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Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

FDA Approves Flibanserin to Treat Female Hypoactive Sexual Desire Disorder: A Billion Dollar Market?

By Jeffrey T. Jensen, MD

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SYNOPSIS: On the third attempt, the FDA approved the mixed serotonin agonist/antagonist flibanserin for the treatment of generalized hypoactive sexual desire disorder in premenopausal women.

SOURCES: U.S. Food and Drug Administration. FDA Briefing Document: Joint Meeting of the Bone, Reproductive and Urologic Drugs Advisory Committee (BRUDAC) and the Drug Safety and Risk Management (DSaRM) Advisory Committee. Available at www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM449088.pdf. Accessed August 24, 2015.

Katz M, et al. Efficacy of flibanserin in women with hypoactive sexual desire disorder: Results from the BEGONIA trial. *J Sex Med* 2013;10:1807-1815.

Thorp J, et al. Treatment of hypoactive sexual desire disorder in premenopausal women: Efficacy of flibanserin in the DAISY study. *J Sex Med* 2012;9:793-804.

On August 18, the FDA approved flibanserin to treat acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women. The dose of flibanserin is 100 mg orally daily taken at bedtime. A total of 3548 patients were randomized to treatment (flibanserin n = 2310; placebo n = 1238) in the combined data from the three pivotal trials submitted in the new drug application (NDA) (the two published trials are referenced above). In the combined evaluation group, the mean age of participants was 36 years, and most (~89%) were white and reported being in a relationship with a mean length of 11 years. The overall completion rate was 78% for placebo and 70% for flibanserin (24 weeks of treatment).

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The two co-primary endpoints in the published studies were: 1) change in the number of satisfying sexual events (SSEs) from baseline (28-day interval) to end of study (28-day interval), and 2) change in the eDiary sexual desire score from baseline to end of study (sum of daily sexual desire scores over 28 days). In these studies, subjects used a personal handheld electronic device (eDiary) to record on a daily basis information about sexual activity, including sexual encounters, orgasms, and desire. The third (unpublished) study referenced in the NDA did not use the eDiary to capture data for sexual desire. Instead, the Female Sexual Function Index (FSFI) sexual desire domain questions were assessed every 4 weeks at clinic visits, and the baseline and final clinical visit data were used for the co-primary efficacy endpoint (the FSFI was a secondary endpoint in the other studies). Key secondary endpoints included: 1) how often subjects reported being bothered by low sexual desire ("never," "rarely," "occasionally," "frequently," or "always"), and 2) the number of "satisfying sexual episodes (SSE)," each assessed for the 28-day baseline and end-of-study intervals.

The FDA review panel concluded that flibanserin's treatment effects were consistent across the three trials with respect to increasing overall satisfying sexual events (statistically significant, $P < 0.05$; median increase of 0.5 to 1.0 episodes in 28 days) and reducing distress (mean treatment difference [95% confidence interval]: -0.3 [-0.4 to -0.1], -0.4 [-0.5 to -0.2], and -0.3 [-0.4 to -0.1] in the three studies). Although treatment benefit was also consistently demonstrated for sexual desire, this became statistically significant only when measured using the FSFI-desire domain questions (mean treatment difference [95% CI]: 0.3 [0.2-0.4], 0.4 [0.2-0.5], and 0.3 [0.2-0.5]) but not with the eDiary. Descriptive data presented suggest that the clinical effect takes about 4 weeks to develop.

Side effects occurred significantly more frequently in the treatment group, with twice as many (12.8% vs 5.9%) discontinuations for adverse events (AEs). The most common AEs included dizziness (11.4% vs 2.2%), somnolence (11.2% vs 3.1%), nausea (10.4% vs 3.7%), fatigue (9.2% vs 5%), and insomnia (4.9% vs 2.4%). There was no difference with respect to depression. In a small substudy where subjects consumed moderate (2-4 drinks) amounts of ethanol with and without flibanserin, the combination precipitated hypotension and presyncope/syncope in some participants. Due to these findings, the FDA approved flibanserin with a risk evaluation and mitigation strategy (REMS) to assure safe use. The REMS requires that prescribers and pharmacies complete training and be certified with the REMS. Certified prescribers must counsel patients using a Patient-Provider Agreement form about the increased risk of severe hypotension and syncope and about the importance of not drinking alcohol during treatment. The labeling for flibanserin (Addyi™) will include a black box warning to highlight the risks of severe hypotension and syncope in patients who drink alcohol during treatment, in those who use moderate or strong CYP3A4 inhibitors, and in those who have liver impairment.

