CONTRACEPTIVE TECHNOLOGY UPDATE®

Interpreting News and Research on Contraceptives and STIs

August 2011: Vol. 32, No. 8
Pages 85-96

IN THIS ISSUE

Financial Disclosure:
Consulting Editor **Robert A. Hatcher**, MD, MPH, Author **Rebecca Bowers**, and Executive Editor **Joy Dickinson**, 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.

AHC Media

Use of long-term methods moving up — How can you boost numbers?

(Editor's Note: Read the September 2011 edition of Contraceptive Technology Update for the second of our two-part special coverage of long-acting reversible contraceptives. Included in the upcoming issue is an in-depth look at the American College of Obstetricians and Gynecologists' new practice bulletin on the use of long-acting reversible contraceptives. The new recommendations offer guidance in selecting appropriate candidates for such methods and provide tips on managing clinical issues that might arise.)

The tide might be turning when it comes to use of long-acting reversible contraceptive methods such as intrauterine devices (IUDs) and implants among American women. Results of a new study show use has increased from 2.4% in 2002 to 5.6% in 2006-2008.[1]

What might be leading to the increase? There are several possibilities, says **Megan Kavanaugh,** DrPH, senior research associate at the New York City-based Guttmacher Institute and lead author of the current paper.

The U.S. Medical Eligibility Criteria for Contraceptive Use and guidance on use of intrauterine devices from the American College of Obstetricians and Gynecologists indicate safe use of the IUD in younger women and nulliparous women.[2-4] U.S.-based organizations, such as the Association of Reproductive

EXECUTIVE SUMMARY

The tide might be turning when it comes to use of long-acting reversible contraceptive methods such as intrauterine devices (IUDs) and implants among American women. Results of a new study show use has increased from 2.4% in 2002 to 5.6% in 2006-2008.

• Guidance from national organizations now indicates safe use of the IUD in younger women and nulliparous women.

• In a study evaluating satisfaction and continuance among contraceptive users, the two IUDs available in the United States had the highest 12-month continuation rates: 88% for the levonorgestrel intrauterine system and 84% for the Copper T380A, followed by the contraceptive implant at 83%. In comparison, oral contraceptive users recorded a 55% 12-month continuation rate.

Health Professionals and the Society of Family Planning, also have disseminated evidence-based information on the safety and efficacy of IUDs.[5] Now that medical organizations are recognizing that IUDs are safe, effective, and are desired in these younger populations, epidemiologists are seeing an increase, Kavanaugh notes.

In the past, the Copper T380A IUD (ParaGard, Teva Women's Health, North Wales, PA) and the levonorgestrel intrauterine system (LNG IUS, Mirena, Bayer HealthCare Pharmaceuticals, Wayne, NJ) had listed parity as a criteria for using the method in their package labeling. This situation is no longer the case with the Copper T380A. The Food and Drug Administration in 2005 approved a change in its labeling, removing a section titled "recommended patient profile" and deleting language that stated, "T380A is recommended for women who have had at least one child…".[5] The Mirena package insert states that the device "is recommended for women who have had at least one child."

When the LNG IUS was approved in the United States in 2000, its 2001 marketing launch began an era of heightened awareness about the device, says Kavanaugh. Researchers hypothesize that the large marketing emphasis has contributed to an overall increase in IUD use, as well as boosted use among younger populations.

Women like the IUD

New data from the Contraceptive Choice Project in St. Louis show that women who use intrauterine contraception have the highest rates of continuation and satisfaction at 12 months among women who chose oral contraceptives, contraceptive vaginal ring, transdermal contraceptive, intrauterine devices, contraceptive implant, and contraceptive injection.[6] The project is designed to promote reversible long-term methods such as subdermal implants and intrauterine devices and to assess satisfaction and discontinuation rates with various contraceptive methods. In the study, 45% chose the levonorgestrel intrauterine system, 10% chose a copper IUD, and 13% chose the contraceptive implant. About 11% of participants chose oral contraceptive pills, 10% chose the vaginal ring, 8% chose the contraceptive injection, and 2% chose a transdermal patch.

The two IUDs had the highest 12-month continuation rates: 88% for the levonorgestrel intrauterine system and 84% for the Copper T380A, followed by the contraceptive implant at 83%. In comparison, oral contraceptive users recorded a 55% 12-month continuation rate.

Satisfaction mirrored continuation, researchers report. More than 80% of users were satisfied with the IUD, compared with 54% satisfied with oral contraceptives.[6] "Given that long-acting reversible contraception methods have the highest contraceptive efficacy, these methods should be the first-line contraceptive methods offered to patients," the researchers conclude.

Many myths remain in the minds of clinicians when it comes to IUD use, says **Jeffrey Peipert**, MD, MPH, MHA, Robert J. Perry professor of obstetrics

Contraceptive Technology Update® (ISSN 0274-726X), including STI Quarterly™, is published monthly by AHC Media, a division of Thompson Media Group LLC, 3525 Piedmont Road, NE, 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 105109, Atlanta, GA 30348.

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), $449. 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.) Photocopying: No part of this newsletter may be reproduced in any form or incorporated into any information retrieval system without the written permission of the copyright owner. For reprint permission, please contact AHC Media. Address: P.O. Box 105109, Atlanta, GA 30348. Telephone: (800) 688-2421. World Wide Web: http://www.ahcmedia.com.

Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

AHC Media is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

This activity has been approved for 15 nursing contact hours using a 60-minute contact hour.

Provider approved by the California Board of Registered Nursing, Provider #14749, for 15 Contact Hours.

AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media designates this enduring material for a maximum of 18 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This activity is intended for OB/GYNs, nurses, nurse practitioners, and other family planners. It is in effect for 24 months from the date of publication.

Editor: **Rebecca Bowers.**
Executive Editor: **Joy Daughtery Dickinson** (229) 551-9195 (joy.dickinson@ahcmedia.com).
Production Editor: **Kristen Ramsey.**

Editorial Questions

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

and gynecology and vice chair for clinical research at Washington University School of Medicine in St. Louis. Peipert is directing the Contraceptive Choice study.

Many clinicians continue to mistakenly believe that the IUD is inappropriate for young women and women who have not had children, Peipert says. A second myth revolves around concerns of infection; that risk is very low with current IUDs, Peipert states.[7] Some clinicians still might harbor concerns about impaired future fertility with intrauterine contraception; again, research has shown its use to be safe in this respect, says Peipert.[8]

Training also has been a barrier, Peipert notes. Many clinicians trained in an era when IUDs were not commonly used and subsequently didn't learn to insert them. However, the push is on to train more clinicians. In 2011, the Office of Populations Affairs provided funding to the Kansas City, MO-based Clinical Training Center for Family Planning, in joint sponsorship with the Association of Reproductive Health Professionals (ARHP) in Washington, DC, for four intrauterine contraception trainings. The trainings were held in Portland; Kansas City, MO; Denver; and Baltimore. *(ARHP plans a session on the ParaGard IUC at its 2011 Reproductive Health conference scheduled for Sept. 15-17. Visit the ARHP web page, www.arhp.org, and click on the 2011 Reproductive Health icon to obtain more information.)*

Don't forget EC use

Clinicians need to remember another use of the Copper T380A IUD: as the first-line choice for emergency contraception, says **Robert Hatcher**, MD, MPH, professor of gynecology and obstetrics at the Emory University School of Medicine in Atlanta.

