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IN THIS ISSUE

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Status report on the female condom: What will increase use in the U.S.?

Female Health Co. to seek federal approval for updated condom

When you counsel on protection against HIV and other sexually transmitted diseases (STDs), where does the female condom fit into your message? While the female condom represents a woman-controlled form of protection against HIV and other STDs, its use has lagged in the United States since its introduction in 1993.

This fact may change if the Female Health Co. (FHC) is successful in gaining Food and Drug Administration (FDA) approval of the second generation of its original female condom, known as the Reality or FC1 condom. Documentation for the FC2 is in final stages of preparation. At press time, the application was scheduled to be filed with the FDA by the end of December 2007.

The FC2 is available to several countries outside the United States. To date, approximately 7 million units have been distributed, according to

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The Female Health Co. plans to seek Food and Drug Administration approval of the second generation of its original female condom, known as the Reality or FC1 condom. The FC2, made of nitrile, is less expensive to manufacture than the original condom, and offers comparable safety and efficacy.

- Program for Appropriate Technology in Health researchers are preparing another version of the female condom, known as the Woman's Condom, for a combined Phase 2/3 clinical trial.
- Despite strides in microbicide development, there still is no commercially available product, outside of the female condom, that women can use to help protect themselves against HIV/AIDS. Women now account for more than one-quarter of all new HIV/AIDS diagnoses in the United States.

Jack Weissman, company vice president. The company has partnered with the United Nations Population Fund to scale up education programs and distribution of the female condom in more than 20 countries, including nationwide distribution programs in Zambia, Zimbabwe, and Malawi. FHC moved forward in 2005 with the second-generation FC2 Female Condom; large-scale distribution of the FC2 began in 2007.

The FC2, made of nitrile, looks and performs in a statistically similar manner to the original FC Female Condom,[1] yet it is less expensive to manufacture. Due to the manufacturing process involved in making the FC1, its price (about 72 cents per unit) was not impacted by bulk purchasing. Since the FC2 carries a less expensive manufacturing cost, it can be made available for as little as 22 cents per unit.[2]

As a contraceptive, female condoms are slightly less effective than male condoms, but are slightly more effective than other barrier methods.[3] Six-month failure rates for the female condom range from 0.8% to 9.5%.[4,5] It is estimated 21% of women will experience an unintended pregnancy during the first year of typical use; with perfect use, that rate falls to 5%.[6] On the other hand, results of use-effectiveness studies indicate that the female condom is at least as effective as the male condom in preventing STDs.[7-9]

Research indicates that women in public STD clinics will try, and some will continue, to use female condoms when they are promoted positively and when women are trained to use them correctly and to promote them to their partners.[10] Current U.S. use of the female condom is low. According to results of a New York state study, while 69% of females said they had heard about the method, less than three in 100 women (2.6%) reported actually having used one.[11] New York state is committed to increasing usage numbers; its Female Condom Promotion Program plans to work with about 60 agencies that provide risk-reduction counseling to heterosexual women.[12] Agency directors and counselors will receive a multi-level intervention to promote FC use.

PATH eyes female condom

Researchers at the Program for Appropriate Technology in Health (PATH) are developing another form of the female condom, the Woman's Condom. Working with couples in Khon Kaen, Thailand; Cuernavaca, Mexico; Durban, South Africa; and Seattle, researchers have looked at more than 50 design generations in more than 300 unique prototypes. The current prototype replaces the inner ring of the current female condom with four small dots of soft, absorbent foam. The dots adhere to the interior of the vagina, hold the condom in place during use, and release from the vaginal walls on removal. To make for easy

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Editorial Questions

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insertion, a rounded cap has been added to the end of the condom; it gathers the condom pouch together until after insertion. Once the condom is inserted, the tip quickly dissolves.[13]

After extensive evaluation and testing, the Woman's Condom is ready for a combined Phase 2/3 clinical trial, the last step before FDA approval. Its first step is to obtain a commercially produced product. According to **Joanie Robertson**, PATH's team leader for the Woman's Condom, the agency is identifying a manufacturer to produce the condom. Family Health International has completed a study of the PATH Woman's Condom; it has not yet been published, states Robertson. Results of a small short-term acceptability study indicate the PATH condom is easy to use, stable during use, comfortable, and satisfactory during sex among users.[14]

