CONTRACEPTIVE TECHNOLOGY UPDATE®

Interpreting News and Research on Contraceptives and STIs

March 2011: Vol. 32, No. 3
Pages 25-36

IN THIS ISSUE

Enclosed in this issue:
STI Quarterly: Pre-exposure prophylaxis for HIV prevention; HPV vaccine gets new indication

Financial Disclosure:
Consulting Editor **Robert A. Hatcher**, MD, MPH, Author **Rebecca Bowers**, Executive Editor **Coles McKagen**, Senior Managing Editor **Joy Dickinson**, **Anita Brakman** and **Melanie Gold** (Guest Columnists) 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.

Prepare to update your practice: updated STD guidelines released

Expanded prevention recommendations include HPV vaccination

Clinicians now have the latest guidance in managing patients who have, or are at risk for, sexually transmitted diseases (STDs) with the just-released 2010 *STD Treatment Guidelines*.[1] The guidance was developed by the Centers for Disease Control and Prevention (CDC) after consultation with a panel of national experts who convened in April 2009.

The 2010 guidelines, which update a similar 2006 publication, serve as a source of clinical guidance and advise health care providers on the most effective treatment regimens, screening procedures, and prevention and vaccination strategies for STDs, according to CDC officials. The agency revises the guidance periodically, using a scientific, evidence-based process that includes CDC and external expert review of current scientific literature.

The guidelines are intended to assist clinicians with the management of persons who have, or are at risk for, sexually transmitted diseases, noted **Kimberly Workowski**, MD, infectious diseases specialist in the CDC's Division of STD Prevention, in a podcast debuting the new guidance. Although the guidelines emphasize treatment, prevention strategies

EXECUTIVE SUMMARY

Clinicians now have the latest guidance in managing patients who have, or are at risk for, sexually transmitted diseases (STDs) with the just-released 2010 *STD Treatment Guidelines*, developed by the Centers for Disease Control and Prevention (CDC).

- The CDC plans webinars associated with the new guidance, as well as formats for the iPhone and e-books.
- Some of the key changes in the 2010 guidance include the prevention and treatment of human papillomavirus virus, gonorrhea, and lymphogranuloma venereum proctocolitis.

AHC Media LLC

and diagnostic evaluation are also discussed, said Workowski, who served as lead author for the publication.

CDC officials have been busy making sure practitioners receive the updated guidelines, says **Rachel Powell**, a CDC spokesperson. The agency has worked to get the word out to trade press, as well as with its prevention partners, to spread news of the new publication, she says. Powell encourages clinicians to visit the dedicated web page, www.CDC.gov/STD/treatment/2010, to download the guidance, check for updates, and access outreach tools. Printed copies, wall charts, and pocket guides will be available for order in the coming months. The web site will have updates on these materials, as well as other educational opportunities, says Powell. The site also includes the erratum contained in the Jan. 10, 2011 "Dear Colleague" letter, which contains corrections for recommended regimens for gonococcal infections, which include gonococcal dual therapy, and the alternative regimens for bacterial vaginosis.

The CDC is planning some population-specific webinars, Powell reports. An adolescent one is in the planning process, she states. Also look for iPhone and e-book applications to come, says Powell.

What's new?

The 2010 guidelines highlight expanded prevention recommendations for sexually transmitted infections, said Workowski. Some of the key changes include the prevention and treatment of human papillomavirus virus (HPV), gonorrhea, and lymphogranuloma venereum proctocolitis.

"Preexposure vaccination is one of the most effective methods to prevent transmission of HPV," noted Workowski. Clinicians have two HPV vaccines licensed for females ages 9 through 26 to prevent cervical precancer and cancer: the quadrivalent HPV vaccine, Gardasil, and the bivalent HPV vaccine, Cervarix. Gardasil also is indicated for prevention genital warts, she noted.

Routine vaccination of females ages 11 or 12 is recommended with either vaccine, as is the catch-up vaccination for females ages 13 through 26, stated Workowski. Gardasil also may be given to males ages 9 through 26 to prevent genital warts.

Neisseria gonorrhoeae, or GC, has developed resistance to many classes of antimicrobials recommended for treatment, stated Workowski. Quinolone-resistant *Neisseria gonorrhoeae* strains are widely disseminated throughout the United States and the world, and as a result, quinolones are not recommended for the treatment of gonorrhea. *(*Contraceptive Technology Update *reported on the change in recommendations; see "New recommendations out for gonorrhea treatment," June 2007, p. 64.)*

"Although currently recommended regimens are

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 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), $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 740056, Atlanta, GA 30374. Telephone: (800) 688-2421. World Wide Web: http://www.ahcmedia.com.

effective for gonorrhea within the United States, the susceptibility of gonococcal isolates to cephalosporins has been decreasing, and treatment failures with oral cephalosporins have been documented in Southeast Asia," noted Workowski. "Based on prior experience with quinolone-resistant *N. gonorrhoeae*, it is probable that such isolates may spread to the United States."

Due to these reports, ceftriaxone 250 mg intramuscularly or cefixime 400 mg orally are recommended for urogenital infection. Since many with gonorrhea are coinfected with chlamydia, therapy with azithromycin or doxycycline is recommended.

Lymphogranuloma venereum proctocolitis (LGV) is being increasingly recognized especially among HIV-positive men who have sex with men, Workowski pointed out. In persons with painful perianal ulcers or those detected on anoscopy, presumptive therapy should include treatment for LGV, which is doxycycline 100 mg twice daily for 21 days.

Check genital wart option

A new patient-applied treatment for genital warts is available, stated Workowski. The treatment of 15% sinecatechins ointment should be applied by the patient three times daily until complete clearance of the warts. The ointment, Veregen Ointment, is manufactured by PharmaDerm, a division of Nycomed US in Florham Park, NJ.

The guidance also offers a new alternative treatment for bacterial vaginosis: 2 g of tinidazole taken daily for three days or 1 g taken daily for five days. For episodic outbreaks of herpes simplex virus, an additional treatment option is 500 mg of famciclovir followed by two days of 250 mg taken twice daily, stated Workowski.

There also are some data that moxifloxacin — 400 mg daily for seven days — is effective in nongonococcal urethritis treatment failures due to *Mycoplasma genitalium*, she stated.

Put guidance into gear

Now that clinicians have the guidance in hand, it is time to brush up on skills that can aid in obtaining a thorough sexual history and effectively delivering prevention messages.

Consider the following strategies to facilitate rapport with patients:

• Use open-ended questions, such as "Tell me about any new sex partners you've had since your last visit" and "What's your experience with using condoms been like?

• Incorporate understandable language, such as "Have you ever had a sore or scab on your penis?

• Use normalizing language, such as "Some of my patients have difficulty using a condom with every sex act. How is it for you?"

Consider using the "Five Ps" to help obtain the necessary information for a thorough sexual history. *(See story, below.)* Remember that effective interviewing and counseling skills, characterized by respect, compassion, and a nonjudgmental attitude toward all patients, are essential to gathering information for a successful treatment plan.[1]

REFERENCE

1. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. *MMWR* 2010; *59*(RR12);1-110. ■

Use the five Ps in your practice

Be sure to include the "five Ps" when obtaining a sexual history:

• **Partners.**

Ask: Do you have sex with men, women, or both? In the past two months, how many partners have you had sex with? In the past 12 months, how many partners have you had sex with? Is it possible that any of your sex partners in the past 12 months had sex with someone else while they were still in a sexual relationship with you?

• **Prevention of pregnancy.** Ask: What are you doing to prevent pregnancy?

• **Protection from STDs.** Ask: What do you do to protect yourself from STDs and HIV?

• **Practices.** Say: To understand your risks for STDs, I need to understand the kind of sex you have had recently. Have you had vaginal sex, meaning penis-in-vagina sex? If yes, do you use condoms: never, sometimes, or always? Have you had anal sex, meaning penis-in-rectum/anus sex? If yes, do you use condoms never, sometimes, or always? Have you had oral sex, meaning mouth on penis/vagina?

