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Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

Marijuana in Pregnancy

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

SYNOPSIS: A group of investigators posing as pregnant patients called marijuana dispensaries in Colorado to determine whether the stores' staff recommended it for nausea and vomiting, if there were risks in pregnancy, and if providers should be consulted. The results were enlightening.

SOURCE: Dickson B, Mansfield C, Guiahi M, et al. Recommendations from cannabis dispensaries about first-trimester cannabis use. *Obstet Gynecol* 2018;131:1031-1038.

Legalization of marijuana has been a highly charged subject. Certainly its use in pregnancy has been no less controversial. Recently, there has been a growing public impetus, now backed by some legislators, to legalize marijuana as a medicine and, in some states, to allow its recreational use. Like smoking and alcohol, the universal admonition has been to apprise the pregnant consumer of its possible risks through product labeling, public education, and their providers.

Marijuana has become a vibrant industry in Colorado and, seemingly, on every few blocks there is a store displaying a green sign. A team from the University of Colorado decided to query the type of upfront information provided by marijuana dispensary staff members to prospective pregnant users. The authors called 465 dispensaries and obtained useful information from 400. The mystery callers, posing as eight-week pregnant patients, recorded the interactions with the staff members answering the calls. Employees were asked whether they had products that were "recommended for morning sickness." Even if the employee said it was against the company policy to make recommendations and then went on to do so, this represented an affirmative answer. The callers' script also included asking about any known fetal or maternal risks and whether they should check with their medical providers.

Sixty-nine percent recommended its use for morning sickness and 36% said it was safe to use in pregnancy. Although only 32% initially recommended that the callers check with their doctors, 81% eventually did so with prompting. According to one dispensary employee "after eight weeks, everything should be good with

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consuming [marijuana] like alcohol and weed and stuff, but I would wait an extra week."

■ COMMENTARY

The study addresses the information provided by dispensaries to those wrestling with nausea and vomiting in pregnancy. Fortunately, most dispensary employees eventually defaulted to an "ask your doctor" response. However, the bulk of pregnant buyers of marijuana are recreational users who may not be asking their provider for advice. Those doing so probably will elicit widely varying, and sometimes biased, opinions. Here is an attempt to lay out a brief objective summary of the possible risks of marijuana in pregnancy.

The marijuana plant contains up to 100 cannabinoids, some of which mimic endogenous cannabinoids acting in the brain through cannabinoid receptors. The two ingredients of greatest interest are tetrahydrocannabinol (THC) and cannabidiol (CBD). THC acts on CB1 receptors responsible for the euphoria or "high" that most marijuana users seek. CBD acts through its effect on serotonin, and not generally through CB1 receptors. There is low- to moderate-quality evidence for its medicinal properties, which include suppression of nausea and vomiting (generally for patients undergoing chemotherapy), pain modification, anti-seizure activity, and anti-inflammatory properties. It also can temper some of the unwanted psychotropic effects of THC.

Pure weed contains varying amounts of THC and CBD, but through the miracle of modern chemistry, it is possible to adjust the levels of each in many manufactured ingestibles and inhaled products. The weed that the Woodstock and Haight-Ashbury generations smoked contained only about 2-4% of THC. Now, through selective engineering of the marijuana plants, the THC can be jacked up to 15% concentrations, and some concentrated extracts now can contain more than 50% THC. For those only wanting the possible medical benefits of marijuana, the ratio of CBD/THC can be adjusted in vapes to above 10 to 1.

The main maternal risk is the same as it is for a nonpregnant user: addiction. Marijuana dependence is thought to occur in 2.7 million individuals in the United States and affects about 9% of users — compared with the 15% of the population addicted to alcohol.[1] However, addiction is far less common in new or occasional users, and is unlikely to happen in pregnant users only seeking relief from nausea and vomiting.