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What would you pay for a drug that must be taken daily to have (at best) a marginal impact on female sexual desire and is associated with serious side effects particularly when coadministered with moderate amounts of alcohol? How about $1 billion? That's the amount of money that Valient Pharmaceuticals paid to acquire Sprout Pharmaceuticals, the company that successfully received FDA approval for flibanserin. The approval came on the third round, and was controversial.[1] It took three pivotal studies and a patient advocacy campaign to gain approval. The initial NDA was submitted by Boehringer Ingelheim (BI) in 2010. At that time, the committee voted unanimously that the risks exceeded potential benefits, and BI discontinued development of the drug. Rights were sold to Sprout Pharmaceuticals, a company with no other products. Sprout filed a second NDA in 2013 and the application was again rejected. After the second NDA was denied, an advocacy group called Even the Score was formed to advocate for what it called "gender equality" in access to treatments for sexual dysfunction. The group promoted the claim that there are 26 approved medications for male sexual dysfunction but none for women; however, it failed to mention that none of these treatments were approved for low sexual desire.[1] The male products include forms of testosterone and the phosphodiesterase (PDE)-5 inhibitors used to treat erectile dysfunction. Although the claim may have been inaccurate, the advocacy appeared to work and Addyi is now approved.

Flibanserin is classified as a mixed post-synaptic 5HT1A receptor agonist and 5HT2A receptor antagonist.[2] It initially was studied for activity as an antidepressant. While the drug was no more effective than placebo in treating depression, flibanserin was more effective than placebo in terms of study participants' responses to the question, "How strong is your

sex drive?" This led BI to the clinical development program for treatment of sexual desire. The *Diagnostic and Statistical Manual of Mental Disorders* (DSMD), 4th edition, defined HSDD as "persistently or recurrently deficient or absent sexual fantasies and desire for sexual activity" accompanied by "marked distress and interpersonal difficulty" that is not accounted for by a nonsexual mental disorder, medication, severe relationship stress, or general medical condition. In 2013, the DSMD, 5th edition, combined HSDD with female sexual arousal disorder into female sexual interest/arousal disorder (FSIAD). The FDA has recognized that there are no approved treatments for these disorders.[3]

But is flibanserin the answer? First, this is not like treating an arousal disorder with a PDE5 inhibitor dosed a few times per month. Daily treatment is required. And it appears to take about a month to show any benefit at all. That, coupled with serious side effects like hypotension and syncope in some individuals (particularly with alcohol use) and annoying less serious adverse events like headache and nausea in others, doesn't make this a dream drug.

Still, the allure of a drug to treat desire is intoxicating. Imagine the conversation that ends with "if you loved me, you would get that medicine that makes you more interested in sex." While women are generally motivated to improve relationships, it is important to recognize that the diagnosis of FSIAD requires that the lack of desire is accompanied by "marked distress and interpersonal difficulty." Guilt and desire to please a partner should not be deciding factors.

The FDA did a good thing requiring that providers receive training to become certified to prescribe flibanserin, but I hope that goes far enough. While it is important not to dismiss a therapeutic opportunity, it is critical that you make an accurate diagnosis. In my practice, I refer patients with sexual desire disorders to a qualified sexual therapist for counseling and treatment. I suspect a minority may benefit from flibanserin. However, I imagine that Valient Pharmaceuticals is banking on widespread over-prescription of this product. That's the $1 billion dollar answer. ■

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ABSTRACT & COMMENTARY

Quality of Information on Pelvic Organ Prolapse on the Internet

By Chiara Ghetti, MD

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Dr. Ghetti reports no financial relationships relevant to this field of study.