For condom answers: If answer is "never," ask, "Why don't you use condoms?" If answer is "sometimes," ask, "In what situations (or with whom) do you not use condoms?"

• **Past history of STDs.** Ask: Have you ever had an STD? Have any of your partners had an STD?

Additional questions to identify HIV and viral hepatitis risk include: Have you or any of your partners ever injected drugs? Have any of your partners exchanged money or drugs for sex? Is there anything else about your sexual practices that I need to know about?

Source: Adapted from: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. *MMWR* 2010; 59(RR12);3. ■

Counsel on efficacy of contraceptive implant

Clinician office phones might be ringing following news reports of women in the United Kingdom (UK) who experienced unintended pregnancies while using the contraceptive implant Implanon. How do you counsel women on this form of long-acting contraception?

Several women in the UK have taken legal action after they received the contraceptive implant and became pregnant. According to the UK Department of Health, 584 official reports of pregnancies among implant users have been recorded in the UK since the device was introduced in 1999. About 1.4 million UK women have used Implanon; at present, 800,000 women are estimated to be relying on the device for contraception.[1]

It is important to put the some 600 pregnancies into perspective, 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. Implanon has the highest efficacy among available contraceptive methods.[2] In an overview of the clinical data, zero pregnancies were recorded during 53,530 cycles (4,103 woman-years), resulting in a Pearl index of 0.0 (95% confidence interval, 0.00-0.09).[2]

Implanon is a highly effective method of birth control, states **Abbey Berenson**, MD, MMS, professor in the Department of Obstetrics and Gynecology and director of the Center for Interdisciplinary Research in Women's Health, both at University of Texas Medical Branch in Galveston. Its advantage lies in that it does not require the patient to remember to take a pill every day or come in to the clinic and get a shot every three months, she notes. Thus, the actual pregnancy rate is much lower with Implanon than most other contraceptive methods, Berenson states.

Check for insertion

There have been reports of problems with inserting and removing Implanon, according to the UK Department of Health.[1] In some women who experienced an unintended pregnancy, Implanon was found not to have been inserted, the department states. These issues have been kept under close review by the agency.[1]

All healthcare providers must receive training before inserting or removing Implanon, according to the package insert. Prior to inserting the device, instructions call for the clinician to carefully remove the Implanon applicator from its blister pack, keep the shield on the needle, and look for the Implanon rod, seen as a white cylinder, inside the needle tip. If the Implanon rod is not visible, the clinician should tap the top of the needle shield against a firm surface to bring the implant into the needle tip.

Following visual confirmation, instructions state to lower the Implanon rod back into the needle by tapping it back into the needle tip, then remove the needle shield while holding the applicator upright. Because Implanon can fall out of the needle, clinicians should keep the applicator in the upright position after the needle shield is removed until the moment of insertion.[3]

Confirm that Implanon has been inserted by inspecting the needle tip for the absence of the Implanon rod and the visualization of the grooved obturator tip. Palpate the arm to check for the implant, and have the patient to do so as well.

EXECUTIVE SUMMARY

Recent news reports say women in the United Kingdom (UK) experienced unintended pregnancies while using the contraceptive implant Implanon.

- According to the UK Department of Health, 584 official reports of pregnancies among implant users have been recorded in the UK since the device was introduced in 1999.
- There have been reports in the UK of problems with inserting and removing Implanon. Providers now use an updated form of the implant, which features a new preloaded applicator designed to reduce the risk of insertion errors.

New device under review

Insertion errors might be diminished with Nexplanon, an advanced generation of Implanon. Introduced in the UK in October 2010, Nexplanon contains the same amount of etonogestrel (68 mg) and is bioequivalent to Implanon. It also is indicated for three years of use and has similar removal instructions.

Nexplanon differs from Implanon in two ways.

It features a new preloaded applicator, which is designed to reduce the risk of insertion errors. The device also is radio-opaque and can be located on an X-ray or CT scan if necessary.

The device is not available in the United States. However, it is now under review by the Food and Drug Administration as IMPLANON NXT, confirms **Lee Davies**, a spokesman for Merck & Co., the device manufacturer.

Review the options

In counseling women, it is important to note that no contraceptive is 100% effective, says Berenson. For women who can't remember to take the Pill everyday, don't want anything implanted in their uterus, and do want long-term contraception, Implanon is a good match, she states.

As with any contraceptive method, Implanon has advantages and disadvantages, according to *A Pocket Guide for Managing Contraception*. Implanon offers decreased menstrual and ovulatory cramping, and dysmenorrhea decreases by 48%. A disadvantage might lie in unpredictable or irregular menstrual bleeding. While such bleeding might persist, it usually is light and well-tolerated.[4]

"The spotting/bleeding is a real challenge, but many women really appreciate the true efficacy," says Nelson.

REFERENCES

1. National Health Services Knowledge Base. Implanon contraceptive implant examined. Accessed at http://www.nhs.uk/news/2011/01January/Pages/info-implanon-contraceptive-implant.aspx.
2. Croxatto HB, Mäkäräinen L. The pharmacodynamics and efficacy of Implanon. An overview of the data. *Contraception* 1998; 58(6 Suppl):91S-97S.
3. Schering-Plough Corp. Implanon prescribing information. Accessed at http://www.spfiles.com/piimplanon.pd.pdf.
4. Zieman M, Hatcher RA, Cwiak C, et al. *A Pocket Guide for Managing Contraception*. Tiger, GA: Bridging the Gap Foundation. 2010. ■

Shot, OC impact eyed on glucose, insulin levels

Results of a new study indicate fasting glucose and insulin levels remain within normal range for women using injectable or oral contraception, with only slight increases among women using depot medroxyprogesterone acetate (DMPA).[1]

The study, which was conducted over three years, is the largest to measure fasting glucose and insulin levels among women using DMPA, an oral contraceptive (desogestrel/ethinyl estradiol), and non-hormonal methods (bilateral tubal ligation, condom, or abstinence).

Some hormonal contraceptives, such as contraceptive implants and injections, have been associated with changes in carbohydrate metabolism.[2,3] These changes might include decreased glucose tolerance and increased insulin resistance, which are risk factors for Type 2 diabetes mellitus and cardiovascular disease. "Previous studies were limited in scope and offered conflicting results, which led physicians to question whether hormonal contraception could lead to diabetes," says **Abbey Berenson**, MD, MMS, professor in the Department of Obstetrics and Gynecology and director of the Center for Interdisciplinary Research in Women's Health, both at University of Texas Medical Branch in Galveston.

Further studies are needed to determine how women with diabetes are affected by DMPA and oral contraception, but results of the current study are reassuring for non-diabetic women already receiving the shot or on the Pill, says Berenson.

EXECUTIVE SUMMARY

Results of a new study indicate fasting glucose and insulin levels remain within normal range for women using injectable or oral contraception, with only slight increases among women using depot medroxyprogesterone acetate (DMPA).

- The study, which was conducted over three years, is the largest to measure fasting glucose and insulin levels among women using DMPA, an oral contraceptive, and non-hormonal methods
- Some hormonal contraceptives have been associated with changes in carbohydrate metabolism. These changes might include decreased glucose tolerance and increased insulin resistance, which are risk factors for Type 2 diabetes mellitus and cardiovascular disease.

The Texas investigators hope to pursue additional research on the topic, she says.

Check the results

To conduct the longitudinal study, researchers measured fasting glucose and insulin levels in 703 white, African-American, and Hispanic women.

After counseling on the different types of contraception available and their efficacies, women were allowed to select one of three types of birth control: 245 selected an oral contraceptive (0.15 mg desogestrel plus 20 mcg ethinyl estradiol for 21 days, followed by two days of placebo and five days of 10 mcg ethinyl estradiol); 240 chose DMPA; and 218 chose a nonhormonal method. Women in the study also completed questionnaires containing demographic and behavioral measures every six months.