Despite strides in microbicide development, there still is no commercially available product, outside of the female condom, that women can use to help protect themselves against HIV/AIDS. Protection is desperately needed: Women now account for more than one-quarter of all new HIV/AIDS diagnoses in the United States.[15] Women of color are especially affected by HIV infection and AIDS; in 2004, HIV infection was the leading cause of death for black women (including African-American women) ages 25-34 and the fourth leading cause of death for Hispanic women ages 35-44.[15]

Women who are in marriages or are cohabitating (in a union) with a man are particularly vulnerable to HIV and STDs, says **Robert Hatcher**, MD, MPH, professor of gynecology and obstetrics at Emory University School of Medicine in Atlanta. These relationships have been called "trust" relationships; for women in these types of relationships, use of a male condom is fraught with problems, unless that male condom is being used as a contraceptive as well, Hatcher notes.

"Use of male condoms in marriages, in unions, and with long-time boyfriends imply a lack of trust, hence the importance of an effective, inexpensive female condom, microbicides, and vaccines against HPV, HIV, and other sexually transmitted infections," says Hatcher.

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Menstrual suppression — What do women say?

While you may be comfortable with menstrual suppression through use of continuous oral contraceptives (OCs), are your patients? According to results from a national survey, more than 66% of women say that they are interested in suppressing their menstrual periods, but many of

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Results from a national survey show that more than 66% of women say that they are interested in suppressing their menstrual periods, but many of them aren't sure if it's safe. However, 97% of polled physicians say that continuous oral contraceptive therapy to suppress menstruation is medically safe and acceptable.

- Use of continuous or extended-cycle OC regimens that eliminate or decrease the menstrual cycle represents a viable and attractive option for many women.
- There is no physiological requirement for the monthly hormone withdrawal bleed that is experienced by women taking cyclic oral contraceptives.

them aren't sure if it's safe. However, when physicians are polled, 97% say that continuous oral contraceptive therapy to suppress menstruation is medically safe and acceptable.[1]

What will it take to close the gap? Patient education and counseling will play important roles, predicts **Kurt Barnhart**, MD, MSCE, associate professor and director of clinical research for the Department of Obstetrics & Gynecology at the University of Pennsylvania School of Medicine. Barnhart presented results of the surveys at the fall meeting of the Association of Reproductive Health Professionals.

"The gap between physician and patient understanding concerning the necessity of monthly periods is obvious," Barnhart says. "It is our hope that based on these findings, physicians will begin to more readily initiate dialogue with their female patients about continuous therapy — helping to eliminate the misconception that periods are a medical necessity and to emphasize the safety and viability of menstrual suppression."

With a dedicated continuous oral contraceptive product (Lybrel; Wyeth Pharmaceuticals, Collegeville, PA) on the market, health care providers will need to deliver clear information to eliminate confusion regarding menstrual suppression. **(*Contraceptive Technology Update* reported on the approval of the new drug in the article "Continuous-use oral contraceptive receives FDA regulatory approval," July 2007, p. 73.)**

Some of the confusion about menstrual suppression may lie in simple semantics, according to the surveys' results. Among the 12% of patients who said they had discussed the idea of eliminating or reducing periods with their doctor, nearly half said they were the ones to raise the issue, not their providers. In contrast, four out of five physicians reported discussing continuous-use oral contraceptive use with their patients, and 77% said they raised the topic.

Providers and their patients may discuss this topic differently, with providers using the medical term "menstrual suppression," while patients simply talk about not having a period. Providers need to break down the language barrier by speaking in simpler, more patient-friendly terms, says Barnhart.

A total of 500 women ages 18 to 49 participated in the online patient study, and 299 professionals were included in the practitioner survey.[1]

How do women feel?

The use of continuous or extended-cycle OC regimens that eliminate or decrease the menstrual cycle represents a viable and attractive option for many women. There is no physiological requirement for the monthly hormone withdrawal bleed that is experienced by women taking cyclic oral contraceptives.[2]

However, amenorrhea needs careful explanation, advises **Robert Hatcher,** MD, MPH, professor of gynecology and obstetrics at Emory University School of Medicine in Atlanta. Hatcher presented on the subject at the recent *Contraceptive Technology* Quest for Excellence conference in Atlanta.[3] For most women, the benefits of a hormonal contraceptive, vis a vis menstrual cycle symptoms (including no bleeding at all), exceed the side effects or complications related to the menstrual cycle, notes Hatcher.

