Add clarity to your assessment of pelvic mass patients

Combine CA125 + HE4 as ROMA™ to compute likelihood of malignancy

With CA125 + HE4, ROMA gives you the security to safely keep the majority of benign disease patients.¹

Assessment of adnexal mass is now more clear.¹⁻³ Data from a study of 472 patients published in August 2011 in Obstetrics & Gynecology showed that:

- ROMA correctly stratified 94% of women with epithelial ovarian cancer into a high-risk group¹
- ROMA correctly stratified 75% of women with benign disease into a low-risk group¹

Better Assessment of Adnexal Masses

- Epithelial Ovarian Cancer
  - High Likelihood: 94%
  - Low Likelihood: 6%
- Benign
  - High Likelihood: 25%
  - Low Likelihood: 75%
From the company that brought you CA125, Fujirebio Diagnostics brings you HE4, the first FDA-cleared biomarker in 25 years for ovarian cancer management.¹

- Unique CPT code and Medicare reimbursable
- Vast body of multi-national peer-reviewed and published clinical evidence supporting the use of HE4⁵

Learn more about ROMA™ and how CA125 + HE4 provides greater diagnostic clarity

The Risk of Ovarian Malignancy Algorithm (ROMA™) is a qualitative serum test that combines the results of HE4 EIA, ARCHITECT CA125 II™ and menopausal status into a numerical score. ROMA is intended to aid in assessing whether a premenopausal or postmenopausal woman who presents with an ovarian adnexal mass is at high or low likelihood of finding malignancy on surgery. ROMA is indicated for women who meet the following criteria: over age 18; ovarian adnexal mass present for which surgery is planned, and not yet referred to an oncologist. ROMA must be interpreted in conjunction with an independent clinical and radiological assessment. The test is not intended as a screening or stand-alone diagnostic assay.

REFERENCES:
Osteoporosis
Taking a tailored approach
Holly Thacker, MD

How to manage respiratory failure in pregnancy
Sonya Abdel-Razeq, MD

Rethinking HT evidence
Lubna Pal, MBBS, MRCOG, MS

NEW SERIES
Fetal monitoring mythbusters
David A. Miller, MD
For your menopausal patient

**IS PAINFUL INTERCOURSE GETTING IN THE WAY?**

PREMARIN Vaginal Cream provides relief from moderate to severe painful intercourse by treating the underlying source of the problem. By restoring estrogen, PREMARIN Vaginal Cream rebuilds vaginal tissue during treatment, which may help to make intercourse more comfortable.¹

*Ease the pain, start treating with PREMARIN Vaginal Cream.*

**Indication**

PREMARIN Vaginal Cream is indicated for the treatment of atrophic vaginitis and kraurosis vulvae and for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.

**Important Safety Information**

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding.

Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia.

The Women’s Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 7.1 years of treatment with daily oral conjugated estrogens (CE) (0.625 mg), relative to placebo.

The WHI Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with daily CE (0.625 mg) alone, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women.

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and MPA, and other combinations and dosage forms of estrogens and progestins.

PREMARIN Vaginal Cream therapy should not be used in women with any of the following conditions: undiagnosed abnormal genital bleeding; known, suspected, or a history of breast cancer; known or suspected estrogen-dependent neoplasia; active deep vein thrombosis, pulmonary embolism or a history of these conditions; active arteriovenous thromboembolic disease (for example, stroke, and myocardial infarction), or a history of these conditions; known liver dysfunction or disease; known thrombophilic disorders; known or suspected pregnancy.

In a prospective, randomized, placebo-controlled, double-blind study, the most common adverse reactions (≥5%) were headache, infection, abdominal pain, back pain, accidental injury, and vaginal infections.


Please see brief summary of Full Prescribing Information, including boxed warning, on the following pages.

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vaginal cream

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Cardiovascular Disorders and Endometrial Cancer

Cardiovascular Disorders

An increased risk of stroke and deep vein thrombosis (DVT) has been reported with estrogen-alone therapy. A statistically significant increased risk of stroke was reported in women 50 to 79 years of age during 7.1 years of treatment with daily CE (0.625 mg) alone relative to placebo. It is unknown whether this finding applies to younger postmenopausal women [see Warnings and Precautions (5.3), and Clinical Studies (14.2) in full prescribing information].

The WHI estrogen plus progestin substudy reported increased risks of stroke and DVT with estrogen plus progestin therapy compared to estrogen-alone therapy or placebo. Stroke, DVT, and myocardial infarction in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding [see Warnings and Precautions (5.4), Use in Specific Populations (8.5), and Clinical Studies (14.2) in full prescribing information].

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and other dosage forms of estrogen.

Premenopausal women with documented heart disease (n = 2,763), average age 66.7 years, in a controlled clinical trial of secondary prevention of cardiovascular disease (Heart and Estrogen/Progestin Replacement Study [HERS]), treatment with daily CE (0.625 mg) plus MPA (2.5 mg) demonstrated no cardiovascular benefit. During an average follow-up of 4.1 years, treatment with CE plus MPA did not reduce the overall rate of CHD events in postmenopausal women with established coronary heart disease (n = 4,311), average age 63.7 years. Furthermore, the CE plus MPA-treated group in the placebo group in year 1, but not during subsequent years. Two thousand, three hundred and twenty-one (2,321) women from the original HERS trial agreed to participate in an open-label extension of HERS, in which CE plus MPA was continued for a total of 6.8 years overall. Rates of CHD events were comparable among women in the CE (0.625 mg) plus MPA (2.5 mg) group and the placebo group in HERS, HERS II, and overall.

Endometrial Neoplasms

Endometrial Cancer

An increased risk of endometrial cancer has been reported with the use of unopposed estrogen therapy in a 10,000-women-years. In some epidemiologic studies, the use of estrogen-alone therapy was associated with an increased risk of endometrial cancer.

In the WHI estrogen-alone substudy, an average follow-up of 7.1 years, daily CE (0.625 mg) was not associated with an increased risk of invasive breast cancer compared to placebo (risk ratio [RR] 0.80) [see Warnings and Precautions (5.3), Use in Specific Populations (8.3), and Clinical Studies (14.2) in full prescribing information].

The most important randomized clinical trial providing information about breast cancer in estrogen plus progestin users was the WHI substudy of daily CE (0.625 mg) plus MPA (2.5 mg). After a mean-follow-up of 5.6 years, the WHI estrogen plus progestin substudy reported no increased risk of developing breast cancer with estrogen plus progestin therapy compared to placebo. In this substudy, prior use of estrogen-alone or estrogen plus progestin therapy was reported by 26 percent of the women. The relative risk of invasive breast cancer was 1.14, and the absolute risk was 41 versus 37 cases per 10,000 women-years (RR 1.14; 95 percent confidence interval [CI] 0.85-1.50). The absolute risk for CE plus MPA versus placebo was 40 versus 36 cases per 10,000 women-years for estrogen plus progestin compared with placebo. In the same substudy, invasive breast cancers were later diagnosed and a more advanced stage in the CE 0.625 mg plus MPA (2.5 mg) group compared with the placebo group. Metastatic disease was rare, with no apparent difference between the two groups. Other prognostic factors, such as histologic subtype, grade, and estrogen receptor status did not differ between the groups [see Clinical Studies (14.2) in full prescribing information].

Consistent with the WH clinical trial, observational studies have also reported an increased risk of breast cancer for estrogen plus progestin therapy, and a smaller increased risk for estrogen-alone therapy, after several years of use. The risk increased with duration of use, and appeared to return to baseline over about 5 years after stopping treatment (only the observational studies have substantial data on risk after stopping). Observational studies also suggest that the relative risk of breast cancer was greater, with an increased risk of cancer among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.86, and the absolute risk was 46 versus 25 cases per 10,000 women-years for estrogen-alone plus progestin therapy compared to placebo. Observational studies have also suggested that endometrial hyperplasia or endometrial carcinoma.

Ovarian Cancer

The WHI estrogen plus progestin substudy reported a statistically significant non-increased risk of ovarian cancer. After an average follow-up of 5.6 years, the relative risk for ovarian cancer for CE plus MPA versus placebo, was 1.09 (95 percent CI 0.77-1.54). The absolute risk for CE plus MPA versus placebo was 4 versus 3 cases per 10,000 women-years (RR 1.09) [see Warnings and Precautions (5.4), Use in Specific Populations (8.4), and Clinical Studies (14.4) in full prescribing information].

The risk among estrogen-alone and estrogen plus progestin therapy has been reported to result in an increase in abnormal mammograms, requiring further evaluation.

All women should receive yearly breast examinations by a healthcare provider and perform monthly breast self-examinations. In addition, mammography examinations should be scheduled based on patient age, risk factors, and prior mammogram results.

Prostate Dose

In the estrogen-alone Women's Health Initiative Memory Study (WHIMS), an ancillary study of WHI, a population of 2,947 hysterectomized women 65 to 79 years of age was randomized to daily CE (0.625 mg) or placebo. In this substudy, prior use of estrogen-alone or estrogen plus progestin therapy was reported by 26 percent of the women. The relative risk of invasive breast cancer was 1.24, and the absolute risk was 41 versus 33 cases per 10,000 women-years (RR 1.24; 95 percent CI 1.04-1.48). The absolute risk for CE plus MPA versus placebo was 37 versus 25 cases per 10,000 women-years [see Use in Specific Populations (8.3), and Clinical Studies (14.3) in full prescribing information].

The absolute risk of probable dementia for CE plus MPA versus placebo was 35 versus 25 cases per 10,000 women-years [see Use in Specific Populations (8.5), and Clinical Studies (14.4) in full prescribing information].

Prostate Dose

In the estrogen-alone Women's Health Initiative Memory Study (WHIMS), an ancillary study of WHI, a population of 2,947 hysterectomized women 65 to 79 years of age was randomized to daily CE (0.625 mg) plus MPA (2.5 mg) or placebo. After an average follow-up of 4 years, 40 women in the CE plus MPA group and 21 women in the placebo group were diagnosed with probable dementia. The relative risk for probable dementia for CE plus MPA versus placebo was 2.05 (95 percent CI 1.21-3.48). The absolute risk of probable dementia for CE plus MPA versus placebo was 45 versus 22 cases per 10,000 women-years [see Use in Specific Populations (8.3), and Clinical Studies (14.3) in full prescribing information].

Galbladder Disease

A 2- to 4-fold increase in the risk of gallbladder disease requiring surgery in postmenopausal women receiving estrogen has been reported.

Hypercaldemia

Hyperparathyroidism may lead to severe hypercalcemia in women with breast cancer and bone metastases. If hypercalcemia occurs, use of the drug should be stopped and appropriate measures taken to reduce the serum calcium level.

(continued on next page)
Addition of a Progestin When a Woman Has Not Had a Hysterectomy
Studies of the addition of a progestin for 10 or more days of a cycle of estrogen administration or daily with estrogen in a continuous regimen have reported a lowered incidence of endometrial hyperplasia than would be induced by estrogen treatment alone. Endometrial hyperplasia may be a precursor to endometrial cancer. There can, however, possible risks that may be associated with the use of progestins with estrogens compared to estrogen-alone regimens. These include an increased risk of breast cancer.

Elevated Blood Pressure
In a 12-week, randomized, double-blind, placebo-controlled trial of PREMARIN Vaginal Cream (PVC), a total of 427 women received at least 1 dose of study medication and were included in all safety analyses: 143 women in the PVC 2% treatment group (0.5 mg PVC daily for 21 days, then 7 days off), 72 women in the matching placebo treatment group; 140 women in the PVC 2x/wk treatment group (0.5 g PVC twice weekly), and 62 women in the matching placebo treatment group. A 42-week, open-label, extension study, in which a total of 394 women received treatment with PVC, including those subjects randomized at baseline to placebo, in this study the treatment-related adverse events ≥5% presented are shown below (Table 1) [see Clinical Studies (14.1) in full prescribing information].

Table 1: Number (%) of Patients Reporting Treatment Emergent Adverse Events ≥5% Percent Only

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Body Systema</th>
<th>Adverse Event</th>
<th>Placebo (%)</th>
<th>PVC (%)</th>
<th>Placebo (%)</th>
<th>PVC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasoconstriction</td>
<td>5 (3.5)</td>
<td>4 (5.6)</td>
<td>7 (5.0)</td>
<td>1 (1.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>4 (2.8)</td>
<td>2 (2.8)</td>
<td>10 (7.1)</td>
<td>1 (1.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (3.5)</td>
<td>4 (5.6)</td>
<td>3 (2.1)</td>
<td>3 (4.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal System</td>
<td>Arthralgia</td>
<td>3 (5.3)</td>
<td>5 (8.9)</td>
<td>6 (4.3)</td>
<td>4 (5.9)</td>
<td></td>
</tr>
<tr>
<td>Nervous System</td>
<td>Respiratory System</td>
<td>Cough Increased</td>
<td>6 (4.2)</td>
<td>3 (4.2)</td>
<td>4 (2.9)</td>
<td>4 (5.9)</td>
</tr>
<tr>
<td></td>
<td>Pharyngitis</td>
<td>3 (2.1)</td>
<td>2 (2.8)</td>
<td>7 (5.0)</td>
<td>3 (4.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sinusitis</td>
<td>1 (0.7)</td>
<td>3 (4.2)</td>
<td>2 (1.4)</td>
<td>4 (5.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Skin And Appendages</td>
<td>12 (8.4)</td>
<td>7 (9.7)</td>
<td>16 (11.4)</td>
<td>3 (4.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ophthalmologic System</td>
<td>Blepharitis</td>
<td>8 (5.6)</td>
<td>7 (10.4)</td>
<td>6 (4.3)</td>
<td>7 (5.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vaginitis</td>
<td>6 (4.2)</td>
<td>3 (4.2)</td>
<td>7 (5.0)</td>
<td>3 (4.4)</td>
</tr>
</tbody>
</table>

* Body system totals are not necessarily the sum of the individual adverse events, since a patient may report two or more different adverse events in the same body system.