Researchers report that DMPA users, but not Pill users, experienced slightly greater increases in glucose and insulin as compared with nonhormonal users (P<.001). Among DMPA users, a small but steady increase in serum glucose levels (2 mg/dL at six months to 3 mg/dL at 30 months) was observed throughout the first 30 months, but it leveled off after that time. In contrast, serum insulin levels showed an upward trend (three units at six months to four units at 18 months) for the first 18 months of DMPA use; it then remained almost flat thereafter. Elevation of insulin and glucose levels was slightly more pronounced in obese and overweight DMPA users than those who were of normal weight.

These observed increases, which were less than those reported in previous studies,[4,5] were not significant enough to cause concern, researchers report.

The Texas study adds solid evidence to the emerging body of research regarding contraceptives' impact on carbohydrate metabolism. In a 2007 Cochrane Review on the effect of steroidal contraceptives' impact on carbohydrate metabolism in women without diabetes mellitus, investigators concluded that such methods have limited effect on metabolism in non-diabetic women.[6]

While the reviewers noted the available evidence suggested that hormonal contraceptives have limited effect on carbohydrate metabolism in women without diabetes, they noted that strong statements could not be made due the small number of studies that compared any particular types of contraceptives.

Many trials had small numbers of participants and some had large losses, investigators said. Many studies had poor reporting of methods, and no information was available regarding the effects among women who were overweight, they state.[6]

In performing their data analysis, investigators did a computer search for studies of birth control methods containing hormones and how carbohydrates are handled in the body. Outcomes were glucose or insulin levels in the blood. Birth control methods included types with estrogen and progestin or progestin-only options. Types of birth control included in the review were pills, shots (injections), implant, the vaginal ring, and an intrauterine device. To undertake the review, investigators included randomized trials in any language that had at least three treatment cycles. Studies included in the review had to compare two types of birth control, or one type of contraception with a placebo method.

Investigators found 43 trials that met the inclusion criteria; however, no study stratified by body weight (normal weight versus overweight women). While results for desogestrel often were favorable regarding carbohydrate metabolism, investigators found they were inconsistent overall. Glucose and insulin means were more favorable for norethisterone in studies of progestin-only contraceptives. For other progestins, little or no difference was noted across trials, investigators reported.[6]

REFERENCES

1. Berenson AB, van den Berg P, Williams KJ, et al. Effect of injectable and oral contraceptives on glucose and insulin levels. *Obstet Gynecol* 2011;117:41-47.
2. Dorflinger LJ. Metabolic effects of implantable steroid contraceptives for women. *Contraception* 2002;65:47-62.
3. Kahn HS, Curtis KM, Marchbanks PA. Effects of injectable or implantable progestin-only contraceptives on insulin-glucose metabolism and diabetes risk. *Diabetes Care* 2003; 26:216-225.
4. Fahmy K, Abdel-Razik M, Shaaraway M, et al. Effect of long-acting progestagen-only injectable contraceptives on carbohydrate metabolism and its hormonal profile. *Contraception* 1991;44:419-430.
5. Vermeulen A, Thiery M. Hormonal contraceptives and carbohydrate tolerance. II. Influence of medroxyprogesterone acetate and chronic oral contraceptives. *Diabetologia* 1974; 10:253-259.
6. Lopez LM, Grimes DA, Schulz KF. Steroidal contraceptives: effect on carbohydrate metabolism in women without diabetes mellitus. *Cochrane Database of Systematic Reviews* 2009. Doi:10.1002/14651858.CD006133.pub3. ■

Put same-sex behavior of teens in the spotlight

Numbers almost doubled from prior studies

Results of a new study suggest that nearly one in 10 sexually active teens have same-sex partners, which is almost twice as many as previous research studies have found.[1]

Researchers at the New York City Department of Health and Mental Hygiene looked at results from the 2005–2007 New York City Youth Risk Behavior Surveys, which included responses from more than 17,000 teens in the city. Their analysis indicates that teens that had sex with only their own gender or with both genders were more likely to engage in risky sexual behaviors, putting themselves at greater risk for sexually transmitted diseases (STDs).

Past research indicates that youth who have sexual experiences with partners of the same sex are vulnerable in that they report high rates of depression, suicidal ideation, substance abuse, and experience with violence, among other issues,[2,3] says **Preeti Pathela**, DrPH, research scientist in the Department of Health's Bureau of Sexually Transmitted Disease Control and lead author of the current study. Past findings suggest that the subset of adolescents who have partners of both sexes might be more prone to these experiences and outcomes, she says.[4] However, analyzing information on this group has not been easy because large sample sizes are needed to draw generalizable conclusions; therefore, studies looking at these issues often have not separated males and female respondents or they have combined respondents with bisexual and exclusively homosexual behavior in order to yield larger groups, she notes.

"In New York City, we are fortunate to have biennial surveys of large numbers of adolescents that could provide us with data," Pathela notes.

Analyze the results

To perform the study, researchers looked at results from the 2005-2007 New York City Youth Risk Behavior Surveys, which look at different behaviors among high school students. Of 15,009 students who answered the question on sexual intercourse, 55.2% (3,898 of 7,021) of male and 43.8% (3,501 of 7,988) of female adolescents reported that they had ever had sex.

Similar numbers of sexually active male and female adolescents (3.2%) reported only same-sex behavior, but fewer male than female adolescents reported both-sex partners (3.7% versus 8.7%; P < .001). Male adolescents with both-sex partners reported a higher prevalence of sexual risk behaviors than male adolescents with only opposite-sex or only same-sex partners. For example, male adolescents with both-sex partners were much less likely to report using a condom at last sex (44.1%) compared with those with opposite-sex partners (79.8%; P = .0002). Female adolescents with both-sex or only same-sex partners also reported a higher prevalence of risk behaviors than female adolescents with only opposite-sex partners, researchers note. Teen girls were more likely to report the use of alcohol/drugs with the last sexual encounter if they had both-sex partners (23.0%) or only same-sex partners (22.3%) than if they had only opposite-sex partners (10.0%). Adolescents with both-sex partners reported a marked prevalence of dating violence and forced sex (males: 34.8% partner violence, 31.6% forced sex; females: 35.8% partner violence, 34.1% forced sex).

What's your approach?

Many adolescents in the New York City survey with only same- or both-sex partners (38.9%) self-identified as straight. That is why clinicians should inquire about behaviors, and not identity, to determine teen's risks for STDs, the researchers note. Education about STDs should include information appropriate for youth with same-sex partners, they add.

Getting clinicians up to speed in dealing with sexual orientation might be a challenge.

EXECUTIVE SUMMARY

Results of a new study suggest that nearly one in 10 sexually active teens have same-sex partners, which is almost twice as many as previous research studies have found.

- Researchers at the New York City Department of Health and Mental Hygiene looked at results from the 2005–2007 New York City Youth Risk Behavior Surveys, which included responses from more than 17,000 teens in the city.
- Their analysis indicates that teens that had sex with only their own gender or with both genders were more likely to engage in risky sexual behaviors, putting themselves at greater risk for sexually transmitted diseases.

According to information presented at the 2009 *Contraceptive Technology* conference, 70% of pediatricians in one survey did not report addressing the issue.[5]

To make sure your office is "teen-friendly" when it comes to sexual behaviors, the California Adolescent Sexual Health Work Group suggests offering sexual health education materials with age-appropriate language in the waiting room that are inclusive of a diverse audience. Also check your intake/history forms and questionnaires to make sure it has gender-inclusive language.

