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A monthly update of developments in female reproductive medicine

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Trends in Alternative Medicine Use in the United States, 1990-1997

A B S T R A C T & C O M M E N T A R Y

This article reports a 1997 survey of a national randomized sample of households. The purpose of the questionnaire was to determine the rate of usage of alternative medicine by U.S. households, and to compare the results of the 1997 survey to a 1991 survey. There is a general impression that the use of complementary and alternative medicine (CAM) has increased during the past few years. Most medical schools now offer courses in CAM and the National Institutes of Health has developed a branch to study it.

The design of this type of study is complicated. In all such studies, there are compromises and great chances for the introduction of bias. Eisenberg and colleagues used random digit-dialing of a select sample of households throughout the United States. One household resident was interviewed. The household member must have been 18 years of age or older, and must have been able to use English to complete the questionnaire. Because it was recognized at the time of the survey that Americans are increasingly reluctant to answer telephone surveys, Eisenberg et al offered a financial incentive, though one was not offered at the time of the 1991 survey.

The initial sample included 9750 telephone numbers of which 52% were not working or were non-household numbers. An additional 5% were ineligible because the contact did not speak English. Forty-one percent of the remaining sample completed the interview at the time of the initial request. A subsample was recontacted, offered more money, and one-third of these individuals responded. It was known from a power calculation that approximately 2000 households would need to complete the interview for the results to be able to detect small significant differences.

Most of the information collected in the 1997 interview was similar to that collected in 1991. Care received from physicians (MD or DO degree) was distinguished from that received from any other practitioner. Participants in the questionnaire process were given a list of common medical conditions and asked whether they had any of these diseases. They were then asked about both their lifetime and past year usage of 16 alternative therapies. They were asked for which medical condition they used these therapies. Patients also

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were asked whether they discussed the use of CAM with their physician. Questions were asked concerning insurance coverage of CAM. The statistical analyses were appropriate for the type of study.

Eisenberg et al found that CAM was used by a wide array of societal members. However, usage was more common among women, non-African Americans, the 35-39 year age group, those with college education, and those with annual incomes of more than \$50,000. There was a 65% increase in the use of CAM between 1990 and 1997, increasing from 577 therapies per 1000 to 953 per 1000. The use of herbal medicines, massage, megavitamins, self-help groups, folk remedies, energy healing, and homeopathy showed the biggest increases.

There was also an increase in the number of individuals who saw alternative medicine practitioners in 1997 (46.3% vs 36.3%). Massage, chiropractic, hypnosis, biofeedback, and acupuncture were the most used providers. Visits to alternative medicine therapists were estimated to exceed the number of visits to primary care physicians in 1997.

There was a wide array of diseases for which individuals sought CAM help. Back problems and allergies led the list but were followed closely by fatigue, arthritis, headache, neck problems, and high blood pressure. Many individuals saw both a physician and an alternative medicine provider.

Most of the costs of alternative therapy were self paid.

Although there is a trend toward coverage of these therapies by insurance companies, approximately 58.3% of the patients paid for the entire alternative therapy themselves. In 1997, approximately \$21.2 billion was spent on alternative therapy. This greatly exceeds out-of-pocket expenses for all hospitalizations. In their comment section, Eisenberg et al carefully point out the limitations of their study. The study was restricted to individuals who speak English, have telephones, and were willing to answer a questionnaire. Nonetheless, it is reasonable to estimate that nearly one of every two adults aged 35-49 years used at least one alternative therapy in 1997. (Eisenberg DM, et al. *JAMA* 1998;280:1569-1575.)

■ COMMENT BY KENNETH NOLLER, MD

This is an important article. Despite what we, as physicians, might individually think of complementary and alternative therapy, the message is clear: The general public endorses and uses CAM to a great degree. I was raised in and received my education in the post-war years when science was king and nothing in medicine was effective unless it was proven in the laboratory. Alternative medicine was either ignored or laughed at. Obviously, such a one-sided view cannot be completely correct.

