CONTRACEPTIVE TECHNOLOGY UPDATE®

A Monthly Update on Contraception and Sexually Transmitted Diseases

AHC Media LLC

IN THIS ISSUE

Statement of Financial Disclosure:
Consulting Editor **Robert A. Hatcher**, MD, MPH, Author **Rebecca Bowers**, Associate Publisher **Coles McKagen**, Senior Managing Editor **Joy Dickinson**, and **Adam Sonfield** (Washington Watch Columnist) report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. **Sharon Schnare** (Nurse Reviewer) discloses that she is a retained consultant and a speaker for Barr Laboratories, Berlex, and Organon; she is a consultant for 3M Pharmaceuticals; and she is a speaker for FEI Women's Health, Ortho-McNeil Pharmaceuticals, and Wyeth-Ayerst Pharmaceuticals.

NOVEMBER 2008
VOL. 29, NO. 11 • (pages 121-132)

New guidance underscores DMPA's safety, efficacy in long-term use

Concerns about bone density should not prevent provision or limit use

Concerns about the effects of the contraceptive injection depot medroxyprogesterone acetate (DMPA, Depo-Provera, Pfizer, New York City; Medroxyprogesterone Acetate Injectable Suspension USP, Teva Pharmaceuticals USA, North Wales, PA) on bone mineral density (BMD) should not prevent clinicians from prescribing the method, nor should its use be limited to two years, according to a new committee opinion released by the American College of Obstetricians and Gynecologists (ACOG).[1]

In November 2004, the Food and Drug Administration (FDA) added a "black box" warning to the drug's labeling to highlight that prolonged use may result in BMD loss. The warning advised that bone loss in women who use Depo-Provera is greater with increased duration of use and may not be completely reversible. The injectable contraceptive should be used as a long-term birth control method (longer than two years) only if other birth control methods are inadequate, the updated label advised.

DMPA has been associated with losses of BMD at the hip and spine of 0.5% to 3.5% after one year of use, and 5.7% to 7.5% after two years.[2-5] DMPA's greatest effect on BMD occurs during the first few years of use.[5,6] However, BMD has been demonstrated to return to levels at or near baseline at two years after the discontinuation of DMPA.[7,8]

Women should be thoroughly counseled about the risks and benefits

Start the new year with results from the Contraception Survey

Looking for the results of the 2008 Contraception Survey, mailed to readers of *Contraceptive Technology Update*? Results of the annual survey will be included in the January 2009 issue. To obtain a comprehensive overview of current contraceptive use, read the January 2009 issue!

of DMPA so they can make an informed decision about whether it is right for them," says **Denise Jamieson**, MD, chair of ACOG's Committee on Gynecologic Practice.

"Many women would choose the theoretical risk of future fracture over the very real risk of an unintended pregnancy," says Jamieson. "For example, a teen at high risk of pregnancy, who faces a similar rate of bone loss from either pregnancy or DMPA use, may find the risk worthwhile."

Contraceptive Technology Update® (ISSN 0274-726X), including **STD Quarterly**™, is published monthly by AHC Media LLC, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to *Contraceptive Technology Update*®, P.O. Box 740059, Atlanta, GA 30374.

Subscriber Information

Customer Service: (800) 688-2421 or fax (800) 284-3291. E-mail: (customerservice@ahcmedia.com). Hours of operation: 8:30 a.m.-6 p.m. Monday-Thursday; 8:30 a.m.-4:30 p.m. Friday, EST.

Subscription rates: U.S.A., one year (12 issues), $499. Add $17.95 for shipping & handling. Outside U.S., add $30 per year, total prepaid in U.S. funds. Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482. **Back issues**, when available, are $75 each.(GST registration number R128870672.)

Editor: **Rebecca Bowers**.
Associate Publisher: **Coles McKagen** (404) 262-5420 (coles.mckagen@ ahcmedia.com).
Senior Managing Editor: **Joy Daughtery Dickinson** (229) 551-9195 (joy.dickinson@ahcmedia.com).
Senior Production Editor: **Nancy McCreary**.

Editorial Questions

Questions or comments?
Call **Joy Daughtery Dickinson** (229) 551-9195.

Use affirmed by WHO

The ACOG opinion falls in line with a similar review issued by the World Health Organization in 2005. The international health agency convened a technical consultation to review the complete body of evidence regarding the effects of hormonal contraception on bone mineral density and fracture risk. Guidance issued following the consultation advises:

- There should be no restriction on the use of DMPA, including no restriction on duration of use, among women ages 18-45 who are otherwise eligible to use the method.
- Among adolescents (menarche to those below age 18) and women over 45, the advantages of using DMPA generally outweigh the theoretical safety concerns regarding fracture risk. Since data are insufficient to determine if circumstances are similar in long-term use among these age groups, the overall risks and benefits for continuing use of the method should be reconsidered over time with the individual user.[9]

While a 2005 editorial in the journal *Contraception* called for the FDA to "consider revising or rescinding the black box warning to reflect current science regarding DMPA use and

EXECUTIVE SUMMARY

Concerns about the effects of depot medroxyprogesterone acetate (DMPA) on bone mineral density (BMD) should not prevent clinicians from prescribing the method, nor should its use be limited to two years, states a new committee opinion released by the American College of Obstetricians and Gynecologists.

