use, knowing that there might be something available at least gives us another option to consider. As with men, the medication is used prior to sexual activity. This study started with 50 mg and allowed the patient to take up to 100 mg. In other studies involving male subjects, doses of up to 200 mg have been reported. When I offer this choice to patients, I typically start with the lowest dose, 25 mg, then increase from there.

Patient education is critical when considering applying these data. First, the clinician should recognize that depression itself can have a deleterious effect on sexual functioning. Also, an antidepressant, be it SRI or not, has the potential for adversely affecting libido and other aspects of sexual functioning. Sometimes, it becomes the proverbial “Which came first, the chicken or the egg?” quandary, trying to sort out whether the sexual dysfunction antedated the use of the antidepressant or, more specifically, the SRI. The patient should be told specifically that the goal is not to increase libido directly. In men, it does not increase libido, but does increase blood flow to the penis, thereby generating the erection that allows the man to be sexually functional.

Other small series or case reports have suggested other approaches to these complaints, none of which has shown more than limited efficacy. The concept of a “drug holiday” in which the patient takes the SRI only on weekdays in order to be more sexually functional on the weekends has now been marginalized because of the tendency of the patient to be less compliant with taking the medication on a regular basis. Adding a non-SRI medication such as bupropion has shown limited success. Reports on yohimbine, urecholine, and periactin have been published. Any of you out there who has tried to deal with this problem has certainly found it frustrating and difficult.

Perhaps this report might allow some of us to step out and try it more often. We will continue to be asked by patients, so we might as well be open to new possibilities. As products are tested and new reports come out, we’ll be watching. The testosterone patch has still not gotten here

despite much anticipation. We know that women’s sexual functioning is a different issue when compared to men’s. As I tell my patients, “Men use sex as stress relief, while women need to have stress relieved before they can have sex.” Yes, it’s different, not as simple, but certainly worth our continued efforts. ■

CME Questions

28. Regarding prenatal care access, which of the following is correct regarding first contact information?

- In only one of three instances was information about LMP requested.
- The most common question asked was how many times the patient had been pregnant.
- The least common question asked was insurance status.
- Information regarding high risk conditions was requested 33% of the time.

29. Women reported less pain with IUD removal and insertion if they received misoprostol prior to their procedures.

- True
- False

30. Which of the following does not fit the findings in the amniotic sheet study?

- The composite morbidity was higher in those with sheets.
- The birth weights were lower in the sheet group.
- The cesarean section rate was similar in both groups.
- Neonates in the sheet group spent more time in the nursery.

31. Which of the following statements best reflects the design or outcome of the ovarian cancer trial?

- The study’s primary endpoint was time to progression.
- Patients were randomly allocated to the early vs delayed arm when the registered on the trial.
- Patients on the delayed arm received more effective therapy.
- Although patients in the early group were informed of their CA125 results, they reported poorer and quicker deterioration in quality of life.

Answers: 28. a, 29. b, 30. c, 31. d.

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