Postmarketing Experience
The following adverse reactions have been reported with PREMARIN Vaginal Cream. Because these reactions are volunteered from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal
Abnormal uterine bleeding/dysmenorrhea/bladder pain, increase in size of uterine leiomyoma, vaginitis (including vaginal candidiasis), change in cervical secretions, cystitis-like syndrome, exacerbation of symptoms of vulvovaginal discomfort, (including burning, irritation, and genital pruritus), endometrial hyperplasia, endometrial cancer, precocious puberty, leukorrhea.

Breast
Tenderness, enlargement, pain, discharge, fibrocystic breast changes, breast cancer, gynecoma in males.

Cardiovascular
Deep venous thrombosis, pulmonary embolism, myocardial infarction, stroke, increase in blood pressure.

Gastrointestinal
Nausea, vomiting, abdominal cramps, bloating, increased incidence of gallbladder disease.

Skin
Chloasma that may persist when drug is discontinued, loss of scalp hair, hirsutism, rash.

Eye
Retinal vascular thrombosis, intolerance to contact lenses.

Central Nervous System
Headache, migraine, dizziness, mental depression, nervousness, mood disturbances, irritability, dementia.

Miscellaneous
Increase or decrease in weight, glucose intolerance, edema, arthralgias, leg cramps, changes in libido, urticaria, anaphylactic reactions, exacerbation of asthma, increased triglycerides, hypersexuality.

Additional postmarketing adverse reactions have been reported in patients receiving other forms of hormone therapy.

Dietary Interactions
No formal drug interaction studies have been conducted for PREMARIN Vaginal Cream.

Metabolic Interactions
Exogenous estrogens may induce or exacerbate symptoms of angioedema, particularly in women with hereditary angioedema.

Other binding proteins may be elevated in serum, for example, corticosteroid binding globulin (CBG), sex hormone-binding globulin (SHBG), leading to increased total circulating corticosteroids and sex steroids, respectively. Free hormone concentrations, such as testosterone and estradiol, may be decreased. Other plasma proteins may be increased (angiotensinogen/renin substrate, alpha-1-antiproteinase, plasminogen).

Lab studies conducted in women receiving estrogens. Caution should be exercised when PREMARIN Vaginal Cream should not be used during lactation. Estrogen administration to nursing mothers has been shown to decrease the quantity and quality of the breast milk. Detectable amounts of estrogens have been identified in the breast milk of mothers receiving estrogens. Caution should be exercised when PREMARIN Vaginal Cream is administered to a nursing woman.

Nursing Mothers
PREMARIN Vaginal Cream should not be used during lactation. Estrogen administration to nursing mothers has been shown to decrease the quantity and quality of the breast milk. Detectable amounts of estrogens have been identified in the breast milk of mothers receiving estrogens. Caution should be exercised when PREMARIN Vaginal Cream is administered to a nursing woman.

Pediatric Use
PREMARIN Vaginal Cream is not indicated in children. Clinical studies have not been conducted in the pediatric population.

Geriatric Use
There have not been sufficient numbers of geriatric women involved in clinical studies utilizing PREMARIN Vaginal Cream to determine whether those over 65 years of age differ from younger subjects in their response to PREMARIN Vaginal Cream.

The Women's Health Initiative Study
In the Women's Health Initiative (WHI) estrogen-alone substudy (daily conjugated equine estrogens 0.625 mg versus placebo), there was a higher relative risk of stroke in women greater than 65 years of age [see Clinical Studies (14.3) in full prescribing information].

In the WHI estrogen plus progestin substudy, there was a higher relative risk of nonfatal stroke and invasive breast cancer in women greater than 65 years of age [see Clinical Studies (14.2) in full prescribing information].

The Women's Health Initiative Memory Study
In the Women's Health Initiative Memory Study (WHIMS) of postmenopausal women 65 to 79 years of age, there was an increased risk of developing probable dementia in women receiving estrogen-alone or estrogen plus progestin when compared to placebo [see Clinical Studies (14.3) in full prescribing information].

Since both ancillary studies were conducted in women 65 to 79 years of age, it is unknown whether these findings apply to younger postmenopausal women [see Clinical Studies (14.3) in full prescribing information].
For nearly a half century, busy practitioners have trusted Contemporary OB/GYN to translate the latest research into outstanding patient care. We are dedicated to providing them with evidence-based information on scientific advances in a clinically useful format.
GRAND ROUNDS
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HOLLY THACKER, MD, FACP, CCD, NMCP
KRISTI TOUGH, MD, NCMP

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GENEVIEVE NEAL-PERRY, MD, PhD
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The authors review the risks and benefits of short-term hormone therapy for healthy women and reexamine its relevance in managing symptomatic menopause.
Yale-New Haven Hospital doctors and nurses conducted a four-year patient safety study that led to a 40 percent decrease in the hospital’s obstetrical adverse events. Their interventions included team training for hospital staff, standardizing interpretation of fetal monitoring, improved communication between staff and creating the role of patient safety nurse. While interventions of this sort involve fundamental culture change, commitment and persistence, the improved outcomes proved that the hard work paid off. In addition to positive results that continue to this day, the program’s pioneering work recently led to an Award of Research Excellence from the Society for Maternal-Fetal Medicine. Our efforts are not only changing how we care for patients at Yale-New Haven, but they are leading the way in the obstetrical patient safety movement across the country.
Is abdominal hysterectomy obsolete?

The first successful attempt to surgically remove a uterus was a vaginal hysterectomy performed by Dr. Conrad Langenbeck in 1813 in his living room. He had to hold the suture with his teeth at one point during the operation. The patient survived despite what was described as a “great hemorrhage.” Since then, vaginal hysterectomy has remained the most cost-effective approach to surgically removing a uterus.

In a recent survey, practicing gynecologists in the United States were asked what kind of hysterectomy they would choose for themselves or their spouse. Only 8% preferred an abdominal approach; the vast majority opted for either a vaginal or a laparoscopic approach. The results were even more interesting because the majority of hysterectomies were being performed abdominally at the time. Thus, although gynecologists recognize the benefits of a minimally invasive approach, they are not able to offer this universally to their patients. This dilemma has been compounded by increased patient awareness of alternative options for hysterectomy and new developments in gynecologic surgery.

It is generally accepted that patients do better postoperatively from a vaginal hysterectomy than an abdominal hysterectomy, with less pain and earlier return to daily activities. Nevertheless, vaginal hysterectomy has never really caught on, with only approximately 20% of hysterectomies performed in this manner. This may be due in part to low surgical volume among gynecologic surgeons, who perform on average 30 hysterectomies per year.

Although a standard vaginal hysterectomy is a fairly simple procedure, it can be challenging to acquire proficiency to perform the surgery in scenarios such as a narrow introitus, poor descent, and uterine fibroids. Enthusiastic champions for vaginal surgery are able to remove almost all uteri in this manner, but this has not been the case for the majority of gynecologic surgeons.

To complicate matters, we now have five viable options for uterine removal: abdominal, vaginal, laparoscopic, robotic, and single-port hysterectomy. Clearly, most gynecologists are not able to obtain and maintain adequate proficiency in all approaches. As a result, many choose to specialize in only 1 or 2 minimally invasive approaches, most commonly laparoscopic and robotic hysterectomy.

According to data from Intuitive Surgical, 120,000 robotic hysterectomies were performed in the United States in 2010. This represents approximately 20% of the 600,000 hysterectomies performed annually. Unfortunately, we do not have current numbers for other approaches because the last published nationwide data are from 2005 and things probably have changed significantly since then. For example, at Brigham and Women’s Hospital, abdominal hysterectomy rates decreased from 64.7% in 2006 to 35.8% in 2009, with the majority of hysterectomies being performed laparoscopically from 2009 and onward.

This is especially interesting because approximately 1,100 hysterectomies are performed each year by more than 40 surgeons with a wide variety of surgical volume and experience. In the current environment at this teaching hospital, an abdominal hysterectomy has become a sought-after chief resident case, while a laparoscopic hysterectomy is an everyday occurrence.

Why is this happening? There probably are many factors at play, but it seems that the laparoscopic/robotic approach is easier to teach since it is more “visual” and it may be more applicable to a variety of clinical situations, such as prior surgery, adhesions, pelvic pain, endometriosis, adnexal masses, and planned adnexal removal. There also has been strong educational emphasis from industry supporting laparoscopic and robotic hysterectomy with a multitude of workshops, courses, and seminars, while vaginal hysterectomy perhaps has not received the credit it deserves.

It is interesting that while vaginal hysterectomy has been touted as the least-invasive hysterectomy, recent randomized trials have indicated that recovery is slightly faster after the laparoscopic approach.

Whatever the cause, the advent of laparoscopic and robotic surgery has helped to push abdominal hysterectomy...
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rates lower than vaginal hysterectomy ever could. I would guess that in 2011, close to 50% of hysterectomies will be performed laparoscopically or robotically with perhaps only 30% to 35% being performed via a laparotomy and the remainder via a vaginal approach. I suspect that this trend will continue and that experienced vaginal surgeons will continue to offer their patients a vaginal approach, while a greater number of abdominal hysterectomies will be replaced by either a robotic or a laparoscopic hysterectomy.

Although robotic and laparoscopic hysterectomies may be more expensive with regard to operating room costs, the societal costs are lower than for abdominal hysterectomy because of shorter hospital stays and faster return to daily activities. This is especially true for the laparoscopic approach because the higher operative cost of the robot significantly offsets the savings associated with a shorter hospital stay and faster recovery. We found that operative cost for robotic hysterectomy was $3,000 more than for a laparoscopic hysterectomy. We therefore favor the laparoscopic approach at our institution, and we are able to offer patients a minimally invasive approach without compromising their safety. A significant decrease in perioperative complications was demonstrated at our hospital with the transformation from abdominal to laparoscopic.

What should practicing gynecologists do when selecting a mode of access for hysterectomy? Clearly, surgeons who routinely perform vaginal or laparoscopic hysterectomies should continue to offer these options to their patients. For those performing mainly abdominal hysterectomy, a critical factor to consider is surgical volume. Considering that the typical learning curve for a hysterectomy is approximately 30 cases, it may be unrealistic for some to acquire the necessary skills to perform a minimally invasive hysterectomy efficiently and safely. We found that gynecologists who perform fewer than 2 hysterectomies per month had significantly higher perceived barriers to offering a minimally invasive option to their patient. Thus, if the current preferred mode of access is abdominal and a physician’s surgical volume is less than 30 hysterectomies per year, it may be appropriate to refer these patients to a high-volume surgeon for consultation, surgery, and postoperative follow-up. The patient returns to the referring physician for her yearly health maintenance. This model ensures that the patient is operated on by an expert surgeon, which may in turn reduce complication risk and improve postoperative outcomes.

An alternative approach for a larger practice is to identify one or two individuals and develop their skills in performing a minimally invasive hysterectomy. They can work with a more experienced surgeon initially and then together to increase their collective surgical volume while becoming comfortable with the techniques required to safely perform these surgeries. More challenging cases should be referred directly to a surgeon who is performing at least 50 minimally invasive hysterectomies per year.

Is abdominal hysterectomy obsolete? Not yet. There still are scenarios in which an abdominal hysterectomy is appropriate, such as a large uterus in the setting of a malignancy where morcellation is not an option. In addition, if a surgeon in a remote area does not have the skills or referral availability, an abdominal approach may be the safest option. Nevertheless, with more training, available subspecialists, and patient awareness, a 90% minimally invasive hysterectomy rate is a realistic goal for the foreseeable future. Implemented correctly, this will greatly enhance perioperative outcomes and safety for patients while lowering overall cost for society: truly a win-win situation.

**REFERENCES**

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Zoledronic acid benefits some with breast cancer

The latest study to look at whether adding zoledronic acid to the management of early stage breast cancer provides any additional benefit concludes that the answer is “no” for most younger women. However, the addition may provide a small survival advantage as well as some skeletal protection to postmenopausal women with breast cancer.

In an open-label phase III study, researchers from the United Kingdom randomly assigned 3,360 women from 174 centers in 7 countries to receive standard adjuvant systemic therapy with or without zoledronic acid administered every 3 to 4 weeks for 6 doses, then every 3 to 6 months for the remainder of 5 years of total treatment.

The percentage of women who were alive and disease-free after about 5 years of follow-up was virtually identical in both groups (76.9% vs 77% in the treatment and control groups, respectively; adjusted hazard ratio [HR] in the zoledronic acid group, 0.98; 95% confidence interval [CI], 0.85-1.13; P=0.79). Disease recurrence or death occurred in 377 women in the former and in 375 women of the latter groups. Rates of survival were 85.4% and 83.1%, respectively (adjusted HR, 0.85; 95% CI, 0.72-1.01; P=0.07).

The zoledronic acid group had 17 confirmed cases of osteonecrosis of the jaw (cumulative incidence, 1.1%; 95% CI, 0.6-1.7; P<0.001) and 9 suspected cases; no cases occurred in the control group.

Rates of adverse effects were similar in both groups, although the zoledronic acid group had a reduced fracture rate, particularly among women with disease recurrence.

The authors commented that important population distinctions were responsible for the marked difference in results from some previous studies.

A previous study found that addition of zoledronic acid conferred benefit. The women in that study started receiving goserelin and endocrine therapy before the initiation of bisphosphonate therapy and had disease with a good prognosis (ie, fewer than 5% of subjects received chemotherapy). In contrast, the women in this study had a poorer prognosis, with 95% receiving chemotherapy, and all had premenopausal levels of reproductive hormones at study entry; only 3 of the premenopausal women received goserelin.