Although bleeding less or not at all is desirable in the eyes of most clinicians, amenorrhea is the leading cause of discontinuation of Depo Provera (depot medroxyprogesterone acetate or DMPA; Pfizer, New York City) and an important discontinuation factor in all hormonal contraceptives taken in a continuous manner, says Hatcher. Be sure that women understand the rationale for dropping the scheduled period:

- The "pill period" is artificial/arbitrary, without health benefits.
- The potential for increased efficacy is present when the pill-free interval is eliminated. There is less follicular recruitment, the potential for fewer pregnancies, less confusion of start/stop, and fewer pharmacy trips.

Women need to understand that continuous use of pills will not make it more difficult to

become pregnant once the continuous regimen is stopped, says Hatcher.[3]

Take the time

Women have assumed for years that a regular menstrual bleeding episode is a sign of normality, says **David Archer,** MD, professor of obstetrics and gynecology and director of the Clinical Research Center at the Eastern Virginia Medical Center in Norfolk. To change this perception will take a significant effort, he notes.

"The understanding of the suppression of ovulation and the thinning of the endometrium are two concepts that need long-term information and consumer understanding and acceptance," says Archer.

When clinicians first started making DMPA available, extra counseling regarding the absence of regular menses and the increasing likelihood of amenorrhea with ongoing use was the order of the day, reflects **Andrew Kaunitz**, MD, professor and associate chairman of the Department of Obstetrics and Gynecology at the University of Florida College of Medicine–Jacksonville. Now, while patients still benefit from such counseling, if they know other women who use DMPA, less time can be devoted to discussions of why it is acceptable not to bleed each month, says Kaunitz.

Women's acceptance of the absence of the monthly withdrawal bleed with oral contraceptives is a work in progress, says Kaunitz. As the approach becomes more common, and more patients know someone else who has done well with menstrual suppression on OCs, less counseling time and effort will be needed, he predicts.

"Meanwhile, women continue to benefit from clinicians who are willing to put extra time and effort into patient education regarding menstrual suppression or who effectively use other resources such as office staff or educational materials in this endeavor," says Kaunitz.

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Counsel on correct, consistent condom use

When men leave your family planning clinic, they may leave with a supply of condoms in hand. But do they leave with good information on the importance of correct, consistent condom use?

Many clinicians may talk about using condoms consistently, but don't spend much time talking about correct use, says **William Yarber**, HSD, senior director of the Rural Center for AIDS/STD Prevention at Indiana University in Bloomington and lead author of a new research paper on condom use. Incomplete use of condoms is a "big issue," Yarber notes, because it can lead to exposure to sexually transmitted disease and unintended pregnancies.

Results from the new study indicate that men who are highly motivated to wear condoms are more likely to put the condom on before having sex with a woman.[1] However, men who have trouble with the fit and feel of their condoms or experience an erection loss while wearing protection are more likely to take the condom off prior to the end of intercourse, data suggest.

Ask the questions

In the study, investigators focused on the factors involved in why male patients at an urban Midwestern STD clinic would don condoms after initiation of vaginal intercourse and remove them before sex ended. A total of 278 male patients participated in the survey.

Nearly one in five men (18.7%) reported starting sex prior to donning a condom in the past three times a condom was used. Of the 278 participants, 88 reported that their condom had broken on one or more occasions; of the remaining 190 men, 23.7% said they had removed the condom before sex ended during at least one of the past three times they used condoms.

Engage patients in a discussion about how condoms are used, suggests **Richard Crosby**, PhD, professor in the College of Public Health at the University of Kentucky, Lexington and a co-author of the current paper. Ask questions such as "Have you ever noticed that your partner or yourself may sometimes put the condom on after sex begins?" Crosby advises.

If the patient acknowledges this fact, Crosby

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Results from a new Indiana University study indicate that men who are highly motivated to wear condoms are more likely to put the condom on before having sex with a woman.

- Men who have trouble with the fit and feel of their condoms or experience an erection loss while wearing protection are more likely to take the condoms off prior to the end of intercourse.
- While it is important to tailor messages to individual patients, one objective about condom use needs to be stressed with all condom users: Condoms don't work well unless they are used from start to finish of penetrative sex.

suggests to affirm the condom use by saying, "You know, it's wonderful that you're using condoms, and as long as you're using condoms, it makes so much sense to go the extra effort that it takes to make sure that the condom is on before you first penetrate, and make sure it stays on until that penetration ends."

While it is important to tailor messages to individual patients, Crosby says one objective about condom use needs to be stressed with all condom users: Condoms don't work well unless they are used from start to finish of penetrative sex.

