

reviewed the charts of 3,400 patients who visited the ultrasound division of the department of obstetrics and gynecology at the University of Miami between August 2007 and August 2009. Of these patients, 103 (3%) were referred specifically for inadequate pelvic examinations.

“This translates into 1-10 patients per month, depending on how busy a practice is,” he said.

The mean age of the 103 patients was 50 years, 37% were black, 37% were Hispanic, and 26% were white. Their mean body mass index was 33 kg/m<sup>2</sup>;

and 67 patients (65%) were obese, while the remaining 36 (35%) were overweight or had a normal BMI.

When the chief complaint of patients was analyzed, 57 (55%) were seen for a routine exam while the remaining 46 (45%) had different complaints including pelvic pain, abnormal uterine bleeding, and urinary dysfunction.

Nearly two-thirds of the ultrasound exams (69%) were found to be normal. But the ovaries were not detectable on ultrasound 25% of the time. The most common findings on ultrasound were fibroids (17%) and ovarian cysts (15%).

When the researchers compared obese patients with nonobese patients, they found that obese patients were significantly less likely to have a complete ultrasound assessment (62% vs. 81%), yet they were significantly more likely to have abnormal findings detected on ultrasound (48% vs. 22%).

“We have to counsel obese patients that because of their body habitus, they have an increased chance of having an incomplete pelvic assessment and an increased chance of having findings on ultrasound,” Dr Cruz-Pachano concluded. ■

# Race a Factor In Completing HPV Series

BY DEBRA L. BECK

FROM THE ANNUAL MEETING OF THE SOCIETY FOR ADOLESCENT HEALTH AND MEDICINE

TORONTO — Girls who identified themselves as white were twice as likely as those who identified themselves as black to complete the three-shot vaccination series against the human papillomavirus, according to a retrospective investigation of medical records. “This is concerning because, historically, black women have had lower rates

**Major Finding:** Eleven percent of girls who self-identified as black received all three doses of the HPV vaccine, compared with 22% of the white girls and 15% of those identified as other races.

**Data Source:** A retrospective study of medical records on 3,297 girls between ages 9 and 26 years who received the first HPV vaccine dose between June 2006 and June 2008 from an urban medical center.

**Disclosures:** None was reported.

of cervical cancer screening and been more at risk from dying of cervical cancer. With unequal distribution of the vaccine, the racial disparity in cervical cancer may worsen,” Dr. Lea Widdice said in a poster at the meeting.

Moreover, overall, only 14% of girls initiating the HPV vaccine series actually completed the three-shot series within 7 months of the first dose.

Clinical recommendations for the vaccine are to get the third shot 6 months after the first.

Dr. Widdice and her colleagues conducted a retrospective investigation of medical records on 3,297 girls between ages 9 and 26 years who received the first HPV vaccine dose between June 2006 and June 2008 from an urban, academic pediatric medical center with multiple primary care and specialty clinics.

Overall, 11% of the black girls received all three doses of the vaccine, compared with 22% of the white girls and 15% of those identified as other races, reported Dr. Widdice, a pediatrician at the Cincinnati Children’s Hospital Medical Center.

Patients were predominantly from primary care (95%) and 65% used Medicaid. The majority (67%) self-identified as black, 29% said they were white, and 4% were classified as other races.

Even after investigators controlled for factors such as type of insurance and the different types of clinics giving the vaccine (primary care pediatrics, adolescent primary care, adolescent specialty clinics, or other specialty clinics), race was still strongly associated with getting all three of the doses on schedule. ■

## Visual Abnormalities

Retinal vascular thrombosis has been reported in patients receiving estrogens. Discontinue medication pending examination if there is sudden partial or complete loss of vision, or a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, estrogens should be permanently discontinued.

## 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 are, 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 small number of case reports, substantial increases in blood pressure have been attributed to idiosyncratic reactions to estrogens. In a large, randomized, placebo-controlled clinical trial, a generalized effect of estrogen therapy on blood pressure was not seen.

## Hypertriglyceridemia

In patients with pre-existing hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis. Consider discontinuation of treatment if pancreatitis occurs.

## Hepatic Impairment and/or Past History of Cholestatic Jaundice

Estrogens may be poorly metabolized in women with impaired liver function. For women with a history of cholestatic jaundice associated with past estrogen use or with pregnancy, caution should be exercised, and in the case of recurrence, medication should be discontinued.