It is very difficult to sort out the fetal risks of marijuana in the animal model because of difficulties in creating experimental methods analogous to the human experience. Also, based on the nonuniformity of products consumed or inhaled by chronic users, whom most observational studies have targeted, it is difficult to apply the results to those seeking relief from nausea and vomiting. By necessity, investigations have compared the effect of marijuana on pregnancy outcomes between users and nonusers, with the former more likely to expose their fetuses to confounding variables such as cigarette smoke (active or passive) and alcohol. Also, marijuana users often come from different socioeconomic backgrounds and have different nutritional habits than nonusers. Nevertheless, some studies have shown children exposed in utero performed more poorly in visual problem-solving, motor coordination, and attention deficits compared with unexposed controls.[2,3,4] This has concerned some investigators because of the possibility that over-exposing developing brains to cannabinoids may interfere with neuronal migration. Other possible effects are a slightly increased risk of stillbirth[5] (but not perinatal death),[6] low birth weight in those using it more than once a week,[7] and preterm birth (mostly in those who also are cigarette smokers).[7] A few older studies have not shown any differences in adverse outcomes.[8,9] Most studies did not show an association with anomalies, although one study did find a higher rate of anencephaly (but marijuana users are less likely to take folic acid during fetal organogenesis).[10]

Since providers have been handed the marijuana advice baton, what can we say about its use in pregnancy? Based on the data at hand, it would be hard to prove that marijuana in pregnancy is innocuous, especially in a chronic user. Therefore, despite the "yes, but" confounders engrained into many of the studies, a cautious approach is warranted. However, it is far easier to tell the recreational user (as suggested by American College of Obstetricians and Gynecologists)[11] that any evidence of possible harm should make abstaining during pregnancy the obvious option, than to forcefully advise against its use in a patient who says that it is the only "medicine" she has tried, or been prescribed, that relieves her debilitating, and often dangerous, hyperemesis. Under these circumstances, one must wonder whether the possible risks outweigh its benefits. ■

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ABSTRACT & COMMENTARY

A New Treatment for Early Pregnancy Loss

By Rebecca H. Allen, MD, MPH

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Dr. Allen reports she is a Nexplanon trainer for Merck.

SYNOPSIS: In a recent trial, researchers found that pretreatment with mifepristone followed by treatment with misoprostol resulted in a higher likelihood of successful management of first-trimester pregnancy loss than treatment with misoprostol alone. The rate of surgical evacuation also was reduced in the mifepristone pretreatment arm compared to the misoprostol-alone arm.

SOURCE: Schreiber CA, Creinin MD, Atrio J, et al. Mifepristone pretreatment for the medical management of early pregnancy loss. *N Engl J Med* 2018;378:2162-2170.

In this multicenter, randomized trial, researchers compared the efficacy of pretreatment with mifepristone followed by treatment with misoprostol vs. treatment with misoprostol use alone for managing anembryonic gestation and embryonic or fetal death. Women had to be between five and 12 completed weeks of gestation with a documented intrauterine pregnancy, clinically stable with a closed cervical os, and with a hemoglobin level of at least 9.5 g/dL. Participants received either pretreatment with 200 mg of mifepristone administered orally followed by 800 mcg of misoprostol administered vaginally approximately 24 hours later (mifepristone group), or standard therapy with 800 mcg of misoprostol alone administered vaginally (misoprostol-only group) 24 hours after randomization. The primary outcome was gestational sac expulsion by the first follow-up visit with one dose of misoprostol and no additional surgical or medical intervention within 30 days after treatment. Participants were scheduled for a follow-up visit from 48 hours up to four days after randomization. A transvaginal ultrasound was performed by a blinded investigator. If the gestational sac was absent, the participants were followed for 30 days after treatment. If the gestational sac was present, women were offered a second dose of misoprostol, expectant management, or surgical management. Participants who chose expectant management or a second dose of misoprostol returned for an additional follow-up visit approximately eight days after randomization for evaluation by a blinded investigator and then were followed for a total of 30 days. Other data collected included bleeding, pain, and acceptability of the treatment.

Between May 2014 and April 2017, researchers enrolled 300 women, with 149 assigned to mifepristone pretreatment and 151 to misoprostol only. The treatment was successful by the first follow-up visit, with no additional need for intervention in 124 of 148 women (83.8%; 95% confidence interval [CI], 76.8-89.3) in the mifepristone group and in 100 of 149 women (67.1%; 95% CI, 59.0-74.6) in the misoprostol-only group. For those women who still had a gestational sac, 41% chose expectant management, 27% chose a second dose of misoprostol, and 31% underwent surgical evacuation. Thirty days after randomization, the cumulative rate of gestational sac expulsion with up to two doses of misoprostol was 91.2% (95% CI, 85.4-95.2) in the