"That's a very clear and concise message for anyone in a clinic. I think saying it any other way leaves too much of a loophole for people," Crosby reflects. "The word 'penetrative' is fairly easy for just about anyone to understand when it comes to sex, and it suggests that when the penis goes in the vagina, there needs to be a condom on and it needs to stay on until that penetration ends."

Take a positive approach when it comes to condom counseling, advises Crosby. Counseling messages may go further if delivered in a positive manner, he notes. "Most STD clinics require long waiting periods, so people may be irritated, frustrated, and it is all too common that they feel judged," says Crosby. "With an STD, people feel stigmatized, so the last thing we want to do as providers is add to that. We want to emphasize the positive."

Mix styles, sizes

If there's just one choice when it comes to sizes and styles of male condoms at your clinic, check into expanding your selection, advises Yarber. Men reporting difficulties with the fit and feel of condoms in the new research were 2.5 times more likely to remove condoms early.[1]

"We found out that a lot of people have their own style [of condom] that they like, and once they find that, they like to use that," says Yarber. "If the clinic has a variety, patients have a greater chance of acquiring that — at least it gives them some choices."

Provide patients with printed information on correct condom use, advises Yarber. (The Center for Health Training in Oakland, CA, offers a male condom information sheet for free download on its site, www.centerforhealthtraining.org. Click on "Materials & Resources," "Contraceptive Fact Sheets," and "Male Condom.") Penile models also help demonstrate correct condom usage, notes Yarber. **(Get more ideas about increasing condom use; see the *Contraceptive Technology Update* articles "Condoms: Does your clinic cover the bases?" December 2006, p. 139, and "Your clinic can boost condom use," December 2006, p. 140.)**

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Clinicians, patients need to boost herpes IQ

What is your level of knowledge when it comes to genital herpes, its methods of virus transmission, risks to others, and appropriate treatment? If results of an online survey are any indication, many health care providers and patients with herpes are poorly informed about herpes.[1]

In an online survey of 200 Canadian family physicians and 401 patients, 45% of doctors and 51% of patients underestimated the risks of passing on the infection during periods when there are no obvious outward symptoms. (Research indicates up to 70% of transmission of herpes may occur during periods of asymptomatic viral shedding.[2]) In addition, only 40% of patients were aware that daily antiviral therapy is available to reduce the risk of transmission.

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Results of an online survey of health care providers and patients with herpes indicate both population segments are poorly informed about herpes.

- Less than half (45%) of providers and 51% of patients underestimated the risks of passing on the infection during periods when there are no obvious outward symptoms. Just 40% of patients were aware that daily antiviral therapy is available to reduce the risk of transmission.
- Genital herpes is ranked second for social stigma out of all sexually transmitted diseases, with only HIV outranking it, according to a survey of U.S. adults. For those with genital herpes, most said that revealing their condition to their partner(s) was troubling to them.

The survey was prompted by researchers' belief that management of genital herpes can be improved, says **Barbara Romanowski**, MD, FRCPC, FACP, a clinical professor in the Division of Infectious Diseases in the Department of Medicine at the University of Alberta in Edmonton. To achieve that goal, the researchers wanted to have a better understanding of the issues for patients and physicians, she explains.

Why did physicians and patients get it wrong when it comes to the risk of transmission during periods of asymptomatic viral shedding? Romanowski cites lack of information as the culprit.

Review the basics

Genital herpes is a sexually transmitted disease (STD) caused by the herpes simplex viruses type 1 (HSV-1) and type 2 (HSV-2). Most genital herpes is caused by HSV-2. Most patients have no or minimal signs or infection; when signs do occur, they typically present as one or more vesicles on or around the genitals or rectum. When the blisters break, they leave small sores that may take two to four weeks to heal at the first time of occurrence. The initial outbreak typically is followed by subsequent outbreaks that can appear weeks or months after the first. Such reoccurrences almost always are less severe and shorter than the first outbreak. Although the infection can stay in the body indefinitely, the number of outbreaks tends to decrease over a period of years.[3]

While HSV-1 and HSV-2 can be found in and released from the sores that the viruses cause, they also are released between outbreaks from skin that does not appear to be broken or to have a sore, known as asymptomatic shedding. Generally, a person can only get HSV-2 infection during sexual contact with someone who has a genital HSV-2 infection, according to the Centers for Disease Control and Prevention. Transmission can occur from an infected partner who does not have a visible sore and may not know that he or she is infected.[3]

While there is no cure for herpes, antiviral medications can shorten and prevent outbreaks during the period of time the person takes the medication. In addition, daily suppressive therapy for symptomatic herpes can reduce transmission to partners. Correct and consistent use of condoms also helps to prevent viral transmission.