This study found that a small, but significant survival advantage existed in a subgroup of women who had undergone menopause at least 5 years before study entry, suggesting that the initial phase of treatment, when zoledronic acid is combined with chemotherapy, may be most important.

Pregnancy not affected by FH, Norwegian study reports

Although women with familial hypercholesterolemia (FH) are prone to early cardiovascular disease and death, FH does not appear to adversely affect pregnancy, according to the findings of a registry-based study from Norway.

Researchers analyzed 40 years of data on women with FH who were at least 14 years of age and able to bear children and on roughly 2 million women in the general population. They identified 1,093 women with heterozygous FH who delivered 2,319 children. Mean maternal age at first birth was 28 years for both the FH women and controls. Norway’s reference range for serum total cholesterol in fertile women is 2.9 to 6.1 mmol/L. The mean prepregnancy level in the FH women was 9.59 mmol/L. Low-density lipoprotein (LDL) levels also were highly elevated.

No significant differences between the FH group and the general population were found in prematurity (6.8% vs 6.2%, respectively), low birth weight rates (5.0% and 5.2%, respectively), and congenital malformation rates (3.3% vs 3.2%, respectively). Corresponding ORs were 1.11 (95% CI, 0.94-1.31; P=0.23); 0.96 (0.79-1.15; P=0.64); and 1.09 (0.87-1.37; P=0.45). When the researchers looked at a subgroup of women with FH taking lipid-lowering agents during pregnancy, they found no difference in birth weights compared with women with FH not taking lipid-lowering medication and no babies born with congenital malformations.

The researchers cautioned that in addition to hyperlipidemia, activation of coagulation and vascular endothelium may confer increased risks for CVD among pregnant women with FH. Although CVD-related morbidity was low in this study, the low numbers made it impossible to formally evaluate CVD risk and pregnancy
in FH. They recommend a prospective trial with CVD morbidity and mortality as endpoints required.


**Dr. Phelan comments:** This Norwegian study that encompassed over 40 years of birth registry showed that despite concerns, there was no increase in adverse outcomes in women with familial hypercholesterolemia. There was no significant increase in adverse fetal (eg, preterm delivery, SGA, or congenital anomalies) or maternal (eg, cardiovascular events or hypertensive issues) complications compared with the general population. Even when comparing the highest with the lowest quartile of cholesterol levels, there were no significant differences. In fact, the risk of LGA may be lower, perhaps because of more educated patients regarding optimal diet choices. This is reassuring for women and continues to support that improved diet can be of help even for this group.

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**British study links fibroids with recurrent miscarriages**

Researchers now know that fibroids are associated with midtrimester pregnancy loss in women who suffer recurrent miscarriages (RM; defined as 3 or more consecutive miscarriages) and that removal of the benign tumors can eliminate the risk for midtrimester pregnancy loss.

The finding is significant because although research has linked fibroids to spontaneous miscarriage, until now no evidence has existed for an association of these tumors with RM.

 Researchers from the United Kingdom looked at retrospective and prospective data from 996 women attending a large tertiary referral clinic specializing in RM. They diagnosed fibroids using combined transvaginal ultrasound and hysterosalpingography, and they resected fibroids distorting the uterine cavity with hysteroscopy.

They found the prevalence of fibroids to be 8.2%. There were 25 women with intracavity-distorting fibroids (submucosal) who underwent myomectomy. These women reduced their midtrimester miscarriage rate from 21.7% to 0% \( (P<0.01) \), which more than doubled their live birth rate \( (23.3\% \text{ to } 52.0\%; \ P<0.05) \). Without any intervention, the 54 women with fibroids not distorting the uterine cavity also reduced their midtrimester miscarriage rate, from 17.6% to 0%, resulting in a 70.4% \( ( \text{up from } 20.0\% ) \) live birth rate in subsequent pregnancies.

The 285 women with unexplained RM also decreased their midtrimester miscarriage rate from 8% to 1.8%, and their live birth rate increased from 20.6% to 71.9%.

The authors report that the primary limitation of the study is the absence of a control group for the women who had their fibroids removed. This makes it impossible to know whether these women would have fared better without surgery.


**Dr. Kilpatrick comments:** Saravelos et al attempted to answer the questions: Do uterine fibroids cause repetitive miscarriages; and would removal of fibroids reduce repetitive miscarriages? This retrospective review is of interest but suffers from the usual flaws associated with retrospective studies, so at best their data suggest the need for a randomized trial. The women studied were those with a history of repetitive miscarriage, defined as at least 3 consecutive miscarriages up to 24 weeks’ gestation, who were seen in their practice. They defined 3 groups: 25 women who had cavity-distorting fibroids (submucosal) and who had had surgery to remove the fibroids; 54 women who had noncavity-distorting fibroids (intramural) and hence had had no surgery; and 285 control women who had a history of repetitive miscarriages and no surgical treatment. The researchers stated the controls were matched to group 2, but never clarified for what they were matched. They compared pregnancy outcomes within these groups between pregnancy history and the outcome of the first pregnancy after referral to their practice. The results are somewhat confusing because their denominator shifts throughout the paper. For example, they report that the total women studied was 364 but report the incidence of fibroids to be 8% \( (79/966) \). These confusing numbers detract from the validity of the study. The main finding was that in the women who underwent surgery for fibroids, there was a significant reduction in midtrimester loss and significant increase in live birth rate comparing after and before the surgery. Again, the comparison is confusing because the denominator for before surgery was 80 versus 25 for after surgery. The only difference between those women with fibroids with no surgical removal and the control group of women with recurrent miscarriages was significantly more midtrimester losses in the fibroid group before referral to their practice. However, after referral there were no differences between these 2 groups of women in pregnancy outcomes. The authors concluded that fibroids are associated with increased midtrimester losses in women with recurrent miscarriage, and that removal of cavity-distorting fibroids can increase live birth rates and reduce midtrimester losses. I would be very cautious with these results, given the methodologic flaws and state only that these data warrant interest and the development of a randomized trial.
When electronic fetal heart rate monitoring (EFM) was introduced into clinical practice 40 years ago, the medical community knew little about its capabilities or limitations. Early descriptive studies generated a wealth of theories, only a few of which were later proven to be correct. Many early notions regarding EFM have surprisingly little supporting evidence in the literature. Fortunately, medicine has made significant progress toward the standardization of EFM nomenclature and evidence-based interpretation.

In 1997, the National Institute of Child Health and Human Development (NICHD) Research Planning Workshop proposed unambiguous definitions for fetal heart rate (FHR) tracings that subsequently were endorsed by the American College of Obstetricians and Gynecologists (ACOG), the Association of Women’s Health, Obstetric, and Neonatal Nurses (AWHONN); and the American College of Nurse-Midwives (ACNM).1-4

In 1999, the Institute of Medicine committee on the Quality of Health Care in America identified standardization as an essential element of patient safety.5 Since then a growing body of evidence has demonstrated that standardization can significantly reduce adverse outcomes.6,7 In 2008, a second NICHD Research Planning Workshop reaffirmed that the FHR definitions proposed in 1997 and introduced a new classification system that groups FHR tracings into three categories.8

In addition, the 2008 consensus report identified a number of FHR observations that require further investigation to determine clinical significance. Examples include decelerations with additional characteristics, such as a slow return of the FHR after the end of a contraction, biphasic decelerations, accelerations preceding and/or following decelerations (sometimes referred to as “shoubergs”), a prolonged acceleration after a deceleration (sometimes referred to as “overshoot”), and fluctuation of the FHR in the trough of a deceleration. Furthermore, the consensus report stated that systems for grading decelerations on the basis of depth and duration (ie, “mild,” “moderate,” and “severe” decelerations) require further investigation to determine their predictive value. Such subclassification is not included in the NICHD’s standard FHR nomenclature.

Other FHR observations described in the literature include “wandering baseline,” “lambda” pattern, “checkmark” pattern, “pseudo-sinusoidal” pattern, “sporadic uniform accelerations,” “sporadic variable accelerations,” “periodic uniform accelerations,” “periodic variable accelerations,” the “conversion” pattern, the “Hon” pattern, and various fetal arrhythmias.9-17

This article is the first in a bimonthly series that will highlight these and other FHR observations, review the existing scientific data, and provide readers with a contemporary foundation for evidence-based FHR interpretation and management. Scientific evidence will be stratified according to the method outlined by the US Preventive Services Task Force.18 Level I evidence derives from at least 1 properly designed, randomized controlled trial and is considered to be the most robust. Level II evidence comes from well-designed controlled trials without randomization, from cohort or case-control analytic studies, or from multiple time series studies. Levels I and II evidence constitute analytic evidence that is capable of establishing statistically significant relationships. Level III evidence derives from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees. Level III descriptive evidence can generate hypotheses, but is not capable of testing them. Therefore, Level III evidence is considered the least robust. Specifically, Level III evidence is not capable of proving statistically significant relationships. It is extremely important to recognize and acknowledge the difference between analytic evidence (Level I and Level II) and descriptive evidence (Level III).
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The Table summarizes the standard FHR nomenclature that was proposed by the NICHD in 1997, endorsed by ACOG and AWHONN in 2005, endorsed by the ACNM in 2006, and reaffirmed in the 2008 NICHD consensus report.1–4,8

**Standard FHR nomenclature**

It is important to start with a common set of definitions. The Table summarizes the standard FHR nomenclature that was proposed by the NICHD in 1997, endorsed by ACOG and AWHONN in 2005, endorsed by the ACNM in 2006, and reaffirmed in the 2008 NICHD consensus report.1–4,8

**Standard FHR interpretation**

A shared mental model regarding FHR interpretation is essential to ensure effective communication and teamwork. Intrapartum fetal monitoring is intended to assess the adequacy of fetal oxygenation during labor. Fetal oxygenation reflects the transfer of oxygen from the environment to the fetus and potential interruption of that transfer. Intrapartum FHR interpretation can be summarized in three basic principles that are evidence-based and reflect consensus in the literature.

**Principle 1.** Oxygen is carried from the environment to the fetus by maternal and fetal blood along a pathway that includes the maternal lungs, heart, vasculature, uterus, placenta, and umbilical cord. Interruption of the oxygen pathway at one or more points can result in FHR deceleration. For example, interruption of the oxygen pathway by compression of the umbilical cord can result in a variable deceleration.9 Reduced placental perfusion and transient fetal hypoxemia during a uterine contraction can trigger a reflex late deceleration.20 Interruption at any point along the pathway can result in a prolonged deceleration. Variable, late, and prolonged decelerations have slightly different physiologic mechanisms. However, the common trigger that is shared by all clinically significant decelerations is interruption of the oxygen pathway at 1 or more points (Figure).

**Principle 2.** Interruption of fetal oxygenation of sufficient duration and degree can result in hypoxic neurologic injury. The pathway from normal fetal oxygenation to hypoxia capable of inflicting potential hypoxic injury progresses through a series of physiologic steps. The first step, hypoxemia, is defined as decreased oxygen content in the blood. Hypoxemia can lead to hypoxia, defined as reduced oxygen content in the tissues. Hypoxia can trigger anaerobic metabolism, lactic acid production, and metabolic acidosis in the tissues. Eventually, the blood...
pH falls, causing metabolic acidemia. The 2008 NICHD Research Planning Workshop identified moderate variability and/or accelerations as the 2 FHR observations that reliably predict the absence of fetal metabolic acidemia at the time they are observed.

**Principle 3.** In 1999 and 2003, the International Cerebral Palsy Task Force, ACOG, and the American Academy of Pediatrics published consensus statements identifying specific criteria that must be met before acute intrapartum oxygen deprivation can be considered a possible cause of neurologic injury. Both consensus statements, supported by more than 20 international organizations, concluded that significant fetal metabolic acidemia (umbilical artery pH <7.0 and base deficit ≥12 mmol/L) is an essential precondition to acute intrapartum hypoxic neurologic injury in the form of cerebral palsy.

Using a shared mental model of standard FHR definitions and basic principles of interpretation, the next article in this series will review the scientific evidence behind “atypical variable decelerations.”

**REFERENCES**


One in two women over the age of 50 years will have an osteoporosis-related fracture during her lifetime. These life-altering fractures affect community-living and nursing-home populations alike. Prevention and treatment of osteoporosis often falls to the obstetrician/gynecologist. This article reviews the pathophysiology of bone loss, current definitions of osteoporosis, causes of primary and secondary bone loss, and currently available prevention and treatment options for postmenopausal osteoporosis.

Epidemiology and pathophysiology
More than 10 million Americans have osteoporosis, and 34 million more have low bone mineral density (BMD). From a global viewpoint, osteoporotic fractures (particularly hip fractures) occur more often in women and carry significant morbidity and mortality risk.

The skeleton is shaped by hormonal, biochemical, and physical influences. Two types of bone tissues are trabecular (found predominantly in the spine, hip, and calcaneus) and cortical (found predominantly in the long bones of the femur and radius). Bone undergoes a constant process of resorption (via osteoclasts) and formation (via osteoblasts).

Bone building begins in utero. Peak bone mass is achieved by the early thirties, after which natural bone loss begins to occur, amounting to about 2% of cortical bone and 5% of trabecular bone each year in early life.

Take-home messages
- Menopause is commonly associated with osteoporosis, which increases the risk of fracture.
- Osteoporosis management entails individualized screening, prevention, diagnosis, treatment, and frequent follow-up bone scans.
During the menopause transition, loss of estrogen produces an excessive amount of receptor activator of nuclear factor-kB ligand (RANKL) from osteoblasts, leading to an increase in the number and activity of osteoclasts and the associated decrease in BMD.  