- A "black box" warning was added to DMPA labeling in 2004 advising that prolonged use may result in BMD loss. The labeling cautioned that DMPA should be used as a long-term birth control method (longer than two years) only if other birth control methods were inadequate.
- There should be no restriction on the use of DMPA, including no restriction on duration of use, among women ages 18-45 who are otherwise eligible to use the method, according to the World Health Organization.

skeletal health," the FDA has not revised the drug's labeling.[10]

Put it in perspective

Bone loss in reproductive-age women is not exclusive to DMPA users, the ACOG opinion notes. Adult women show similar rates of temporary bone loss during pregnancy and breastfeeding (2-8% and 3-5%, respectively) when compared with BMD loss sustained by DMPA users (approximately 3-5%).[11-12]

Teens who use DMPA lose BMD at a time when their BMD typically would increase, which can be a cause of concern, the opinion notes. However, while low BMD is linked to an increased risk of fracture in older women, no studies have linked DMPA-related BMD loss with increased rates of fracture in younger women with a low-fracture risk, the opinion states.[1]

Shot makes its mark

More than two million American women use DMPA, including approximately 400,000 teens, according to national data.[13] With correct and consistent use, the probability of pregnancy is only 0.3%.[14]

"DMPA has a number of characteristics that make it particularly appealing to certain populations such as adolescents or women who may have a hard time successfully using a daily or partner-dependent method of contraception," says Jamieson. "Some women also prefer it over other methods of contraception because of the privacy that it provides."

Daily exercise and age-appropriate calcium and Vitamin D intake should be encouraged in DMPA users, especially in teens, who often do not get enough calcium. The Institute of Medicine recommended average daily intake of calcium for teens ages 14-18 is 1,300 mg; for women ages 19-50, 1,000 mg.[15] While studies have shown that low-dose estrogen supplementation slows bone DMPA bone loss, ACOG does not currently recommend such practice.[1] This research, however, also demonstrates that in adult and adolescent women, BMD recovers after DMPA is discontinued, which renders it unlikely that women in either group would benefit from estrogen supplementation.[16]

In counseling women on DMPA use, be sure to counsel on breakthrough bleeding to help women continue on the method.[1] Language suggested by *Contraceptive Technology* might help explain DMPA's impact on periods:

"DMPA makes a woman's periods less regular, and spotting between periods is fairly common. Eventually most women stop having periods completely. This is not harmful. Do not choose DMPA unless you do not mind having your periods change."[13]

References

1. ACOG Committee Opinion No. 415: Depot Medroxyprogesterone Acetate and Bone Effects. *Obstet Gynecol* 2008;112:727-730.
2. Berenson AB, Radecki CM, Grady JJ, et al. A prospective, controlled study of the effects of hormonal contraception on bone mineral density. *Obstet Gynecol* 2001; 98:576-582.
3. Ulrich CM, Georgiou CG, Snow-Harter CM, et al. Bone mineral density in mother-daughter pairs: relations to lifetime exercise, lifetime milk consumption, and calcium supplements. *Am J Clin Nutr* 1996; 63:72-79.
4. Santelli JS, Abma J, Ventura S, et al. Can changes in sexual behaviors among high school students explain the decline in teen pregnancy rates in the 1990s? *J Adolesc Health* 2004; 35:80-90.
5. Clark MK, Sowers MR, Nichols S, et al. Bone mineral density changes over two years in first-time users of depot medroxyprogesterone acetate. *Fertil Steril* 2004; 82:1,580-1,586.
6. Scholes D, LaCroix AZ, Ichikawa LE, et al. Injectable hormone contraception and bone density: results from a prospective study. *Epidemiology* 2002; 13:581-587.
7. Scholes D, LaCroix AZ, Ichikawa LE, et al. Change in bone mineral density among adolescent women using and discontinuing depot medroxyprogesterone acetate contraception. *Arch Pediatr Adolesc Med* 2005; 159:139-144.
8. Kaunitz AM, Miller PD, Rice VM, et al. Bone mineral density in women aged 25-35 years receiving depot medroxyprogesterone acetate: recovery following discontinuation. *Contraception* 2006; 74:90-99.
9. World Health Organization. *Technical Consultation on the Effects of Hormonal Contraception on Bone Health.* Geneva, Switzerland; 2005. Accessed at www.who.int/reproductive-health/publications/hc_bonehealth/consultation_rpt.pdf.
10. Kaunitz AM. Depo-Provera's black box: time to reconsider? *Contraception* 2005; 72:165-167.
11. Karlsson C, Obrant KJ, Karlsson M. Pregnancy and lactation confer reversible bone loss in humans. *Osteoporos Int* 2001; 12:828-834.
12. Sowers M, Corton G, Shapiro B, et al. Changes in bone density with lactation. *JAMA* 1993; 269:3,130-3,135.
13. Mosher WD, Martinez GM, Chandra A, et al. Use of contraception and use of family planning services in the United States: 1982-2002. *Adv Data* 2004; 350:1-36.
14. Hatcher RA, Trussell J, Nelson AL, et al. *Contraceptive Technology*. 19th revised edition. New York: Ardent Media; 2007.
15. National Institutes of Health. *Dietary Supplement Fact Sheet: Calcium.* Fact sheet. Accessed at ods.od.nih.gov/fact-

sheets/calcium.asp.
16. Association of Reproductive Health Professionals. Labeling Changes for Depot Medroxyprogesterone Acetate. Fact sheet. Accessed at www.arhp.org/Publications-and-Resources/Clinical-Fact-Sheets/DMPA. ■

Research focuses on rapid HIV testing

Is rapid HIV testing in use in your family planning facility? Findings from a 2007 survey conducted by the National Alliance of State and Territorial AIDS Directors Rapid point to "yes"; 94% of health departments indicated they use rapid HIV testing as part of health department-supported HIV testing programs.[1]

Results from a recently released study indicate that the OraQuick Advance test (OraSure Technologies, Bethlehem, PA), when conducted on oral fluid in a low-prevalence emergency department population, might lead to a high rate of false-positive results.[2]

In the study, researchers at Brigham and Women's Hospital (BWH) in Boston report that out of 849 adults tested with the oral rapid HIV test, 31 had reactive results. Five patients were truly HIV-infected upon confirmation. Investigators found 84% of positive rapid screening tests turned out to be false when further testing documented that the patient did not have HIV infection.[2]

The news follows recent reports regarding similar false-positive readings from the New York City Department of Health and Mental Hygiene. Between October 2007 and April 2008, the agency documented a higher-than-usual percentage of false-positive oral HIV tests in its sexually transmitted disease (STD) clinics, with the false-positive rate reaching 1.1% in some months.[3] While the rate is below the Food and Drug Administration (FDA) threshold of 2%, it is higher than expected.