SYNOPSIS: After review of more than 400 websites, most web-based information available to women regarding pelvic organ prolapse treatment is incomplete. The best-quality information was found on government-sponsored websites.

SOURCE: Kakos AB, et al. Quality of information on pelvic organ prolapse on the Internet. *Int Urogynecol J* 2015;26:551-555.

The objective of this study was to evaluate the quality of patient-centered information regarding pelvic organ prolapse treatment available on the Internet. Two independent investigators reviewed the content of websites obtained after performing Internet search for four prolapse-related terms. Google, Yahoo, and Bing search engines were used to search for the terms: bladder prolapse, dropped bladder, uterine prolapse, and dropped uterus. Websites were evaluated using a modified DISCERN instrument. The DISCERN tool, which uses a two-stage, six-point rating scale with score range per question 0–5, is reliable in estimating the quality of web-based health care information. A greater score indicated more complete information. Sixteen questions were used: 12 were based on the DISCERN instrument, rendering a maximum score of 80, and four focused on information availability and quality regarding conservative treatment (pessary, watchful waiting, and physical therapy). In addition, websites were identified as having Health On the Net (HON) certification. The HON Foundation uses health-specific criteria to estimate website health information quality. A separate Internet search was completed using the four search terms to identify the relative proportions of domain suffix for the top 100 sites identified per term.

The study reviewed a total of 218 websites. Of these, 23 (9.5%) sites were HON certified. Sites that were HON certified had higher DISCERN scores ($P < 0.0001$). For the three questions referencing conservative treatments (i.e., pessary, physical therapy, watchful waiting), 115 (52%) sites had a summed mean score of ≤ 3, indicating less complete information regarding these conservative treatment options. Searches performed using the medically precise term "prolapse" identified sites with better quality information using the assessment scale than searches using the term "dropped" (mean scores 32.75 and 21.3, respectively;

$P < 0.02$). The summary of 400 sites reviewed across the four search terms identified sites with the following domains: 64% .com, 19% .org, 8% .edu, 6% other, and 3% .gov. Overall .gov sites yielded the highest quality information.

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Pelvic organ prolapse is a prevalent condition that is estimated to affect as many as 38-50% of women.[1,2] Despite its high prevalence, very little is known about the quality of information women are able to access online regarding this condition and its treatment options.

This study found that overall information available to women online regarding prolapse is incomplete and often biased toward surgical treatment. The authors suggest that .com and .net sites seemed to emphasize surgical treatment and were more likely to have industry bias. Searches using more medical terminology resulted in websites with higher quality information. This study also ascertained that .gov sites had the most high-quality information regarding prolapse. In addition, while some sites did better than others in describing the range of treatment options, few comprehensively described the relative benefits of each of the treatment options.

Based on this study, women may come to us with a range of information regarding their prolapse. In an era in which we often rely on information acquired online, the poor quality of online information about prolapse and its treatment options impacts not only the patient but has significant repercussions for her provider. Patients will be looking to their physicians to fill the gaps in their health information. Physician counseling is increasingly important in educating women about all available treatment options.

Informed consent is the foundation for any health care intervention, whether it is surgery or conservative treatment. While this is true in any field of medicine, the importance of impartially educating our patients with pelvic floor disorders seems to take on almost magnified importance due to the intimate nature of the disorders, perhaps because these conditions affect so many aspects of a woman's quality of life, including social, psychological, physical, sexual, body image, and overall well-being.[3,4] As physicians, we are under the moral, ethical, and legal obligation to provide patients with an unbiased and evidence-based review of all treatment alternatives, their corresponding risks and benefits, and answers to any questions they may have. We need to ensure that the poor quality of online information about prolapse does not affect the quality of information we use in physician counseling and informed consent. ■

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ABSTRACT & COMMENTARY

Can Cerebroplacental Ratio Predict Neonatal Mortality?

By John C. Hobbins, MD

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Dr. Hobbins reports no financial relationships relevant to this field of study.