mifepristone group and 75.8% (95% CI, 68.2-82.5) in the misoprostol-alone group. Thirteen women (8.8%) in the mifepristone group and 35 women (23.5) in the misoprostol-only group underwent surgical evacuation (relative risk, 0.37; 95% CI, 0.21-0.68). There was no difference in the effect of the intervention when stratified by gestation, gravidity, parity, or type of missed abortion. There were no significant differences in mean scores for bleeding intensity or pain between the two groups, and both groups found the treatment acceptable (89.4% mifepristone group vs. 87.4% misoprostol-only group). The number of serious adverse events was no different between the two groups. Three women in the mifepristone group and one woman in the misoprostol-only group required a blood transfusion, and two women in each group were diagnosed with pelvic infection.

■ COMMENTARY

Early pregnancy loss, also known as missed abortion, typically is defined as an intrauterine pregnancy in the first trimester that is not viable, whether because the gestational sac is empty or because the embryo has no cardiac activity.[1] Most commonly, diagnosis is made by ultrasound and the patient may or may not be symptomatic. For women who are stable without hemorrhage or infection, the three main options for the management of early pregnancy failure are expectant management, medical management with misoprostol, and surgical management. Women's preferences should guide treatment decisions, given that all three options are medically safe. Overall, the success rates of each method depend on the time allowed for completion. With misoprostol management, the authors of a large U.S. randomized, controlled trial reported success rates of 71% by day 3 with 800 mcg of vaginal misoprostol.[2] The success rate was increased to 84% when women took a second dose of 800 mcg of vaginal misoprostol, if needed. Given its efficacy in inducing abortion with misoprostol,[3] mifepristone has been researched as a supplementary drug for the treatment of early pregnancy failure to improve patient experience and success rates.[4] This is the largest trial to date evaluating the efficacy of combining mifepristone with misoprostol for medical treatment of missed abortion. The important findings from this study are that pretreatment with mifepristone increased the success of complete evacuation of the uterus without the need for additional medication or surgery. The number of mifepristone doses needed for one additional treatment success (i.e., the number needed to treat) was six. This was true across gestational age categories. Critically, the investigators kept the study population relatively homogeneous in that all women had to have a missed abortion, either an anembryonic pregnancy or embryonic fetal demise. The authors did not include incomplete abortions or inevitable abortions, which have higher success rates with misoprostol alone. The use of mifepristone as a pretreatment to misoprostol certainly will decrease the need for additional visits, ultrasounds, and interventions for those women opting for medical management of their early pregnancy loss.

[The use of mifepristone as a pretreatment to misoprostol certainly will decrease the need for additional visits, ultrasounds, and interventions for those women opting for medical management of their early pregnancy loss.]

However, mifepristone is a medication that has carried a U.S. Food and Drug Administration (FDA) Risk Evaluation and Mitigation Strategy (REMS) requirement since its approval in 2000. Typically, REMS requirements are used for drugs associated with the risk of serious complications that cannot be addressed by labeling information alone, and the requirements often limit drug supply. Because of the REMS, mifepristone is not permitted to be sold in retail pharmacies. The medication must be stocked in physician offices or hospitals, and it must be dispensed by a certified prescriber. To become a certified prescriber, the provider must attest to the drug distributor that they can date a pregnancy, diagnose ectopic pregnancy, and provide or refer for surgical evacuation of the uterus if needed. Finally, under the REMS requirement, women must be given an FDA-approved medication guide and sign an FDA-approved patient agreement form outlining the instructions for use and potential risks. Nevertheless, the safety of mifepristone and misoprostol for induced abortion has been well established since 2000. Only 19 deaths have been reported to the FDA out of more than 3 million women who have used mifepristone, and, as in this trial, the rate of hospital admission, blood transfusion, or serious infection is rare.[5] Therefore, the REMS restrictions are unnecessary and only make mifepristone more difficult to access for both patients and providers. Mifepristone has many uses in obstetrics and gynecology, having been shown to work for induced abortion with misoprostol, cervical ripening for surgical abortion, and to shorten the duration of labor for induction abortions. With this new indication for the use of mifepristone now established, hopefully we can work on improving the availability of mifepristone across the United States. ■

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ABSTRACT & COMMENTARY

Screening for von Willebrand Disease: Warranted in Young Women With Heavy Menstrual Bleeding

By Robert W. Rebar, MD

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Dr. Rebar reports he is the chair of two data safety monitoring boards for Myovant Sciences.