In a statement issued to *Contraceptive Technology Update*, OraSure officials say that test accuracy rates remain within the FDA-approved and expected range of performance, based on monthly data from "hundreds of thousands of tests" conducted annually in New York and around the nation.[4] However, the company states it takes every customer inquiry or discordant situation very seriously and is working closely with BWH and the New York City health department to resolve any concerns about the performance of the test.

EXECUTIVE SUMMARY

Results from a recently released study indicate that the OraQuick Advance rapid HIV test, when conducted on oral fluid in a low-prevalence emergency department population, might lead to a high rate of false-positive results.

- The news follows recent reports regarding similar false-positive readings from the New York City Department of Health and Mental Hygiene, with the false-positive rate reaching 1.1% in some months. The manufacturer of the test is working with both organizations to alleviate any concerns about the test.
- The Centers for Disease Control and Prevention continues to encourage the use of oral fluid rapid HIV tests due to their role in HIV prevention.

Review the study

To perform the current study, BWH researchers recruited adults without known HIV disease who were patients at the hospital emergency department. Investigators collected oral samples from the patients and processed them in the emergency department laboratory, where they were read within 20-40 minutes. If results were negative, patients received no further testing for HIV; if results were reactive, patients had a blood test to confirm HIV infection. Confirmatory tests included a serum enzyme-linked immunoassay, a Western blot test, CD4 (cluster of differentiation 4) count, and plasma HIV-1 RNA (ribonucleic acid) level.

Researchers then examined the number of patients who had both reactive results and confirmed HIV infection. Of the 849 adults included in the study, 39 had a reactive rapid oral HIV test. Confirmatory tests showed that five of the 39 patients were HIV-infected, which yielded a 0.6% prevalence rate of HIV infection in the study population. Specificity of the oral test in this setting was 96.9% (95% confidence interval, 95.7% to 98.1%).

Tests key in HIV fight

In 2006, the Centers for Disease Control and Prevention (CDC) called for voluntary HIV screening among all patients ages 13-64.[5]

Does the CDC still recommend oral fluid rapid HIV tests? Yes, according to information released following the New York report.[6] The agency says

it continues to encourage the use of oral fluid rapid HIV tests "not only because they allow for testing to be done in many more settings than before, particularly non-clinical settings, but also because they offer the potential to increase the number of persons who are tested and who receive their test results."[6]

"It is important to note, however, that users need to be aware of the potential for unexplained variability in the rate of false-positive test results and the need to follow a reactive (positive) oral fluid rapid test with a confirmatory test," states the CDC guidance. "Finally, before using any rapid HIV test, patients should be informed that reactive rapid HIV test results are preliminary and require confirmation."

In the United States, there are six FDA-approved rapid HIV tests: OraQuick Advance, Clearview Stat-Pak, Clearview Complete (both from Inverness Medical Professional Diagnostics, Waltham, MA), Trinity Uni-Gold (Trinity Biotech, Bray, Ireland), Reveal G-3 Rapid HIV-1 Antibody Test (MedMira, Halifax, Nova Scotia, Canada), and MultiSpot HIV-1/HIV-2 Rapid Test (BioRad Laboratories, Hercules, CA). Such tests have been in use for many years in international markets; sensitivity data provided in support of licensure indicate such tests are at least as sensitive as traditional enzyme immunoassay tests.[7]

Rapid HIV testing represents an expanding field of knowledge; the more providers use these tests in different settings, the more is learned, states **Rochelle Walensky**, MD, MPH, associate professor at Harvard Medical School and an infectious disease physician at BWH. "We continue to use the OraSure test in the emergency department," says Walensky, who served as lead author of the current study.

With rapid testing, providers need to keep in mind two important points, says Walensky. First, all results should be considered preliminary until they are confirmed, and second, patients should be encouraged to follow up on test results, with providers responsible for facilitating that follow-up, she states. "We offer confirmation testing onsite, and we stay in close contact with the patient so that we can facilitate linkage of care for them," states Walensky.

References

1. National Alliance of State and Territorial AIDS Directors. *Report on Findings from an Assessment of Health Departments Efforts to Implement HIV Screening in Health Care Settings.* Accessed at www.nastad.org/Docs/highlight/2008717_NASTAD_Rapid_Testing_Implementation_Report_071608.pdf.

2. Walensky RP, Arbelaez C, Reichmann WM, et al. Revising expectations from rapid HIV tests in the emergency department. *Ann Intern Med* 2008; 149:153-160.

3. Centers for Disease Control and Prevention (CDC). False-positive oral fluid rapid HIV tests -- New York City, 2005-2008. *MMWR* 2008; 57:660-665.

4. OraSure Technologies. Nationwide Data Indicate a Very High Degree of Accuracy for OraQuick ADVANCE Rapid HIV-1/2 Antibody Test with Oral Fluid. Press release. Accessed at phx.corporate-ir.net/phoenix.zhtml?c=99740&p=irol-newsArticle&ID=1166494&highlight=.

5. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep* 2006; 55(RR-14):1-17; quiz CE1-4.