When Hatcher began as a family planning clinician 45 years ago, 50% of all U.S. pregnancies were unintended, and that figure still stands today, Hatcher says. Long-acting reversible contraceptives (LARCs) such as the IUD offer the best hope for lowering that number, he states.

While many interventions might help increase use of long-acting contraceptive methods, Hatcher sees the insertion of a Copper T380A IUD as the most promising option. Provider use might be swinging that way. There are clinicians who have inserted over a hundred Copper T380A IUDs as emergency contraceptives, he states. In a recent study of women who had a Copper T380A inserted as an emergency contraceptive, no pregnancies were recorded in the 1,963 women who received the device.[9]

"Each clinician who is serious about increasing the use of LARC methods should move in the direction of recommending Copper T380A insertion as the method of choice for a woman who has had unprotected sex," says Hatcher.

Hatcher also recommends that insertion of IUDs be done immediately after first trimester abortions. This practice leads to higher continuation rates and lower pregnancy rates than delaying IUD insertion for 2-6 weeks post procedure. *(Results of a just-published study will be discussed in detail in the next issue of* Contraceptive Technology Update.*)*[10]

REFERENCES

1. Kavanaugh ML, Jerman J, Hubacher D, et al. Characteristics of women in the United States who use long-acting reversible contraceptive methods. *Obstet Gynecol* 2011; 117:1,349-1,357.
2. Centers for Disease Control and Prevention (CDC). U S. medical eligibility criteria for contraceptive use, 2010. *MMWR Recomm Rep* 2010; 59(RR-4):1-86.
3. American College of Obstetricians and Gynecologists. ACOG practice bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 59, January 2005. Intrauterine device. *Obstet Gynecol* 2005; 105:223-232.
4. American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 392, December 2007. Intrauterine device and adolescents. *Obstet Gynecol* 2007; 110:1,493-1,495.
5. Hubacher D, Finer LB, Espey E. Renewed interest in intrauterine contraception in the United States: evidence and explanation. *Contraception 2011*; 83:291-294.
6. Peipert JF, Zhao Q, Allsworth JE, et al. Continuation and satisfaction of reversible contraception. *Obstet Gynecol* 2011; 117:1,105-1,113.
7. Grimes DA. Intrauterine device and upper-genital-tract infection. *Lancet* 2000; 356:1,013-1,019.
8. Hubacher D, Lara-Ricalde R, Taylor DJ, et al. Use of copper intrauterine devices and the risk of tubal infertility among nulligravid women. *NEJM* 2001; 345:561-567.
9. Wu S, Godfrey EM, Wojdyla D, et al. Copper T380A intrauterine device for emergency contraception: a prospective, multicentre, cohort clinical trial. *BJOG* 2010; 117:1,205-1,210.
10. Bednarek PH, Creinin MD, Reeves MF, et al; Post-Aspiration IUD Randomization (PAIR) Study Trial Group. Immediate versus delayed IUD insertion after uterine aspiration. *NEJM* 2011; 364:2,208-2,217. ■

Treat HIV infection to protect partners

New research indicates that early initiation of antiretroviral treatment in people infected with HIV prevents them from transmitting the

virus to their partners.

Results from a study set to run until 2015 were released early in May 2011 by an independent data safety monitoring board after findings indicated that HIV-infected men and women with relatively healthy immune systems who received immediate oral antiretroviral therapy were 96.3% less likely to pass on the infection to their uninfected partners and remained healthier than those whose treatment was delayed. The findings of the Phase III clinical trial, conducted by the HIV Prevention Trials Network as HPTN 052 and sponsored by the National Institute of Allergy and Infectious Diseases, were released early after data indicated the benefits of early treatment were clear. The results represent the first findings from a major randomized clinical trial to indicate that treating an HIV-infected individual can reduce the risk of sexual transmission of HIV to an uninfected partner.

What the science shows is what many HIV clinicians have long suspected: Earlier treatment is not only better for patient outcome, but it also is better for lowering transmission, says **Michael Horberg**, MD, vice chair of the Arlington, VA-based HIV Medicine Association (HIVMA) and director of HIV/AIDS at Kaiser Permanente in Rockville, MD. "The earlier you test, the earlier you screen for HIV risk and other sexually transmitted disease risk, diagnose early, and get patients into care, there is now not only a treatment, but a public health imperative," states Horberg, who serves on the Presidential Advisory Council on HIV/AIDS.

Look closer at results

To conduct the study, researchers began in 2007 to enroll discordant patients at 13 study sites in nine countries, including Botswana, Brazil, India, Kenya, Malawi, South Africa, Thailand, the United States and Zimbabwe. All participants were at least 18 years of age with a median age of 33 at the time of enrollment; 52% of the participants were male, and 97% of the couples were heterosexual. A total of 1,763 couples were enrolled in the study.

Couples randomly were assigned to two study groups: 886 were placed in the "immediate" arm, where the HIV-infected partners began receiving a three-drug HIV treatment combination, with the other 877 assigned to the "deferred" arm, where the HIV-infected partners received antiretroviral therapy only after their CD4 count dropped below a pre-determined level or an AIDS-related event occurred. Both groups received regular HIV testing, safe-sex counseling, free condoms, testing and treatment for sexually transmitted infections, and treatment for any HIV-related complications.

The study retained 90% of its participants, with only one case of HIV infection occurring among the couples assigned to receive immediate treatment, compared to 27 cases of HIV infection among those who delayed treatment. Seventeen cases of previously undiagnosed extrapulmonary tuberculosis also occurred among the HIV-infected partner in the deferred treatment arm, with only three cases occurring in the immediate arm.

The HIV drugs that were used in various combinations in the trial included atazanavir (300 mg once daily), didanosine (400 mg once daily), efavirenz (600 mg once daily), emtricitabine/tenofovir disoproxil fumarate (200 mg emtricitabine/300 mg tenofovir disoproxil fumarate once daily), lamivudine (300 mg once daily), lopinavir/ritonavir 800/200 mg once daily or lopinavir/ritonavir 400/100 mg twice daily, nevirapine (200 mg taken once daily for 14 days, followed by 200 mg taken twice daily), ritonavir (100 mg daily, used only to boost atazanavir), stavudine (weight-dependent dosage), tenofovir disoproxil fumarate (300 mg once daily), and zidovudine/lamivudine (150 mg lamivudine/300 mg zidovudine taken orally twice daily). A separate non-affiliated study is looking at the optimal time for asymptomatic HIV-infected individuals to begin antiretroviral treatment.

What happens next?

While the study findings were released early, the study will continue for at least one year, with all infected subjects being offered antiretroviral

EXECUTIVE SUMMARY

New research indicates that early initiation of antiretroviral treatment in people infected with HIV prevents them from transmitting the virus to their partners.