Reduce the stigma

According to a Harris Interactive poll of U.S. adults, participants ranked genital herpes second for social stigma, out of all STDs, with only HIV outranking it. For those with genital herpes, 61% said that revealing their condition to their partner(s) was troubling to them, and only 32% said they were open about their condition with their close family and friends.[4]

RESOURCES

Download a free copy of English or Spanish versions of *The Updated Herpes Handbook* from the Westover Heights web site, www.westoverheights.com. Click on "Genital Herpes" and "Updated Herpes Handbook." Also, view *Taking Charge of Your Life: Learning to Live with Genital Herpes*, a free video resource designed to answer the most common questions and concerns. Click on "Herpes" and "Counseling DVD."

Direct patients to browse the WebMD Genital Herpes Health Center web site, which features a community board and a blog authored by Terri Warren. Go to the Web MD site, www.webmd.com. Under "Health Centers," click on "Genital Herpes." While at the Westover Heights site, click on "Herpes," "Resources & Links," and "WebMD Genital Herpes Health Center."

What can providers do to help lessen the stigma of herpes? First, it's important to understand what stigma represents, says **Terri Warren,** RN, ANP. Warren is the owner of Westover Heights Clinic in Portland, OR, a private clinic specializing in the diagnosis and treatment of STDs, and the co-author of two books, *The Updated Herpes Handbook* and *Tender Talk, a Guide to Intimate Conversations*. **(See the resource listing on p. 19 for ordering information.)**

Stigma is defined as occurring when someone has a characteristic, in this case genital herpes infection, that is considered to be universally undesirable, is uncommon, and is within the control of the person who has it, explains Warren. Herpes is not uncommon. According to the American Social Health Association, about one in five persons in the United States has genital herpes; however, as many as 90% are unaware that they have the virus.

Encourage patients to utilize educational materials that also include the discussion about the emotional aspects of having herpes, not just the facts about herpes, says Warren. Give patients the information they need to take charge of their diagnosis, she advocates.

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Note the benefits of calcium supplementation

Good news for your older female patients: Calcium, or calcium in combination with vitamin D, may prevent osteoporosis in those age 50 and older, results from a new meta-analysis show.[1]

Women need to be informed on osteoporosis: It is estimated that 10 million people older than age 50 have osteoporosis in the United States, and almost 34 million have low bone mass that puts them at increased risk for developing the disease, according to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).[2] Four out of five people who have osteoporosis are women, estimates NIAMS. One in two women older than age 50 will have an osteoporosis-related fracture in their lifetime, according to NIAMS statistics.[2]

To perform the meta-analysis, researchers at University of Western Sydney's Center for Complementary Medicine Research identified 29 randomized trials via electronic databases, supplemented by a hand-search of reference lists, review articles, and conference abstracts. All randomized trials that recruited people ages 50 years or above were eligible. The main outcomes were fractures of all types and percentage change of bone mineral density from baseline. Data were pooled by use of a random-effect model.

In trials that reported fracture as an outcome (17 trials, n = 52,625), treatment was associated with a 12% risk reduction in fractures of all types, the scientists note. In trials that reported bone mineral density as an outcome (23 trials, n = 41,419), the treatment was associated with a reduced rate of bone loss of 0.54% (0.35–0.73; $p < 0.0001$) at the hip and 1.19% (0.76–1.61%; $p < 0.0001$) in the spine. Reduction of fracture

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Calcium, or calcium in combination with vitamin D, may prevent osteoporosis in those age 50 and above, results from a new meta-analysis show. Scientists report that treatment effect was better with daily calcium doses of 1,200 mg or more and with daily vitamin D doses of 800 IU or more.

- An estimated 10 million people over age 50 have osteoporosis in the United States, and almost 34 million have low bone mass that puts them at increased risk for developing the disease. Four out of five people who have osteoporosis are women. One in two women over age 50 will have an osteoporosis-related fracture in her lifetime.
- Talk about vitamin D when counseling on calcium intake. Calcium cannot be absorbed without vitamin D. More than half of North American women receiving therapy to treat or prevent osteoporosis have vitamin D inadequacy.

risk was significantly greater (24%) in trials in which the compliance rate was high. Scientists report that treatment effect was better with calcium doses of 1,200 mg or more than with doses less than 1,200 mg, and with vitamin D doses of 800 IU or more than with doses less than 800 IU.