SYNOPSIS: A large, retrospective cohort study using a national claims database revealed that fewer than 20% of young women with heavy menstrual bleeding were screened for von Willebrand disease.

SOURCE: Jacobson AE, Vesely SK, Koch T, et al. Patterns of von Willebrand disease screening in girls and adolescents with heavy menstrual bleeding. *Obstet Gynecol* 2018;131:1121-1129.

Heavy menstrual bleeding (HMB) occurs commonly in young women. It is well known that bleeding disorders must be considered as one of the underlying causes. A quantitative or qualitative deficiency of von Willebrand factor, von Willebrand disease is the most common bleeding disorder in women, affecting an estimated 1.6 million U.S. individuals.[1] In 2001, the American College of Obstetricians and Gynecologists (ACOG) first recommended that adolescents with menorrhagia be screened for von Willebrand disease.[2]

Jacobson et al used the Truven Health MarketScan Research Databases to identify women between 10 and 17 years of age with a diagnosis of HMB based on ICD-9 codes to investigate the frequency of screening for von Willebrand disease. The Truven Health MarketScan Research Databases include medical prescription claims of more than 109 million total covered lives in the United States and Medicaid data on 8.6 million patients from 14 states from 2011 to 2013. Based on a prior study of Ohio Medicaid patients,[3] the authors hypothesized that the frequency of screening in this population, representative of the entire United States, would be low.

Of the 202,000 young women in the database, 23,888 met the inclusion criteria with a diagnosis of HMB, and 986 (4%) met the study definition for severe HMB (defined as heavy menstrual bleeding plus evidence of iron deficiency anemia, a blood transfusion, or an inpatient stay for bleeding). Of the total, 28% were seen at the first visit by obstetrician-gynecologists and 13% were seen by family practitioners. Fewer than one in 10 (8%) of the total population and fewer than one in five of the women with severe HMB (16%) were screened for von Willebrand disease. The younger women (aged 10-13 years) were screened more often than the older women (aged 14-27 years; 13.9% vs. 6.4%; $P < 0.001$). Logistic regression analysis indicated that women with severe HMB had a significantly increased likelihood of undergoing screening compared to those without severe HMB (16.2% vs. 7.8%; odds ratio [OR], 1.58; 95% confidence interval [CI], 1.31-1.91). Of additional note is that the logistic regression analysis showed that privately insured patients were significantly more likely to be screened for von Willebrand disease than Medicaid patients (8.8% vs. 6.5%; OR, 1.66; 95% CI, 1.47-1.87). Women seeing family practitioners for the initial visit were less likely to undergo screening compared to those seeing obstetrician-gynecologists (3.2% vs. 6.0%; OR, 0.43; 95% CI, 0.34-0.54), but screening by both groups was low.

■ COMMENTARY

Perhaps the seminal study calling attention to the high incidence of bleeding disorders among young women was a 1981 series published from the Toronto Hospital for Sick Children reporting that 19% of adolescents with menorrhagia had a bleeding disorder.[4] Because of the heightened realization of the increased incidence of bleeding disorders in young women with HMB, ACOG first issued a Committee Opinion in 2001 urging practitioners to screen adolescents with menorrhagia for von Willebrand disease.[2] In a subsequent Committee Opinion, ACOG refined the recommendation to urge testing in young women with HMB and one or more of the following: menses longer than seven days or bleeding through a pad or tampon in two hours, anemia, a family

history of a bleeding disorder, and a history of bleeding after a hemostatic challenge (i.e., tooth extraction, surgery, delivery).[5]

Despite such recommendations, the Jacobson et al study documents that screening for von Willebrand disease rarely is performed among young women with HMB. Why is this the case? Certainly, taking an appropriate history is the first step and is accomplished easily by all clinicians. The testing can be complicated, but initial testing for HMB is straightforward. A blood type and crossmatch are warranted for any woman who is hemodynamically unstable on initial presentation. A complete blood count with differential and platelet count and a pregnancy test always are indicated. Initial testing for a bleeding disorder should include prothrombin time, partial thromboplastin time, thrombin time, and fibrinogen level. At this point, referral to a hematologist probably is warranted because no simple, single laboratory test is available to screen for von Willebrand disease. The initial laboratory assessment for von Willebrand disease includes measurement of von Willebrand factor antigen, ristocetin cofactor activity, and factor VIII coagulant activity.[6] All three tests are recommended for initial evaluation and also may suggest the type and severity of von Willebrand disease.