Talk with staff members to be sure they are careful to avoid making assumptions about gender or sexual orientation with teen patients. Staff should be ready to maintain sensitivity for the sexual orientation, family structure, and lifestyle choices of all patients and their loved ones, the work group recommends.[6]

REFERENCES

1. Pathela P, Schillinger JA. Sexual behaviors and sexual violence: adolescents with opposite-, same-, or both-sex partners. *Pediatrics* 2010; 126:879-886.
2. Saewyc EM, Skay CL, Pettingell SL, et al. Hazards of stigma: the sexual and physical abuse of gay, lesbian, and bisexual adolescents in the United States and Canada. *Child Welfare* 2006;85:195-213.
3. Garofalo R, Wolf RC, Wissow LS, et al. Sexual orientation and risk of suicide attempts among a representative sample of youth. *Arch Pediatr Adolesc Med* 1999;153:487-493.
4. Saewyc EM, Bearinger LH, Heinz PA, et al. Gender differences in health and risk behaviors among bisexual and homosexual adolescents. *J Adolesc Health* 1998;23:181-188.
5. Dahan R, Feldman R, Hermoni D.Is patients' sexual orientation a blind spot of family physicians? *J Homosex* 2008; 55:524-532.
6. Monasterio E, Combs N, Warner L, et al. Sexual Health: An Adolescent Provider Toolkit. San Francisco, CA: Adolescent Health Working Group, 2010. Accessed at http://www.ahwg.net/assets/library/104_sexualhealthtoolkit2010bw.pdf. ■

Pelvic exam necessary for contraception Rx?

"Clinicians at my family planning facility often refuse to give a birth control method if the patient is late for her annual exam," says a respondent to the 2010 *Contraceptive Technology Update* Contraception Survey. Is this practice prevalent in the United States?

While some providers might continue to require a pelvic exam prior to providing hormonal contraception, results of a national survey indicate many providers are dropping such restrictions.[1] In a poll of obstetrician-gynecologists (OB/GYNs), family medicine physicians, and advanced practice nurses specializing in obstetrics and gynecology and women's health or family medicine, less than one third of OB/GYNs (29%) and exactly one-third of family medicine physicians (33%) said they always require a pelvic examination when prescribing oral contraception. Almost half of advanced practice nurses in primary care (45%) and some advanced practice nurses in reproductive health (17%) reported always requiring an exam.

Is a pelvic examination necessary? No, according to national and international guidance. Hormonal oral contraception can be prescribed safely without a pelvic examination, according to guidelines from the World Health Organization and the American College of Obstetricians and Gynecologists.[2,3] While weight, blood pressure, and health history are required before prescription of hormonal contraception, screening for sexually transmitted infections and cancer are not necessary to evaluate patients for initiation of oral contraceptive use for birth control, according to authors of the recently published survey results.[1]

Requiring a pelvic exam to access birth control is really a "tragic leftover from the past," 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.

"In a beneficent effort to gain more comprehensive care for women, we linked many of the

EXECUTIVE SUMMARY

Hormonal oral contraception can safely be prescribed without a pelvic exam, according to guidelines from the World Health Organization and the American College of Obstetricians and Gynecologists.

- In a poll of obstetrician/gynecologists, family medicine physicians, and advanced practice nurses specializing in OB/GYN and women's health or family medicine, less than one-third of OB/GYNs (29%) and exactly one-third of family medicine physicians (33%) said they always require a pelvic exam when prescribing oral contraception.
- Some advanced practice nurses in primary care (45%) and advanced practice nurses in reproductive health (17%) reported always requiring an exam.

aspects of reproductive health care," says Nelson. "To motivate women to take their care seriously, doctors did the same."

Today, clinicians know that requiring an annual pelvic exam prior to continuance of birth control only causes problems, she states. "The truth is that there is nothing in the exam, except the blood pressure, that could keep a woman from being eligible to continue her method, if it contains estrogen," Nelson observes. "If it is a progestin-only method, even elevated blood pressure would not be a problem."

There is generally no need for withholding a method of contraception because someone is late for her exam, advises **Susan Wysocki**, WHNP-BC, FAANP, president and chief executive officer of the Washington, DC-based National Association of Nurse Practitioners in Women's Health. It is better to be late for an exam than late for her period, she points out.

There absolutely is no connection between methods of contraception and getting a Pap test or a pelvic exam, as the most important parts of the yearly exam (as it relates to hormonal methods) are the history and a blood pressure, says Wysocki. The history review can be done quickly over the telephone, which allows the clinician to note changes in medical history and use of new medications, she says. A blood pressure reading can be obtained at any local chain drug store, if the clinician thinks it is necessary. However, the history and the blood pressure can be deferred until the woman can make it into the office for an appointment, states Wysocki.

Knock down barriers

Requiring asymptomatic women to undergo a pelvic examination before dispensing contraception "poses an unnecessary medical hurdle before a critical and time-sensitive medication," say authors of the current survey analysis.[1] In a 2001 study, research shows that hormonal contraception can be provided safely based on careful review of medical history and blood pressure measurement. For most women, no further evaluation is necessary, the 2001 study states.[4]

Refusing to call in a prescription for pills, rings, or patches because a woman is late is "thoughtless," says **Robert Hatcher**, MD, MPH, professor of gynecology and obstetrics in the Emory University School of Medicine in Atlanta. In fact, since there is often a delay in scheduling visits, one might even suggest that refusing to call in a prescription for a woman who will be late for her annual exam by the time she needs to obtain a package of pills, patches, or a ring is "perfectly outrageous," states Hatcher.

"You wonder why 50% of all pregnancies in the United States are unintended?" he observes. "This practice suggests one little part of the answer."

REFERENCES

1. Henderson JT, Sawaya GF, Blum M, et al. Pelvic examinations and access to oral hormonal contraception. *Obstet Gynecol* 2010;116:1257-1264.
2. World Health Organization. *Selected Practice Recommendations for Contraceptive Use*. Second ed. Geneva: WHO; 2004. Available at http://whqlibdoc.who.int/publications/2004/9241562846.pdf.
3. American College of Obstetricians and Gynecologists. *Guidelines for women's health care: a resource manual*. Third ed. Washington, DC: American College of Obstetricians and Gynecologists; 2007.
4. Stewart FH, Harper CC, Ellertson CE, et al. Clinical breast and pelvic examination requirements for hormonal contraception: Current practice vs. evidence. *JAMA* 2001;285:2232-2239. ■

States eye benefits as family planning expands

By **Adam Sonfield**
Senior Public Policy Associate
Guttmacher Institute
Washington, DC

Among the seemingly countless provisions in the March 2010 health reform law is one that greatly simplifies the process by which a state may extend Medicaid eligibility for family planning services and supplies to individuals ineligible for comprehensive health coverage under the program.[1] These expansions have the potential to greatly expand the capacity of family planning clinics and private providers to help thousands of women and couples avoid unplanned pregnancies, births, and abortions, and in the process improve public health and save millions in public dollars.[2]

Before the new law, states had been able to initiate a Medicaid family planning expansion only as a temporary demonstration program, under the complicated, time-consuming process of seeking a "waiver" from Medicaid law and regulations. Despite the red tape, a geographically and politically diverse group of 22 states have taken this approach since the mid-1990s. Those states have extended eligibility to women, and sometimes men, typically up to the same income eligibility level used in the state for coverage of pregnancy-related care. In most states, that level is at or near 200% of the federal poverty level.[3] *(Six additional states have more limited expansions in place, typically for postpartum women. See list on p. 35.)*

Under their new authority, states may set up a family planning expansion under a streamlined process, known as a state plan amendment (SPA). The programs must cover all of the family planning services and supplies available under the state's full-benefit Medicaid program. Those usually include the complete range of contraceptive methods and associated examinations and lab tests. States pay for only 10% of the costs of these services, with the federal government reimbursing them for the other 90%. States must also cover transportation costs and at least some of a broader set of related services, such as treatment for sexually transmitted infections or the human papillomavirus vaccine, provided as part of or follow-up to a family planning visit. The costs for those services are split more evenly between the state and federal governments.