**Definitions and etiology**

BMD is reported in T and Z scores, which represent standard deviations around a population mean. The T score is the postmenopausal patient’s BMD compared with that of an average healthy young woman. The World Health Organization (WHO) diagnoses osteoporosis on the basis of the T score, as shown in Table 1. The International Society for Clinical Densitometry (ISCD) also recommends using the WHO diagnostic standard for osteoporosis (T score -2.5 or lower). WHO defines severe osteoporosis as a BMD T score less than -2.5 and presence or history of fracture. The Z score is a measure of BMD used for comparisons of individuals of similar age, sex, and race. It is important to note that premenopausal osteoporosis and osteopenia are defined by low Z scores; it is not appropriate to use T scores in these individuals. A Z score less than -2.0 warrants a workup for primary and secondary causes of osteoporosis. In the authors’ opinion, the workup should include a comprehensive metabolic panel with calcium and phosphorus, complete blood count, thyroid-stimulating hormone, 25-hydroxyvitamin D [25(OH)D], intact parathyroid hormone (PTH), and 24-hour urine calcium collection. Other testing can include serum protein electrophoresis, 24-hour urine cortisol, and antibody testing for celiac enteropathy.

**Diagnosis and risk stratification**

The diagnosis and severity of bone loss shape the treatment goals. A formal diagnosis of osteoporosis can be made clinically if a patient sustains a fragility fracture, or objectively by dual-energy x-ray absorptiometry (DXA) scan. DXA measures BMD at the lumbar spine and the nondominant hip. (It is important to note that degenerative disk disease may cause false elevations of DXA.) The T score assigns a diagnostic category of bone loss and guides therapy, but the T score alone is insufficient for predicting fracture risk. Current recommendations by organizations such as the ISCD regarding repeat DXA scanning are not clearly defined. However, serial BMD measurements should be taken to monitor the effectiveness of treatment. The ISCD recommends follow-up 1 year after initiation or changes in therapy and allows longer intervals between screenings for patients with stable BMD on therapy. We repeat DXA testing every 3 to 5 years for average-risk postmenopausal patients with normal baseline T scores. Timing of DXA requires an individualized patient approach that takes into consideration therapy and clinical risk factors.
Osteoporosis is assessed by risk factors, fracture history, bone scanning, and bone mineral density T scores.

| Bone building begins in utero. Peak mass is achieved by the early thirties, after which bone loss begins to occur naturally. |

The National Osteoporosis Foundation (NOF) and the American College of Obstetricians and Gynecologists have identified several major risk factors for fractures (see “Major risk factors for osteoporotic fractures,” page 20) and secondary causes of osteoporosis (Table 2). We recommend use of the NOF guidelines, which are available on the NOF Web site and in print.

After evaluating risk factors and DXA testing, fracture risk can be estimated using WHO’s FRAX model (Fracture Risk Assessment Tool) to identify patients at highest risk for fracture who require treatment. FRAX calculation is indicated only for previously untreated women and men over 50 years of age with low BMD. FRAX uses 7 clinical risk factors with or without femoral neck BMD; they include body mass index, previous fragility fracture, use of glucocorticoids, parental history of fracture, current smoking, current alcohol use, and rheumatoid arthritis. Treatment is indicated and cost-effective if the 10-year risk of hip fracture is greater than 3% or the 10-year risk of any osteoporotic fracture is greater than 20% when using the model. The FRAX tool is available at www.shef.ac.uk/FRAX.

Although the FRAX tool helps guide appropriate therapy, it has limitations. As stated above, use of FRAX is limited to untreated patients aged 50 years or older, it estimates risk with a single-site BMD score, and it can oversimplify complex clinical risk factors. Further, patients in the immediate postmenopausal period have a greater loss of trabecular bone (ie, in the spine) before loss is detected in the cortical (hip) bone.

Serum and urine biomarkers do not play a role in the diagnosis of osteoporosis; however, they can be clinically useful in risk stratification during treatment. Osteoclastic bone resorption is marked by increased circulating levels of type-1 collagen cross-linked N-telopeptide and C-telopeptide. For patients who are considering transitioning off therapy with bisphosphonates, for example, we evaluate the rate of turnover of these biochemical markers. If it is low and patients have a low fracture risk, we consider monitoring with serial DXA in the absence of therapy. In addition, biochemical markers help evaluate the bone turnover rate in patients who continue to experience fractures or lose height or BMD in spite of being compliant with “adequate” treatment. Such an occurrence necessitates changing to a different or stronger class of medication. Thus, bone turnover markers can be used to assist in the decision to stop or alter treatment.

**Lifestyle and dietary treatments**

**LIFESTYLE FACTORS**

All persons should be encouraged not to smoke; older persons who smoke have accelerated rates of bone loss and a higher risk of fracture. Alcohol use among women should be limited to fewer than 7 drinks per week (12 oz of beer, 1.5 oz of liquor, or 5 oz of wine). Routine weight-bearing exercise, such as walking, running, or aerobics, is recommended. Walking for at least 4 hours per week was associated with a 41% decrease in hip fracture risk in postmenopausal patients. In addition, exercises that promote balance and stability (such as yoga and tai chi) can decrease the risk of falls.

Patients at the highest risk for fractures or falls (ie, frail elderly or severely osteoporotic women) should have a home assessment that should include removal of loose rugs and wires, installation of handrails in bathrooms, and providing adequate lighting. Hip pad protectors (www.safehip.com) can be purchased commercially, but a meta-analysis did not show them to be effective in preventing hip fractures in community-dwelling individuals.

**CALCIUM**

Calcium is present in dairy products, fortified foods, and dietary supplements. The
Institute of Medicine (IOM) suggests that women older than 50 years receive 1,200 mg per day of elemental calcium, with an upper limit of 2,000 mg per day. Calcium-rich foods such as low-fat yogurt, cheese, and milk are obvious sources, but spinach, kale, salmon, tofu, and sardines also contain high levels of calcium.

A maximum of 500 mg of elemental calcium can be absorbed at one time. Patients should be advised to consume calcium in divided doses. Certain antibiotics (eg, tetracyclines) can block calcium absorption. Lactose-intolerant patients can obtain calcium from foods, but often need supplementation with calcium citrate, which does not require gastric secretion for its absorption. Calcium carbonate preparations and calcium phosphate options may cause constipation and should be taken with food for maximum absorption.

It is critical to avoid excess calcium supplementation in patients with renal failure, many of whom have secondary or tertiary hyperparathyroidism. Patients with kidney stones need not avoid calcium-containing foods, but they should be advised to stay hydrated and use calcium citrate as a supplement if needed.

**VITAMIN D**

Optimal vitamin D status has not been clearly defined, and the recommended daily allowance (RDA) is still being investigated. The two sources of vitamin D are synthesis in sun-exposed skin and dietary intake. Many individuals avoid sun exposure for fear of sunburn and skin cancer, and some data indicate that vitamin D deficiency is common, particularly among patients living in northern latitudes. Osteomalacia is an important cause of secondary bone loss.

Recently, the IOM updated the RDA of both calcium and vitamin D with the assumption that most people obtain adequate essential vitamins from dietary sources. For women aged 51 to 70 years, the RDA of vit-amin D is 600 IU; for women over age 70 years, the RDA is 800 IU. The upper limit of safe intake is 4,000 IU. These are population-based guidelines, and a value less than 20 ng/mL of 25(OH)D is used to define deficiency. Our practice recommends 1,000 to 2,000 IU per day of vitamin D3 supplementation because we have found this to be consistent with 25(OH)D levels of about 40 to 50 ng/mL. Toxicity has been reported with doses exceeding 10,000 IU of vitamin D3 daily and can present as symptoms of hypercalcemia (ie, bone pain, nausea, polyuria, and

**TABLE 2: Common secondary causes of osteoporosis**

<table>
<thead>
<tr>
<th>Category</th>
<th>Specific cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrine conditions</td>
<td>Early menopause (age &lt;45 years) or estrogen deficiency states</td>
</tr>
<tr>
<td></td>
<td>Prolonged amenorrhea</td>
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<tr>
<td></td>
<td>Cushing syndrome</td>
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<tr>
<td></td>
<td>Hypogonadism (ie, hyperprolactinemia)</td>
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<tr>
<td></td>
<td>Eating disorders</td>
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<tr>
<td></td>
<td>Hyperthyroidism</td>
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<td></td>
<td>Hyperparathyroidism</td>
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<tr>
<td>Gastrointestinal conditions</td>
<td>Celiac disease</td>
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<tr>
<td></td>
<td>Malabsorption syndromes (eg, inflammatory bowel disease)</td>
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<td></td>
<td>Gastric bypass</td>
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<tr>
<td>Hematologic conditions</td>
<td>Multiple myeloma</td>
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<td></td>
<td>Sickle cell disease</td>
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<tr>
<td>Other conditions</td>
<td>Chronic renal failure</td>
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<tr>
<td></td>
<td>Hypercalcuria</td>
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<tr>
<td></td>
<td>Lupus</td>
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<td></td>
<td>Rheumatoid arthritis</td>
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<tr>
<td></td>
<td>Cystic fibrosis</td>
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<tr>
<td></td>
<td>Osteomalacia</td>
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<tr>
<td>Lifestyle factors</td>
<td>Excess alcohol use</td>
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<tr>
<td></td>
<td>Physical inactivity</td>
</tr>
<tr>
<td>Medication use</td>
<td>Anticonvulsants (eg, phenytoin)</td>
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<tr>
<td></td>
<td>Glucocorticoids</td>
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<tr>
<td></td>
<td>Gonadotropin-releasing hormone agonists (eg, leuprolide acetate)</td>
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<tr>
<td></td>
<td>Aromatase inhibitors</td>
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<tr>
<td></td>
<td>Chronic depe- medroxypregesterone</td>
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<td></td>
<td>Lithium</td>
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<td></td>
<td>Cyclosporine</td>
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</tbody>
</table>

Data from National Osteoporosis Foundation; ACOG, Women’s Health Care Physicians.

**POWER POINTS**

The T score is the postmenopausal patient’s BMD compared with that of an average healthy young woman.

The Z score is a measure of BMD used to compare individuals of similar age, sex, and race.

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polydipsia). We treat vitamin D deficiency with high-dose prescription vitamin D2 or D3 given at 50,000 IU once weekly for 6 to 12 weeks and followed by daily supplementation as described above.

**Prescription medications**

A comprehensive list of osteoporosis medications approved by the US Food and Drug Administration (FDA) may be found online at www.contemporaryobgyn.net/Osteo3. Indications, significant side effects (including concerns about osteonecrosis of the jaw19), and costs are highlighted. Several newer medications are available, including denosumab and slow-release risedronate sodium. The use of combination therapy generally is not advised. Treatment goals should be assessed annually.

**HORMONE THERAPY**

Estrogen therapy (ET) and estrogen-progestogen therapy (EPT) are highly effective at preventing osteoporosis, but are not indicated for the treatment of osteoporosis. Hormone therapy relieves vasomotor symptoms, treats genitourinary atrophy, and prevents inevitable bone loss. In the Women’s Health Initiative randomized trial, oral ET (conjugated equine estrogen [CEE] 0.625 mg/day) or EPT (CEE 0.625 mg/day + medroxyprogesterone acetate [MPA] 2.5 mg/day) reduced all types of fractures in non-osteoporotic postmenopausal populations. Hip and vertebral fractures in both the unopposed ET and EPT arms were decreased by 30% to 40% compared with placebo.19,20

Increasingly lower doses of estrogen and transdermal preparations have been prescribed in recent years. Low-dose CEE (0.3 mg/day or 0.45 mg/day) compared with the standard 0.625 mg/day CEE, with and without MPA (1.5 or 2.5 mg/day), achieved increases in BMD at both the hip and spine compared with placebo.21 In addition, an ultra-low-dose estradiol weekly patch that delivers 0.014 mg/day was used in 208 postmenopausal women without or with osteoporosis (T score less than -2.5) but with normal lumbar spine BMD for age (Z score -2.0 or higher).22 After 2 years, the study showed modest increases in hip and spine BMD with the patch compared with placebo.

Hormone therapy has the greatest benefit if it is started in the early postmenopausal (or perimenopausal) years and can concomitantly treat other problems facing midlife women. There is no time limit on the use of hormone therapy, although safety and efficacy should be readdressed. We recommend following the guidelines of the North American Menopause Society of using the lowest effective dose consistent with individual treatment goals, benefits, and risks.23

**BISPHONONATES**

The bisphosphonate class is the “grandmother” of osteoporosis medications, and these are the most commonly prescribed agents. They have a strong affinity for bone mineral (ie, binding to hydroxyapatite) and prevent osteoclast activation by promoting osteoclast apoptosis. All bisphosphonates reduce both vertebral and non-vertebral fractures in postmenopausal women (except ibandronate, which reduces vertebral fractures only). Both alendronate and risedronate and, most recently, zoledranate, are FDA approved to treat glucocorticoid-induced osteoporosis.24 This indication is important among women affected by rheumatoid arthritis, lupus, or other corticosteroid-dependent conditions. We use risedronate or zoledronate in patients who receive more than 7.5 mg/day of glucocorticoid for more than 3 months.

### Major risk factors for osteoporotic fractures

- Low bone mineral density
- Advancing age
- Personal history of a fragility fracture (ie, low-impact fracture)
- Family history of fracture (eg, hip) in first-degree relative
- Low body weight (<58 kg or 127 lb)
- Cigarette smoking
- Use of corticosteroids (eg, prednisone >7.5 mg/day for 3 months)

Data from National Osteoporosis Foundation; ACOG, Women’s Health Care Physicians.
One drawback of the bisphosphonates is the need to wait 30 minutes (60 minutes with ibandronate) before eating or drinking. The newest formulation of risedronate sodium is a 35-mg, once-weekly, delayed-released tablet, which is taken after breakfast and thus negates this waiting period, but patients still should be advised to sit or stand upright for 30 minutes after taking any bisphosphonate.