6. Centers for Disease Control and Prevention. *Questions and Answers: False-Positive Oral Fluid Rapid HIV Tests.* Accessed at www.cdc.gov/hiv/topics/testing/rapid/oral-fluid_qa.htm.

7. Paul SM, Martin EG. H*IV Test Recommendations, Assay Selection.* Accessed at lpn.advanceweb.com/Article/HIV-Test-Recommendations-Assay-Selection.aspx?CP=4. ■

Time to step up HIV testing in women

Review the last three patient charts: a 19-year-old college student, a 26-year-old mother of two, and a 43-year-old woman who is newly divorced. Which women were offered screening for HIV?

All of them, if your practice is following new guidance issued by the American College of Obstetricians and Gynecologists (ACOG).[1] The ACOG recommendations fall in line with those issued in 2006 by the Centers for Disease Control and Prevention (CDC) calling for voluntary HIV screening among all patients ages 13-64.[2]

The ACOG recommendations call for routinely screening all women between ages 19 and 64 for HIV. Targeted screening should be performed in women outside the age range who are at high risk, such as sexually active teens under age 19 and women older than 64 who have had multiple partners in recent years, the ACOG guidance advises.[1]

HIV testing rates have remained fairly stable from 2001 through 2006. While 10% of adults ages 18-64 report getting tested each year, the percentage of people who report ever being tested in their lifetimes has not increased, according to

EXECUTIVE SUMMARY

New guidance issued by the American College of Obstetricians and Gynecologists (ACOG) calls for routinely screening all women between the ages of 19 and 64 for HIV.

- Targeted screening should be performed in women outside the age range who are at high risk, such as sexually active teens under age 19 and women older than 64 who have had multiple partners in recent years.
- While all women should be screened for HIV, providers and their patients must be aware that women of color are disproportionately affected by the disease, according to a second advisory issued ACOG.

new surveillance from the Centers for Disease Control and Prevention (CDC).[3]

HIV testing is the essential first step in linking people with HIV to medical care and ongoing support to help them maintain safer behaviors, says Melissa Shepherd, acting chief of the CDC's Division of HIV/AIDS Prevention's Technical Information and Communications Branch. Most new infections are believed to be transmitted by individuals who are unaware of their infection, says Shepherd. Studies show that once individuals learn they are HIV-infected, most will take steps to protect their partners, she notes.

Women of color at risk

While all women should be screened for HIV, providers and their patients must be aware that women of color are disproportionately affected by the disease, advises a second committee opinion issued by ACOG.[4]

The CDC estimates 56,300 HIV infections occurred in the United States in 2006. According to the CDC analysis, infection rates among blacks were seven times as high as whites (83.7/100,000 people versus 11.5/100,000) and almost three times as high as Hispanics (29.3/100,000 people).[5]

Women of color are acquiring HIV at higher rates compared with other groups, says **Maureen Phipps**, MD, MPH, director of the research division of the obstetrics and gynecology department and associate professor in the departments of obstetrics and gynecology and community health at the Warren Alpert Medical School of Brown University in Providence, RI. "Being able to diagnose a person with HIV early on is important because they need to receive appropriate medications and on-going health care," says Phipps, who served as a co-author of the ACOG committee opinion. "Early diagnosis is also important for the person to become well-educated about how to prevent transmitting the disease to others."

The CDC is working to fight HIV among African Americans through the Heightened National Response, a partnership of CDC, public health partners, and African American community leaders. The partnership is designed to build upon progress in four key areas: expanding prevention services, increasing testing, developing new interventions, and mobilizing broader community action. One such initiative is "Take Charge. Take the Test," a one-year HIV testing social marketing campaign for African-American women in Cleveland and Philadelphia. The campaign, held October 2006 to 2007, promoted local toll-free HIV testing hotlines through radio, print, and billboard advertisements. Preliminary findings indicate that the campaign exposure led to increases in information-seeking behavior.[6]

Shepherd says, "Social marketing campaigns such as `Take Charge, Take the Test' about HIV testing are designed to increase knowledge of HIV status and to promote HIV risk reduction. "These campaigns are important components of the CDC's comprehensive program for HIV prevention."

References

1. American College of Obstetricians and Gynecologists. ACOG committee opinion. Routine human immunodeficiency virus screening. *Obstet Gynecol* 2008; 112(2 Pt 1):401-403.
2. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep* 2006; 55(RR-14):1-17; quiz CE1-4.
3. Centers for Disease Control and Prevention (CDC). Persons tested for HIV -- United States, 2006. *MMWR* 2008; 57:845-849.
4. American College of Obstetricians and Gynecologists. ACOG committee opinion. Human immunodeficiency virus and acquired immunodeficiency syndrome and women of color. *Obstet Gynecol* 2008; 112(2 Pt 1):413-416.
5. Hall HI, Song R, Rhodes P, et al. Estimation of HIV Incidence in the United States. *JAMA* 2008; 300:520-529.
6. Davis K, Uhrig J, Goetz J, et al. Effectiveness of an HIV testing campaign in increasing HIV hotline calls and HIV testing rates among African American women. Presented at the 136th annual American Public Health Association meeting. San Diego; October 2008. ■

Cost-effectiveness study eyes HPV vaccine

What is the most cost-effective approach to administering vaccination against human papillomavirus (HPV)? A just-released analysis concludes vaccination will be optimized by achieving universal vaccine coverage in young adolescent girls, targeting initial "catch-up" efforts to vaccinate women younger than age 21, and by revising current screening policies.[1]

Gardasil (Merck & Co., Whitehouse Station, NJ) is the only HPV vaccine approved by the Food and Drug Administration (FDA). It is designed to protect against infection from four HPV types, including two types (HPV 16 and 18) that cause about 70% of cervical cancers. The vaccine received an additional approval in September 2008 for the prevention of vaginal and vulvar cancer caused by HPV types 16 and 18.[2] Given in three doses over six months, the vaccine series costs about $360.