I chose to highlight this paper because I was so surprised by the findings. From my early days of medical school, it was always emphasized to rule out a bleeding disorder in any individual with unexplained heavy bleeding. That admonition still rings true today, and this paper emphasizes the need for evaluation in women with HMB. Study after study now have reported that approximately 20% of young women with HMB have a bleeding disorder, and von Willebrand disease is the most common. Let us never forget to evaluate young women who present with HMB. ■

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ABSTRACT & COMMENTARY

Can Hormone Therapy Prevent the Development of a 'Dowager's Hump'?

By Jeffrey T. Jensen, MD, MPH

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Dr. Jensen reports that he is a consultant for and receives grant/research support from Bayer, Merck, ContraMed, and FHI360; he receives grant/research support from Abbvie, HRA Pharma, Medicines 360, and Conrad; and he is a consultant for the Population Council.

SYNOPSIS: Postmenopausal hormone therapy may reduce the risk of developing age-related hyperkyphosis, commonly known as a "Dowager's hump," and the benefit from hormone therapy use in early menopause may provide long-term benefit.

SOURCE: Woods GN, Huang MH, Cawthon PM, et al. Patterns of menopausal hormone therapy use and hyperkyphosis in older women. *Menopause* 2018;25:738-743.

The abnormal exaggerated curvature of the dorsal spine with compensatory cervical lordosis that commonly occurs in elderly postmenopausal women colloquially is referred to as a "Dowager's hump" and medically is known as hyperkyphosis. Women with hyperkyphosis are at risk for other fragility health concerns, including poor physical function, falls, fractures, and early mortality. The risk factors for hyperkyphosis include low bone mineral density (BMD), bone loss, and vertebral fractures. Since menopausal hormone therapy (HT) reverses bone loss and prevents vertebral fractures, the authors hypothesized that use of HT would reduce the risk for developing hyperkyphosis.

As an initial step to evaluate this hypothesis, they used data available from the Study of Osteoporotic Fractures (SOF), a longitudinal, multicenter, observational study of 9,704 community-dwelling ambulatory women aged 65 years and older recruited between 1986 and 1988 from four clinics in Baltimore; Minneapolis; Monongahela

Valley, PA; and Portland, OR. Out of the total study population of 9,704 women, they selected a random group of 1,063 women from a subset of participants with longitudinal follow-up (seven study visits) that detailed HT use spanning an average of 15 years and adequate spinal radiographs at baseline and at year 15 suitable for determination of a modified Cobb angle of kyphosis. The modified Cobb angle uses the anchors of T4 and T12 to measure the angle in lateral spine radiographs instead of T1 to T3, as the higher thoracic vertebral bodies typically are not well visualized on lateral X-rays (available in the SOF). Readers of the films were blinded to HT status of the women.

They relied on self-report during the study period to classify HT: continuous (current use reported at six or more of seven visits), 12% of sample; intermittent (current use reported at between one and five of seven visits), 17%; remote past (reported past use at study baseline but no current use at any visit), 24%; or never, 46%. Evaluation of the demographic characteristics of participants revealed no clinically important or statistically significant differences between HT pattern groups and age (overall mean at follow-up, 83.7 years), body weight, or family history of hyperkyphosis (26%).

Compared to never users (52.6°), continuous HT users had the smallest mean Cobb angle (48.9°), followed by remote past (49.9°) and intermittent use (51.5°). Consistent with this effect, users of continuous HT also had higher BMD (0.805 g/cm^2) compared to never use (0.704 g/cm^2), with a dose effect observed with intermittent (0.733 g/cm^2) and remote past (0.715 g/cm^2) use. The authors did not report statistical significance.

The differences in the Cobb angle with continuous and remote past use of HT were statistically significant in the age- and clinic-adjusted model (P = 0.01). In the fully adjusted model, which also included the number of prevalent vertebral fractures, family history of hyperkyphosis, the presence of degenerative disc disease, total hip BMD, and body weight, the strength of association decreased and became nonsignificant (only -2.8°; P = 0.06) for continuous use. Of interest, this full adjustment did not attenuate the beneficial association seen with remote past use (-2.8°; P = 0.02).