- Results from a study set to run until 2015 were released early after findings indicated that HIV-infected men and women with relatively healthy immune systems who received immediate oral antiretroviral therapy were 96.3% less likely to pass on the infection to their uninfected partners and remained healthier than those whose treatment was delayed.
- The results represent the first findings from a major randomized clinical trial to indicate that treating an HIV-infected individual can reduce the risk of sexual transmission of HIV to an uninfected partner.

therapy while researchers consider the best way forward, says **Myron Cohen**, MD, J. Herbert Bate Distinguished Professor of Medicine, Microbiology and Immunology, and Public Health at the University of North Carolina at Chapel Hill. Cohen serves as lead investigator of the HPTN 052 trial. At press time, full findings of the study were scheduled to be presented at the July 2011 annual session of the International AIDS Society in Rome, Italy.

"Confirmation of the protective effect of treatment on HIV transmission to sexual partners is a giant step forward in confronting the HIV epidemic," said **Wafaa El-Sadr**, MD, MPH, professor of clinical epidemiology at the Mailman School of Public Health at Columbia University and a member of HIVMA's Center for Global Health Policy's Scientific Advisory Committee in a statement accompanying news of the study findings. "The finding of a protective effect of HIV treatment on the development of extrapulmonary tuberculosis may play an important role in avoiding this deadly complication in HIV-infected individuals."

While research continues on HIV prevention, clinicians can continue to emphasize the consistent and correct use of condoms by all women and men infected with HIV, notes **Robert Hatcher**, MD, MPH, professor of gynecology and obstetrics at the Emory University School of Medicine in Atlanta. ■

Do OCs cause weight gain? No, says research

Thumbing through your inbox charts, you see your next patient is a 19-year-old who began use of oral contraceptives (OCs) about six months ago. When you talk with her in the examination room, however, you find that she has discontinued use of the Pill after she began to gain weight.

Family planning clinicians are all too familiar with this scenario. Perceived weight gain is the leading reason cited for pill discontinuation in U.S. women.[1] However, studies have not conclusively established if OCs do indeed cause weight gain; in fact, results of a new study in primates indicate that the Pill is not the culprit.[2]

Why has popular belief leaned toward associating oral contraceptive use with weight gain? For women, weight regulation is a major concern, says **Alison Edelman**, MD, MPH, associate professor in the Department of Obstetrics/Gynecology and assistant director of the Family Planning Fellowship at the Oregon Health & Science University (OHSU) in Portland.

"People tend to gain weight as they age, even if they don't change anything, because as we age, metabolism changes and slows," says Edelman, who served as lead author of the current research. "So you can imagine with birth control pills being one of the most common things that women use during their reproductive lives, that pills become an easy thing to blame for the weight gain."

In Edelman's study, researchers followed a group of rhesus macaque monkeys at the OHSU Oregon National Primate Research Center for almost a year. Rhesus monkeys were used as study subjects since their reproductive system is nearly identical to humans, and variables such as exact food intake can be controlled and measured.

At the beginning of the study, half the animals were obese, and half were normal weight. During the eight-month treatment period, animals received oral contraceptives, dosed to achieve equivalent human serum levels for a 30 mcg ethinyl estradiol/150 mcg levonorgestrel pill. Researchers looked at weight, food intake, activity levels, body fat, and lean muscle mass. At the study's conclusion, researchers report the normal weight group remained stable in weight, while the obese group lost a significant amount of weight (8.5%) and percent of body fat (12%) due to an increase in basal metabolic rate. No changes were seen in food intake, activity, or lean muscle mass for either group, they note.[2]

EXECUTIVE SUMMARY

While weight gain is the leading reason cited for pill discontinuation in U.S. women, studies have not conclusively established if oral contraceptives do indeed cause weight gain. Results of a new study in primates indicate that the Pill is not the culprit.

- At the beginning of the study, half the animals were obese, and half were normal weight. During the eight-month treatment period, animals received oral contraceptives, dosed to achieve equivalent human serum levels for a 30 mcg pill.
- Researchers report the normal weight group remained stable in weight, where the obese group lost a significant amount of weight (8.5%) and percent of body fat (12%) due to an increase in basal metabolic rate.

Check lifestyle factors

Women generally start using the Pill at a time in life when weight gain is apt to happen, observes **Susan Wysocki**, WHNP-BC, FAANP, president and chief executive officer of the Washington, DC-based National Association of Nurse Practitioners in Women's Health.

Late night snacks in the college dorm room, dates where dinner and cocktails add up to caloric excess, and post-pregnancy food choices all can lead to weight gain, she notes. Lack of sleep has been shown to increase cravings, says Wysocki.[3] If a woman has been studying late for exams, staying out later than usual, or getting up with a baby at night, these might be the culprits that can lead to added weight that coincide with starting the Pill.

"However, if a woman tells me that she has gained weight from the Pill and truly believes it is the Pill, even after going over lifestyle factors, she may not be a terrific candidate for staying on the Pill," Wysocki notes. "She may stop on her own, so finding her a method she would be more satisfied with is prudent."

How do you approach the topic of weight gain prior to initiation of oral contraceptives? Placebo-controlled studies of OCs used for noncontraceptive indications have demonstrated no difference in weight gain between Pill users and placebo users, says **Anita Nelson**, MD, professor in the Obstetrics and Gynecology Department at the David Geffen School of Medicine at the University of California in Los Angeles.[4] Nelson points to a recent journal commentary that discusses the power of the "nocebo phenomenon" in which if women are told to expect noxious side effects, these complaints occur due of the power of suggestion.[5] If the nocebo phenomenon holds true, warning women about potential side effects with oral contraceptives, such as weight gain, might not only be unwarranted, but possibly unethical, the commentary concludes.

Clinicians might consider using optimistic counseling, where women are told that they will feel well and do well on the Pill, the commentary notes. Unless established by randomized placebo-controlled trials, non-specific side effects should not be mentioned, it suggests.[5]

REFERENCES

1. Rosenberg M. Weight change with oral contraceptive use and during the menstrual cycle. Results of daily measurements. *Contraception* 1998; 58:345-349.
2. Edelman A, Jensen JT, Bulechowsky M, et al. Combined oral contraceptives and body weight: do oral contraceptives cause weight gain? A primate model. *Hum Reprod* 2011; 26:330-336.
3. Morselli L, Leproult R, Balbo M, et al. Role of sleep duration in the regulation of glucose metabolism and appetite. *Best Pract Res Clin Endocrinol Metab* 2010; 24:687-702.
4. Redmond G, Godwin AJ, Olson W, et al. Use of placebo controls in an oral contraceptive trial: methodological issues and adverse event incidence. *Contraception* 1999; 60:81-85.
5. Grimes DA, Schulz KF. Nonspecific side effects of oral contraceptives: nocebo or noise? *Contraception* 2011; 83:5-9. ■

Out-of-pocket expenses for OCs targeted

Findings from a new analysis indicate that women pay a higher percentage out of pocket when it comes to oral contraceptive (OC) expenditures.[1] The analysis shows that women pay about 58% in total expenditures for the Pill, compared to about 30% for other maintenance medications. A red-light finding for family planners: Researchers say young and uninsured women are likely to pay more out of pocket for the Pill, which might impact their ability to continue using them.