The pendulum is swinging more toward the middle and, I believe, it is incumbent upon us as physicians who care for the entire patient to be aware of alternative medicine and the good it can do. There are literally thousands of articles (many of them randomized clinical trials) that have shown the effectiveness of at least some of the alternative medicine measures. NIH has started a branch to investigate complementary and alternative medicine. They are finding a rich literature that "proves" effectiveness of many traditional folk medicines while, at the same time, they have also found some therapies not to be effective.

I see three major problems for which we, as physician guardians of our patients' health, must take leadership. First, we must make it clear to our patients that it is important that we know of all medications they may be ingesting, whether these are prescription or nonprescription. Serious interactions occur between medications and we must strive to avoid them. However, patients will not freely admit to seeking CAM care unless we ask our questions in a nonthreatening manner and do not poke fun at these other treatment strategies.

Second, we must protect our patients from those practitioners of CAM who are clearly taking advantage of a distressed patient. Unfortunately, licensing of alternative medicine practitioners varies greatly, and, in many states, no license is necessary for some practices. While I have had many patients who have seen alternative providers and been happy, I cannot help but remem-

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Questions & Comments

Please call **Robin Mason**, Assistant Managing Editor, at (404) 262-5517 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

ber the recent patient who saw an “herbal immunologist” who took her history, talked to her for 20 minutes, and charged her \$483. Obviously, he had figured out she could afford to pay his exorbitant fee.

Third, we must join the lobby that is pushing Congress to require content labeling of all “food supplements.” These substances are not required to undergo testing for content. When bottles have been purchased off shelves in health food stores and pharmacies, there has been a wide variation in the amount of actual active ingredients in the pills from a tiny fraction of the labeled amount to many-fold greater amount.

CAM has always been here and is here to stay. We should learn what is good and reject what is bad. Most important, we must keep an open mind. ❖

Burning Herbs to Correct Breech Presentation

ABSTRACT & COMMENTARY

Synopsis: *Moxibustion, when used in primigravidas at 33 weeks gestation, is an effective therapy for inducing an increase in cephalic presentations.*

Source: Cardini F, Weixin H. *JAMA* 1998;280:1580-1584.

Moxibustion is a burning herb used to stimulate an acupuncture point beside the outer corner of the fifth toenail. To determine the efficacy and safety of moxibustion to promote version of fetuses in the breech presentation, Cardini and Weixin conducted a randomized, controlled, open clinical trial of primigravidas at 33 weeks gestation with a normal pregnancy and an ultrasound-confirmed diagnosis of breech presentation ($n = 130$). The moxibustion material in a “cigar-shaped roll” was applied for 30 minutes each day for seven days in the first 87 subjects, and twice daily in 43 subjects. Women in the control group ($n = 130$) received routine prenatal care. At 35 weeks, subjects in either group with a persistent breech presentation could elect to undergo external cephalic version (ECV). Because the beneficial effect of moxibustion may be through the stimulation of fetal activity, study subjects in both groups counted fetal movement for one hour each day.

At 35 weeks, 75.4% (98/130) of fetuses in the intervention group were in a cephalic presentation compared to 47.7% (62/130) of fetuses in the control group—a significant difference ($P < 0.001$). One patient in the inter-

vention group had a failed ECV, while 19 of 24 ECVs in the control group were successful. Overall, even after ECV, the number of fetuses in a cephalic presentation remained significantly greater in the moxibustion-treated patients. Of note, fetal movements were significantly greater during the seven days of monitoring in the moxibustion patients, 48.45 per hour vs. 35.35 in the controls. Moxibustion treatment was not associated with adverse effects in the mother or neonate.

Cardini and Weixin conclude that moxibustion, when used in primigravidas at 33 weeks gestation, is an effective therapy for inducing an increase in cephalic presentations.

■ COMMENT BY STEVEN G. GABBE, MD

There has been a significant increase in the use of alternative therapies in the United States. (*See article, pages 65-67.*) A nationally conducted random household telephone survey revealed that more than 40% of adults questioned used at least one of 16 alternative therapies during the past year.