The results showed the importance of starting supplements at about the age of 50, when bone mineral loss begins to accelerate, says **Benjamin Tang**, MD, an associate researcher at the university center and lead author of the research paper. This persistence pays off, he notes: People who reported taking their supplements at least 80% of the time experienced a 24% reduction in fractures, while those who were less rigorous with their routine saw the benefit cut in half.

Encourage vitamin D

When talking with women about calcium's role in osteoporosis prevention, be sure to talk about vitamin D as well. Calcium cannot be absorbed without vitamin D. Milk fortified with vitamin D, including lactose-free milk, is a good source, as is sunlight. Being in the sun for just 15 minutes a day helps skin produce vitamin D and activates vitamin D in the body.[3] Recommended daily levels of vitamin D are 10 mcg for women ages 51–70 and 15 mcg for women older than age 70.[3]

Clinicians often overlook vitamin D deficiency, and inadequate supplementation may be more widespread than most realize, a recent study indicates.[4] More than half of North American women receiving therapy to treat or prevent osteoporosis have vitamin D inadequacy, the research suggests.[4]

The epidemic of low vitamin D levels should be highlighted, says **Anita Nelson**, MD, professor in the Obstetrics and Gynecology Department at the University of California in Los Angeles (UCLA) and medical director of the women's health care programs at Harbor-UCLA Medical Center in Torrance. In adults, vitamin D deficiency may precipitate or exacerbate osteopenia, osteoporosis, muscle weakness, fractures, common cancers, autoimmune diseases, infectious diseases, and cardiovascular diseases.[5]

Good for breast health?

Women who consume higher amounts of calcium and vitamin D also may have a lower risk of developing premenopausal breast cancer, according to results of a 2007 research study.[6] While data from animal studies have linked calcium and vitamin D to breast cancer prevention, results from previous epidemiologic studies on humans have been less conclusive.

Study details

Researchers assessed 10,578 premenopausal and 20,909 postmenopausal women age 45 and older who were part of the Women's Health Study. At the beginning of the study, the women completed a questionnaire about their medical history and lifestyle, and they completed a food frequency questionnaire that detailed how often they consumed certain foods, beverages, and supplements during the previous year.

For every six months during the first year and then every subsequent year, participants returned follow-up questionnaires indicating whether they had been diagnosed with breast cancer.

Over an average of 10 years of follow-up, 276 premenopausal women and 743 postmenopausal women developed breast cancer. Premenopausal women who consumed more total calcium and vitamin D were at a lower risk of developing breast cancer; the multivariate hazard ratios (95% confidence intervals) in the highest quintile group relative to the lowest one were 0.61 (0.40–0.92) for total calcium (P = 0.04 for trend) and 0.65 (0.42–1.00) for total vitamin D intake (P = 0.07 for trend).

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Advanced trial under way for oral contraceptive

Could a new combined oral contraceptive (OC) be available to U.S. women? Organon is conducting two Phase 3a trials for the first monophasic oral contraceptive containing estradiol (E2) and a new progestin, nomegestrol acetate (NOMAC). Phase 3 development is scheduled to be completed in 2009, reports **Monique Mols**, an Organon spokeswoman.

The two trials, which involve 4,400 women, are the largest trials in contraception ever undertaken by the company.[1] Recruitment for both trials was completed in May 2007. More than 180 centers in 24 countries, including the United States, are taking part in the trials. Mols declined to identify the U.S. sites.

Nomegestrol acetate is considered a new progestin, along with drospirenone, dienogest, trimegestone, and Nestorone.[2] These new progestins have been designed to bind very specifically to the progesterone receptor and not to other steroid receptors in an effort to avoid androgenic, estrogenic, or glucocorticoid side effects.

Organon was granted development and marketing rights of NOMAC/E2 in 2005 by Laboratoire Théramex, an affiliate of Merck KGaA. Phase 2 research completed by Théramex indicates that the combination of NOMAC/E2 inhibits ovulation with an acceptable cyclic bleeding pattern and safety profile, says Mols.