To perform the observational cohort study, scientists at the University of California, San Francisco analyzed information from the 1996-2006 Medical Expenditures Panel Survey, which gathers material from patients, healthcare providers, and pharmacies to provide nationally representative data. The researchers looked at 8,151 women ages 13-50 who had made at least one OC purchase, examining such factors as out-of-pocket costs and numbers of packs obtained per purchase. Out-of-pocket expenditures were defined as payments made by the survey respondent or other family members.

Researchers determined the number of packs per purchase by looking at data from the pharmacy and then calculated the ratio of out-of-pocket costs versus the total expenditures paid by the woman and her health plan. They also estimated the annual out-of-pocket cost if a woman were to obtain 13 medication cycles per year with a median cost per pack, and then determined the ratio of annual out-of-pocket expenditures for pills versus annual out-of-pocket expenditures for all healthcare services.

The analysis reports that women's out-of-pocket

expenses per Pill pack averaged $16, but uninsured women had the highest out-of-pocket cost at an average of $26. Privately insured women who did not have prescription drug coverage paid an average of $21 per pack, while Medicaid beneficiaries paid $16 per pack. Privately insured women with prescription drug coverage paid the least out-of-pocket costs: an average of $14. Out-of-pocket expenses varied by the number of packs a woman was able to purchase and were highest when women only obtained one pack per purchase, researchers report.

The amount women pay out-of-pocket for OCs often is determined by their insurance coverage, such as whether they have drug coverage, and if so, the type of health plan and benefit they have, such as the formulary tier, and the amount of copayment required by the health plan for oral contraceptives, explains **Su-Ying Liang**, PhD, senior analyst and center data manager at the Center for Translational and Policy Research in Personalized Medicine at the Department of Clinical Pharmacy at the University of California, San Francisco. "In addition to the absolute out-of-pocket amount, we were also interested in examining an additional dimension of financial burden: how this out-of-pocket amount compared to the total OC payment," says Liang, who served as lead author for the paper. "Thus we calculated the ratio of out-of-pocket to total expenditures. When evaluating this measure, the denominator, total expenditures, matters."

In the final analysis, the average out-of-pocket and total payment per OC pack were $16 and $27, By comparison, the average out-of-pocket and total payment are $30 and $101 for Lipitor, a highly prescribed maintenance drug, Liang notes.[2] **Robert Hatcher**, MD, MPH, professor of gynecology and obstetrics at the Emory University School of Medicine in Atlanta, points out that a woman can purchase Sprintec or Tri-Sprintec, two low-dose combined pills, for about $9 a cycle from discount and grocery story chains. Even if she pays 100% of this amount, she is far better off than the copayments women make when purchasing most other pills, he notes. Clinicians should strongly consider the use of one of these two medications if concerned about the cost of OCs for their patients, he states.

When it came to total expenditures, researchers report women on average paid about 58% of total OC expenditures. Women with private insurance paid 56%; women without insurance paid 95%. Women without insurance paid less than 100% because of other federal, state, and local programs that helped pay for their pills.

What other trends did researchers note? Almost half (46%) of women paid more than $15 per physician visit to manage their contraception, and women averaged 1.6 visits per year. When it came to purchasing pill packs, about half (44%) of survey respondents got one pack per purchase, while 27% obtained 2-3 packs, and 29% obtained more than four packs. Dispensing practices also have changed; the proportion of women who obtained only one pack per purchase was significantly lower in recent years: 76% in 1996-1998 versus 35% in 1999-2006.

Researchers report women were more likely to pay at least $15 per pack if they did not have insurance, were younger, or did not have prescription drug coverage. Women enrolled in managed care plans and younger women also were more likely to obtain just one pack per visit, they note.

While the findings suggest that dispensing limitations, whether coming from clinicians or from the insurance industry, are slowly being chipped away, there is still progress to be made when it comes to contraceptive access, the researchers note. "More work needs to be done to remove any barriers that prevent women from obtaining as many pill packs as they want," they conclude.[1]

How to increase access?

What will it take to increase access to contraception for women? One possibility is working with a pharmaceutical company to bring an oral progestin-only pill to market for over-the counter (OTC)

EXECUTIVE SUMMARY

Findings from a new analysis indicate that women pay a higher percentage out of pocket when it comes to oral contraceptive expenditures.

- The analysis shows that women pay about 58% in total expenditures for the Pill, compared to about 30% for other maintenance medications.
- A red-light finding for family planners: Researchers say young and uninsured women are likely to pay more out of pocket for the Pill, which might impact their ability to continue using them.
- Access to contraception might be increased with the availability of an over-the-counter pill. An advocacy group is working to bring an oral progestin-only pill to market for over-the counter use in the near future.

use in the near future. This possibility is being explored by the Oral Contraceptives Over-the-Counter Working Group, an Oakland, CA-based coalition focused on providing easier access to safe, effective, acceptable, and affordable contraception, says **Dan Grossman**, MD, a member of the working group steering committee. *(*Contraceptive Technology Update *reported on the group's push in "Is it time to bring OCs over the counter," July 2010, p. 77.)*

Two recently published reports from the Border Contraceptive Access Study gives insight to potential OTC use, says Grossman.[3,4] Those reports took advantage of a natural experiment along the United States-Mexico border where U.S. residents sometimes purchase OCs over the counter in Mexican pharmacies.

One study found that continuation among women who obtained pills in Mexican pharmacies without a prescription was significantly higher than among those who got pills in U.S. clinics, Grossman notes.[3] The other study examined contraindications among women obtaining combined oral contraceptives over the counter in Mexican pharmacies. It found that the prevalence of World Health Organization Medical Eligibility Criteria Category 3 contraindications (a condition for which the theoretical or proven risks usually outweigh the advantages of using the method) was significantly higher among OTC users compared to women obtaining pills at public clinics.[4,5]

Taken together, these studies suggest that over-the-counter access to oral contraceptives does not adversely affect effectiveness and might improve it, Grossman notes. However, progestin-only pills might be a better option as the first over-the-counter oral contraceptive, given their fewer and rarer contraindications, he states.

REFERENCES

1. Liang SY, Grossman D, Phillips KA. Women's out-of-pocket expenditures and dispensing patterns for oral contraceptive pills between 1996 and 2006. *Contraception* 2011; 83:528-536.

2. Stagnitti MN. The top five outpatient prescription drugs ranked by total expense for children, adults, and the elderly, 2004. Statistical Brief #180. Agency for Healthcare Research and Quality, Rockville, MD; 2007. Accessed at http://www.meps.ahrq.gov/mepsweb/data_files/publications/st180/stat180.pdf.

3. Potter JE, McKinnon S, Hopkins K, et al. Continuation of prescribed compared with over-the-counter oral contraceptives. *Obstet Gynecol* 2011; 117:551-557.

4. Grossman D, White K, Hopkins K, et al. Contraindications to combined oral contraceptives among over-the-counter compared with prescription users. *Obstet Gynecol* 2011; 117:558-565.