The law allows states to cover a broader population than currently covered under any existing waiver program. It also requires states' expansions to cover adolescents and men, two groups excluded under some current waivers. A SPA is a permanent change to a state's Medicaid program. By contrast, a waiver must be renewed every several years and requires ongoing evaluation.

COMING IN FUTURE MONTHS

- Don't miss opportunities to talk about intrauterine contraception
- Research notes uptick in medication abortion
- Reach teens with reproductive health information
- Check approach to treatment of pelvic inflammatory disease

Programs make impact

A large body of evidence from program evaluations and independent studies indicates that the existing programs have had a significant impact.

Waiver programs have been found to expand women's access to contraceptive services and improve their contraceptive use. In turn, those changes have helped thousands of women and couples avoid unplanned pregnancies and the births and abortions that follow. In doing so, the programs have helped women extend their interpregnancy intervals, a key factor in maternal and child health. The cost of providing Medicaid-covered, pregnancy-related care greatly outstrips the cost of providing contraceptive services. Thus, these programs also have generated tens of millions of dollars in state and federal savings annually in states as diverse as Alabama, Arkansas, California, Oregon, and South Carolina.[2,4]

A new Guttmacher Institute analysis, drawing on the experience of existing waiver programs, projects that most states could see this type of impact if they took up the new family planning SPA authority. Twenty-eight states don't have an income-based family planning expansion. Nineteen of them could each serve at least 10,000 individuals, enable women to prevent at least 1,500 unintended pregnancies, and save at least $2.3 million in state funds in a single year, beyond what their Medicaid program is already accomplishing. Nine of the 19 could each serve at least 50,000 individuals, avert at least 7,500 unintended pregnancies, and save at least $17.4 million. Even states that already have a waiver program could benefit from switching to a SPA, because they could cover additional women and men. Among the 22 states with waivers, 11 of them could each serve at least 10,000 new participants, avert at least 1,300 unintended pregnancies, and save at least $1.7 million in state funds annually, beyond what their expansions achieve today.[2]

The ultimate impact of any new expansion would depend greatly on state-level decisions and factors, including the range of services covered, the quality of care provided, and the capacity of the state's provider network and Medicaid systems. Nevertheless, the potential benefits of expansion are clear enough that they might override the numerous fiscal and political pressures that state legislators and officials are facing. Already as of mid-January 2011, two states — Wisconsin and

State Family Planning Expansion Overview

• States with Family Planning State Plan Amendments

South Carolina	Wisconsin

• States with Income-Based Family Planning Waivers

Alabama	Arkansas
California	Georgia
Illinois	Iowa
Louisiana	Michigan
Minnesota	Mississippi
Missouri	New Mexico
New York	North Carolina
Oklahoma	Oregon
Pennsylvania	Texas
Virginia	Washington

• States with Limited Family Planning Waivers

Arizona	Delaware
Florida	Maryland
Rhode Island	Wyoming

Source: Guttmacher Institute, State Medicaid family planning eligibility expansions, State Policies in Brief (as of January 14, 2011), 2011. Accessed at http://www.guttmacher.org/statecenter/spibs/spib_SMFPE.pdf

South Carolina — had received federal approval to shift from a waiver to a SPA and expand the scope of their programs.[3] To date, none of the states without waiver programs have received approval for a family planning SPA, but it was only in July 2010 that the Centers for Medicare and Medicaid Services issued formal guidance to states on the implementation of the new provision.[5]

REFERENCES

1. Patient Protection and Affordable Care Act, P.L. 111–148, Sec. 2303, March 23, 2010.
2. Sonfield A, Frost JJ, Gold RB, Estimating the Impact of Expanding Medicaid Eligibility for Family Planning Services: 2011 Update. New York: Guttmacher Institute, 2011.
3. Guttmacher Institute, State Medicaid family planning eligibility expansions, State Policies in Brief (as of January 14, 2011), 2011. Accessed at http://www.guttmacher.org/statecenter/spibs/spib_SMFPE.pdf.

continued on page 36

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.

9. According to the 2010 *STD Treatment Guidelines*, what is a new patient-applied treatment for genital warts?
A. 15% sinecatechins ointment
B. Clindamycin cream
C. Butoconazole cream

10. How does the contraceptive implant Nexplanon differ from Implanon?
A. It has a higher dose of etonogestrel.
B. It features a new preloaded applicator, which is designed to reduce the risk of insertion errors.
C. It is 5 mm larger in size.

11. According to a 2011 study (Berenson AB, et al. Effect of injectable and oral contraceptives on glucose and insulin levels. *Obstet Gynecol*) how are fasting glucose and insulin levels impacted in women using injectable or oral contraception?
A. Levels are lowered.
B. Levels remain within normal range.
C. Levels remain within normal range, with only slight increases among women using depot medroxyprogesterone acetate.

12. Why is it important that clinicians inquire about behaviors, and not identity, to determine an adolescent's risks for sexually transmitted diseases, according to a 2010 study (Pathela P, et al. Sexual behaviors and sexual violence: adolescents with opposite-, same-, or both-sex partners. *Pediatrics*)?
A. Some adolescents are more comfortable discussing behaviors.
B. Some adolescents gave false information regarding their sexual identity.
C. Many adolescents in the study who had only same- or both-sex partners (38.9%) self-identified as straight.

Answers: 9. A; 10. B; 11. C; 12. C

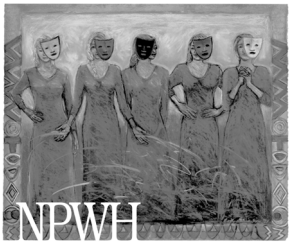
continued from page 35

4. Edwards J, Bronstein J, Adams K. Evaluation of Medicaid Family Planning Demonstrations. Alexandria, VA: CNA Corp., 2003.
5. Centers for Medicare and Medicaid Services. Family planning services option and new benefit rules for benchmark plans. State Medicaid Director Letter, July 2, 2010, SMDL No. 10-013, ACA No. 4. Accessed at http://www.cms.gov/smdl/downloads/SMD10013.pdf. ■

CNE/CME INSTRUCTIONS

Physicians and nurses participate in this continuing nursing 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 June issue, you must complete the evaluation form provided and return it in the reply envelope provided in that issue to receive a letter of credit. When your evaluation is received, a letter will be mailed to you. ■

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.



S·T·I
QUARTERLY™

Update: Use of HIV drugs shrinks infection risk in uninfected people

Can same pre-exposure prophylaxis results be recreated in real life?

Use of powerful antiretroviral drugs, known as pre-exposure prophylaxis (PrEP), is now being weighed as an addition to the HIV prevention arsenal with the results of a new clinical trial.[1]

In the Pre-exposure Prophylaxis Initiative (iPrEx) trial, researchers found that among men who have sex with men (MSM) who took a single daily tablet containing two widely used HIV medications, emtricitabine and tenofovir, subjects experienced an average of 43.8% fewer HIV infections than those who received a placebo pill (95% CI 15.4 to 62.6%; P=0.005).[1]

The iPrEx study, one of the largest HIV prevention clinical trials to focus on men who have sex with men, claims two "firsts:" It is the first HIV prevention study to focus on MSM to be conducted in Africa or Asia, and it is the first demonstration of a biomedical intervention to prevent HIV infection in MSM. The findings represent a "major advance" in HIV prevention research, providing the first evidence that PrEP, when combined with other prevention strategies, can reduce HIV risk among MSM, state the Centers for Disease Control and Prevention (CDC).[2] *[Use a CDC-developed fact sheet to talk with patients about the ramifications of the study, as well as understand the agency's direction on PrEP. A fact sheet is enclosed with the online issue of* Contraceptive Technology Update. *For assistance, contact customer service at (800) 688-2421 or customerservice@ahcmedia.com.]*

The CDC is developing guidance on the safe and effective use of PrEP and determining how to most effectively use it with other prevention strategies to reduce new HIV infections. At press time, interim guidelines tentatively were scheduled to be published in *Morbidity and Mortality Weekly Report* by the end of February 2011, says **Nikki Mayes,** a CDC spokesperson. Full U.S. Public Health Service guidelines are anticipated later in 2011, she states.