It is important to note that the bisphosphonates possess varying chemical, biochemical, and pharmacologic properties. For example, alendronate and zoledronate suppress bone turnover more than risedronate. Additional differences among the bisphosphonates were noted in the Fracture Intervention Trial Long-term Extension (FLEX) and the Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly (HORIZON) trial. Specifically, bone turnover markers remained suppressed for an additional 5 years after patients received 5 years of alendronate, whereas zoledronate kept bone turnover markers suppressed for 1 year after infusion.

A common clinical question is the expected duration of treatment with bisphosphonates. FLEX was the largest study to examine the long-term efficacy of bisphosphonates. In this study, patients were randomized to receive either daily alendronate or placebo for 5 years; all patients already had received alendronate for 5 years in a previous study, the Fracture Intervention Trial (FIT). The authors reported a reduction in clinically recognized vertebral fractures for those receiving 10 years of alendronate treatment (relative risk, 0.45; 95% confidence interval [CI], 0.24-0.85), with no significant reduction in fractures at other sites. However, patients who received alendronate for only 5 years (ie, placebo group) had small but significant decreases in BMD and increases in bone turnover markers without an increased rate of fracture after a total 10 years of follow-up.

There are no data to support bisphosphonate drug holidays; however, from the best current evidence, we extrapolate that patients at lowest risk (ie, those who are properly supplemented with calcium and vitamin D) can be monitored without therapy after completing 5 years of bisphosphonate treatment. For patients at the highest risk for fractures and falls or those with recurrent vertebral fractures, it is acceptable to continue therapy for up to 10 years.

Prolonged bisphosphonate use can result in atypical femoral fractures from excess suppression of bone turnover, which disrupts the balance of bone resorption and formation. An analysis of 3 randomized controlled trials (FIT, FLEX, and HORIZON) revealed that after 10 years of bisphosphonate use, the rates of fracture of the subtrochanteric or diaphyseal femur were very low and nonsignificant compared with placebo. A recent, large case-control study in postmenopausal women aged 68 years or older taking bisphosphonates for at least 5 years found that 0.36% of patients sustained a subtrochanteric or femoral shaft fracture. Treatment for 5 years or more increased the risk of atypical fracture (odds ratio, 2.74; 95% CI, 1.25-6.02). However, the incidence, risk, and morbidity associated with typical osteoporotic fractures far outweigh those of atypical fractures.

Another concern with bisphosphonate therapy prominently reported by the media is osteonecrosis of the jaw. A comprehensive review by a multidisciplinary expert group, however, revealed a relatively low risk ranging from 1 in 10,000 to less than 1 in 100,000 patient-years of treatment.

**ESTROGEN AGONISTS/ANTAGONISTS**

Estrogen agonists/antagonists are medications with tissue-selective actions, intended to produce estrogenic actions in certain tissues and antagonistic (ie, suppressive) actions in others. Raloxifene is FDA approved to reduce the risk of estrogen-receptor-positive breast cancer without stimulating the endometrium. It is known to reduce the risk of vertebral fracture, but not hip fracture. Similar investigational medications in this class (particularly bazedoxifene) are effective at preventing osteoporotic vertebral fracture and improving BMD compared with placebo.

**POWER POINTS**

- Smoking cessation, regular exercise, limiting alcohol, and other lifestyle modifications are useful in reducing fracture risk.
- It is critical to avoid excess calcium in patients with renal failure and to counsel patients with kidney stones about hydration and calcium use.
We’re committed to you and your patients

At Ther-Rx, we take our commitment to you and your patients seriously. We have heard your concerns and have taken steps to make Makena™ (hydroxyprogesterone caproate injection) more accessible for clinically eligible patients.

We believe every woman deserves access to FDA-approved and regulated medications. As the only FDA-approved medication of its kind, Makena helps fulfill important unmet needs for certain at-risk women. We understand the responsibility associated with bringing Makena to market in a reliable manner for the thousands of moms in need of therapy every year.

Our commitment to affordable patient access

With our Patient Assistance Programs, clinically eligible patients can have affordable access to therapy.* Financial assistance is available for clinically eligible insured and uninsured patients upon request.

The Makena Co-pay Assistance Program will reduce co-pay costs for insured patients whose health plan covers Makena. Patients with a household income of up to $120,000† will pay between $0 and $20 per injection for Makena. Since there are no income caps, patients with a household income greater than $120,000 are also eligible for co-pay assistance.

The Makena Patient Assistance Program supports uninsured patients by offering the drug at no cost or reduced cost. Patients who are uninsured and have an annual household income less than $60,000 will receive Makena at no out-of-pocket cost.

Our commitment to product quality and patient safety

We believe that there is a need for a quality FDA-approved treatment.

FDA-approved Makena— a sterile injectable—is manufactured in a facility compliant with current Good Manufacturing Practices (cGMPs). These FDA-enforced regulations help ensure the identity, strength, quality, and purity of the medication by requiring control and monitoring of the manufacturing process and facilities. This also helps ensure consistency from dose to dose and accurate potency according to the amount declared on the label.1 Adherence to these quality-management systems means your patients will receive the FDA-approved formulation for this indication.2

Makena is the only product for this indication that has been studied in clinical trials conducted by the NICHD and subsequently reviewed and approved by the FDA. As an FDA-approved medication, Makena is also subject to ongoing safety monitoring for adverse effects.

Our commitment to ongoing support

In addition to access to FDA-approved Makena, your patients will have access to educational materials and compliance reminders throughout therapy.

We established the Makena Care Connection™ to help facilitate the prescription process via a standardized distribution system. As part of this effort, dedicated specialists are available to support you, your staff, and your patients throughout the prescription process.

Our commitment goes beyond simply bringing Makena to market. We are conducting large follow-up trials on Makena, designed in collaboration with the FDA. These studies will help provide enhanced medical knowledge to patients, families, and society as a whole.

*Each patient’s eligibility is evaluated on an individual basis. Program eligibility criteria are subject to change. Financial assistance programs are administered by the Makena Cares Foundation, which is managed by the Chronic Disease Fund.

†This encompasses 85% of US household incomes. Source: 2009 US census data.


Visit www.makena.com for additional information about Makena.

Please see next page for important safety information.
Makena™ is a progestin indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered <37 weeks of gestation. There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity.

Limitation of use: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. It is not intended for use in women with multiple gestations or other risk factors for preterm birth.

Important safety information for Makena

- Makena should not be used in women with any of the following conditions:
  - Current or history of thrombosis or thromboembolic disorders
  - Known or suspected breast cancer, other hormone-sensitive cancer or history of these conditions
  - Undiagnosed abnormal vaginal bleeding unrelated to pregnancy
  - Cholestatic jaundice of pregnancy
  - Liver tumors, benign or malignant, or active liver disease
  - Uncontrolled hypertension
- Makena should be discontinued if thrombosis or thromboembolism occurs
- Allergic reactions, including urticaria, pruritus and angioedema, have been reported with use of Makena or with other products containing castor oil
- Women receiving Makena should be monitored if they:
  - Are prediabetic or diabetic
  - Have conditions that may be affected by fluid retention, such as preeclampsia, epilepsy, cardiac or renal dysfunction
  - Have a history of clinical depression; Makena should be discontinued if depression recurs
  - Develop jaundice; consider whether benefit of use warrants continuation
  - Develop hypertension
- Certain pregnancy-related fetal and maternal complications or events were numerically increased in Makena-treated subjects as compared to placebo subjects, including miscarriage (2.4% vs. 0%) and stillbirth (2% vs. 1.3%), admission for preterm labor (16% vs. 13.8%), preeclampsia or gestational hypertension (8.8% vs. 4.6%), gestational diabetes (5.6% vs. 4.6%), and oligohydramnios (3.6% vs. 1.3%)
- The most common adverse reactions reported in ≥2% of subjects and at a higher rate in the Makena group than in the control group were injection site reactions (pain [35% vs. 33%], swelling [17% vs. 8%], pruritus [6% vs. 3%], and nodule [5% vs. 2%]), urticaria (12% vs. 11%), pruritus (8% vs. 6%), nausea (6% vs. 5%), and diarrhea (2% vs. 1%)

Please see next page for brief summary of prescribing information.
INDICATIONS AND USAGE
Makena is a progestin indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered >37 weeks of gestation. There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity.

LIMITATION OF USE: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. It is not intended for use in women with multiple gestations or other risk factors for preterm birth.

CONTRAINDICATIONS
Do not use Makena in women with any of the following conditions:
- Current or history of thrombosis or thromboembolic disorders
- Known or suspected breast cancer, other hormone-sensitive cancer, or history of these conditions
- Undiagnosed abnormal vaginal bleeding unrelated to pregnancy
- Cholestatic jaundice of pregnancy
- Liver tumors, benign or malignant, or active liver disease
- Uncontrolled hypertension

WARNINGS AND PRECAUTIONS
Thromboembolic Disorders
Discontinue Makena if an arterial or deep venous thrombotic or thromboembolic event occurs.

Allergic Reactions
Allergic reactions, including urticaria, pruritus and angioedema, have been reported with use of Makena or with other products containing castor oil. Consider discontinuing the drug if such reactions occur.

Decrease in Glucose Tolerance
A decrease in glucose tolerance has been observed in some patients on progestin treatment. The mechanism of this decrease is not known. Carefully monitor prediabetic and diabetic women while they are receiving Makena.

Fluid Retention
Because progestational drugs may cause some degree of fluid retention, carefully monitor women with conditions that might be influenced by this effect (e.g., preeclampsia, epilepsy, migraine, asthma, cardiac or renal dysfunction).

Depression
Monitor women who have a history of clinical depression and discontinue Makena if clinical depression recurs.

Jaundice
Carefully monitor women who develop jaundice while receiving Makena and consider whether the benefit of use warrants continuation.

Hypertension
Carefully monitor women who develop hypertension while receiving Makena and consider whether the benefit of use warrants continuation.

ADVERSE REACTIONS
For the most serious adverse reactions to the use of progestins, see Warnings and Precautions.

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to the rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In a vehicle (placebo)-controlled clinical trial of 463 pregnant women at risk for spontaneous preterm delivery based on obstetrical history, 310 received 250 mg of Makena and 153 received a vehicle formulation containing no drug by a weekly intramuscular injection beginning at 16 to 20 weeks of gestation and continuing until 37 weeks of gestation or delivery, whichever occurred first. (See Clinical Studies.)

Certain pregnancy-related fetal and maternal complications or events were numerically observed in the Makena-treated subjects as compared to control subjects, including miscarriage and stillbirth, admission for preterm labor, preeclampsia or gestational hypertension, gestational diabetes, and oligohydramnios (Tables 1 and 2). Table 1 Selected Fetal Complications

<table>
<thead>
<tr>
<th>Pregnancy Complication</th>
<th>Makena n/N</th>
<th>Control n/N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage (&lt;20 weeks)</td>
<td>5/209</td>
<td>0/107</td>
</tr>
<tr>
<td>Stillbirth (≥20 weeks)</td>
<td>6/305</td>
<td>2/153</td>
</tr>
</tbody>
</table>

Table 2 Selected Maternal Complications

<table>
<thead>
<tr>
<th>Pregnancy Complication</th>
<th>Makena n=310</th>
<th>Control n=153</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission for preterm labor</td>
<td>16.0%</td>
<td>13.8%</td>
</tr>
<tr>
<td>Preeclampsia or gestational hypertension</td>
<td>8.8%</td>
<td>4.6%</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>5.6%</td>
<td>4.6%</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>3.6%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

Table 3 Adverse Reactions Occurring in ≥2% of Makena-Treated Subjects and at a Higher Rate than Control Subjects

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Makena n=310</th>
<th>Control n=153</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site pain</td>
<td>34.8%</td>
<td>32.7%</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>17.1%</td>
<td>7.8%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>12.3%</td>
<td>11.1%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>7.7%</td>
<td>5.9%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2.3%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

In the clinical trial, 2.2% of subjects receiving Makena were reported as discontinuing therapy due to adverse reactions compared to 2.6% of control subjects. The most common adverse reactions that led to discontinuation in both groups were urticaria and injection site pain/swelling (1% each).

Use in Specific Populations

Pregnancy

Pregnancy Category B: There are no adequate and well-controlled studies of Makena use in women during the first trimester of pregnancy. Data from a vehicle (placebo)-controlled clinical trial of 310 pregnant women who received Makena at weekly doses of 250 mg by intramuscular injection in their second and third trimesters, as well as long-term (2-5 years) follow-up safety data on 194 of their infants, did not demonstrate any teratogenic risks to infants from in utero exposure to Makena.

Makena administration produced embryopathy in rhesus monkeys but not in cynomolgus monkeys exposed to 1 and 10 times the human dose equivalent every 7 days between days 20 and 146 of gestation. There were no teratogenic effects in either species.

Labor and Delivery
Makena is not intended for use to stop active preterm labor. The effect of Makena in active labor is unknown.

Nursing Mothers
Discontinue Makena at 37 weeks of gestation or upon delivery. Detectable amounts of progestins have been identified in the milk of mothers receiving progestin treatment. Many studies have found no adverse effects of progestins on breastfeeding performance, or on the health, growth, or development of the infant.

Pediatric Use
Makena is not indicated for use in children. Safety and effectiveness in pediatric patients less than 16 years of age have not been established. A small number of women under age 18 years were studied; safety and efficacy are expected to be the same in women aged 16 years and above as for users 18 years and older. (See Clinical Studies.)

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continued from page 21

PARATHYROID HORMONE

Teriparatide PTH 1-34 is the only anabolic hormone that increases BMD in the spine (and minimally at the hip) when given as a daily dose. It is reserved for patients who have the highest risk of fracture, or those who continue to break bones or show evidence of bone resorption while taking first-line treatments.