5. World Health Organization. Medical Eligibility Criteria for Contraceptive Use. Fourth ed. Geneva; 2009. ■

Boost teen HIV testing with free rapid tests

While adolescents are at risk for HIV, many forego testing. This lack of testing is a major public health concern, as more than 50% of HIV-infected adolescents do not know their infection status.[1]

Good news: Results from new research indicate that teens who are offered free or low-cost rapid HIV testing often are willing to accept the test.[2] The study included 81 at-risk adolescents between ages 15-21; more than half of all participants were boys. Overall, 53% of adolescents in the study agreed to receive the free HIV test, with African-American teens more likely to agree to testing compared to Latino youth (75% versus 39%). Researchers note that teens with only one sexual partner were nearly five times more likely to accept testing than their peers with multiple partners, who are at higher HIV risk.[2]

The Centers for Disease Control and Prevention recommends that healthcare providers routinely offer HIV testing to all adolescents ages 13 and above[3], but this recommendation is seldom followed in practice for a variety of reasons says **Rebecca Swenson**, PhD, a child psychologist with the Bradley Hasbro Children's Research Center and the current study's lead author.

Providers might be pressed for time, not perceive their teen patients to be at risk, or might worry about offending patients by suggesting testing, says Swenson. However, if healthcare providers were aware that more than half of the adolescents would be willing to accept testing, they might be more inclined to offer this service, she notes. "Given that teens in committed relationships are even more likely to accept testing, healthcare providers may present HIV testing to teen patients as a routine health behavior that is part of responsible sexual health care for all couples," says Swenson. "As such, healthcare providers can play an important role in increasing social norms for partner testing among teens." *(Use a*

Centers for Disease Control and Prevention fact sheet,"HIV Testing Among Adolescents," inserted in the online issue, for added counseling information.)

Rapid testing is key

Results from another study published online suggest that while teens and young adults prefer rapid HIV testing that can deliver results in less than an hour, some still worry about whether their tests will be confidential.[4] About 40% of those tested said they had some concerns that their parents and health insurers would discover the results.

Readily-available rapid HIV testing can definitely help to increase testing acceptance, says **Cathryn Samples**, MD, MPH, AAHIV, assistant professor of pediatrics at Harvard Medical School and clinical director of the Boston HAPPENS Program, which provides HIV care and support to youth ages 12-24. "Rapid HIV testing immediately increased both the number of youth testing and the proportion of youth learning their HIV status through our program," says Samples, a co-author of the current online research. "Obtaining results rapidly makes a return visit unnecessary, avoids youth concern about billing for the test, and allows immediate feedback about results and risk and the need for future testing."

While a small grant allowed the Boston researchers to pilot availability of free rapid HIV tests in a large adolescent/young adult clinic setting in 2007-2008, further funding from the state health department maintains rapid testing availability, says Samples. Clinicians continue to find high rates of acceptance for the rapid testing for youth being seen for routine and urgent care, she notes. Grant support also allows the program to offer rapid HIV testing to non-patients, such as the partner or friend of a youth with a sexually transmitted infection (STI), and youth and couples who are seeking HIV testing only.

"I believe rapid HIV testing as a point of care test, similar to pregnancy testing, also fits well in settings focusing on reproductive health and family planning, where it could be offered routinely to new clients and to those needing repeat testing, and where nurses or family planning counselors may be able to be trained to conduct the tests," Samples comments.

Seize the moment

Adolescents often make decisions "in the moment," and rapid HIV testing provides that opportunity with immediate feedback, advises Samples. It is particularly useful when provided in a clinical setting, where reactive results can be confirmed immediately through venous specimen collection, and counseling and immediate access to medical advice also are available, she notes.

"We encourage couples, especially those in new relationships or considering pregnancy, to test together, and availability of barrier-free rapid HIV testing makes that possible," Samples states. "We also have noticed that friends have encouraged other friends to test, once they have been through the experience."

Providers at the Boston clinic strive to normalize HIV testing, as well as repeat testing, for youth who are sexually active or otherwise at risk, working to make it less scary to them and their peers, says Samples. The program offers routine clinician-ordered HIV testing and rapid testing. While both are valuable, rapid health testing is particularly useful for young people who are first time testers, concerned about confidentiality and privacy of insurance billing, anxious about test results, presenting only for HIV or other STI screening, or not otherwise engaged in medical care, she notes. "Our study showed that without universal health care and billing mechanisms to protect privacy, rapid HIV testing may not be self-supporting for adolescents and young adults," states Samples. "If a clinical program lacks grant support and cannot totally support the cost of rapid testing with reimbursement or wishes to decrease financial and confidentiality barriers, partnership with local testing programs, cross-training of support staff, or co-location of testers from other programs may enable successful implementation."

EXECUTIVE SUMMARY

Results from new research indicate that teens who are offered free or low-cost rapid HIV testing often are willing to accept the test. Availability of such testing might lower the number of teens who don't know their HIV status. More than 50% of U.S. HIV-infected adolescents fall into that category.

- The Centers for Disease Control and Prevention recommends that healthcare providers routinely offer HIV testing to all adolescents ages 13 and above.
- Adolescents often make decisions "in the moment," and rapid HIV testing provides that opportunity with immediate feedback.

REFERENCES

1. Centers for Disease Control and Prevention. HIV Testing Among Adolescents. Fact sheet. Accessed at http://www.cdc.gov/HealthyYouth/sexualbehaviors/pdf/hivtesting_adolescents.pdf.
2. Swenson RR, Hadley WS, Houck CD, et al. Who accepts a rapid HIV antibody test? The role of race/ethnicity and HIV risk behavior among community adolescents. *J Adolesc Health* 2011; 48:527-529.
3. Branson BM, Handsfield HH, Lampe MA, et al; Centers for Disease Control and Prevention (CDC). Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep* 2006; 55(RR-14):1-17.
4. Tuysuzoglu S. Corliss HL, Fitzgerald SM, et al. Acceptability and feasibility of rapid HIV testing in an adolescent clinic setting: youth testing attitudes, knowledge, and behaviors. *J Adoles Health* 2011; Doi: 10.1016/j.jadohealth.2011.03.007. ■

HPV vaccines on time via text messaging

Research indicates that while many young women might initiate vaccination for human papillomavirus (HPV), they do not complete the three-injection course of treatment. In a 2010 study of more than 9,600 adolescent and young adult women in the Baltimore area, researchers report that fewer than 30% of those eligible to receive the HPV vaccine chose to get it, and about one-third of those who began receiving the vaccine completed the three-dose course.[1]

What can clinicians do? Findings from a new study indicate text messaging might serve as an effective reminder.[2] In the new study, researchers implemented and evaluated a text message reminder system to promote on-time receipt of the second and third HPV vaccine doses at nine pediatric clinical sites in New York City. Parents of adolescents ages 9-20 years who received the vaccine during the time period of January-June 2009 were offered enrollment cards with instructions to sign up for English or Spanish language text message reminders for the next vaccine dose. Parents who enrolled in the program received up to three weekly text message reminders for their daughter's next vaccine dose. Medical records were reviewed for up to four months after the next vaccine dose was due.