EXECUTIVE SUMMARY

Use of powerful antiretroviral drugs, known as pre-exposure prophylaxis (PrEP), is being weighed as an addition to the HIV prevention arsenal with the positive results from a new clinical trial.

- Researchers found that among men who have sex with men who took a single daily tablet containing two widely used HIV medications, emtricitabine and tenofovir, subjects experienced an average of 43.8% fewer HIV infections than those who received a placebo pill.
- The Centers for Disease Control and Prevention is developing guidance on the safe and effective use of PrEP and determining how to most effectively use it with other prevention strategies to reduce new HIV infections.

Statement of Financial Disclosure:
Consulting Editor **Robert A. Hatcher**, MD, MPH, Author **Rebecca Bowers**, Executive Editor **Coles McKagen**, and Senior Managing 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.

To conduct the iPrEx study, investigators enrolled 2,499 individuals at high risk of HIV infection in Brazil, Ecuador, Peru, South Africa, Thailand, and the United States. All study participants received a comprehensive package of prevention services designed to reduce their risk of HIV infection throughout the trial, including HIV testing, intensive safer sex counseling, condoms, and treatment and care for sexually transmitted infections. Half of study participants also received the PrEP pill, while the other half received a placebo drug. The pill is marketed by Gilead Sciences of Foster City, CA under the brand name Truvada. Each pill contained 200 mg of emtricitabine and 300 mg of tenofovir.

Investigators recorded 64 HIV infections among the 1,248 study participants who received a placebo pill, while 36 HIV infections were recorded among the 1,251 participants who received the study drug. The average reduction in HIV infection risk of 43.8% includes all study participants, even those who did not take the daily pill consistently.[1]

PrEP was more protective among those who reported taking the pill more regularly, researchers report. Among those who used the drug on 50% or more of days, as measured by pill counts, bottle counts, and self-reports, risk of HIV infection fell by 50.2% (95% CI 17.9-69.7%; P = 0.006); among those who used the drug on 90% or more of days, as determined by the same measures, the PrEP pill reduced infection risk by 72.8% (95% CI 40.7-87.5%; P = 0.001).[1]

What's next for PrEP?

PrEP research has been have been hailed by national news media as some of the most important medical achievements of 2010, observes **Ward Cates**, MD, MPH, president of research at Family Health International in Research Triangle Park, NC. The iPrEX trial follows the 2010 publication of results of the CAPRISA 004 trial, which looked at 1% tenofovir gel. The gel formulation was found to be 39% effective in reducing a woman's risk of becoming infected with HIV during sex and 51% effective in preventing genital herpes infections.[3] *(Read more about the CAPRISA 004 trial; see the* Contraceptive Technology Update *articles, "Tenofovir gel makes strides in development," January 2011, p. 5, and "HIV breakthrough: Trial results offer promise," October 2010, p. 114.)*

While the two trials were "diametrically different" in terms of population, site of exposure, and formulation, they both yielded "remarkably similar" results in terms of study endpoints, effectiveness, dosing, and antiretroviral therapy, Cates observes.

For CAPRISA and iPrEX, Cates says the implications for the future of PrEP now center around the following three precepts:

- Biology. Antiretrovirals work for PrEP, if the drug is present at site of exposure, Cates notes.
- Behavior. High adherence is key to PrEP success, just as with condoms, states Cates.
- Impact. Increased coverage is necessary if PrEP is to reduce HIV spread, according to Cates.

PrEP research is ongoing, says **Robert Grant**, MD, MPH, Betty Jean and Hiro Ogawa endowed investigator at the Gladstone Institute of Virology and Immunology, and associate professor of medicine at the University of California, San Francisco. Grant served as protocol chair for the iPrEX research team.

There are nine studies taking place in several parts of the world that will provide interesting and important information to complement the iPrEx study results in different populations: men and women at risk, serodiscordant couples, and injecting drug users, Grant notes.

"The next steps in PrEP research are being planned in this very moment and have to do basically with the use of PrEP intermittently," Grant says. "The HIV Prevention Trials Network has designed the ADAPT study to evaluate the pharmacokinetics and behaviors associated to the use of PrEP intermittently, (and) the International AIDS Vaccine Initiative is about to be complete or probably completed by now."

There are several research questions still to be answered in the PrEP field, but one of the most important ones are the ones related to the implementation of PrEP programs, says Grant. Demonstration projects should be designed to evaluate the feasibility of PrEP in different parts of the world.

IPrEx will have an open label roll-over extension in which all participants that have been enrolled in the blinded phase of the study can consent to be enrolled in the open label phase targeted at observing changes in sexual and adherence behaviors, he explains. The rollover study also will provide additional information to help determine whether adherence and drug exposure increases, or if risk behavior changes, when trial participants receive the information that the original iPrEx study has provided regarding the safety and efficacy of PrEP.

A more ambitious study that needs to be discussed is a "non-inferiority trial" of daily versus intermittent PrEP, says Grant. This undertaking would be "challenging," he says. Such a study would require a huge sample size, more than 20,000 individuals, the number of participants that are enrolled in all of the PrEP ongoing studies, he notes.

REFERENCES

1. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010;363:2587-2599.
2. Centers for Disease Control and Prevention. Pre-Exposure Prophylaxis (PrEP) for HIV Prevention: Promoting Safe and Effective Use in the United States. Fact sheet. Accessed at: http://www.cdc.gov/nchhstp/newsroom/PrEPforHIVFactSheet.html.
3. Abdool Karim Q, Abdool Karim SS, Frohlich JA, et al. CAPRISA 004 Trial Group. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science* 2010;329:1168-1174. ■

New indication OK'd for HPV vaccine

Add new information in your counseling dialogue regarding the human papillomavirus (HPV) vaccine Gardasil. The Food and Drug Administration (FDA) has approved the Merck & Co. quadrivalent vaccine for prevention of anal cancer and associated precancerous lesions related to HPV types 6, 11, 16, and 18 in people ages 9-26.

Gardasil already has approval for the same age population for the prevention of cervical, vulvar, and vaginal cancer and the associated precancerous lesions caused by HPV types 6, 11, 16, and 18 in females. It also is approved for the prevention of genital warts caused by types 6 and 11 in males and females. *(Read more about the vaccine in* Contraceptive Technology Update. *See "Updated guidance issued on use of HPV vaccines," August 2010, p. 93, and "Gardasil approved for use in males — Cervarix gets OK for use in females," December 2009, p. 133.)*

Treatment for anal cancer is challenging, stated **Karen Midthun**, MD, director of the FDA's Center for Biologics Evaluation and Research, in a statement released with the December 2010 indication approval. The use of Gardasil as a method of prevention is important as it might result in fewer diagnoses and the subsequent surgery, radiation, or chemotherapy that individuals need to endure, she said.

Check study results

Approval for the new indication was based on a single randomized, controlled trial of 4,065 patients, including 602 men who have sex with men (MSM). Among the MSM population, the point estimate of efficacy for Gardasil was 78% (95% confidence interval [CI], 40-93) for the primary composite endpoint of prevention of any grade anal intraepithelial neoplasia and anal cancer. Efficacy was 75% (95% CI, 9-93) for grade 2 or higher anal intraepithelial neoplasia. No cases of invasive anal cancer were noted in the study.

The study yielded overall efficacy of 50% (95% CI, 26-27) for any grade anal intraepithelial neoplasia and anal cancer. For grade 2 or higher anal intraepithelial neoplasia, efficacy was 54% (95% CI, 18-75).[1]

Because anal cancer is the same disease in males and females, the effectiveness data was used to support the indication in females as well.