Results from the Phase 2 program, which involved 265 women, indicates that a monophasic combination of 2.5 mg of NOMAC and 1.5 mg of E2 given in a cyclic regimen provides good ovulation inhibition and an acceptable monthly bleeding pattern and safety profile.[3]

Phase 2 studies for NOMAC/E2 looked at three doses of NOMAC (0.625 mg, 1.25 mg, and 2.5 mg) in combination with 1.5 mg of E2. Scientists studied suppression of ovarian function by measuring follicular growth via vaginal ultrasonography and circulating serum levels of luteinizing hormone (LH), follicle-stimulating hormone, E2, and progesterone. Research indicates daily dosages of 2.5 mg of NOMAC combined with 1.5 mg of E2 represents the optimal dose combination for suppression of ovarian activity.[3]

The NOMAC 2.5 mg /E2 1.5 mg combination appears to be associated with a cyclic and regular vaginal bleeding pattern. Results from a separate Phase 2 study indicate a consistent ovulation inhibition combined with a regular cyclic bleeding pattern in women who used the drug combination in a 24 days active tablet, four days placebo regimen. Full Phase 2 results will be published during the Phase 3 development program, Mols states.

Implant uses NOMAC

Nomegestrol acetate has been studied in use in a contraceptive implant form, Uniplant. Developed by South-to-South Cooperation in Reproductive Health, Uniplant is a single silicone rubber implant that is designed to slowly release the progestin over a year's time. A multicenter clinical trial of 1,803 women of reproductive age was conducted; 276 of the women discontinued prior to completing one year of study, with medical reasons for discon-

EXECUTIVE SUMMARY

Organon is conducting two Phase 3a trials for the first monophasic oral contraceptive containing estradiol and a new progestin, nomegestrol acetate. Phase 3 development is scheduled to be completed in 2009.

- Nomegestrol acetate — along with drospirenone, dienogest, trimegestone, and Nestorone — have been designed to bind very specifically to the progesterone receptor and not to other steroid receptors in an effort to avoid androgenic, estrogenic, or glucocorticoid side effects.
- Nomegestrol acetate has been studied for contraceptive use in a single rod implant, Uniplant. It also has been eyed for use in perimenopausal women.

COMING IN FUTURE MONTHS

- Check advances in female sterilization
- Urine-based test for ovarian cancer?
- How to stem the rise in HIV infections
- What's behind teen birth rate rise?
- Phase 1 trial planned for breast cancer vaccine

tinuation principally menstrual-related. Fifteen pregnancies occurred during the one-year study period, which resulted in a 12-month net cumulative pregnancy rate of 0.94%.[4] Uniplant is not commercially available.

In a separate study, researchers enrolled women of reproductive age to examine the effect of Uniplant on plasma levels of sex hormone-binding globulin (SHBG), testosterone, free testosterone, and androstenedione, as well as its impact on blood pressure, body weight, and the development of common acne.[5] All changes observed in the study were within normal range, researchers report. SHBG was not affected by Uniplant use, and no significant increase was observed in androgen levels or in the development of acne vulgaris.[5]

Because of the lack of androgenic activity of NOMAC, the progestin does not modify glucose and insulin response in oral glucose tolerance tests and does not induce changes in the lipid profile.[6,7]

NOMAC also has been studied in use of perimenopausal women.[8] In a study designed to evaluate whether progestin administration increases resting metabolic rate and influences body composition of perimenopausal women, results indicate cyclic NOMAC administration may contribute to reduce negative modification of body composition.[8]

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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.

5. What material is used to manufacture the FC2 female condom?
A. Linen
B. Nitrile
C. Polyurethane
D. Sheep cecum

6. When the viruses that can cause genital herpes are released between outbreaks from skin that does not appear to be broken or to have a sore, it is called:
A. sequential eruption.
B. sloughing.
C. paraphimosis.
D. asymptomatic shedding.

7. Calcium cannot be absorbed without:
A. vitamin D.
B. bisphosphonates.
C. isoflavones.
D. vitamin C.

8. Which progestin is NOT considered a new progestin?
A. Drospirenone
B. Dienogest
C. Norethisterone acetate
D. Trimegestone

Answers: 5. B; 6. D; 7. A; 8. C.

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CNE/CME Instructions

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

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.*

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S·T·D QUARTERLY™

Despite progress, STD numbers continue to rise; diseases remain a major challenge

Chlamydia, syphilis, gonorrhea cases increase for second year in a row

Review the number of sexually transmitted diseases (STDs) detected in your patient population over the last year. Have the numbers gone up? If so, don't be surprised. National numbers from 2006 show that cases of chlamydia, as well as gonorrhea and syphilis, continued to increase in the United States for the second year in a row, according to a new report by the Centers for Disease Control and Prevention (CDC).[1]

The CDC estimates that approximately 19 million STD infections occur each year in the United States, with almost half among young people ages 15 to 24.[2] Young women, racial and ethnic populations, and men who have sex with men (MSM) are particularly hard hit by these diseases, says **John Douglas Jr.**, MD, director of the Division of STD Prevention in the CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. STDs can have serious health consequences, particularly if they are undiagnosed and left untreated, he notes.