During the intervention period, of 765 eligible HPV vaccine events, enrollment instructions were distributed to parents (56.7% of doses). Parents of 124 adolescent girls (28.6% of those handed instructions) activated text message reminders. On-time receipt of the next HPV vaccine dose occurred in 52% of teens whose parents signed up for reminders, 35% among those whose parents did not sign up, and 38% among those who served as historic controls.[2]

While the system was effective for those who signed up for the text reminder program, the intervention could be improved if the system were more automated and did not require as much action from the parent to activate the reminders, says **Elyse Kharbanda**, MD, MPH, who served as lead author of the study while at Columbia University in New York City.

"Next steps would also be to implement similar systems in larger settings with more diverse populations," says Kharbanda, now a research investigator with HealthPartners Research Foundation in Bloomington, MN. "Additionally, we would encourage further studies to implement systems to directly text the teenagers, rather than their parents."

COMING IN FUTURE MONTHS

- ■ QR codes: communication option for prevention messages?
- ■ Add couples-focused services to family planning
- ■ Counsel patients on breaking STD news to partners
- ■ Reach Hispanic teens with contraceptive message

EXECUTIVE SUMMARY

Research indicates that while many young women may initiate vaccination for human papillomavirus (HPV), they do not complete the three-injection course of treatment.

- In a 2010 study of more than 9,600 adolescent and young adult women in the Baltimore area, researchers report that fewer than 30% of those eligible to receive the HPV vaccine chose to get it and only about one-third of those who began receiving the vaccine completed the three-dose course.
- Using text messaging as reminders might be effective in helping teens and young adults complete the three-course vaccination schedule. A study in New York City indicates text messaging's effectiveness; another study is under way in Baltimore.

What stops the shots?

Why might young women not complete the course of HPV vaccination? Researchers suspect the answer is related in large part to the fact that the HPV vaccination requires three doses for maximum protection, says **Kathleen Tracy**, PhD, assistant professor in the Department of Epidemiology and Public Health at the University of Maryland School of Medicine in Baltimore. Tracy presented findings from the Baltimore study at a 2010 national conference of the American Association for Cancer Research.[1]

Tracy and other Baltimore researchers looked at 9,658 adolescent and young adult women, ages 9 to 26, who potentially were eligible for the vaccine and attended the University of Maryland Medical Center's outpatient gynecology clinics from August 2006 until August 2010. A total of 2,641 young women (27.3%) started the vaccination process; 39.1% completed one dose, 30.1% completed two doses, and 30.78% completed all three doses. Two-thirds of those who began taking the vaccine were African-American.

Young women between ages 18-26 were the least likely to complete more than a single dose of the vaccine, the researchers found. African-American women were less likely than young white women to complete all three doses, findings indicate.[1]

The researchers don't know why the young women in the study opted not to take the vaccine or failed to complete the three-dose regimen; how-

continued on p. 96

CNE/CME INSTRUCTIONS

To earn credit for this activity, please follow these instructions.

1. Read and study the activity, using the provided references for further research.
2. Log on to **www.cmecity.com** to take a post-test; tests can be taken after each issue or collectively at the end of the semester. *First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.*
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly. ■

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;
- provide practical information that is evidence-based to help clinicians deliver contraceptives sensitively and effectively.

5. Parity is listed as a recommendation for use in
   A. ParaGard
   B. Mirena
   C. ParaGard and Mirena
   D. Neither ParaGard nor Mirena

6. Which antiretroviral drug was NOT used in the HPTN 052 trial?
   A. Atazanavir
   B. Didanosine
   C. Rilpivirine
   D. Efavirenz

7. What primates were used to conduct research (Edelman A, et al. *Hum Reprod* 2011; 26:330-336) regarding oral contraceptive use and weight gain, since their reproductive system is nearly identical to humans, and variables such as exact food intake could be controlled and measured?
   A. Owl monkeys
   B. Squirrel monkeys
   C. Chimpanzees
   D. Rhesus macaque monkeys

8. According to the Centers for Disease Control and Prevention, what percentage of U.S. HIV-infected adolescents do not know their infection status?
   A. 10%
   B. 25%
   C. 35%
   D. More than 50%

continued from p. 95

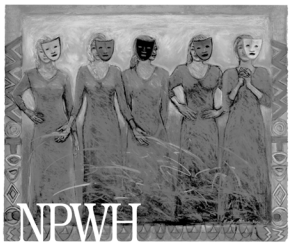
ever, they see the study's results pointing strongly to the need to develop strategies to encourage eligible women to take the vaccine as directed for maximum protection, Tracy notes. Parents might have to take a more active role in making sure their daughters receive all the necessary doses, she states.

"Studies that have looked at compliance with multiple-dose vaccine schedules find relatively poor adherence to dosing schedules that require multiple doses," observes Tracy. "For younger women, we think having parental involvement likely increases adherence rates because parents may be involved in making sure they attend subsequent visits for follow-up doses."

REFERENCES

1. Tracy JK, Terplan M, Lydecker, AD, et al. HPV vaccine adherence in urban youth. Presented at the Ninth Annual American Association for Cancer Research (AACR) International Conference on Frontiers in Cancer Prevention Research. Philadelphia; November 2010.
2. Kharbanda EO, Stockwell MS, Fox HW, et al. Text message reminders to promote human papillomavirus vaccination. *Vaccine* 2011; 29:2,537-2,541. ■

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 healthcare professionals.



OB/GYN
QUARTERLY UPDATE

Painful sex: Look at how far we've come , and yet how far we have left to go

By **Frank W. Ling**, MD
Clinical Professor, Department of Obstetrics and Gynecology
Vanderbilt University School of Medicine
Nashville, TN

Source: Bergeron S, Rosen NO, Morin M. Genital pain in women: Beyond interference with intercourse. *Pain* 2011; 152:1223-1225.

Understanding sexual pain remains limited. With multiple etiologies and lack of evidence-based outcomes research, future investigations should focus on evaluating the intimacy of the couple, the partner relationship, and biomedical sources of pain such as the pelvic floor muscles.

The article by Bergeron et al is not new science, but, instead, is a "topical review." In addition, it doesn't appear in a journal that most women's health providers read. Both are reasons it makes a compelling focus for this supplement. This is not an article that is likely to get full attention in other publications since it doesn't adhere to the traditional scientific methods that so populate our classic journals. Nonetheless, I think that a summary of this review and its clinical implications for us as patient advocates is warranted.

For those not familiar with the Diagnostic and Statistical Manual of Mental Disorders-V, the authors inform us that the upcoming fifth edition of this categorization of psychiatric diagnoses will group vaginismus and dyspareunia into a single entity called "genito-pelvic pain/penetration disorder." Although this wording appears to be a better descriptor, it still is categorized as a sexual dysfunction with strong emphasis on a specific sexual act: intercourse. The authors suggest that a broader view of the problem would make even more sense, focusing not just on the coital act, but also emphasizing such critical components as the cognitive, affective, behavioral, and interpersonal aspects of pain associated with sex. The new disorder will include specific elements: proportion of successful vaginal penetration, pain with vaginal penetration, fear of vaginal penetration, pelvic floor dysfunction, and medical comorbidities.