Disease is spreading

While anal cancer is uncommon in the general population, the incidence is increasing, according to the FDA. HPV is associated with about 90% of anal cancer. The American Cancer Society estimates that about 5,300 people are diagnosed with anal cancer each year in the United States.[2] It is estimated that about 1,600 new cases of HPV-associated anal cancers are diagnosed in women, and about 900 are diagnosed in men each year in the United States.[3] More white women are diagnosed with anal cancer than women of other races; more black men are diagnosed with anal cancer than men of other races.

There is no standardized screening recommended for the general population for anal cancer. A digital rectal exam will find some cases of anal carcinoma early. This test is sometimes used to look for prostate cancer in men and is a routine part of a woman's pelvic exam. The odds that anal cancer can be found early depend on the location and type of the cancer, according to the American Cancer Society.

For people at high risk for anal intraepithelial neoplasia (AIN), such as men who have sex with men, women who have had cervical cancer or vulvar

EXECUTIVE SUMMARY

The Food and Drug Administration (FDA) has approved Gardasil, the quadrivalent human papillomavirus (HPV) vaccine, for prevention of anal cancer and associated precancerous lesions related to HPV types 6, 11, 16, and 18 in people ages 9-26.

• While anal cancer is uncommon in the general population, the incidence is increasing, according to the FDA. HPV is associated with about 90% of anal cancer. The American Cancer Society estimates that about 5,300 people are diagnosed with anal cancer each year in the United States.

• About 1,600 new cases of HPV-associated anal cancers are diagnosed in women and about 900 are diagnosed in men each year in the United States.

cancer, those who are HIV-positive, and all transplant recipients, some experts recommend screening with anal cytology testing. Known as an anal Pap test or anal Pap smear, the test is performed by swabbing the anal lining, with swab contents examined under a microscope.

Science has not yet determined how often an anal Pap test should be done or if it reduces the risk of anal cancer, according to the American Cancer Society. Some experts recommend the test be repeated on an annual basis in HIV-positive men who have sex with men and every two to three years if the men are HIV-negative.[4]

REFERENCES

1. FDA approves HPV vaccine for anal cancer. Infectious Disease News. Jan. 1, 2011. Accessed at http://www.infectiousdiseasenews.com/article/78864.aspx.
2. American Cancer Society. How many people get anal cancer? Last revised Dec. 23, 2010. Accessed at http://www.cancer.org/Cancer/AnalCancer/OverviewGuide/anal-cancer-overview-key-statistics.
3. Joseph DA, Miller JW, Wu X, et al. Understanding the burden of human papillomavirus-associated anal cancers in the US. *Cancer* 2008;113(S10):2892–2900.
4. American Cancer Society. Can anal cancer be found early? Accessed at http://www.cancer.org/Cancer/AnalCancer/DetailedGuide/anal-cancer-detection. ■

Signs of progress seen on STI prevention front

Despite the continued high burden of sexually transmitted infections (STIs) in the United States, an analysis of 2009 national data by the Centers for Disease Control and Prevention (CDC) shows some signs of progress on the prevention front:

• The national gonorrhea rate is at the lowest level ever recorded. In 2009, a total of 301,174 cases of gonorrhea were reported in the United States, which corresponds to a rate of 99.1 cases per 100,000 population. The 2009 rate is a 10.5% decrease from the rate of 110.7 cases per 100,000 population in 2008.

• In 2009, a total of 1,244,180 cases of sexually transmitted *Chlamydia trachomatis* infection were reported to the CDC, the largest number of cases ever reported to CDC for any condition. While increases in chlamydia diagnoses continue in the United States, this trend likely reflects expanded screening efforts, rather than a true increase in disease burden, the analysis states

• For the first time in five years, reported syphilis cases did not increase among women overall, the CDC reports. Likewise, cases of congenital syphilis did not increase for the first time in four years.[1]

Data in the report are based on state and local STI case reports from a variety of private and public sources, most of which come from non-STI clinic settings, such as private physicians and health maintenance organizations.

Vigilance is needed

STIs remain a major public health challenge in the United States, states the new report. The CDC estimates there are about 19 million new STI infections each year, which cost the U.S. healthcare system $16.4 billion annually and cost individuals even more in terms of acute and long-term health consequences.

Undetected and untreated STIs can increase a person's risk for HIV and cause other serious health consequences, such as infertility. STI screening can help detect disease early and, when combined with treatment, is one of the most effective tools available to protect one's health and prevent the spread of STIs to others, the report notes.

Untreated gonorrhea and chlamydia in women can result in pelvic inflammatory disease, a condition that can cause infertility. Each year, STIs cause at least 24,000 women in the United States to become infertile, the CDC states. Untreated syphilis can lead to serious long-term complications, including brain, cardiovascular, and organ damage. Syphilis in pregnant women also can result in congenital syphilis, which can cause stillbirth, death soon after birth, and physical deformity and neurological complications in children who survive. Untreated syphilis in pregnant women results in infant death in up to 40% of cases.

Research findings suggest that people with gonorrhea, chlamydia, or syphilis are at increased risk for HIV. This increase is especially concerning for young black men, among whom the rate of syphilis is increasing, the CDC notes.

Syphilis rates increased among black men ages 15-19 from 10.6 per 100,000 population in 2005 to 28.3 per 100,000 population in 2009. A similar rise was seen in black men ages 20–24, jumping from 30.2 per 100,000 population in 2005 to 94.2 per 100,000 population in 2009. These increases are the largest observed in any age, sex, or racial/ethnic group, reports the CDC.[1]

REFERENCE

1. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2009. Atlanta: Department of Health and Human Services; 2010. ■

Centers for Disease Control and Prevention
Your Online Source for Credible Health Information

Fact Sheet

For immediate release: November 23, 2010
Media Contact: NCHHSTP (http://www.cdc.gov/nchhstp/) - News Media Line, 404.639.8895, NCHHSTPMediaTeam@cdc.gov (mailto:NCHHSTPMediaTeam@cdc.gov)

Pre-Exposure Prophylaxis (PrEP) for HIV Prevention: Promoting Safe and Effective Use in the United States

New Tool to Reduce the Risk of HIV infection among Gay and Bisexual Men

In November 2010, the National Institutes of Health (NIH) announced the results of the iPrEx trial, a large research study examining whether a pill containing drugs used to treat HIV can also help prevent HIV infection – an approach called pre-exposure prophylaxis, or PrEP. These findings represent a major advance in HIV prevention research, providing the first evidence that PrEP, when combined with other prevention strategies, can reduce HIV risk among men who have sex with men (MSM) (see box).

iPrEx Trial: Key Findings

- *Efficacy:* The trial found that a once-daily pill containing tenofovir plus emtricitabine (brand name Truvada) provided an average of 44 percent additional protection to men who have sex with men (MSM) who also received comprehensive prevention services which included monthly HIV testing, condom provision, counseling, and management of other sexually transmitted infections (95% CI 15 to 63%).
- *Consistent use of PrEP*: The level of protection shown varied widely depending on how consistently participants used PrEP. Among those whose data (based on self-

reports, bottles dispensed, and pill counts) indicates use on 90 percent or more days, HIV risk was reduced by 73 percent (95% CI 41 to 88%), while among those whose adherence by the same measure was less than 90 percent, HIV risk was reduced by only 21 percent (95% CI, from a 52% reduction to a 31% increase).

- *Risk behavior:* Risk behavior among participants declined overall during the trial both in terms of decreases in the number of sexual partners and increases in condom use, likely as a result of the intensive risk reduction counseling provided as part of the trial.

The iPrEx results have immediate implications for the U.S., since tenofovir-emtricitabine pills are already FDA-approved and available with a prescription for the treatment of HIV infection. As the agency responsible for protecting public health, CDC is taking steps to promote the safe and effective use of PrEP in the United States.