Gardasil is approved for women ages 9-26. The Centers for Disease Control and Prevention (CDC) recommends the vaccine for all girls ages 11-12, with "catch-up" doses for those ages 13-26 who missed earlier vaccination.

To perform the analysis, researchers at the Harvard School of Public Health synthesized epidemiologic, clinical, and demographic information using sophisticated computer models to simulate the U.S. population. Researchers designed computer models to predict the health outcomes of girls and women who get the vaccination as well as Pap tests or other screenings, which still are recommended for vaccine recipients. Calculations included the cost of the vaccine, screenings, and treating cervical cancer and other illnesses targeted by the vaccine. While the study focused on the prevention of cervical disease, investigators also looked at the benefits of the vaccine on genital warts and its possible benefits of averting other HPV-related cancers and conditions.

What were the results?

Analysis findings indicate that vaccination against HPV-16 and HPV-18 would lead to lower cervical cancer rates and be economically attractive if high coverage can be achieved in the most important target group of 12-year-old girls, and if vaccine protection against infection lasted for at least 20 years. If most 12-year-old girls are vaccinated, their future cervical cancer screening could begin somewhat later than currently recommended and be conducted less frequently, the analysis suggests.

A catch-up program for girls ages 13-18 appears to offer benefits and be reasonably cost-effective, compared to other vaccine programs in the United States, researchers note. The cost-effectiveness of extending the catch-up program to age 21 is less certain and depends on whether the vaccine eventually will be proven to prevent other cancers caused by HPV-16 and -18. Extending the catch-up program to those up to age 26 was consistently not cost-effective due to the vaccine's expense, investigators conclude.

Results of the analysis could change if future information shows that vaccine protection does not last, or if there is an unexpected increase in other cancer-causing HPV types not included in the vaccine, caution the researchers. "Our results are the best prediction we can make with the information available now, but it will be critical to update the analysis as we learn more about the long-term vaccine effects," states **Jane Kim**, PhD, MSc, assistant professor of health decision science in the Department of Health Policy and Management at Harvard School of Public Health and co-author of the paper.

Why is it so important to continue with the current strategy of universal vaccination with pre-adolescent girls together with a "catch up" program for older females who have not been

EXECUTIVE SUMMARY

Vaccination against human papillomavirus (HPV) will be optimized by achieving universal vaccine coverage in young adolescent girls, targeting initial "catch-up" efforts to vaccinate women younger than age 21, and by revising current screening policies, states a new analysis.

- The HPV vaccine Gardasil is approved for women ages 9-26. It is recommended for all girls ages 11-12, with "catch-up" doses for those ages 13-26 who missed earlier vaccination.
- Gardasil is designed to protect against infection from four HPV types, including two types that cause about 70% of cervical cancers. The vaccine also has received an additional approval for the prevention of vaginal and vulvar cancer caused by HPV types 16 and 18.

vaccinated? Gardasil works best when given prior to exposure to HPV types 6, 11, 16, and 18, explains **Tracy Ogden**, a Merck spokesperson. The optimal administration of the vaccine is before the onset of sexual activity, Ogden notes.

A catch-up vaccination program works because even among those who are sexually active, it is unlikely that anyone would have been exposed to all four types of the HPV virus that Gardasil protects against, states Ogden. People who are infected with one type of HPV still would receive protection from the other three HPV types covered by the vaccine, says Ogden. "That's why the CDC's Advisory Committee on Immunization Practices [ACIP] recommends catch-up vaccination for females aged 13 to 26 years who have not been previously vaccinated," Ogden states.

ACIP has not considered changing its current recommendation for catch-up vaccination of females ages 13-26, according to a press statement issued by the CDC.[3] It recently reviewed the HPV cost-effectiveness analysis during its deliberations on recommendations for use of HPV vaccine in women age 27 years and older. The committee continues to review new information and data as they become available.[3]

Opportunity to discuss contraceptives

The provision of the HPV vaccine for girls ages 11-12 offers family planning programs an important way to serve young girls and initiate at a very young age the discussion of the use of contraception to prevent unintended pregnancy, says **Robert Hatcher**, MD, MPH, professor of gynecology and obstetrics at Emory University School of Medicine in Atlanta.

"This discussion is one of the most important components of preconceptional care, offering providers the opportunity to discuss the importance of folic acid for all women in their reproductive years, delaying intercourse until a girl is certain that it is something she wants to do, and of course, the use of condoms to prevent infection and other effective contraceptive methods," Hatcher says.

References

1. Kim JJ, Goldie SJ. Health and economic implications of HPV vaccination in the United States. *N Engl J Med* 2008; 359:821-832.

2. Food and Drug Administration. FDA Approves Expanded Uses for Gardasil to Include Preventing Certain Vulvar and Vaginal Cancers. Press release. Sept. 12, 2008. Accessed at www.fda.gov/bbs/topics/NEWS/2008/NEW01885.html.

3. Centers for Disease Control and Prevention. HPV Vaccine -- Cost-Effectiveness of HPV Vaccine. Press release. Aug. 28, 2008. Accessed at www.cdc.gov/vaccines/vpd-vac/hpv/cost-effect-hpv-vac.htm. ■

Extend the option of extended contraception

Take a poll among your female patients about their preferences surrounding their menstrual cycle. How many would prefer to get their periods less often?