The review summarizes what is known about biomedical factors; pelvic floor dysfunctions; cognitive, behavioral, and affective factors; and interpersonal factors. Suffice it to say that each of these areas of exploration has been shown to be a potential contributor to the end result of painful sexual experiences. Because of the complexity of any given patient's case, the authors recommend a more holistic approach to research in the future, to allow for understanding more than just the biomedical aspects of this condition.

So what's a well-intentioned clinician to do? Even the best data dealing with dyspareunia are flawed. Randomized, controlled trials are few and far between. Evidence-based medicine offers precious little insight into how best to treat that woman sitting in your office complaining of dyspareunia. The office schedule is full, and time pressures limit what can be offered. Even though this article tended to ask more

Statement of Financial Disclosure:
Frank W. Ling, MD, guest author, and **Catherine Leclair**, MD, peer reviewer, report no financial relationship to this field of study. **Jeffrey T. Jensen,** MD, MPH, guest author, receives research support from, is a consultant to, and serves on the speakers bureau of Bayer Healthcare/Bayer Schering; receives research support from Merck Abbott Laboratories, Wyeth, and Warner-Chilcott; and is a consultant to Schering Plough.

questions than it answered, it does provide us with food for thought that leads us to some general guidelines which can be extrapolated to help our patients:

• **"Dyspareunia is better than no pareunia at all."** Surely you've heard that one, haven't you? This old boys' network adage blatantly ignores the importance of the interpersonal and intimacy aspects of sexual activity. In reality, the devastation between partners caused by sexual pain can be tremendous, even to the point of undermining the entire relationship as well as the woman's mental health. We've probably all seen it in one way or another. Message: Don't ignore or trivialize a woman's complaint of pain with sex.

• **HATAH.** Coined by Dr. **Ray Good**, a psychiatrist and obstetrician/gynecologist (although many of us think of ourselves as part-time psychiatrists also), this palindrome reminds us to ask the patient "How are things at home?" This is a shortcut into seeing what kind of environment the patient is in. The stressors, the obstacles, the support systems, etc. can be ferreted out using this fairly non-threatening question. Message: Identify where the woman is with regard to significant people and circumstances.

• **"Doesn't it take too long to obtain a sexual history?"** Not really. Here is an easy approach:

Question 1: Are you sexually active? (Three seconds including question and answer.)

Question 2: Do you have any questions or problems? (10 seconds including question and answer and allowing time for the patient to think about her answer.)

So it takes less than 15 seconds to inquire, to open the door, to let the patient see that you consider this aspect of her health to be of significance. After all, if you didn't think it was important, why would you ask? There are three logical outcomes:

— issues;

— issues that are expressed and that can be addressed now and/or at a separate visit;

— or no issues expressed, but she brings up something at a subsequent visit because she sees that you are open to this type of concern.

If an issue is raised that can be addressed in an efficient fashion, doing so at the same visit makes sense. If, on the other hand, it sounds more complex requiring more time, then the patient should have her concern acknowledged, but addressed when there is more time to focus on it. This approach keeps the office from backing up unexpectedly. Message: It takes no time at all to take a brief sexual history.

• **"I don't have the time or interest to be trained as a sex therapist."** That's fine, because, in fact, becoming a certified sex therapist is a significant undertaking. The clinician can, however, with little effort, become a practitioner who identifies a problem and refers the woman/couple to an appropriate resource. Knowing what is available in your community is even something that can be delegated to office staff, but the key is to ask around to find individuals or clinics who can effectively address patients' sexual pain problems. Message: There is no shame in referring a patient for "genito-pelvic pain/penetration disorder."

• **"If I try to take a history, I really don't know how to approach it."** Actually, you already know how to, because you can take a thorough history for pain in your sleep. It's just what we learned in our medical school class on history-taking: describe the pain, where is it, how long has it been there, when does it hurt, does it happen every time, what makes it better or worse, what treatments have helped/not helped it?

In this case, it's just a question of focusing on the sexual activity that brings about the pain. For example, does it hurt at the beginning (entrance or insertional dyspareunia) or upon deep thrusting? Such a question might differentiate vestibulodynia (vulvar vestibulitis syndrome) from pelvic endometriosis. Message: Taking a history for painful sex is not significantly different from taking a history for any other pain.

• **What role can the physical exam play? In fact, it can tell you why she hurts with sex.** As long as the examination is thorough and systematic, the cause of the pain is likely apparent by the end of the examination. Thinking anatomically, the exam is straightforward including the vulva, vagina, pelvic organs, and pelvic floor muscles.

Ask the patient to point to where the pain is, using one finger only (that gives you a better chance to identify the specific location of the pain).

Gently palpate the area of pain to see if you can elicit the pain that is bothering her.

If the area of pain is over the lower abdomen, ask the patient to tense the abdominal wall by lifting her head off the table/trying to touch her chin to her chest (like doing an abdominal crunch) and/or lift her legs off the table without bending her knees (like doing a leg lift).

Ask the patient specifically, "Is this the pain?" (Don't assume that all pain is the same pain that she is complaining of).

Palpate the vestibule (specifically the Skene's and Bartholin duct openings) with a moist cotton-tipped swab to identify potential tenderness.

Gently insert an index finger into the vagina to press posteriorly and laterally to identify potential pelvic floor muscular pain.

Rotate the index finger 180 degrees and palpate urethra and bladder.

Palpate the vaginal cuff (if the patient has had her uterus removed) or cervix to see if that recreates her pain.

Palpate the adnexa cautiously because the abdominal wall might well be the source of pain.

Perform a recto-vaginal exam if her symptoms and other signs warrant. Message: When examining, always ask the patient, "is this the pain?"

• **You see what you look for. You look for what you know.** This bit of wisdom sums up how far our diagnostic acumen will take us. Chances are that you will identify the conditions that are in your intellectual and clinical database. The more entities in that database, the more likely you'll be able to find the ultimate diagnosis. Even if your database is small, just trying is more than the patient might have gotten from others; plus, since you looked for a cause of the pain, you're far more likely to refer her to someone else who can continue the search. Message: The more conditions you know about, the more likely you'll find the right one. ■

ABSTRACT & COMMENTARY

An outline: Prognosis and treatment of DIV

By **Jeffrey T. Jensen**, MD, MPH, Leon Speroff Professor and Vice Chair for Research,
Department of Obstetrics and Gynecology
Oregon Health & Science University
Portland

Synopsis: Desquamative inflammatory vaginitis represents a chronic inflammatory process that responds well to anti-inflammatory treatment and requires long-term maintenance.

Source: Sobel JD, et al. Prognosis and treatment of desquamative inflammatory vaginitis. *Obstet Gynecol* 2011; 117:850-855.