The study by Cardini and Weixin, performed at two hospitals in the People’s Republic of China, demonstrates that the herb moxibustion applied to a specific acupoint is associated with an increased likelihood of version in primigravid women treated during the 33rd week of pregnancy. Because there was an associated increase in fetal movement during the first week of treatment, this effect was thought to be the mechanism for the change in fetal position. Of note, the cesarean delivery rate was no different for either of the study groups—approximately 35% with most for cephalopelvic disproportion. While the trial was randomized and controlled, it was not blinded. Nevertheless, this report provides an interesting and alternative approach to the treatment of a common obstetrical problem. ❖

Fertility-Sparing Surgery in Uterine Leiomyosarcoma

ABSTRACT & COMMENTARY

Synopsis: *Selected cases of uterine leiomyosarcoma may be conservatively managed in young nulliparous women desiring pregnancy.*

Source: Lissoni A, et al. *Gynecol Oncol* 1998;70:348-350.

Lissoni and associates have reported eight patients with a diagnosis of uterine leiomyosarcoma between 1982 and 1996 who were managed conservative-

ly after myomectomy. After myomectomy, surveillance consisted of physical examination, vaginal sonography, and hysteroscopy every three months for the first two years and every six months thereafter. Median age was 29 years (range, 19-32 years). All were nulliparous. The tumor was confined to the myoma in all patients. The mean mitotic count of the leiomyosarcomas was 6/10 high-power fields, with a range of 5-33. At a median follow-up of 42 months, three pregnancies were reported. Two patients had a spontaneous delivery at term. The third patient had a diagnosis of recurrent disease at the time of cesarean section. Despite further surgery and chemotherapy, she died of disseminated tumor 26 months after diagnosis. The remaining seven patients are alive and well. Two patients underwent a second surgical procedure after diagnosis of leiomyosarcoma, 24 and 16 months after primary surgery; both were found to have leiomyomas. Lissoni et al conclude that selected cases of uterine leiomyosarcoma might be managed conservatively in young nulliparous women desiring pregnancy. They emphasized that a strict follow-up is mandatory, and, at completion of childbearing, a hysterectomy could be considered.

■ COMMENT BY DAVID M. GERSHENSON, MD

This is a provocative report of fertility-sparing surgery after diagnosis of leiomyosarcoma treated with myomectomy. Lissoni et al are clearly pushing the envelope in terms of what is considered standard care. Leiomyosarcoma is an extremely rare malignancy, accounting for only about 25% of all uterine sarcomas. It is found arising in a benign leiomyoma in less than 1% of cases. It should be noted that the histopathologic definition of leiomyosarcoma has changed recently, with more emphasis placed on the presence of atypia and necrosis than on mitotic count alone. Standard treatment for high-grade leiomyosarcomas consists of abdominal hysterectomy and bilateral salpingo-oophorectomy. Approximately 50% of patients whose tumor is apparently confined to the uterus will ultimately develop recurrence. There is no known effective adjuvant therapy. Pelvic irradiation probably reduces the incidence of pelvic recurrence but has no effect on survival. Chemotherapy is relatively ineffective in treating metastatic disease. As emphasized by Lissoni et al, in considering a conservative approach after myomectomy, the patient and her family must be advised of the risks. Unfortunately, the precise risk of recurrence is unknown. Lissoni et al refer to two other series detailing 11 cases of conservative management after myomectomy for leiomyosarcoma; only one patient recurred and six pregnancies were documented. In the present series, one patient recurred and died. Therefore, based on small numbers, one could estimate the risk of recurrence in such

patients as 10-15%. However, it is important to underscore the fact that recurrence almost always equals death. In addition, it would seem advisable to retrospectively review the pathology from the world experience using modern criteria. In the interim, extreme caution is recommended until more experience is reported. ❖

Increased Levels of Cigarette Use Among College Students

ABSTRACT & COMMENTARY

Synopsis: Rates of cigarette smoking among college students increased between 1993 and 1997.

Source: Wechsler H, et al. *JAMA* 1998;280:1673-1678.

Several independent surveys have documented the fact that smoking rates have been increasing among adolescents since the early 1990s. However, little study has been completed on smoking among college students.