SYNOPSIS: Recent articles show the cerebroplacental ratio to be a useful predictor of immediate and later neonatal morbidity, particularly, in late-onset intrauterine growth restriction.

SOURCE: Khalil AA, et al. Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission? *Am J Obstet Gynecol* 2015;213:54.e1-10.

The July issue of the *American Journal of Obstetrics and Gynecology* included three articles on the cerebroplacental ratio. Back-to-back papers from the same institution, Kings College Hospital in London,[1,2] were accompanied by an excellent review on the subject by Gregory DeVore.[3] This month I will focus on one of the studies[1] by the British authors.

In Doppler wave form analysis, the pulsatility index (PI) and systolic/diastolic (S/D) ratios quantify the relationship between systole and diastole in a cardiac cycle. Normally there is increased resistance in the cerebral circulation, which is reflected in an increased distance between systole and diastole in the waveform, resulting in (normally) high PIs and S/D ratios in the middle cerebral artery (MCA). In contrast, the placental circulation, by necessity, is very lush. This lowered resistance results in proportionally greater diastolic flow in the umbilical artery (UA) as demonstrated by low PIs and S/D ratios, with ratios in the latter of generally less than 3:1 in the third trimester.

In intrauterine growth restriction (IUGR) when the PO2 drops below a certain point in a gradually worsening progression, the fetus will feel a need to protect the brain by vasodilation, thereby increasing flow during diastole. This causes a decrease in the PIs and S/D ratios in the MCA. In early-onset IUGR, the fetal circulation in the placenta has fewer villus branches and terminal villi. The umbilical arteries, therefore, will encounter more resistance downstream, causing lower flow during diastole, thus resulting in an increase in the PIs and S/D ratios. Interestingly, as the fetal condition worsens, the wave forms from the MCA (with diastolic flow trending upward) and the UA (with progressively lower diastolic flow) begin to look very much alike. Since the umbilical artery reflects the adequacy of the placental circulation and the MCA is indicative of how well the fetus tolerates the deprivation process, a ratio of the two PIs, cerebroplacental ratio, has emerged as a way to provide even more useful information than either alone. Any value < 1.08 is thought to be concerning.

The featured retrospective cohort study involved patients who were delivered between 2000 and 2013. Each of these patients had UA and MCA Dopplers done within 2 weeks of delivery. Although the managing physicians were privy to the individual results, the cerebroplacental ratios were calculated later for the purpose of the study. The only Doppler criterion used in decision-making was the UA.

The results should get our attention: The higher the birth weight and the higher the cerebroplacental ratio, the lower the chances of having an operative delivery for fetal distress. Specifically, if the cerebroplacental ratio was reassuring, the risk of operative delivery was significantly lower (odds ratio [OR], 0.67; 95% confidence interval [CI], 0.52-0.77). This association held up even if small for gestational age infants were excluded from the analysis. The cerebroplacental ratio was also an independent predictor of newborn special care unit admissions (OR, 0.55; 95% CI, 0.33-0.92), while birth weight was not. It is of note that operative delivery was more common in appropriate for gestational age babies with low cerebroplacental ratios than small for gestational age babies with normal cerebroplacental ratios.

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First, it is clear that there are two forms of IUGR: early onset and late onset. The early onset type is associated with an early fall off in fetal growth secondary to insufficient placental flow. Affected fetuses generally have birth weights below the third percentile, have a more predictable course, often are delivered very early, and have a high rate of perinatal mortality and morbidity. Late-onset IUGR is associated with late plateauing of fetal growth and, although perinatal mortality is uncommon, later morbidity is not. Their courses are generally unpredictable and any diagnostic help in managing these pregnancies should be welcomed.