The authors performed a descriptive analysis of all cases of desquamative inflammatory vaginitis (DIV), defined as symptomatic vaginitis (discharge, dyspareunia, pruritus, burning, or irritation) associated with vaginal inflammation (such as focal or linear erosions), a vaginal pH higher than 4.5, and saline microscopy showing an increase in parabasal and inflammatory cells in the absence of an infectious etiology (such as trichomonas, candida, or bacterial vaginosis). A review of clinic charts was conducted to identify women diagnosed with DIV by the lead author between 1996 and 2007 in a referral university-based vaginitis clinic. Clinical findings, laboratory findings, and treatment outcomes were documented during the first 12 months and at two and four years for subjects with longer follow-up. The authors identified 130 patients who met the case definition, but 32 were excluded (mainly due to a suspicion of erosive lichen planus). All of the patients presented with symptomatic vaginal inflammation, and 72% had vestibular findings (e.g., evidence of erythema, erosion, or thinning).

Initial treatments included topical 2% clindamycin (54%) or 10% hydrocortisone (46%). Both of these treatments relieved symptoms within three weeks (median) in the majority (86%) of patients. Among 53 women who discontinued treatment after an initial favorable clinical response, 17 (32%) were noted to relapse within six weeks. At one year, cure was achieved in 25/98 patients (26%) with the initial treatment only, while an additional 57/98 (58%) were asymptomatic but remained dependent on maintenance treatment. Symptoms were only partially controlled in 15/98 (16%). The authors conclude that DIV is an inflammatory condition that typically requires long-term maintenance therapy.

Commentary

I did not bring this paper to your attention because it was well written (it was not) or great science (single-site case series are the lowest level of medical evidence). However, little is written about difficult vaginitis, and the problem is highly disruptive to affected women. Vaginitis generally is considered to be a fairly mundane problem for most gynecologists; something for the office nurse to manage over the phone or a midlevel provider to triage in the office. Most cases of common vaginitis are indeed common. We are fortunate to have great treatments for yeast vulvovaginitis, bacterial vaginosis, and trichomoniasis. But, if you've ever seen a patient who presents with recurrent difficult-to-manage inflammatory vaginitis and felt unsure what to do, read on.

Most practitioners recognize a variety of causes of epithelial disorders on the external body surface (including the vulva) due to infectious, allergic, and irritant responses. The immune-based skin disorders, dermatoses (non-neoplastic epithelial disorders such

as psoriasis and lichen sclerosus), and neoplastic conditions such as vulvar intraepithelial neoplasia and squamous cancers also generally are recognized by most providers. If not, the presence of a distinct lesion usually leads to the appropriate action (biopsy or referral).

Why then the reluctance to consider that this diversity of disorders also may exist in the vagina? Many clinicians think that vaginal discharge can only mean infection or cancer. When screening tests for these conditions come up empty, the patient often receives yet another round of antifungal or antibiotic treatment. If you haven't found a way to effectively diagnose and manage difficult vaginitis, you might not even know it; these women probably have left your practice.

So what can we learn from this case series? First, the author's practice is a large university referral clinic for vulvovaginal disorders, so the cases represent a substantial accumulation of experience. This case series also comes with long-term follow-up (at least 30 months for most patients), so it provides us with some insight into the natural history of the condition. Finally, the manuscript represents a change in thinking by the author. Although DIV originally was recognized in the 1960s by Gray and Barnes[1] and described by Gardner,[2] the etiology and approach to therapy have been controversial. Almost 30 years after these initial reports, Sobel published a paper describing DIV as an infectious disease, and suggested that the condition was caused by an uncharacterized anaerobic bacterial overgrowth.[3] The absence of protective lactobacillus and clinical response to intravaginal clindamycin provided the basis for this conclusion. Although the science of the 1995 paper was similar to the current manuscript (case series), the lack of competing theories made it influential. The approach to treatment of DIV became antibiotics: usually clindamycin but sometimes penicillin (for the Group B Streptococcus [GBS] culture fans).

How did GBS become a vaginal pathogen? Guilt by association. Some clinicians began culturing difficult vaginitis and, not surprisingly, GBS was identified. Since GBS is present in about 20% of our obstetrical population, this finding should not be a surprise, but this colonization was accepted (and treated) as an infection by many providers.

Unfortunately, antibiotic treatment is not without risk. Penicillin and clindamycin kill lactobacillus, the bacterium we rely on to maintain the normal vaginal ecosystem. It is not surprising then that these therapies typically fail to reestablish normal flora. Leclair published an important (but not widely seen) paper last year in the Journal of Lower Genital Tract Disease that considered the question of GBS.[4] In this manuscript, non-pregnant reproductive age women with and without vaginitis underwent vaginal culture for GBS. Of the 215 women recruited, 68% showed no evidence of vaginitis, 19% had evidence of a common vaginitis (such as candida, BV, or trich), and 13% showed evidence of inflammatory vaginitis. The overall prevalence rate of GBS was 22.8%. Both common vaginitis (odds ratio [OR] 2.7, 95% confidence interval [CI] 1.1-6.2) and inflammatory vaginitis (OR 2.9, CI 1.1-8.0) were associated with an increased odds of GBS colonization. These findings demonstrate that disruption of the normal vaginal bacterial environment is an important predictor of GBS colonization. In other words, GBS fills a void when lactobacillus became scarce. GBS colonization is a result, and not a cause of disrupted flora, and treatment of gynecologic patients with penicillin for vaginitis is not warranted.

What about clindamycin? It works primarily due to its anti-inflammatory effects through a mechanism similar to macrolides and steroids. This mechanism is why clindamycin provides an effective benefit in treating acne as a topical product. It is also why metronidazole was not effective in treating DIV. The current manuscript by Sobel corrects the erroneous conclusions reached in 1995 that DIV has an infectious etiology and firmly establishes an inflammatory (possibly autoimmune) basis.

So how should you manage DIV? At our University Vulvar referral practice, we typical initiate therapy with hydrocortisone 25 mg rectal suppositories (used vaginally) at a dose of ½ to 1 suppository twice daily. See the patient back in two weeks to evaluate response. Usually, the inflammation and discharge (and symptoms) are greatly reduced as are the number of parabasal cells seen on wet smear. When adequate control is achieved, wean the therapy, but recognize that many patients will require long-term maintenance. Consider judicious use of intravaginal tacrolimus or clobetasol to manage difficult-to-treat cases. My personal belief is that most DIV represents a variant of erosive lichen planus, so look for signs of this dermatosis on the vestibule and vulva.

REFERENCES

1. Gray LA, Barnes ML. Vaginitis in women, diagnosis and treatment. *Am J Obstet Gynecol* 1965; 92:125-136.
2. Gardner HL. Desquamative inflammatory vaginitis: A newly defined entity. *Am J Obstet Gynecol* 1968; 102:1102-1105.
3. Sobel JD. Desquamative inflammatory vaginitis: A new subgroup of purulent vaginitis responsive to topical 2% clindamycin therapy. *Am J Obstet Gynecol* 1994; 171:1215-1220.
4. Leclair CM, Hart AE, Goetsch MF, et al. Group B streptococcus: Prevalence in a non-obstetric population. *J Low Genit Tract Dis* 2010; 14:162-166. ■