Wechsler and associates used the data collected from the Harvard School of Public Health College Alcohol Study surveys of 1993 and 1997 to determine smoking rates among college students at the time of these two surveys and to compare the data.

One hundred forty colleges participated in the 1993 survey and 130 participated in the 1997 survey. The schools were randomly selected with correction for school subtypes and geographic distribution. A random sample of 230 students was obtained from each school, except for the small schools, where 108 students were chosen. Data from schools with low participation rates were dropped.

The questionnaire that was used was largely concerned with the use of alcohol. However, smoking and other high-risk behaviors were the focus of some questions. Students were encouraged to respond to questionnaires with cash awards. Despite the monetary inducement, the response rate declined from 70% in 1993 to 60% in 1997.

When the data were analyzed, Wechsler et al found that there had been a 27.8% increase in smoking among college students between the two surveys. This increase was observed at 99 of the 116 colleges in the final sample. Most of the increase was in light smokers, with a 16% decrease noted in students who smoked one pack or greater a day. Smoking was highest in Caucasian students, non-seniors, students at public colleges, and less competitive schools. Smoking was lowest in the western part of the United States.

■ **COMMENT BY KENNETH NOLLER, MD**

I am troubled by the results of this survey. For many years, it has been shown repeatedly that the level of education is negatively associated with smoking. That is, the better educated an individual, the less likely that individual will smoke. For example, smoking among professionals with degrees beyond a basic college education is extremely low. In contrast, smoking rates among poor, urban adolescents and individuals who have not completed a high school education is disproportionately high, and most antismoking efforts in the United States have been aimed at these groups.

Now we have data to suggest that college students are also increasing cigarette consumption. Perhaps we have been negligent in our efforts to discourage tobacco use in this group since it has been assumed that they are at low risk for initiating and continuing smoking because of their education.

Since cigarette smoking is the leading preventable cause of serious medical illness in the United States at the present time, we, as physicians, have a duty to discourage all of our patients from smoking. This article suggests that we should not forget to include college students in our efforts. ❖

Atypical Glandular Cells of Undetermined Significance

ABSTRACT & COMMENTARY

Synopsis: *Atypical glandular cells of undetermined significance on Pap smears were correlated with significant findings in 45% of patients.*

Source: Veljovich DS, et al. *Am J Obstet Gynecol* 1998; 179:382-390.

Veljovich and associates conducted a five-year retrospective review of screening cervical cytologic examinations diagnosed as atypical glandular cells of undetermined significance (AGCUS) to ascertain the types and frequency of pathologic conditions associated with this diagnosis. Three hundred forty-five evaluable patients were identified. The incidence of AGCUS was 0.53%. Pathologic findings for the respective Pap smears with the diagnosis of AGCUS—not otherwise specified—favor benign, squamous intraepithelial lesions, and favor neoplasia through the follow-up interval were as follows: squamous intraepithelial lesions in 11%, 8%, 38%, and 20%; adenocarcinoma in situ in 3%, 0%, 0%, and 10%; endometrial hyperplasia in 3%, 5%, 1%, and 2%; and cancer in 8%, 3%, 1%, and 7%. Overall, 63 patients (32%)

had preinvasive or invasive lesions. Veljovich et al conclude that AGCUS on Pap smears were correlated with significant findings in 45% of patients (32% with preinvasive or invasive lesions and 13% with benign lesions). A prompt and aggressive workup was recommended.