HIV among MSM in the U.S.: The HIV epidemic among MSM in the U.S. is severe, and additional risk reduction strategies for this population are urgently needed. MSM represent more than half of new HIV infections and nearly half of all people living with HIV in the U.S., and the rate of new HIV diagnoses among MSM is more than 44 times that of other men. Moreover, data suggests that HIV infections have been steadily increasing in this group since the mid-1990s.

Implications of findings for other PrEP trials: While we don't yet know if PrEP will work for preventing HIV transmission in other populations, these findings give us hope that this approach might also prove effective among heterosexuals at high-risk for HIV and injection drug users. CDC, NIH, and other institutions are conducting trials around the world to determine the safety and effectiveness of PrEP for these populations; those results are expected within the next few years. The iPrEx results may also be the first step toward other effective and potentially more feasible options for PrEP, as other regimens and dosing strategies are also being evaluated.

CDC next steps: CDC will pursue two primary goals in the wake of the iPrEx trial findings: developing guidance on the safe and effective use of PrEP and determining how to most effectively use PrEP in combination with other prevention strategies to reduce new infections in the U.S. The following pages describe these goals in greater detail, and discuss key remaining questions about PrEP as an HIV prevention tool.

Working Toward Safe and Effective Use in the U.S.

Given the availability of the medication proven effective in this trial and the possibility of immediate interest in using PrEP among some high risk gay and bisexual men and their physicians, CDC's most urgent priority is to develop guidance for health-care providers, public health agencies, and gay and bisexual men on its safe and effective use.

CDC will fully review the trial data and publish interim guidance for physicians in the coming weeks in the *Morbidity and Mortality Weekly Report*, to be followed by formal U.S. Public Health Service guidelines. We urge individuals and providers to wait for those guidelines. However, because the drug is commercially available in the U.S. with a prescription, CDC is providing a number of immediate cautions (see box).

Immediate Cautions from CDC

What Gay and Bisexual Men and Doctors in the U.S. Should Know Now About PrEP

For MSM at high risk for HIV infection, PrEP may represent a much-needed additional prevention tool. However, PrEP should be used only in combination with other strategies, requires strict adherence, and is an intensive approach that won't be right for everyone. Anyone considering using or prescribing PrEP should know:

- To date, PrEP has only been shown to reduce HIV infection among men who have sex with men, and there are no data regarding its benefit among heterosexuals or injection drug users.
- Truvada taken once daily is the only regimen shown to be safe and effective for PrEP, and therefore Truvada is the only medication that should be prescribed for PrEP. Providers and patients should be aware that HIV prevention is not a labeled indication for use of the medication.
- PrEP should only be used among individuals who have been confirmed to be HIV-negative. Initial and regular HIV testing are critical for anyone considering using PrEP. All individuals considering PrEP must also be evaluated for other health conditions that may impact PrEP use.
- PrEP should never be seen as the first line of defense against HIV. It was only shown to be partially effective when used in combination with regular HIV testing, condoms, and other proven prevention methods, and it does not protect against other sexually transmitted infections. Men who have sex with men should still:
    - Use condoms consistently and correctly
    - Get tested to know their status and that of their partner(s) for certain
    - Get tested – and treated if needed – for other sexually transmitted infections that can facilitate HIV transmission, such as syphilis and gonorrhea
    - Get information and support to reduce drug use and sexual risk behavior
    - Reduce their number of sexual partners
- Taking PrEP daily is critical. This study found that PrEP provided a high level of protection only to those who took the pills regularly; protection was very low among those who did not adhere to the daily regimen well.
- PrEP must be obtained and used in close collaboration with health care providers to ensure regular HIV testing, risk reduction and adherence counseling, and careful safety monitoring.

Developing Guidelines for Health Care Providers on PrEP Use

CDC will be the lead federal agency in developing U.S. Public Health Service guidelines, in

collaboration with other federal health agencies. The guidelines will be based on a full review of trial data and other research, and will incorporate input from providers, HIV prevention partners, and affected communities. The guidelines will help ensure both physicians and MSM have accurate information to guide decisions about the use of PrEP.

Topics to be addressed in the guidelines will include:

- Specific populations of MSM for which PrEP is recommended
- Procedures for health care providers to assess whether PrEP is appropriate for individual patients (e.g., methods for evaluating patients' risk behavior)
- Recommended support services to help ensure adherence to the daily PrEP regimen
- Recommended risk reduction counseling to prevent inadvertent increases in risk behavior (known as "risk compensation" or "disinhibition"), as well as to provide referrals to—and/or transition individuals to—other, more effective prevention interventions
- Procedures for initial HIV testing and health screening, as well as ongoing monitoring for side effects, clinical toxicities, HIV infection, and possible drug resistance among those who become infected despite taking PrEP

Maximizing the Potential Benefits of PrEP in the U.S.

The iPrEx trial findings offer a new tool to help combat HIV among MSM, one of the hardest hit populations in the U.S. and many areas of the world.

We will have to carefully consider how to most effectively use this tool in combination with other prevention strategies to reduce the continuing toll of HIV and AIDS. There are a significant number of HIV-positive individuals in the U.S. and around the world who do not have access to antiretroviral drugs to treat their infection, and we know that treatment not only benefits infected individuals, but can also reduce transmission to others. But, we also know that treatment alone will not end the epidemic. With 2.7 million people becoming infected annually worldwide, including approximately 56,000 in the U.S., we must capitalize on every available prevention tool.

Ultimately, the impact of PrEP on the U.S. HIV epidemic will depend on difficult decisions and many things that remain unknown, including the feasibility, cost, and impact of this strategy in real-world settings.

Available data suggest that PrEP, used strategically and effectively among MSM, could have a positive impact on the U.S. epidemic and be cost-effective, but only if certain conditions are met, including:

- Reaching the MSM at highest risk for HIV infection
- Effectively delivering PrEP in tandem with effective risk reduction counseling, condoms, and other prevention tools as were delivered in the trial setting. This will be critical to prevent increases in risk behavior that could offset the benefits of PrEP
- Identifying ways to achieve the high levels of adherence needed for maximum protection

CDC's Next Steps

CDC will be implementing a range of activities to promote the effective and strategic use of PrEP in the U.S. In addition to developing public health guidelines, CDC will:

- Conduct research to determine how to most effectively communicate about the use of PrEP in conjunction with other risk reductions strategies
- Develop comprehensive risk reduction guidelines for MSM, which will incorporate PrEP and all proven strategies
- Adapt national HIV surveillance and program monitoring systems to help evaluate the use and impact of PrEP in the U.S.
- Examine potential program costs, impact, and cost-effectiveness compared to other interventions
- Communicate guidance to providers and MSM through multiple information channels
- Hold a consultation with public and private insurers to better assess the potential barriers and facilitators of PrEP coverage

CDC has also identified other activities that could help address remaining research questions and is currently exploring all avenues to identify resources to support them. Key among these is the need for demonstration projects in clinics serving MSM to assess feasibility, acceptability, and the impact of PrEP in real-world settings. It will also be critical for public and private sector partners to begin to collectively address the significant financial barriers that may place PrEP out of reach for many MSM at highest risk for HIV infection.

Given the urgency of addressing the HIV epidemic among gay and bisexual men in this nation, CDC is working to maximize the impact of this important new intervention in combination with all available HIV prevention strategies.

For more information on PrEP and HIV prevention, please visit www.cdc.gov/hiv/prep (http://www.cdc.gov/hiv/prep) .

###

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (http://www.hhs.gov/)

Page last reviewed: November 23, 2010
Page last updated: November 24, 2010
Content source: National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention

Centers for Disease Control and Prevention 1600 Clifton Rd. Atlanta, GA 30333, USA
800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, 24 Hours/Every Day - cdcinfo@cdc.gov