In 1999, Bahado-Singh described cerebroplacental ratio as a way to keep tabs on the placenta and fetus at the same time.[4] The concept languished for many years. However, recently there has been a rebirth of its use in IUGR pregnancies, with studies mostly from Europe correlating abnormal MCAs and cerebroplacental ratios with poor neonatal acid base status,[5] neurological sequelae after birth,[6] neurodevelopmental performance at 2 years of age,[7] and even, indirectly, with childhood cardiovascular abnormalities.[8] Yet, in the United States the concept of brain sparing has been largely ignored, where the only Doppler method that is officially recognized is the UA Doppler — a test that is often within normal range in those late IUGR pregnancies leading to poor neonatal outcome and later neurological morbidity. The latest American College of Obstetricians and Gynecologists (ACOG) practice bulletin on fetal growth restriction (May 2013) makes no mention of early vs late IUGR or the use of MCA Dopplers in the management of IUGR pregnancies. The ACOG bulletin on fetal surveillance (July 2014) also did not distinguish between early and late IUGR, and states that "MCA has not been shown to improve outcome" and its "role remains uncertain."

Well, if the above studies are not sufficient, there are new data from a large multicenter observational study from Ireland[9] to indicate that the cerebroplacental ratio is predictive of immediate outcome and how well the fetus will tolerate labor. Yet with today's emphasis on "evidence-based medicine," nothing appears to be put into play until it is first tested through a prospective, randomized, clinical trial. So, we had better act fast while we are still seemingly clueless about the benefit of information derived from the MCA. And don't bother asking our colleagues in Europe to join us. They already have made up their minds. ■

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SPECIAL FEATURE

Morcellation: Has it Improved Outcomes or Put Women at Risk?

By Molly A. Brewer, DVM, MD, MS

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Dr. Brewer reports that she receives grant/research support from the National Cancer Institute.

SYNOPSIS: Widespread concern over malignant tumor dissemination with morcellation threatens to undermine advances in minimally invasive gynecologic surgery that have benefited women. Before providers abandon this technique, they should put the risks and benefits in perspective.

Over the last 3 decades, rapid advances in laparoscopic techniques have revolutionized gynecologic surgery, leading to a reduction in surgical morbidity and improved postoperative quality of life. In a 2009 review, Nieboer et al concluded that laparoscopic hysterectomy was preferable to abdominal hysterectomy because the return to work was quicker, the blood loss was less, the hospital stay was shorter, and the rate of wound infections was lower.[1] A retrospective cohort study using data from the American College of Surgeons National Surgical Quality Improvement Program compared venous thromboembolism (VTE) events for minimally invasive surgery (MIS) for hysterectomy to an open approach when the hysterectomy was being done for benign indications. This study included 20% vaginal hysterectomies and 51% laparoscopic hysterectomies. There was no difference in VTE rates between the two approaches, so they were combined as MIS and compared to the hysterectomies done with a laparotomy incision. This study found that open hysterectomy was an independent risk factor for VTE with an odds ratio of 2.45 (95% confidence interval, 1.77-3.40) compared to an MIS hysterectomy.[2]

The most common reason for hysterectomy in the United States remains a fibroid uterus. As gynecologists have adopted MIS techniques, they have increasingly offered laparoscopic myomectomy as well as supracervical or total laparoscopic hysterectomy to women with large fibroid uteri. However, surgeons were met with the challenge of removing a large fibroid uterus from the pelvis using an MIS approach, which required a mini-laparotomy incision to remove either a large fibroid or a large uterus. Morcellation, which is cutting tissue into pieces so it can be removed through a smaller incision, was developed to address these limitations. The technique has greatly expanded the ability to do gynecologic procedures with MIS. The first morcellations were done by introducing a scalpel through an incision to cut the uterus into small parts. In 1993, power morcellation was developed to chop up tissue with greater efficiency, allowing the uterus to be extracted through a laparoscopic port site, thus eliminating the need for a larger incision.