Results of a new national survey show that while about three-quarters of women polled would prefer to get their period less often, just 8% report having tried extended or continuous contraceptive pills.[1]

What impedes women from considering continuous contraception with birth control pills? Women polled for the survey noted concern about long-term side effects, belief that it is not healthy to have a period less than once a month, and lack of interest in oral contraceptives.[1]

Continuous contraceptive pills have risks and long-term side effects that are very similar to standard, monthly birth control pills, the most widely used form of contraceptive, says **Elizabeth Battaglino Cahill**, RN, executive director of the National Women's Health Resource Center, which authorized the survey. Women need to talk with their health care provider and learn more about their options when it comes to managing their menstrual cycle to fit with their lifestyle choices, Cahill notes.

When talking with women about menstrual suppression with oral contraceptives, explain that there is no medical or health reason to bleed while on hormonal contraceptives, advises the Association of Reproductive Health Professionals (ARHP).[2] Counsel women that menstrual blood does not build up when they are using hormonal birth control.

What should you tell women when it comes to safety issues? Research on use of extended/continuous methods appears comparable to that of conventional OC regimens, the ARHP states. Women can expect return to fertility after discontinuation of extended/continuous use pills to be the same as that found in conventional pill use.[3]

EXECUTIVE SUMMARY

Results of a new national survey show that while about three-quarters of women polled would prefer to get their period less often, just 8% report having tried extended or continuous contraceptive pills.

- Providers are familiar with suppressing menses with monophasic combined oral contraceptives. There are two dedicated extended-use pills and one dedicated continuous-use pill. Three other pills offer shortened pill-free intervals.
- Extended and continuous regimens of birth control pills can help manage conditions such as polycystic ovary syndrome, endometriosis, menstrual migraine, premenstrual syndrome, and seizures in women that occur exclusively or more commonly at menses.

What are some of the benefits of suppressing menstruation? It can help manage menstruation-related conditions, such as polycystic ovary syndrome, endometriosis, menstrual migraine, premenstrual syndrome, and seizures in women that occur exclusively or more commonly at the time of menses. Menstrual suppression works well for active lifestyles and athletic activities; also, it reduces/eliminates the need to purchase and carry hygiene products.

Continuous oral contraceptives might be more effective than the standard 28-day birth control pills in suppressing the ovary, according to newly published research.[5]

What are some of the chief benefits of the continuous OC regimen when it comes to improvement in pain and behavioral changes? "I believe it is due to the constant suppression of endogenous ovarian activity which creates a stable hormonal environment without fluctuations in ovarian hormones and their associated negative mood and physical effects, [such as] discomfort from ovarian cyst development and withdrawal bleeding," says the study's lead author, **Richard Legro**, MD, professor of obstetrics and gynecology, Penn State College of Medicine.

Talk about bleeding

Women who choose oral contraceptives in extended or continuous regimens should be counseled that unpredictable breakthrough bleeding is initially more common than with conventional pills. according to the ARHP. Bleeding will lessen as the body adjusts to the new hormone balance.[4]

In using pills in an extended or continuous manner, advise patients that it might be more difficult to detect pregnancy, counsels the ARHP.

References

1. Harris Interactive Inc. prepared for The National *Women's Health Resource Center. Menstrual Management Survey Report.* Aug. 29, 2008. Accessed at www.healthywomen.org/Documents/MenstrualManagementReport.pdf.
2. Association of Reproductive Health Professionals. *What You Need to Know. Menstrual Suppression.* Fact sheet. Accessed at www.arhp.org/uploadDocs/menstruationfactsheet.pdf.
3. Legro RS, Pauli JG, Kunselman AR, et al. Effects of continuous versus cyclical oral contraception: a randomized controlled trial. *J Clin Endocrinol Metab* 2008; 93:420-429. ■

Treatment for PMDD? New OC regimen eyed

(Editor's note: This story discusses off label use of a medication)

Review the chart for the next patient. According to her history, for about 10 days of every month, she experiences depression, marked anxiety, sudden mood shifts, persistent irritability, and bloating. While the symptoms disappear with the onset of her menstrual cycle, when they are present, they are severe enough to interfere with her relationships and work activities. What's your call?

Look at premenstrual dysphoric disorder (PMDD). While premenstrual syndrome (PMS) and premenstrual dysphoric disorder are marked by the cyclic nature of symptoms that begin in the late luteal phase of the menstrual cycle and remit shortly after the onset of menstruation. PMDD is distinguished from PMS by the severity of symptoms, predominance of mood symptoms, and role dysfunction, particularly in personal relationships and marital/family relationships.[1]

About 3–9% of women of reproductive age meet the criteria for PMDD.[2] In 2006, the Food and Drug Administration (FDA) gave approval to Yaz (Bayer HealthCare Pharmaceuticals, Wayne, NJ), an oral contraceptive with 24 days of active hormones and four days of placebo pills, for the treatment of emotional and physical symptoms of PMDD. The drug was approved for contraceptive use in March 2006.

Continuous use eyed

Researchers at the University of North Carolina at Chapel Hill (UNC) are studying the possible use of Yaz in a continuous dosing regimen to treat PMDD. The National Institute of Mental Health awarded researchers a $3 million grant to conduct the clinical trial.

The current trial is based on research conducted by **David Rubinow**, MD, the Asad Meymandi distinguished professor and chair of psychiatry in the UNC School of Medicine. Rubinow's earlier work indicates it is the change in, not the level of, reproductive hormones that triggers depression in women who are susceptible to PMDD.[3] Women with the disorder do not have abnormal levels of reproductive hormones, but are more sensitive to the shifts in them that occur prior to menstruation, explains Rubinow. That sensitivity triggers mood symptoms, Rubinow notes.

During the trial, researchers will test three groups of 27 women for three months. One group will take a full 28-day dose of oral contraceptives continuously, while another takes the standard 21-7 regimen each month. A third group will be given a placebo. After the three months, researchers will measure hormone cycling, as well as metabolites of progesterone, which are involved in activating brain centers.