RANK-INHIBITOR AGENTS

Denosumab is a human immunoglobulin G2 monoclonal antibody that inhibits the formation, function, and survival of osteoclasts early in the bone-resorption cascade. A non-inferiority study compared denosumab with alendronate for changes in BMD in postmenopausal women previously treated with alendronate for at least 6 months. Patients were randomized to continue alendronate or to denosumab for 12 months. Total hip BMD was increased by 1.90% (95% CI, 1.61-2.18%) in the denosumab group versus 1.05% (95% CI, 0.76-1.34%) in the alendronate group; BMD also increased significantly with denosumab at other measured sites (spine, femur, and radius). The FREEDOM trial (Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months) documented the efficacy of denosumab for fracture risk reduction in postmenopausal osteoporosis patients. After 3 years of treatment, the investigators recorded relative decreases in both new vertebral fractures (by 68%) and hip fractures (by 40%) among patients treated with denosumab compared with placebo.

We find that Medicare routinely covers this medication, which is useful in patients with contraindications to bisphosphonates such as renal failure or gastrointestinal intolerance.

CALCITONIN

Calcitonin produces significant reductions in new vertebral fractures and increases in BMD of the spine, but this is the last option for osteoporosis treatment because of its cost. Both the intramuscular and nasal preparations of calcitonin may be useful for acute pain relief in patients who have sustained osteoporotic fractures.

Summary

Postmenopausal patients with suspected osteoporosis require careful diagnostic workup and individualized treatment because osteoporosis often is silent until patients sustain clinically recognized fractures. In general, women should be screened within 5 years of menopause, but those with critical risk factors should have earlier screening. Bone health is a dynamic process that must be staged frequently with careful DXA scans.

The foundation of osteoporosis prevention and treatment is appropriate calcium and vitamin D intake. The plethora of pharmacologic therapies, ranging from oral to injectable agents, is constantly evolving. New treatments on the horizon include a recombinant 84-amino acid human PTH and nitroglycerin preparations. Proper prevention, diagnosis, treatment, and follow-up of osteoporosis are necessary in postmenopausal women to reduce fractures, improve bone health, and sustain excellent quality of life.

DR. THACKER is director of the Cleveland Clinic Center for Specialized Women's Health, and associate professor of surgery, Cleveland Clinic Lerner College of Medicine, Case Western Reserve University, Cleveland, Ohio. She is also executive director of National Speaking of Women's Health, a not-for-profit organization. DR. TOUGH has a fellowship in women's health at the Cleveland Clinic Center for Specialized Women's Health. Dr. Tough reports that she has served as a speaker for Amgen, Novartis, Proctor and Gamble, sanofi-aventis, Bayer Healthcare, the Better Bone Alliance, Upsher-Smith, Novoogyne, Warner Chilcott, and Ther-Rx, for which she has been compensated. She has received CME honoraria from Horizon CME, Baylor School of Medicine, the University of Toledo, the North American Menopause Society, Menopause Management, and the Cleveland Clinic Journal of Medicine. She has been a consultant to Myriad Genetics, and she may receive educational honoraria from Pfizer. Dr. Tough has received consulting fees from Myriad Genetics and coauthored a chapter titled “Topics in Gynecology” for the Deja Review board review series.

References

3. American College of Obstetricians and Gynecologists,
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Obstetric emergencies

Respiratory distress

Acute respiratory distress is uncommon, but its consequences can be dire. Understanding the causes, anatomic influences, and management of acute respiratory distress are essential for increasing the likelihood of mother and fetus surviving.

BY SONYA S. ABDEL-RAZEQ, MD

Although acute respiratory failure (RF) occurs in fewer than 0.1% of pregnancies, the potential maternal and fetal consequences are devastating. Defined as an inability to maintain adequate gas exchange or adequate ventilation, RF can be separated into two distinct groups based on the cause of decompensation: failure of oxygenation (hypoxic RF), the most common cause; or failure to eliminate carbon dioxide (hypercapnia). The distinction between isolated hypoxia and combined hypercapnic-hypoxia RF allows for differentiation among the predominant etiologies of these subtypes (Table 1).

Anatomic and physiologic changes of pregnancy
The gravid woman undergoes a number of respiratory adaptations, some of which increase her risk for respiratory compromise. Progesterone stimulates a 30% increase in minute ventilation, which is achieved by an increase in tidal volume; respiratory rate does not change significantly. Because the respiratory rate remains constant across gestation, tachypnea often is a sign of underlying pathology.

Maternal partial pressure of carbon dioxide (PaCO$_2$) drops from a range of about 36 mm Hg to 44 mm Hg to a range of 28 mm Hg to 32 mm Hg, but renal compensation helps maintain arterial pH between 7.40 and 7.47. Because of this change in PaCO$_2$, established normal ranges in nonpregnant patients do not apply during gestation. Thus, a seemingly minor increase in PaCO$_2$ above 40 mm Hg may reflect significant respiratory compro-
mise in the gravid woman. Maternal \( \text{PaO}_2 \) increases slightly to an average of 100 mm Hg to 105 mm Hg at sea level.\(^3\) Oxygen consumption during pregnancy increases by 15% to 20% because of increased maternal metabolism and the needs of the growing fetus.\(^4\)

Three noteworthy changes occur in the thorax during pregnancy: an increase in the circumference of the lower chest wall with increases in anteroposterior and transverse diameters; elevation of the diaphragm with cephalad displacement of 4 cm to 5 cm, reducing functional residual capacity by 10% to 25%; and as much as a 50% widening of the costal angle.\(^5,6\) These changes peak at the 37th week of pregnancy and normalize within 6 months of delivery, translating to an overall reduced respiratory reserve and putting the pregnant woman at risk for precipitous drops in oxygenation during significant illness. Pregnant women have reduced capacity for respiratory compensation in response to metabolic acidosis. All this can lead to more rapid development of hypoxia, hypercarbia, and acidosis.

In addition, increased estrogen levels can produce mucosal edema, hyperemia, mucus hypersecretion, capillary congestion, and increased fragility in the upper respiratory tract, most markedly during the third trimester. Hormonally mediated rhinitis affects 30% of pregnant women and is characterized by nasal congestion and inflammation.\(^7\) Thus, placement of endotracheal tubes, face masks, and nasogastric tubes in these women may be more difficult and smaller tubes may be required.

**Etiologies of acute RF**

Etiologies of RF can be divided into pregnancy-specific and nonspecific types (Table 2).\(^7\)

**PREGNANCY-SPECIFIC ETIOLOGIES**

Amniotic fluid embolism

Although estimates vary, amniotic fluid embolism, also referred to as anaphylactoid syndrome of pregnancy, occurs in from 1 in 40,000 to 1 in 60,000 deliveries, with a reported mortality rate reaching 86%.\(^8-10\) Amniotic fluid embolism usually occurs during labor or delivery, but has been reported as early as 20 weeks’ gestation and as late as 48 hours postpartum, as well as after a first- or sec-
Acute respiratory failure occurs in fewer than 0.1% of pregnancies.

Established normal ranges for assessing the nonpregnant patient do not apply to the gravid patient.

**Pulmonary edema**

Pulmonary edema occurs when fluid is filtered into the lungs faster than it is removed, which interferes with alveolar gas exchange. Pregnant women are particularly at risk given their already increased circulating volume and alterations in sodium metabolism and water retention. The clinical presentation includes dyspnea, tachypnea, tachycardia, hypoxemia, and diffuse crackles. Tocolytics, particularly the beta-adrenergics, are associated with iatrogenic pulmonary edema and are more common in pregnancies involving multiple gestation, maternal infection, or simultaneous use of multiple tocolytic agents.

Tocolytic-associated pulmonary edema is multifactorial and reflects enhanced vasodilation and tachycardia in response to these medications, as well as increased sodium and fluid resorption after stimulation of antidiuretic hormone. Iatrogenic fluid loading is a contributing factor.

Management of pulmonary edema includes discontinuation of possible precipitating medication, supplemental oxygen, fluid restriction, and diuresis. Furosemide administered at 20 mg or 40 mg intravenously over 1 to 2 minutes usually elicits the desired response of pulmonary lymphatic vasodilation with improved alveolar draining and systemic rapid diuresis. If an inadequate response is noted 1 hour after administration, a second dose may be given. The same dose of furosemide may be administered 6 to 8 hours after an adequate response; however, the underlying etiology of acute pulmonary edema should be addressed. These women also should receive appropriate electrolyte replacement.

Preeclampsia can be associated with pulmonary edema. In this situation, pulmonary edema again is thought to be multifactorial and related to fluid overload, decreased plasma oncotic pressure, increased capillary permeability, increased pulmonary capillary hydrostatic pressure, and possibly to the use of magnesium. Experts believe increased pulmonary capillary hydrostatic pressure arises from generalized arterial vasospasm leading to contraction of the intravascular volume. Presentation is as mentioned previously. Management involves treatment of preeclampsia/eclampsia, supplemental oxygen, fluid restriction, and diuresis therapy with close monitoring of intake and output.

**Peripartum cardiomyopathy**

Peripartum cardiomyopathy (PP CDM) accounts for a substantial proportion of reported pregnancy-related deaths, with a mortality rate reaching 19%. Diagnostic criteria for PP CDM include onset of heart failure in the last month of pregnancy or within 5 months of delivery; absence of other determinable causes for cardiac failure; and absence of demonstrable heart disease before the final month of pregnancy. Some experts have proposed a fourth criterion: left ventricular systolic dysfunction demonstrated by classic echocardiographic findings, such as depressed shortening fraction (less than 30%), ejection fraction less than 45%, and left ventricular end-diastolic dimension of more than 2.7 cm per m² of body surface area. Cardiomegaly almost always is present on chest x-ray. Etiology of the disease is unknown. In contrast to PP CDM, heart failure from underlying structural heart disease usually presents in the second trimester when hemodynamic changes are most appreciable.

**NONPREGNANCY-SPECIFIC ETIOLOGIES**

**Pneumonia**

Prevalence and hospitalization rates for pneumonia are similar in pregnant and nonpregnant women. However, RF due to pneu-
Pneumonia was the third leading indication for intubation during pregnancy and accounted for 12% of intubated obstetric patients in one series. Severe pneumonia and RF lead to more preterm deliveries and higher fetal mortality related to prematurity.

In spite of the changes in immunity that occur during gestation, pneumonia in pregnancy most often is community-acquired. In as many as two-thirds of cases, the offending microbe is not recovered. Comorbid illnesses play an important pathological role.

Immunologic and physiologic changes that occur during pregnancy place women at increased risk for severe viral infections. Secondary bacterial infections, frank RF, and acute respiratory distress syndrome frequently complicate viral pneumonias.

Common symptoms of pneumonia include dyspnea, fever, cough (productive and nonproductive), tachycardia, tachypnea, and sometimes hypoxia. Patients often complain of chills, gastrointestinal symptoms, and pleuritic chest pain. A chest x-ray and findings of focal crackles, rhonchi, or evidence of consolidation (eg, egophony) are required for diagnosis.

**Influenza**

The recent H1N1 influenza pandemic raised awareness of the potential for catastrophic illness during pregnancy. During the 2009 flu season in New York City, pregnant women were 7 times more likely to be hospitalized than nonpregnant reproductive-age women and 4 times more likely to develop severe infection, defined as a need for admission to the intensive care unit (ICU) or ultimate death. This latter finding suggested that pregnant women experienced more severe disease and were not simply hospitalized more frequently.

A large database accumulated by the US Centers for Disease Control and Prevention (CDC) showed that between April and August 2009, 65% of 788 pregnant women with proven H1N1 infection were hospitalized. Of those hospitalized, nearly one-quarter developed severe disease necessitating ICU-level care and one-fifth required intubation. Approximately half of pregnant women diagnosed with H1N1 had an underlying comorbid condition, such as obesity, asthma, or diabetes (both pregnancy-related and nonpregnancy-related). Influenza infection had a significant impact on the fetus as well; one-third of live-born babies were delivered prematurely. Pregnant women accounted for 5% of influenza-related deaths reported to the CDC in the same period.

The study also highlighted the importance of early recognition and treatment; pregnant women given oseltamivir within 48 hours did well as indicated by a 0.5% maternal mortality rate. Among survivors, earlier treatment was associated with less severe disease even when it was provided outside the FDA-approved 48-hour window.

**Pulmonary embolism**

Embolic diseases are the primary cause worldwide of acute hemodynamic and respiratory
collapse during gestation. Contributing factors include changes in clotting protein profiles, inhibition of the fibrinolytic system, and venous stasis. Risk of venous thromboembolism (VTE) begins to increase in the first trimester and continues through the postpartum period. Other conditions that increase the risk of VTE include prolonged bed rest, instrumentation or cesarean delivery, hemorrhage, sepsis, multiparity, and increased maternal age. Clinical features include dyspnea, pleuritic chest pain, cough, leg pain/edema, tachypnea, tachycardia, and hypoxia. Diagnosis is confirmed by imaging (computed tomography pulmonary angiography or low-dose ventilation perfusion scanning). If suspicion of VTE is high, anticoagulation therapy instituted before completion of the diagnostic evaluation is appropriate, as is maintaining adequate maternal and fetal oxygenation and circulation.

Venous air embolism
Venous air embolism (VAE) is a rare but potentially fatal condition that manifests after the introduction of air into the vasculature. Typically, air enters the venous circulation through the subplacental myometrial veins, travels to the right side of the heart, and lodges within the pulmonary circulation, where it can cause endothelial damage and mechanical obstruction. Increases in fibrin deposition, clot formation, and platelet aggregation occur in the vasculature as a result of turbulent blood flow, while release of histamine and serotonin in the lung lead to pulmonary vasoconstriction and increased capillary permeability. The result is pulmonary hypertension and pulmonary edema. Incidence likely is underestimated.