■ **COMMENT BY DAVID M. GERSHENSON, MD**

The classification of AGCUS was proposed as part of the Bethesda system in 1988. Although other such studies have recently been reviewed in these pages, the importance of this finding cannot be overestimated. Not only do Veljovich et al place their findings in perspective, they also review the published reports on the subject. In seven other studies, the incidence of AGCUS was 0.48%, a figure similar to that found in the present study. In addition, the incidence of squamous intraepithelial lesions, adenocarcinoma in situ, endometrial hyperplasia, and cancer in these studies was 29.1%, 3.6%, 5.4%, and 5.8%, respectively. Recently, the American Society for Colposcopy and Cervical Pathology published guidelines for management of women with AGCUS on Pap smear. According to their recommendations, all women with AGCUS should undergo colposcopy of the cervix and vagina as well as endocervical curettage (ECC). Colposcopic-directed biopsies of abnormal areas should be performed. Patients with unqualified AGCUS who have negative colposcopy and ECC should have a repeat Pap smear every 4-6 months until four normal smears are reported. Patients with either AGCUS favoring neoplasia or unqualified AGCUS with positive ECC should undergo cervical conization. If cells appear to be of endometrial origin, endometrial biopsy, hysteroscopy, or curettage is recommended. In summary, the message is clear: the finding of AGCUS on Pap smear should be taken very seriously since the associated incidence of both preinvasive and invasive lesions is relatively high. Appropriate workup should be performed and physicians need to counsel their patients regarding the significance of this finding. ❖

Special Feature

Understanding the Perimenopause

By Sarah L. Berga, MD

The perimenopause is a time of confusion. bleeding patterns become erratic. Hormone levels fluctuate.

ate unpredictably. Symptoms come and go. To make matters worse, the physician is often at a loss for effective therapies and may dismiss the symptom complex because of diagnostic or therapeutic uncertainty. The way out of this limbo, for both patients and physicians, is to have a clear understanding of what the perimenopausal transition entails.

Perimenopause refers to those years in the reproductive life cycle during which ovarian cyclicality becomes irregular because of a decline in oocyte competence and count. Generally, this phase occurs during the years from ages 40-55.¹ The reproductive life cycle is characterized by a progression of states that involve the interplay between oocyte competence and hypothalamic-pituitary functioning. In a sense, the perimenopause is the "mirror image" of puberty. The timing and tempo of puberty is primarily a function of hypothalamic events and the reactivation of GnRH pulsatility, but, for puberty to be clinically manifested, the ovaries must contain responsive follicles. In contrast, the timing and tempo of perimenopause reflects follicular availability and responsiveness, but, for the perimenopause to be clinically apparent, the hypothalamic-pituitary unit must provide gonadotropin drive.

The cause of perimenopause and menopause is progressive follicular depletion. The store of primordial follicles is fixed in utero, and, thereafter, the number of primordial follicles declines with age. Across each interval of time, a certain percentage of these resting follicles die or become atretic. It has been estimated that menopause occurs when the number of primordial follicles falls below 1000.² The usual age for this degree of follicular depletion is 51 years. The age of menopause is not thought to be influenced by socioeconomic factors, but rather, it has been found to be a relatively universal biological constant.³ It is estimated that the number of primordial follicles at birth is about 1 million and that the rate of atresia is relatively constant until the remaining follicles number about 25,000. The customary age at which the rate of follicular atresia accelerates is estimated to be 37.5 years.² The probability of being menopausal increases with duration of amenorrhea and age.⁴

Considerable evidence suggests that serum FSH and serum inhibin levels are biomarkers for the number or quality of remaining follicles.⁴ However, in the perimenopause, each menstrual cycle is a relatively independent event,⁵ so measuring a single, isolated FSH level does not help to predict when menopause will occur and an untimed FSH level is a poor discriminator of follicular reserve. It remains to be determined if inhibin levels, which also change with follicular development, will pre-

dict ovarian reserve. While the biological basis for changing rates of atresia is not known, there is some empirical support for the notion that elevated FSH accelerates the rate of atresia.⁶ This might be one reason that rates of atresia accelerate in the perimenopause. According to one analysis, smokers tend to reach menopause an average of 1.74 years earlier than nonsmokers.⁷ However, family history is a good predictor of early menopause. In one study, women with a family history of early menopause were not more likely to have inborn errors of galactose metabolism or stigmata of Turner's syndrome, but they were less likely to have brothers.⁸ The strength of this familial association is such that a history of menopause before age 46 in a mother or sister increases the probability that a woman will have her menopause before age 46 years from 5-25%. Given that the cause of ovarian failure in girls with Turner's syndrome and those with deletions of the long arm of the X chromosome is thought to be an accelerated rate of atresia, Cramer and associates suggested that the low incidence of male siblings suggested that microdeletions of the long arm of the X chromosome might account for these observations.⁸ The exact gene product encoded for at the distal end of the long arm of the X chromosome is unknown, but it presumably influences oocyte longevity, and, thus, it would be potentially useful to identify. More information about the molecular events regulating follicular apoptosis also is expected to aid our understanding of the "ovarian clock."⁹