Continuous oral contraceptives potentially would benefit PMDD by stabilizing the levels of these hormones, explains Rubinow. Thus, after the initial administration, which would increase hormone levels and potentially precipitate symptoms, further symptoms should be prevented, he says. The way that oral contraceptives usually are given, with their pill-free intervals, would be expected to be ineffective in treating PMDD for that very reason, Rubinow believes.

Yaz contains drospirenone, a spironolactone antagonist that binds to the androgen receptor. Drospirenone does help with PMS/PMDD symptoms, says **Mary Jane Minkin**, MD, clinical professor in the Department of Obstetrics and Gynecology at the Yale University School of Medicine. Minkin presented on PMS, PMDD, and depression at the 2008 Contraceptive Technology seminar.[4]

Since premenstrual symptoms occur almost exclusively in ovulatory cycles, inhibiting ovulation could be expected to reduce or eliminate these symptoms, research indicates.[5] Yaz's current shortened pill-free interval addresses this, Minkin observes.

She believes an extended cycle pill with drospirenone would work. Some providers already are using drospirenone-containing OCs in this off-label manner, Minkin reports.

[Review "Managing Premenstrual Symptoms," a quick reference guide for clinicians prepared by the Association of Reproductive Health Professionals (ARHP). To download a free guide, go to www.arhp.org. Click on "Publications & Resources," "Quick Reference Guides for Clinicians," and the publication title.]

References

1. Steiner M, Pearlstein T, Cohen LS, et al. Expert guidelines for the treatment of severe PMS, PMDD, and comorbidities: the role of SSRIs. *J Womens Health* (Larchmt) 2006; 15:57-69.

2. Freeman EW, Sondheimer SJ. Premenstrual dysphoric disorder: recognition and treatment. Primary Care Companion *J Clin Psychiatry* 2003; 5:30-39.

3. Huo L, Straub RE, Roca C, et al. Risk for premenstrual dysphoric disorder is associated with genetic variation in

EXECUTIVE SUMMARY

Researchers are studying the possible use of the oral contraceptive Yaz in a continuous dosing regimen in treating premenstrual dysphoric disorder (PMDD).

- Premenstrual syndrome (PMS) and PMDD are marked by the cyclic nature of symptoms that begin in the late luteal phase of the menstrual cycle and remit shortly after the onset of menstruation,
- PMDD is distinguished by the severity of symptoms, predominance of mood symptoms, and role dysfunction, particularly in personal relationships and marital/family relationships.

COMING IN FUTURE MONTHS

- New approaches to polycystic ovary syndrome
- Combined hormonal contraceptives on horizon
- Focus on managing contraceptive side effects
- Reach out to culturally diverse women
- Herpes update: new tests, treatments

ESR1, the estrogen receptor alpha gene. *Biol Psychiatry* 2007; 62:925-933.

4. Minkin MJ. Mood Disorders in Women: PMS, PMDD and Depression. Presented at the 2008 *Contraceptive Technology* conference. Boston; March 2008.

5. Sulak PJ. Ovulation suppression of premenstrual symptoms using oral contraceptives. *Am J Manag Care* 2005; 11(16 Suppl):S492–S497. ■

CNE/CME Instructions

Physicians and nurses participate in this continuing medical education/continuing education program by reading the articles, using the provided references for further research, and studying the questions at the end of the issue. Participants should select what they believe to be the correct answers and refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity with the **December** issue, you must complete the evaluation form included in that issue and return it in the reply envelope provided in that issue to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you. ■

CNE/CME Questions

After reading *Contraceptive Technology Update*, the participant will be able to:

- **identify** clinical, legal, or scientific issues related to development and provisions of contraceptive technology or other reproductive services.
- **describe** how those issues affect services and patient care.
- **integrate** practical solutions to problems and information into daily practices, according to advice from nationally recognized family planning experts.

17. Adult women experience temporary bone loss during
    A. Pregnancy and breastfeeding.
    B. Pregnancy and dysfunctional uterine bleeding.
    C. Breastfeeding and dysfunctional uterine bleeding.
    D. Dysfunctional uterine bleeding and perimenopause.

18. What are the six rapid HIV tests approved by the Food and Drug Administration?
    A. OraQuick, Clearview Stat-Pak, Clearview Complete, Reveal G-3, MultiSpot, and POCkit
    B. OraQuick, Clearview Stat-Pak, Clearview Complete, Reveal G-3, MultiSpot, and Trinity Uni-Gold
    C. QuikFIT, Reveal G-3, MultiSpot, Clearview Stat-Pak, Clearview Complete, and Trinity Uni-Gold
    D. OraQuick, BVBlue, Clearview Complete, Trinity Uni-Gold, Reveal G-3, and MultiSpot

19. Which three combined oral contraceptive pills have reduced pill-free intervals?
    A. Ortho Tri-Cyclen, Yaz, and Loestrin 24-Fe
    B. Mircette, Alesse, and Loestrin 24-Fe
    C. Mircette, Yaz, and Loestrin 24-Fe
    D. Mircette, Yaz, and Demulen

20. What type of drugs is often used for treatment of premenstrual dysphoric disorder?
    A. Mood stabilizers
    B. Antipsychotics
    C. Anticonvulsants
    D. Selective serotonin reuptake inhibitors

Answers: 17. A; 18. B; 19. C; 20. D.