The authors concluded that these results support a role for postmenopausal HT in the prevention of age-related hyperkyphosis.

■ COMMENTARY

At first glance, these results seem obvious. We know that low BMD, bone loss, and vertebral fractures are predictable consequences of menopause, and also are independent risk factors for hyperkyphosis. We also know that HT prevents postmenopausal bone loss, maintains or improves BMD, and prevents fracture.[1,2] However, no studies specifically have evaluated whether HT can reduce the risk of developing hyperkyphosis.

Why study this question? The fact that we have a colloquial expression, "Dowager's hump," for the physical changes of spinal compression fractures and short stature that develop in elderly women reveals the ubiquity of the condition. But we also recognize hyperkyphosis as a fragility sign. While we cannot stop the aging process, I have not met any patient looking forward to the development of this physical change of fragility.

The results of this paper by Woods and colleagues provide additional information useful in the counseling of perimenopausal and early postmenopausal women regarding HT. We now have evidence that the use of HT can reduce the risk of developing a Dowager's hump. This may motivate some women to consider HT more carefully.

The cross-sectional design, simple cohort analysis, and lack of detail on type or dose of HT represent major weaknesses that must be considered in evaluating this research. However, notable strengths include the large sample size and prospective follow-up over 15 years. We see biologic plausibility in the results. Continuous use of HT resulted in the greatest reduction in Cobb angle (almost 4°). I am not bothered that this benefit attenuated and was no longer statistically significant after full adjustment. The full adjustment model included BMD and the presence of degenerative disk disease (DDD). Not surprising, continuous HT users had the highest BMD and the lowest rate of DDD, as HT also improved both of these findings. Thus, these characteristics are not confounders of the association of benefit of HT on the reduced Cobb angle. HT improves BMD and prevents DDD, so we should expect correlation with the benefit through a causal relationship. Also, we should expect that adjusting for these factors would tend to attenuate the overall beneficial effect seen with respect to the Cobb angle.

I am intrigued by the fact that remote past users also showed a significant reduction in the Cobb angle, and that this benefit remained significant even after complete adjustment. The absence in change in the effect supports my previous comment that adjusting for the benefit in BMD diluted the effect seen with continuous use. In contrast to continuous users, the BMD of remote past users was similar to that of never users. Remote past users stopped HT prior to enrolling in the study (mean age, 68 years). This suggests that initiation of HT and strong protection against bone loss in the early postmenopausal years might provide lasting benefit, even if bone loss eventually catches up.

These results may provide clinicians with an additional counseling point to encourage healthy perimenopausal and postmenopausal women to consider initiation of HT as an early intervention. If a patient has reservations about the potential benefits of HT, perhaps these new results will push her over the "hump." ■

REFERENCES

1. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal

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CME/CE INSTRUCTIONS

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CME/CE QUESTIONS

1. **There is some evidence that marijuana has benefit by:**
   a. alleviating nausea and vomiting.
   b. relieving pain.
   c. countering seizures.
   d. All the above

2. **In the study by Schreiber et al, how many women with early pregnancy loss needed to pretreat with mifepristone to attain an additional treatment success by the first follow-up visit?**
   a. Three
   b. Six
   c. Nine
   d. 12

3. **In the study evaluating hyperkyphosis, Woods et al reported that women who reported continuous use of hormonal therapy during 15 years of follow-up showed which of the following?**
   a. A reduction in nonvertebral and vertebral fractures compared to intermittent users
   b. A reduction in the Cobb angle, a marker of kyphosis, compared to never users
   c. A decrease in bone mineral density compared to remote past users
   d. A reduction in weight compared to all reference groups

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- Explain the latest data regarding diagnosis and treatment of various diseases affecting women;
- Discuss new data concerning prenatal care, neonatal health, and complications arising in pregnancy and the perinatal period; and
- Discuss the advantages, disadvantages, and cost-effectiveness of new testing procedures in women's health.

[IN FUTURE ISSUES]

Primary HPV Screening: Ready for Primetime?

Does Every Woman Deserve a High-volume Gynecologic Surgeon?