## Hypothyroidism

Estrogen administration leads to increased thyroid-binding globulin (TBG) levels. Women with normal thyroid function can compensate for the increased TBG by making more thyroid hormone, thus maintaining free T<sub>4</sub> and T<sub>3</sub> serum concentrations in the normal range. Women dependent on thyroid hormone replacement therapy who are also receiving estrogens may require increased doses of their thyroid replacement therapy. These women should have their thyroid function monitored in order to maintain their free thyroid hormone levels in an acceptable range.

## Fluid Retention

Estrogens may cause some degree of fluid retention. Patients with conditions that might be influenced by this factor, such as cardiac or renal dysfunction, warrant careful observation when estrogens are prescribed.

## Hypocalcemia

Estrogens should be used with caution in individuals with hypoparathyroidism as estrogen-induced hypocalcemia may occur.

## Exacerbation of Endometriosis

A few cases of malignant transformation of residual endometrial implants have been reported in women treated post-hysterectomy with estrogen-alone therapy. For women known to have residual endometriosis post-hysterectomy, the addition of progestin should be considered.

## Exacerbation of Other Conditions

Estrogen therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomas and should be used with caution in women with these conditions.

## Effects on Barrier Contraception

PREMARIN Vaginal Cream exposure has been reported to weaken latex condoms. The potential for PREMARIN Vaginal Cream to weaken and contribute to the failure of condoms, diaphragms, or cervical caps made of latex or rubber should be considered.

## Laboratory Tests

Serum follicle stimulating hormone and estradiol levels have not been shown to be useful in the management of moderate to severe symptoms of vulvar and vaginal atrophy.

## Drug-Laboratory Test Interactions

Accelerated prothrombin time, partial thromboplastin time, and platelet aggregation time; increased platelet count; increased factors II, VII antigen, VIII coagulant activity, IX, X, XII, VII-X complex, II-VII-X complex, and beta-thromboglobulin; decreased levels of antifactor Xa and antithrombin III, decreased antithrombin III activity; increased levels of fibrinogen and fibrinogen activity; increased plasminogen antigen and activity.

Increased thyroid-binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by protein-bound iodine (PBI), T<sub>4</sub> levels (by column or by radioimmunoassay) or T<sub>3</sub> levels by radioimmunoassay. T<sub>3</sub> resin uptake is decreased, reflecting the elevated TBG. Free T<sub>4</sub> and free T<sub>3</sub> concentrations are unaltered. Women on thyroid replacement therapy may require higher doses of thyroid hormone.

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-antitrypsin, ceruloplasmin).

Increased plasma HDL and HDL<sub>2</sub> cholesterol subfraction concentrations, reduced LDL cholesterol concentrations, increased triglyceride levels.

Impaired glucose tolerance.

## ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the labeling:

- Cardiovascular Disorders [see Boxed Warning, Warnings and Precautions (5.2)]
- Endometrial Cancer [see Boxed Warning, Warnings and Precautions (5.3)]

## Clinical Study Experience

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

In a 12-week, randomized, double-blind, placebo-controlled trial of PREMARIN Vaginal Cream (PVC), a total of 423 postmenopausal women received at least 1 dose of study medication and were included in all safety analyses: 143 women in the PVC-21/7 treatment group (0.5 g 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), 68 women in the matching placebo treatment group. A 40-week, open-label extension followed, in which a total of 394 women received treatment with PVC, including those subjects randomized at baseline to placebo. In this study, the most common adverse reactions ≥ 5 percent are shown below (Table 1) [see Clinical Studies (14.1) in full Prescribing Information].