United States Postal Service

Statement of Ownership, Management, and Circulation

1. Publication Title	2. Publication No.	3. Filing Date
Contraceptive Technology Update	0 2 7 4 - 7 2 6 X	10/1/08
4. Issue Frequency	5. Number of Issues Published Annually	6. Annual Subscription Price
Monthly	12	$449.00

7. Complete Mailing Address of Known Office of Publication *(Not Printer) (Street, city, county, state, and ZIP+4)*
3525 Piedmont Road, Bldg. 6, Ste. 400, Atlanta, Fulton County, GA 30305

Contact Person: Robin Salet
Telephone: 404/262-5489

8. Complete Mailing Address of Headquarters or General Business Office of Publisher *(Not Printer)*
3525 Piedmont Road, Bldg. 6, Ste. 400, Atlanta, GA 30305

9. Full Names and Complete Mailing Addresses of Publisher, Editor, and Managing Editor *(Do Not Leave Blank)*

Publisher *(Name and Complete Mailing Address)*
Robert Mate, President and CEO
AHC Media LLC, 3525 Piedmont Road, Bldg. 6, Ste. 400, Atlanta, GA 30305

Editor *(Name and Complete Mailing Address)*
Joy Dickinson, same as above

Managing Editor *(Name and Complete Mailing Address)*
Coles McKagen, same as above

10. Owner *(Do not leave blank. If the publication is owned by a corporation, give the name and address of the corporation immediately followed by the names and addresses of all stockholders owning or holding 1 percent or more of the total amount of stock. If not owned by a corporation, give the names and addresses of the individual owners. If owned by a partnership or other unincorporated firm, give its name and address as well as those of each individual. If the publication is published by a nonprofit organization, give its name and address.)*

Full Name	Complete Mailing Address
AHC Media LLC	3525 Piedmont Road, Bldg. 6, Ste 400 Atlanta, GA 30305

11. Known Bondholders, Mortgagees, and Other Security Holders Owning or Holding 1 Percent or More of Total Amount of Bonds, Mortgages, or Other Securities. If none, check box → ☐ None

Full Name	Complete Mailing Address
Thompson Publishing Group Inc.	805 15th Street, NW, 3rd Floor Washington, D.C. 20005

12. Tax Status *(For completion by nonprofit organizations authorized to mail at nonprofit rates.) (Check one)*
The purpose, function, and nonprofit status of this organization and the exempt status for federal income tax purposes:
☐ Has Not Changed During Preceding 12 Months
☐ Has Changed During Preceding 12 Months *(Publisher must submit explanation of change with this statement)*

PS Form **3526**, September 1998 *See instructions on Reverse)*

13. Publication Name: Contraceptive Technology Update

14. Issue Date for Circulation Data Below: September 2008

15. Extent and Nature of Circulation			Average No. of Copies Each Issue During Preceding 12 Months	Actual No. Copies of Single Issue Published Nearest to Filing Date
a. Total No. Copies *(Net Press Run)*			1221	1057
b. Paid and/or Requested Circulation	(1)	Paid/Requested Outside-County Mail Subscriptions Stated on Form 3541. *(Include advertiser's proof and exchange copies)*	577	565
	(2)	Paid In-County Subscriptions *(Include advertiser's proof and exchange copies)*	4	0
	(3)	Sales Through Dealers and Carriers, Street Vendors, Counter Sales, and Other Non-USPS Paid Distribution	227	245
	(4)	Other Classes Mailed Through the USPS	121	121
c. Total Paid and/or Requested Circulation *(Sum of 15b(1) and 15b(2)*			929	931
d. Free Distribution by Mail *(Samples, Complimentary and Other Free)*	(1)	Outside-County as Stated on Form 3541	23	26
	(2)	In-County as Stated on Form 3541	0	0
	(3)	Other Classes Mailed Through the USPS	0	0
e. Free Distribution Outside the Mail *(Carriers or Other Means)*			20	20
f. Total Free Distribution *(Sum of 15d and 15e)*			43	46
g. Total Distribution *(Sum of 15c and 15f)*			972	977
h. Copies Not Distributed			249	80
i. Total *(Sum of 15g, and h.*			1221	1057
Percent Paid and/or Requested Circulation *(15c divided by 15g times 100)*			96	95

16. Publication of Statement of Ownership
Publication required. Will be printed in the November 2008 issue of this publication. ☐ Publication not required.

17. Signature and Title of Editor, Publisher, Business Manager, or Owner: President and CEO — Date: 9/27/08

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including multiple damages and civil penalties).

Instructions to Publishers

1. Complete and file one copy of this form with your postmaster annually on or before October 1. Keep a copy of the completed form for your records.
2. In cases where the stockholder or security holder is a trustee, include in items 10 and 11 the name of the person or corporation for whom the trustee is acting. Also include the names and addresses of individuals who are stockholders who own or hold 1 percent or more of the total amount of bonds, mortgages, or other securities of the publishing corporation. In item 11, if none, check the box. Use blank sheets if more space is required.
3. Be sure to furnish all circulation information called for in item 15. Free circulation must be shown in items 15d, e, and f.
4. Item 15h., Copies not Distributed, must include (1) newsstand copies originally stated on Form 3541, and returned to the publisher, (2) estimated returns from news agents, and (3), copies for office use, leftovers, spoiled, and all other copies not distributed.
5. If the publication had Periodicals authorization as a general or requester publication, this Statement of Ownership, Management, and Circulation must be published; it must be printed in any issue in October or if the publication is not published during October, the first issue printed after October.
5. In item 16, indicate date of the issue in which this Statement of Ownership will be published.
6. Item 17 must be signed.

Failure to file or publish a statement of ownership may lead to suspension of second-class authorization.

PS Form **3526**, September 1999 *(Reverse)*

Contraceptive Technology Update *is endorsed by the National Association of Nurse Practitioners in Women's Health and the Association of Reproductive Health Professionals as a vital information source for health care professionals.*

NATIONAL ASSOCIATION NPWH
National Association of Nurse Practitioners in Women's Health

Association of Reproductive Health Professionals