In 2013, a 38-year-old physician received the unexpected postoperative diagnosis of leiomyosarcoma (LMS), a high-grade and very aggressive stromal malignancy, following total laparoscopic hysterectomy with morcellation for the treatment of her presumed fibroid uterus.[3] She subsequently sued her surgeon and the manufacturer of the morcellator claiming that her cancer was upstaged to Stage IV due to the power morcellation of her uterus, which contained an undiagnosed malignancy. She has been a vocal advocate of removing power morcellation from surgical options, and in response to her advocacy, an FDA statement published in April 2014 stated "If laparoscopic power morcellation is performed in women with unsuspected uterine sarcoma, there is a risk that the procedure will spread the cancerous tissue within the abdomen and pelvis, significantly worsening the patient's likelihood of long-term survival. For this reason, and because there is no reliable method for predicting whether a woman with fibroids may have a uterine sarcoma, the FDA discourages the use of laparoscopic power morcellation during hysterectomy or myomectomy for uterine fibroids."[4] In November 2014, the FDA issued additional warnings stating "While the specific estimate of this risk may not be known with certainty, the FDA believes that the risk is higher than previously understood. Because of this risk and the availability of alternative surgical options for most women, the FDA is warning against the use of laparoscopic power morcellators in the majority of women undergoing myomectomy or hysterectomy for treatment of fibroids."[5]

Although the claim is certainly plausible that morcellation may upstage a malignancy, there are little data on the effect of morcellation on upstaging, recurrence, or survival. LMS is a rare cancer and nearly always diagnosed either on frozen section or on permanent pathology because preoperative evaluation through imaging (MRI) or endometrial biopsy is not reliable.[6,7] The incidence of uterine sarcoma is extremely low, with < 1% of hysterectomy specimens found to have a sarcoma. Uterine sarcomas consist of LMS, an extremely aggressive but rare malignancy; endometrial stromal sarcoma (ESS), a rare and less aggressive malignancy; and STUMP tumors (smooth muscle tumors of uncertain malignant potential), a rarer and less-aggressive sarcoma. One study found a 0.09% risk of sarcoma in a case series of 1091 patients,[8] including ESS, STUMP tumors, and LMS. The most aggressive and the most worrisome of these is

LMS. This study showed that 57% of the LMS recurred as disseminated disease and the majority of these patients died of their disease. More recent articles have attempted to quantitate the risk of malignancy among women undergoing surgery for fibroid uteri. Bojar et al evaluated 10,731 women who underwent laparoscopic supracervical hysterectomy; the rate of ESS was 0.04%, LMS was 0.02%, and endometrial cancer was 0.07%, supporting the contention that malignant conditions of the uterus not diagnosed prior to surgery are extremely rare.[9] Liu et al evaluated two studies of survival in Stages I/II LMS[10] and survival was 51-75% for Stage I and 25-60% for Stage II LMS, which is similar to the recurrence of 57% noted with morcellation.[8] Given that most patients who recur do not survive their cancer, these data suggest that morcellation may only slightly increase the recurrence risk of LMS. The two studies also noted that there was a 0.2-0.8% (2/1000) risk of uterine sarcoma in patients who were not suspected of having a sarcoma.[11,12] The survival for STUMP tumors and ESS is much higher than LMS, with one study of ESS showing an 89% 5-year survival for Stages I/II[12] and another showing an 84% 5-year survival for Stage I and a 62% 5-year survival for Stage II.[13] Another study found no difference in overall survival with morcellation vs no morcellation for Stage I LMS after adjustment for mitotic rate in the tumors,[14] suggesting that the biology of the cancer rather than the mode of surgical removal is the most important prognostic factor in uterine sarcoma.

Liu et al also evaluated the potential cost differential, assuming surgery would have been performed open if morcellation were not available.[10] There are approximately 600,000 hysterectomies done each year.[9] In 2008, 10% of the cases were done laparoscopically and 15% of these laparoscopic cases involved morcellation. If morcellation were not available, the laparotomy rate could have increased by 15%. In real terms, this would mean an open procedure for 9000 additional women, 99,000 more days absent from work, $13.5 million more in health care spending/year, and at least 54 more VTE (0.6% greater risk of VTE).[2] This would translate to even more in 2014, given the dramatic rise of MIS for hysterectomies and myomectomies.