Although most cases of air embolism are asymptomatic and often undetected, presentation may include acute hemodynamic instability and neurologic symptoms. Factors that increase risk include cesarean delivery, trauma, and uterine rupture.

Asthma
Asthma is the respiratory disorder that most often complicates pregnancy. Incidence is reported at between 0.4% to 7%, and prevalence is increasing. Acute exacerbations rarely occur during labor and delivery, however.

During an asthma attack, severity is best judged by clinical appearance and by forced expiratory volume in 1 second (FEV1); physical examination and chest x-rays are poorer measures of disease severity. Symptoms include dyspnea, tachypnea, tachycardia, and wheezing. Clinicians should monitor oxygenation and fetal status throughout the evaluation and treatment. Pulse oximetry provides no information on the patient’s ability to clear CO₂, and thus cannot substitute for arterial blood gas evaluation. Management includes bronchodilators and corticosteroids.

Acute respiratory distress syndrome
Consensus criteria for defining acute respiratory distress syndrome (ARDS) include acute onset of bilateral radiographic infiltrates; absence of clinical evidence on the left side of the heart; and PaO₂/fractional inspired oxygen (FiO₂) ratio less than or equal to 200. Although not strictly required, an underlying cause of lung injury should be sought. Presenting signs and symptoms are nonspecific and include dyspnea, tachypnea, and tachycardia. The list of potential causes is extensive. Physical examination may reveal diffuse or bibasilar crackles or cyanosis. Treatment is supportive and includes management of predisposing factors, fluid status, and hemodynamic status.

Presentation and differential diagnosis of acute RF
Dyspnea is the most common symptom associated with acute RF and usually is characterized by rapid, shallow breathing and the use of accessory respiratory muscles. Investigation into the causes of RF is determined by the suspected mechanism of failure and the primary disease process. Pulse oximetry is a useful tool for monitoring oxygenation and should be instituted in essentially all cases. Arterial blood gas analysis will identify a widened alveolar-arterial gradient and/or hypercapnia. A chest x-ray provides a clear image that will narrow the differential to include pulmonary embolism, anatomic right-to-left shunt, pneumothorax, cirrhosis, and chronic obstructive pulmonary disease. The differential should include pleural effusion, aspiration, lobar pneumonia,
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Permanent Contraception

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atelectasis, and infarction when unilateral infiltrates or effusion are present. If the infiltrates are bilateral, then the differential diagnosis should include pulmonary edema (cardiogenic and non-cardiogenic causes), pneumonia, and pulmonary hemorrhage. The need for advanced imaging modalities, including computerized tomography, is based on the differential diagnosis for suspected primary disease.

**Management**

The actual number of obstetric patients who require ICU admission for RF is low. Little data exist on optimal management of these patients. The most appropriate management strategy is to apply those practices used to manage RF in nonobstetric populations while keeping in mind the anatomic and physiologic changes of pregnancy that affect respiratory goals.

In addition, consultation with a perinatologist or intensivist with experience in caring for the gravida patient is imperative. Ideally, fetal monitoring should be performed by an obstetric nurse in the ICU at least every 4 to 8 hours while the patient is critically ill and more frequently if the degree and/or acuity of respiratory compromise increases. Continuous fetal monitoring is appropriate in the most serious situations. Urgent cesarean delivery may become necessary. Thus, all necessary instruments and staff should be readily available.

The overall goal is to maintain adequate oxygenation and ventilation in these women and treat the primary cause of the RF. For hypoxic RF, the goal is to improve arterial oxygenation and maintain a PaO\(_2\) of greater than 60 mm Hg and an arterial blood oxygen saturation (SaO\(_2\)) of greater than 90%. Administration of supplemental oxygen improves oxygenation in most clinical situations except those involving anatomic shunts. Low-flow oxygen can be delivered using a nasal cannula or a face mask. The maximum fraction of inspired oxygen (FiO\(_2\)) that can be delivered via this route is approximately 0.4. The FiO\(_2\) delivered using noninvasive modes also is dependent on minute ventilation. Adding a reservoir bag to a face mask achieves a higher FiO\(_2\) by minimizing admixture of the supplemental oxygen with room air. Noninvasive positive pressure ventilation and mechanical ventilation via an endotracheal tube are additional approaches for providing supplemental oxygen as well as partial or total support for minute ventilation.

In hemodynamically stable patients with mild or moderate RF, noninvasive positive pressure ventilation may decrease the need for intubation and mechanical ventilation and reduce the length of stay in ICU. Ideal candidates for this mode of ventilation have intact mental status, can protect their airway, are hemodynamically stable, and are at low risk of aspiration. The presence of copious airway secretions is considered a relative contraindication.

In hypercarbic RF, the primary goal of treatment is to maintain arterial pH at greater than 7.30 with a PaCO\(_2\) appropriate for the pH, but less than 45 mm Hg in the gravid patient. Bronchodilators can be delivered via metered dose inhalers or nebulizers; however, patients with respiratory distress and tachypnea may not be able to use metered dose inhalers.

Long-acting beta-adrenergic agonists should not be used to treat acute exacerbations of chronic bronchospasm. Corticosteroids often are used to treat acute exacerbations of disease related to airway inflammation (eg, asthma and chronic obstructive pulmonary disease). Aerosolized steroids may not improve the episode in its acute phase, but are useful for maintenance. Although systemic absorption of aerosol steroids is not significant, some degree of adrenal suppression may occur. Patients who experience change in the production or color of sputum may benefit from a short course of antibiotic therapy.

The need for mechanical ventilation is a clinical decision based on a patient’s increased difficulty in breathing, clearing secretions, and maintaining an adequate airway. When severe hypoxemic RF necessitates intubation, slowed

<table>
<thead>
<tr>
<th>Table 3 Goals of respiratory support</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Markers</strong></td>
</tr>
<tr>
<td>SaO(_2)</td>
</tr>
<tr>
<td>Maternal PaCO(_2)</td>
</tr>
<tr>
<td>Tidal volume</td>
</tr>
<tr>
<td>IBW maternal pH</td>
</tr>
<tr>
<td>Peak or plateau pressures</td>
</tr>
</tbody>
</table>

Adapted from Mighty R.\(^7\)

**POWER POINTS**

- Amniotic fluid embolism, pulmonary edema, and PP CDM are pregnancy-related causes of acute respiratory failure.
- Asthma is the most frequent respiratory disorder complicating pregnancy.

---
gastrointestinal motility, progesterone-mediated loss of lower esophageal sphincter tone, and higher intra-abdominal pressures from the gravid uterus increase the risk of peri-intubation aspiration. Patients should be kept semi-recumbent while preparing for intubation to reduce compression of the inferior vena cava and to decrease pressure on the diaphragm. Specific parameters for management of a gravid patient with respiratory distress are presented in Table 3. Compared with the typical patient with RF, more frequent arterial blood gas measurements are warranted so that trends in PaO2, PCO2, and pH can be monitored carefully.

Pregnancy-related anatomic and physiologic changes increase the risk for RF. Many causes of RF are not unique to pregnancy, including pneumonia, influenza, pulmonary embolism, cardiogenic pulmonary edema, and asthma. Pregnancy-specific etiologies include amniotic fluid embolus, pulmonary edema secondary to tocolytic therapy, pre-eclampsia/eclampsia, and PP CDM. Diagnostic evaluation and management of gravid women is similar to that in nonpregnant women; however, special attention to maintaining appropriate oxygenation is essential for both mother and fetus. This requires a thorough knowledge and understanding of the physiologic changes and pathologic processes that occur in pregnancy. Optimizing maternal outcome ultimately ensures fetal and maternal well being.

REFERENCES

How does transdermal low-dose MHT compare to oral therapy in terms of safety?

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Results from recent double-blind, randomized trials of menopausal hormone therapy (MHT) have dramatically changed the practice of menopausal medicine. Prior to the highly publicized Women’s Health Initiative (WHI) Hormone Trials,1,2 many clinicians encouraged menopausal women to take estrogen. However, premature termination of the WHI trial by the data monitoring safety board because of concerns of increased net harm and an absence of cardioprotection began a tumultuous phase of uncertainty with regard to the role of MHT.3,4

General reaction by clinicians to the findings of the WHI trials was either to eliminate MHT—widely regarded as the most efficacious of existing therapies for menopausal syndrome—from available therapeutic options or to relegate it to the bottom of a relatively finite list of suboptimal alternatives.5-7

Now, several years after the initial reports on the WHI hormone trials, the concept of individualized therapy has gained momentum, thereby encouraging reconsideration of MHT for menopause management.

Perimenopausal/early menopausal women suffer most

The WHI hormone trials1,2 revealed important scientific information and initiated insightful debate among researchers, but left clinicians with the challenge of sifting through conflicting expert opinions and
varying interpretations of data. Caution in prescribing and using MHT ensued, driven, at least in part, by magnified apprehensions regarding MHT-related risks, as well as by heightened concerns relating to medical liability and the potential for litigation. The reluctance on the part of many practitioners to offer MHT in the wake of WHI underscores the need to revisit the absolute risks associated with MHT (Table 1) and to reexamine its relevance in managing symptomatic menopause.

It is important to recall that WHI was designed to determine whether MHT affords cardioprotection (primary outcome) and whether it affects the risks for breast cancer, stroke, colon cancer, and hip fracture (secondary outcomes) in postmenopausal women. It should be noted that the effects of MHT on menopause-related symptoms were not considered in the WHI trial design. Moreover, nearly 75% of the women enrolled in WHI were more than 10 years postmenopause, and the majority did not complain about common menopause-related symptoms. Extrapolating MHT-related adverse occurrences that were primarily observed in older postmenopausal populations remote from the final menstrual period and applying them to symptomatic women early in the menopause transition has been an unfortunate sequela to the WHI trial. Using data from the WHI trials to justify withholding MHT from younger, symptomatic menopausal women warrants a cautionary pause.

Efficacy of estrogen
Most studies suggest that menopausal symptoms, which may include hot flashes, night sweats, insomnia, mood lability, vaginal dryness, and dyspareunia, commence 2 to 3 years before the final menstrual period and gradually resolve within a few years after menopause. Experts hypothesize that the magnitude of symptoms, ranging from mild and dismissible to excessive and debilitating, reflect an altered sensitivity to wide fluctuations in circulating estrogen levels. Hypoestrogenism as an etiology for many menopausal symptoms and efficacy of exogenous estrogen for symptom control are both well established. Indeed, estrogen is one of the most powerful tools for managing menopause-related symptoms.
The intent of the WHI was to determine whether MHT affords cardioprotection and affects risks for cancer, stroke, and fracture in postmenopausal women.

Experts theorize that severity of menopausal symptoms is associated with fluctuating estrogen levels.

Table 1

<table>
<thead>
<tr>
<th>Event</th>
<th>Estrogen + progesterone</th>
<th>Estrogen alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD</td>
<td>+7</td>
<td>-3</td>
</tr>
<tr>
<td>Stroke</td>
<td>+8</td>
<td>+12</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>+8</td>
<td>+6</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>+8</td>
<td>-7</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>-5</td>
<td>-6</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>-6</td>
<td>+1</td>
</tr>
<tr>
<td>Dementia</td>
<td>+18</td>
<td>+4</td>
</tr>
</tbody>
</table>

Mean age of study population 63 years (50 to 79 years) with more than 70% of participants aged 60 to 79 years. Data from Rossouw JE; et al; Anderson GL.

But a focused evaluation of the therapy’s risk-benefit profile (eg, atherosis, stroke, thrombotic events, and breast cancer) in the context of the individual’s overall health status, unique risks, and quality-of-life related concerns must guide the decision to recommend MHT for symptom control. Once the decision to initiate MHT is made, then the choice of pharmacological intervention is further influenced by the presence or absence of a uterus. Given the increased risk for endometrial neoplasia and cancer associated with unopposed estrogen use, a combination of estrogen plus progestin must be offered to nonhysterectomized women. Although the use of estrogen alone is appropriate for women who have had a hysterectomy, combination MHT is preferred for hysterectomized women with a history of pelvic endometriosis in whom a combination strategy mitigates the risk for recrudescence of endometriosis-related symptoms.

In addition, MHT offers skeletal benefit to peri- and early postmenopausal women who are at increased risk for fractures (eg, those with a family history of osteoporosis, a family or personal history of fracture, or known low bone mineral density). However, because effective alternatives to MHT for osteopenia/osteoporosis exist, initiating MHT for skeletal protection alone in otherwise asymptomatic women during the perimenopause or in early menopause remains debatable and should only be considered after individualized assessment of the risk-benefit profile and after discussing with the patient the risks and benefits of MHT compared with alternative pharmacotherapy options.

Placing risks in perspective

Existing data conflict with regard to cardiovascular implications of MHT; observational studies in perimenopausal and early menopausal populations suggest cardioprotective implications of MHT, whereas randomized, controlled trials undertaken in older menopause populations have demonstrated otherwise. Although multiple factors, such as smoking, obesity, diabetes, and family history, increase a woman’s risk for stroke and cardiovascular disease (CVD), the increased risk for CVD and thromboembolic events after initiating MHT in older women cannot be minimized. The beneficial effects of estrogen on in vitro and in vivo models of vascular elasticity and reactivity are well documented, but researchers also have reported that the beneficial effects of estrogen on vascular elasticity may be attenuated or even reversed in the setting of underlying atherosclerosis. These observations raise the possibility that covert atherosclerosis may partially explain the increased CVD and stroke incidence in the elderly postmenopausal population randomized to MHT in the WHI hormone trials.

Attempts to clarify diverging viewpoints about the risk for CVD and stroke in early compared with elderly menopausal women prompted the “timing hypothesis,” first
proposed in a nonhuman primate model by Clarkson et al.20 The primary tenet of this hypothesis is that early initiation of MHT (around or shortly after the onset of menopause) protects against development of vascular disease. This hypothesis further suggests that reintroducing estrogen after a prolonged period of hypogonadism may actually accelerate processes that are detrimental to vascular health.