Clinical Consequences

One of the main reasons for wanting to understand the timing of menopause relates to concerns about predicting the end of fertility. If we could estimate the remaining follicle reserve, we might be able to individually forecast fecundity and menopause. This might be helpful to those who were interested in conceiving as well as to those seeking to avoid fertility. Although the mean age of sterility is estimated to be 44 years and is relatively constant worldwide,³ it is difficult to tell an individual woman when she can stop using contraception or when she can expect a fertility procedure to result in a conception. Maintaining or extending follicular reserve might also be an objective some would desire. Understanding and reversing gonadal dysgenesis might be an outcome that could be achieved if the biology of follicular atresia was better understood. Some experts believe that the ovarian clock reflects the individual's biological as opposed to chronological age and that menopause is a marker for the aging process in a given individual.⁴ Forestalling aging might seem to be an unrealistic goal, but extending disease-free life may not

be. Aging confers vulnerability to a wide variety of disorders that challenge individuals and society; thus, our forays into predicting or retarding the aging process could have multiple dividends.

Another reason for needing to understand the physiology of the menopause is that the changes in ovarian function are associated with a number of clinically apparent symptoms. Santoro and colleagues have shown that perimenopausal cycles are characterized by hyperestrogenism and luteal phase insufficiency.⁵ These alterations in steroidal secretion may lead to endometrial proliferation and menorrhagia. Endometrial sloughing depends on exposure to an orderly sequence of hormonal excursions. Should these not occur, the endometrium may not slough in an orderly fashion and the usual hemostatic mechanisms, particularly the release of prostaglandins and subsequent provocation of uterine “contractions” may be blunted, leading to arteriole dilation. Relative hyperestrogenism may provoke fibroid growth in predisposed individuals, moodiness in those so prone, and mastodynia. Because each menstrual cycle in the perimenopause is an independent event, cycles are irregularly irregular and associated symptoms may come and go. Lack of predictability alone may provoke concern and annoyance, fear, or frustration. It is even more maddening for women seeking medical consultation for these symptoms to be subjected to a dismissive attitude that abrogates their own sense of observation and concern. Thus, the prudent clinician is advised to heed the woman’s own description of the changes she notes and help her to understand that they likely reflect erratic ovarian function that is physiologic. The physician’s role is also to determine when these symptoms herald organic disorders and warrant further assessment and treatment.

Treatment Strategies

Clinically, the major problem is recognizing the perimenopause. Symptoms may be episodic because ovarian function waxes and wanes in an unpredictable fashion. Therefore, management must be based on the symptom complex. While many symptoms may be attributable to erratic ovarian function and amplified hormonal fluctuations, care must be taken not to prematurely assign all symptoms to this physiological event. Organic conditions must be excluded. In short, this is a good time to take a health inventory and to make sure that the perimenopausal woman is up-to-date on health screening. If the past personal or family history indicates problem areas, screening can be tailored or diagnostic studies undertaken.