The American College of Obstetricians and Gynecologists (ACOG) issued a statement in response to these warnings stating "We continue to believe that power morcellation has a role in gynecologic surgery. Power morcellation can make it possible for some women to undergo less-invasive laparoscopic hysterectomy or myomectomy, sparing them the longer recovery time and higher mortality rates associated with a total abdominal procedure. The FDA's clarification of contraindications for morcellation will help to ensure that only women at low risk for an occult malignancy will undergo laparoscopic hysterectomy or myomectomy with morcellation. However, we look forward to working with the FDA to provide additional clarification regarding certain language within the contraindications that could be confusing to patients and physicians."[15] The Society of Gynecolgic Oncology (SGO) issued the following statement: "The SGO asserts that morcellation is generally contraindicated in the presence of documented or highly suspected malignancy. Women being considered for minimally invasive surgery performed by laparoscopic or robotic techniques that might require morcellation should first be evaluated for coexisting uterine or cervical malignancy. Morcellation may also be inadvisable for women with premalignant conditions or who are undergoing cancer risk-reducing surgery, in which there is some risk of occult malignancy. Thus, the SGO does advise caution when using any morcellation technique. But the SGO is not supportive of any overt restriction of power morcellation. As surgical tools, power morcellators allow thousands of women the opportunity to have minimally invasive surgery."[16]

■ COMMENTARY

So given the medico-legal climate of morcellation, what are the surgical options? I believe continuing to do minimally invasive surgery will promote better health in women. MIS includes total vaginal hysterectomy, which is an excellent option with lower cost and equivalent morbidity to laparoscopic surgery. Other options include doing the surgery laparoscopically and making a mini-laparotomy to remove the uterus or the myoma. There is interest in developing a bag to contain the uterus or the myoma and then morcellating it confined to a bag. Given that both ACOG and SGO promote the ongoing use of morcellation due to the advantages of MIS, it is clear that we need to continue to strive for minimally invasive surgery for low-risk women and should not radically change our surgical approach. Can we afford to abandon a technology that saves money and reduces morbidity? We have become a risk averse society when it comes to medical care. As a result, on May 5, 2015, Highmark Insurance stopped covering morcellation, followed by Aetna the next week, confirming that power morcellation in its current state will not continue to be a surgical option for some women. This is even more disappointing given the recent decision analysis by Siedhoff et al who found that women undergoing laparoscopic hysterectomy with morcellation for presumed fibroids had a lower overall mortality than those undergoing abdominal hysterectomy (98 vs 103/100,000).[17]

Medicine is an imperfect science. In the quest to seek perfection and avoid risk at all costs, we have abandoned a valuable and useful procedure. However, this may be an opportunity to enhance our vaginal surgical skills and/or continue to do MIS but remove the specimen through a mini-laparotomy. Currently, there are no data that a mini-laparotomy carries the same risks as an open laparotomy. In addition, if a bag can be developed that eradicates the potential spread of tissue, then morcellation may return to our surgical armamentarium. ■

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CME QUESTIONS

1. **In the clinical trials of flibanserin, compared to placebo, subjects who received active treatment reported which of the following?**
   a. Up to one more additional satisfying sexual episode each month
   b. Significant increases in sexual desire as measured with the eDiary
   c. Better vaginal lubrication and arousal with continued use of the drug past 6 months.
   d. Weight loss and reduction in blood pressure and serum cholesterol
2. **A recent study of Internet searches for information on pelvic organ prolapse found which of the following to be true?**
   a. .edu sites had the most high-quality information regarding prolapse.
   b. The overall quality of health information regarding prolapse on the Internet was excellent.
   c. Performing an online search using the search term "prolapse" resulted in websites with higher quality than when using the term dropped
   d. .gov sites had the most high-quality information regarding prolapse.
3. **In previous studies, abnormal cerebroplacental ratios have not been linked with the following adverse outcomes?**
   a. Poor ability to tolerate labor
   b. Immediate neurological morbidity
   c. Need for cesarean section for fetal distress
   d. Low neurobehavioral scores at 2 years of age
   e. All of the above are true
4. **The poorest prognosis for a uterine sarcoma is:**
   a. leiomysarcoma.
   b. endometrial stromal sarcoma.
   c. STUMP tumor.
   d. adenocarcinoma.

[IN FUTURE ISSUES]

Concomitant Hysteroscopic Sterilization and Endometrial Ablation: What Are the Risks?