Indeed, post hoc analyses of the WHI data concur with the timing hypothesis; data stratified by age and time since final menstrual period indicate that the risk for CVD, thrombotic events, and total mortality was greatest in women taking combined MHT who were older than 60 years and/or were more than 10 years postmenopause at the time of enrollment.21 Furthermore, these analyses identified that, although not statistically significant, the risk for adverse outcomes after initiation of MHT was lowest in the younger postmenopausal WHI enrollees and in those who were within 10 years of their final menstrual period. Thus, the timing hypothesis may largely explain the discrepancy between observational data, which largely found MHT to be cardioprotective, and the results of randomized, controlled trials, which largely found MHT to be cardiotoxic.22 Thus, clinicians must factor in a woman’s age and time since her last menstrual period to her risk profile when considering or refusing MHT as a therapeutic option.

Choice of preparation
MHT embraces a spectrum of hormonal preparations and regimens, all of which modulate an individual’s risk profile differently. Indeed, certain differences in MHT-related risks were apparent in the two hormone arms of the WHI.1,2 Although increased risks for thromboembolism and stroke and reduced fracture risk were associated with both MHT interventions, the risks for breast cancer and CVD were greatest with combination MHT (Table 1).23 Experts have suggested that the excess breast cancer incidence observed in the WHI estrogen plus progestin trial relates to the type of synthetic progestin (ie, medroxyprogesterone acetate [MPA]) and possibly to the progestin regimen used (ie, continuous).23–25 However, some have argued that the hysterectomized women enrolled in the estrogen-alone arm of the WHI trial represent a population quite distinct from the women with uteri enrolled in the WHI estrogen plus progestin arm, such that unquantifiable population differences may underlie the observed discrepancies in MHT risk profiles evident in these trials. Nonetheless, WHI estrogen trial data provide reassurance regarding the risks for breast cancer and CVD with short-term estrogen exposure; this information may be of particular relevance to young women with surgically induced menopause in whom the severity of menopausal symptoms can be particularly overwhelming.

How can inherent risks be mitigated?

**Estrogen dose and route**
The choice of estrogen dose in MHT must...
reflect a balance between therapeutic efficacy and risk burden (ie, higher doses of estrogen increase risks for vascular thrombosis, stroke, gall stones, and endometrial cancer). Although experts are unanimous in their recommendation to use “the lowest dose of MHT for the shortest time,” what constitutes the “lowest dose” and “shortest time” is left to the discretion of the treating clinician. In the absence of explicit guidelines, the lowest estrogen dose that provides symptomatic relief may be considered “optimal,” and MHT use for a duration of 5 or fewer years generally is considered “acceptable.” Of practical consideration are populations with unique needs, such as young women with surgically induced menopause who should be managed with unopposed estrogen, unless endometriosis was the indication for the menopause-rendering surgery; then combination MHT regimens are appropriate. These women may require higher doses of estrogen to achieve adequate symptom relief.  

Even ultra-low doses of estrogen provide skeletal protection. Nevertheless, clinicians should check periodically for skeletal deterioration in all postmenopausal women deemed to have an enhanced fracture risk, especially after discontinuation of MHT, when accelerated bone loss commonly ensues. In addition, although prospective data are sparse, nonoral routes of estrogen administration (ie, transdermal, vaginal) may pose a lower CVD risk.

**Progestin type, regimen, and risks**
When oral or transdermal MHT is used to alleviate menopausal symptoms in women with uteri, combined hormone therapy is needed to prevent uterine neoplasia and cancer. Both natural and synthetic progestin offer protection against endometrial neoplasia in MHT users, but dose and duration are pertinent. Although sequential (ie, 10 to 14 days) and continuous progestin regimens confer comparable endometrial protection, cyclical exposure to progestin for up to 10 days may be associated with an increased risk for endometrial neoplasia.

Experts have proposed strategies for limiting progestin exposure (ie, lower doses and/or less frequent dosing regimens) with the goal of mitigating MHT-related risks. A recent Cochrane Review on the risk for endometrial neoplasia related to MHT use suggested that MPA in a standard dose (ie, 2.5 to 5 mg) or a lower dose (eg, 1.5 mg) given sequentially (≥10 days) or continuously effectively protects against endometrial neoplasia compared with unopposed estrogen.

The Million Women Study, the Heart and Estrogen/Progesterone Replacement Study (HERS), and the WHI trials suggest that the incidence of postmenopausal breast cancer is significantly increased in postmenopausal women taking combination MHT compared with estrogen alone. Follow-up studies from the WHI trials also suggest that breast cancers diagnosed after MHT tend to be more aggressive (ie, positive lymph nodes, negative estrogen/progestin receptor expression, and HER2 overexpression). These observations have recycled old and raised new questions regarding the ways dose, regimen (ie, cyclic vs continuous), and type of progestin might affect the risk for breast cancer in MHT users. The disparate risk profile evident in WHI-estrogen plus progestrone versus WHI-estrogen trials raised concerns regarding the medroxyprogesterone acetate (MPA) component of MHT. In vitro studies with Michigan Cancer Foundation-10A cells (ie, human epithelial, estrogen and progestin receptor-negative, normal breast cells) suggest that MPA, but not other progestin analogs, may increase the risk for breast cancer by increasing the mitotic index of normal breast epithelial tissue.

Similarly, in vivo studies demonstrated that MPA, and not micronized progestin, adversely affects epithelial breast proliferation in nonhuman primates. The French E3N cohort study (ie, the French component of the European Prospective Investigation into Cancer and Nutrition), involving more than 80,000 postmenopausal women suggested that micronized progestin is associated with reduced rates...
Intraperitoneal (IP) chemotherapy was introduced as a way to treat ovarian cancer by administering chemotherapy directly to the abdomen rather than through a vein. While this treatment extended median survival for women, the side effects were harsh and many women were unable to complete treatment. Our faculty at Magee-Womens Hospital of UPMC and UPMC Cancer Centers played a major role in the adaptation of IP to a modern outpatient regimen, reducing side effects and improving outcomes by adjusting dosing and anticipating and controlling symptoms. Oncologists at Magee and throughout UPMC were also among the first to use hyperthermic IP chemotherapy for the treatment of ovarian cancer. Snap the code and learn more at UPMCPhysicianResources.com.
of breast cancer compared with synthetic progestin.\textsuperscript{33,34} The decreased risk for breast cancer with the use of micronized progestin, however, may be offset by an increased risk for uterine neoplasms, especially if it is used sequentially.\textsuperscript{35,36}

A progestin intrauterine device (IUD) is an alternative strategy that offers endometrial protection in estrogen users without increasing the risk for breast cancer.\textsuperscript{37} Researchers have assessed the safety of progestin IUDs in menopausal women and deemed them reliable and efficacious substitutes to oral and transdermal progestin regimens.

In summary, combined MHT is appropriate for symptomatic menopausal women with intact uteri. Moreover, in light of recent evidence, we recommend continuous micronized progestin or a progesterone IUD as acceptable regimens in users of estrogen.

Avoiding the avoidables
When interpreting any relationship between MHT and organ-specific risks, it is important to factor in the patient’s age, weight, and whether she has diabetes, abuses alcohol, or smokes because each of these factors directly correlates with many of the adverse risks attributed to MHT. Healthy lifestyle choices that include a diet rich in fiber, fruits, and vegetables, low animal fat intake, moderate alcohol consumption, avoidance of tobacco, and regular physical activity can mitigate risks for adverse cardiovascular and cerebrovascular events and possibly for breast cancer.\textsuperscript{38-40}

Each risk attributed to MHT has additional and potentially modifiable determinants. The art of medicine lies in using strategies that minimize an individual’s risk while maximizing overall benefit. The benefits of short-term MHT likely outweigh any potential for harm in otherwise healthy women in early menopause.

Conclusion
Concerns regarding the safety of MHT in elderly menopausal women remote from the final menstrual period are highly relevant. Good evidence exists that the risks for breast cancer, cardiac events, dementia, stroke, and venous thrombotic events correlate with the duration, dose, and type of MHT, particularly in the older population. However, when used in healthy young perimenopausal and early menopausal women, the vast majority of studies suggest that MHT is a safe and efficacious strategy for relieving moderate to severe menopausal symptoms and for the prevention of osteoporosis. For symptomatic perimenopausal and early menopausal women, MHT remains a valid and appropriate first-line therapy.

\[\text{REFERENCES}\]


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Mount Carmel Health System, the second largest health care system in central Ohio, is currently seeking a BC/BE Maternal Fetal Medicine physician for an employed position. Join a multidisciplinary team of experts providing a unified approach to perinatal services throughout Mount Carmel. Each physician on the team will have a primary hospital site.

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For more information please contact Julie Hotchkiss, Physician Recruiter, Mount Carmel Health System at 614-546-4398; fax 614-546-4946; email: jhotchkiss@mchs.com.

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Intermountain is frequently referenced nationally as one of the leaders in delivering high quality/low cost health care. Intermountain Healthcare needs one BC/BE OB/GYN in Park City, Utah. Send CV to Intermountain Healthcare, Physician Recruiting, 36 S. State St, 21 Fl, Salt Lake City, UT 84111. 800-888-3134. http://physicianjobsintermountain.org.

Opportunity for early to mid July, 2012 for a Board Certified/Board Eligible physician to join a group of University-trained Board Certified Obstetricians and Gynecologists, including one Board Certified MFM. We have a regional referral center with a Level III NICU and a new state of the art Labor & Delivery unit as of 2012. Winchester is nestled in the Shenandoah Valley of Virginia just 70 miles from downtown Washington, DC. Outdoor and cultural activities abound. Call approximately 1/6 with five weeks vacation to start.

Please contact Janie Smith
c/o Winchester Obstetrics & Gynecology
1330A Amherst Street, Winchester, VA 22601
CALL (540) 667-2313, or EMAIL at janiesm@ntelos.net
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Is this really patient-centered care?

Patient-centered care is the buzzword for a new trend in healthcare. It sounds great, it sounds as if we should pursue it, it sounds politically correct. It sounds as if everyone would vote for it and it might be the fix that US healthcare needs. If only we could be patient centered, then our healthcare woes would be over.

But what does patient-centered care mean? Hasn’t the patient always been the focus of our attention? If we didn’t have patients, we wouldn’t have jobs, hospitals, clinics, drug companies, health insurance companies. So it is hard to argue that patients have not been at the center of US healthcare.

Somehow in the last 20 years, other entities vying for attention, convenience, and resources have gained more control and possibly influenced healthcare for ulterior motives. Healthcare organizations have focused on the business of making money, potentially at the expense of patient experience and safety at times. Insurance companies likewise have as their first priority profit, not patient well-being. Pharmaceutical companies, in the name of saving and improving lives, have created huge corporations that market directly to the consumer wares that are purportedly better than generic drugs. Even physicians in the climate of increasingly higher debt after training and falling healthcare reimbursements have influenced practice strategies to be more convenient for them and less convenient for the patient.

Today I conjecture that the direct physician-to-patient time, whether in the office or the hospital, is dramatically less than it was 20 years ago because we have been forced to become more efficient to make more money for everyone but the patient or to be less efficient to improve safety.

Although these clearly are oversimplified generalizations, they illustrate that medicine no longer is just about what is best for the patient. One of the best examples of the new focus on efficiency is the electronic medical record (EMR). It is a tremendous asset over time: To be able to read the records, not lose the records, and to use automatic queries and safety checks are tremendous steps toward reducing redundancy and improving patient safety. However, the patient does not experience these advantages directly. In fact, the provider spends more time at the computer and less time with the patient. So, ask the patient: Is this better?

There is no doubt that we need to step back and look at what has happened. We need to make the patient the primary focus again and remind ourselves that we are in medicine to make people better or to help them have better health.

We need to remind ourselves that we are in medicine to make people better or to help them have better health.

Dr Kilpatrick is the Helping Hand of Los Angeles Chair, department of obstetrics and gynecology, at Cedars-Sinai Medical Center, Los Angeles, California, and visiting professor, department of obstetrics and gynecology, at the David Geffen School of Medicine, University of California Los Angeles.
patient what she wants and let her choose, like a menu: Today you can choose the day you want to be delivered, what type of delivery you would like, whether you want pitocin, cervical ripening, or an epidural, or—if you really want—to wait for labor and see what happens. Now, what would you like?

Another scenario might be a woman who comes in with ruptured membranes at 22 weeks. She is given an explanation that her baby is not likely to live, but at the same time she is given the option of having pediatricians for full resuscitation at the delivery, doing a cesarean section for fetal distress, or just allowing nature to take its course and give the baby comfort care at delivery. What would you choose if those were your options?

In these simple examples, the patient essentially is being asked to choose her care. She is not being given a recommendation by an experienced provider who really does have the knowledge to make a recommendation based on the most benefits and the least risks for her in that situation.

I am afraid that our move toward patient-centered care has become a model of shirking responsibility in favor of the overriding importance of patient autonomy, perhaps facilitated by less physician confidence in his or her experience and knowledge. Most patients did not go to medical school and do a residency; most do not have years of experience in taking care of other patients and of seeing bad and good outcomes. Our fears of making women unhappy, of losing their business, of being sued are threatening to undermine our responsibility as physicians to knowingly do no harm.

Of course patients should have input. Of course they should understand the plans that we have made for them and why we made them. Maybe if we just spent more meaningful time with patients, face to face, listening and talking, we would get back to where we started: patient-centered care.

Isn’t it really what we all were taught as children: Be caring, be respectful, communicate clearly, and listen? That is the patient-centered care I remember.

Our move toward patient-centered care has become a model of shirking responsibility in favor of the overriding importance of patient autonomy.
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