A common clinical problem is heavy menses at unpredictable intervals (i.e., poor endogenous cycle control). Once conditions such as cancer, polyps, and fibroids have been excluded, the optimal solution for unpredictable ovarian function is the use of low-dose oral contraceptive pills containing 20 mcg of ethinyl estradiol. However, oral contraceptive use must be confined to nonsmokers and women without risk factors for or a history of thromboembolic events. The progestin dominance of ultra-low-dose oral contraceptives may help to reverse any nascent endometrial hyperplasia and because the dose of steroids in oral contraceptives is sufficient to suppress central GnRH drive, endogenous ovarian sex steroid secretion will also be suppressed. Standard hormone replacement regimens used for menopausal women also may have use, but given the propensity of the perimenopausal ovary to oversecrete estrogen, care must be taken to provide sufficient progestin along with estrogen exposure to avoid further stimulating the endometrium and increasing the chance of endometrial hyperplasia. Also, standard HRT regimens may not confer adequate cycle control, because the doses are insufficient to adequately suppress hypothalamic GnRH drive, and, thus, the endometrium may be exposed to both endogenous and exogenous steroid excursions. In perimenopausal women with recent onset of depression, studies suggest that antidepressant therapy has minimal efficacy if estrogen levels are inadequate, so institution of hormonal therapy is suggested prior to a trial of antidepressants.¹⁰ Perimenopausal ovarian function may provide high estrogen levels at some times followed by very low levels after the demise of a dominant follicle and before the recruitment of another. Therefore, the goal of HRT in the perimenopause is to provide “background” sex steroid levels upon which endogenous ovarian steroids fluctuate. Because progestins inhibit GnRH drive, there also may be some slight intermittent suppression of central input and possibly some blunting of ovarian hypersecretion of estrogen. Women with low bone mass can receive concurrent therapy with bisphosphonates, if needed, although low-dose oral contraceptives tend to promote bone accretion.

Summary

Understanding the physiology of the perimenopause helps the patient and clinician to put subtle clinical symptoms, such as mood swings, intermittent hot flashes, and heavy, irregular bleeding, into context. Conditions such as uterine pathology and hypothyroidism need to be excluded, however. Rela-

tive hyperestrogenism and luteal phase insufficiency characterize perimenopausal ovarian function, although there also may be windows of relative hypoestrogenism between the demise and the recruitment of poorly responsive follicles. Menometrorrhagia due to hormonal aberrations may respond to hormonal interventions, particularly oral contraceptives containing 20 mcg of ethinyl estradiol. The erratic nature of perimenopausal ovarian function means that the patient's history is one of the best diagnostic tools available and prudent clinicians are advised to elicit from the patient a prioritization as to which symptoms require intervention vs. reassurance. This is a good time to assess health risks and behaviors and to provide well-care screening. ❖

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CME Questions

1. **The most effective known adjuvant postoperative treatment for patients with uterine leiomyosarcoma apparently confined to the uterus is:**
 - a. Single-agent chemotherapy
 - b. Hormonal therapy
 - c. Radiotherapy
 - d. Combination chemotherapy
 - e. None

2. **The incidence of finding atypical glandular cells of undetermined significance in a Papanicolaou smear is:**
 - a. 0.3-0.8%
 - b. 0.5-1.0%
 - c. 1.0-1.5%
 - d. 2.0-5.0%
 - e. None of the above
3. **According to the telephone survey performed by Eisenberg et al, which of the following individuals would have been most likely to have used an alternative therapy in 1997?**
 - a. Caucasian male.
 - b. African American female.
 - c. Non-high school graduate.
 - d. Annual income greater than \$50,000.
4. **According to the article by Wechsler et al, college students in which geographic area of the United States are least likely to smoke?**
 - a. Northeast.
 - b. South.
 - c. Central
 - d. West
5. **An increase in which of the following is thought to be the mechanism by which moxibustion contributes to a change in fetal position from breech to cephalic?**
 - a. Maternal temperature
 - b. Fetal activity
 - c. Uterine activity
 - d. Uteroplacental blood flow

Correction

An error appeared in the December 1998 issue of *OB/GYN Clinical Alert*. On page 62 in Dr. Speroff's Special Feature, the fifth sentence in the first paragraph should have read: "It is a handsome package that includes four tablets (each containing 50 mcg ethinyl estradiol and 250 mcg levonorgestrel)." In the second column on page 63, the third sentence in the second paragraph should have read: "For women with a contraindication to exogenous estrogen, the progestin-only minipill can be used for emergency contraception (e.g., administering 10 levels onorgestrel tablets [75 mcg], for each of the two doses, or in some countries using the special commercial package." We regret any confusion this may have caused. ❖

In Future Issues:

P53 Protein Overexpression:
A Strong Prognostic Factor in
Uterine Papillary Serous Carcinoma