Body System <sup>a</sup> Adverse Event	Treatment			
	PVC 21/7 (n=143)	Placebo 21/7 (n=72)	PVC 2x/wk (n=140)	Placebo 2x/wk (n=68)
Number (%) of Patients with Adverse Event				
Any Adverse Event	95 (66.4)	45 (62.5)	97 (69.3)	46 (67.6)
<b>Body As A Whole</b>				
Abdominal Pain	11 (7.7)	2 (2.8)	9 (6.4)	6 (8.8)
Accidental Injury	4 (2.8)	5 (6.9)	9 (6.4)	3 (4.4)
Asthenia	8 (5.6)	0	2 (1.4)	1 (1.5)
Back Pain	7 (4.9)	3 (4.2)	13 (9.3)	5 (7.4)
Headache	16 (11.2)	9 (12.5)	25 (17.9)	12 (17.6)
Infection	7 (4.9)	5 (6.9)	16 (11.4)	5 (7.4)
Pain	10 (7.0)	3 (4.2)	4 (2.9)	4 (5.9)
<b>Cardiovascular System</b>				
Vasodilatation	5 (3.5)	4 (5.6)	7 (5.0)	1 (1.5)

System	1	2	3	4
<b>Digestive System</b>				
Diarrhea	4 (2.8)	2 (2.8)	10 (7.1)	1 (1.5)
Nausea	5 (3.5)	4 (5.6)	3 (2.1)	3 (4.4)
<b>Musculoskeletal System</b>				
Arthralgia	5 (3.5)	5 (6.9)	6 (4.3)	4 (5.9)
<b>Nervous System</b>				
Insomnia	6 (4.2)	3 (4.2)	4 (2.9)	4 (5.9)
<b>Respiratory System</b>				
Cough Increased	0	1 (1.4)	7 (5.0)	3 (4.4)
Pharyngitis	3 (2.1)	2 (2.8)	7 (5.0)	3 (4.4)
Sinusitis	1 (0.7)	3 (4.2)	2 (1.4)	4 (5.9)
<b>Skin And Appendages</b>				
	12 (8.4)	7 (9.7)	16 (11.4)	3 (4.4)
<b>Urogenital System</b>				
Breast Pain	8 (5.6)	1 (1.4)	4 (2.9)	0
Leukorrhoea	3 (2.1)	2 (2.8)	4 (2.9)	6 (8.8)
Vaginitis	8 (5.6)	3 (4.2)	7 (5.0)	3 (4.4)

<sup>a</sup> 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 reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

### Genitourinary System

Abnormal uterine bleeding/spotting, dysmenorrhea/pelvic pain, increase in size of uterine leiomyomata, vaginitis (including vaginal candidiasis), change in cervical secretion, cystitis-like syndrome, application site reactions of vulvovaginal discomfort, (including burning, irritation, and genital pruritus), endometrial hyperplasia, endometrial cancer, precocious puberty, leukorrhoea.

### Breasts

Tenderness, enlargement, pain, discharge, fibrocystic breast changes, breast cancer, gynecomastia 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.

### Eyes

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, hypersensitivity.

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

## DRUG INTERACTIONS

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

## Metabolic Interactions

*In vitro* and *in vivo* studies have shown that estrogens are metabolized partially by cytochrome P450 3A4 (CYP3A4). Therefore, inducers or inhibitors of CYP3A4 may affect estrogen drug metabolism. Inducers of CYP3A4, such as St. John's Wort (*Hypericum perforatum*) preparations, phenobarbital, carbamazepine, and rifampin, may reduce plasma concentrations of estrogens, possibly resulting in a decrease in therapeutic effects and/or changes in the uterine bleeding profile. Inhibitors of CYP3A4, such as erythromycin, clarithromycin, ketoconazole, itraconazole, ritonavir and grapefruit juice, may increase plasma concentrations of estrogens and may result in side effects.

## USE IN SPECIFIC POPULATIONS

### Pregnancy

PREMARIN Vaginal Cream should not be used during pregnancy [see Contraindications (4)]. There appears to be little or no increased risk of birth defects in children born to women who have used estrogens and progestins as an oral contraceptive inadvertently during early pregnancy.

### 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 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 (14.2) 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].

## Renal Impairment

The effect of renal impairment on the pharmacokinetics of PREMARIN Vaginal Cream has not been studied.

## Hepatic Impairment

The effect of hepatic impairment on the pharmacokinetics of PREMARIN Vaginal Cream has not been studied.

## OVERDOSAGE

Overdosage of estrogen may cause nausea and vomiting, breast tenderness, dizziness, abdominal pain, drowsiness/fatigue, and withdrawal bleeding in women. Treatment of overdose consists of discontinuation of PREMARIN therapy with institution of appropriate symptomatic care.

This brief summary is based on PREMARIN Vaginal Cream Prescribing Information W10413C018 ET01, Rev 11/09.