Many cases of notifiable STDs go undiagnosed, and some highly prevalent viral infections, such as human papillomavirus and genital herpes, are not reported at all, notes the CDC.[1] In releasing its new publication, *2006 STD Surveillance Report*, the CDC focused special attention on trends in three notifiable STDs: chlamydia, gonorrhea, and syphilis.

EXECUTIVE SUMMARY

Cases of chlamydia, as well as gonorrhea and syphilis, continued to increase in the United States for the second year in a row, according to a new report by the Centers for Disease Control and Prevention.

- The national rate of reported chlamydia in 2006 was 347.8 cases per 100,000 population, an increase of 5.6% from 2005. The national rates for primary and secondary syphilis increased 13.8%, from 2.9 to 3.3 cases per 100,000 population, and the number of cases increased from 8,724 to 9,756.
- In 2006, the gonorrhea rate was 120.9 cases per 100,000 population, representing an increase of 5.5% since 2005 and an increase for the second consecutive year.

How to stem chlamydia?

The national rate of reported chlamydia in 2006 was 347.8 cases per 100,000 population, an increase of 5.6% from 2005.[1] While recent data underscore the impact of innovative screening and prevention strategies, clinicians must continue to adapt to meet new challenges in detect-

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Consulting Editor **Robert A. Hatcher**, MD, MPH, Author **Rebecca Bowers**, Associate Publisher **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.

ing and treating the disease, says **Stuart Berman**, MD, chief of the epidemiology and surveillance branch in the CDC's Division of STD Prevention.

Chlamydia screening for women under the age of 26 is critical, says Berman. While the CDC recommends screening for this group, such recommendations are not always implemented, he notes. **(Several medical and public health groups recommend screening; see the *Contraceptive Technology Update* article, "Spotlight on chlamydia: Boost your screening rate in young women," August 2007, p. 85.)**

"Studies show that chlamydia screening is one of the most effective, yet underutilized, prevention tools," says Berman. "We have seen expanded opportunities for chlamydia screening in recent years, but many young women remain untested."

Simple systems-level changes by clinicians can lead to a significant increase in the number of women screened, notes Berman. For example, placing chlamydia test materials next to Pap test materials during an exam can remind a provider to offer the test and make access to materials convenient, he states.

Recent studies indicate that many women treated for chlamydia may become reinfected by their male partners;[3,4] approaches that help facilitate treatment of these partners may help reduce reinfection, says Berman.

"For example the patient herself may help deliver treatment to the partner," states Berman. "This sort of approach is known as expedited partner therapy, and CDC has recommended that it be available and considered by clinicians as an additional strategy to combat reinfection." **(Read more about strategies to stem repeat infection; see the *STD Quarterly* supplement articles, "Informing partners can help lower STD rates," April 2007, supplement p. 3; and "Repeat chlamydia infection: Improve partner notification and treatment," October 2006, supplement p. 1.)**

Screening and treating men for chlamydia may help decrease transmission to women, says Berman. Several STD programs are conducting such screening, he notes. The CDC has issued guidance that helps STD programs decide which populations of men to test and has indicated that the highest risk populations include men in correctional facilities, he notes. *(Editor's note: The CDC convened an external consultation in March 2006 to address male chlamydia screening. To download a free copy of the consultation results, go to the CDC STD web page, www.cdc.gov/std/default.htm. Under "STD Topics," click on "Chlamydia and LGV." Under "Treatment," click on "Male Chlamydia Screening Consultation."*)

Keep eye on syphilis

While the rate of primary and secondary (P&S) syphilis in the United States decreased throughout the 1990s, national figures show an increase over the past six years. Between 2005 and 2006, the national P&S syphilis rate increased 13.8%, from 2.9 to 3.3 cases per 100,000 population, and the number of cases increased from 8,724 to 9,756.[1] **(*CTU* reported on the gains in syphilis rates in its *STD Quarterly* supplement article, "Syphilis rate on the increase in gay, bisexual men in the U.S.," July 2007, p. 1.)**

To tackle the challenge, the CDC released in May 2006 its updated National Plan to Eliminate Syphilis. The plan is designed to sustain efforts in populations traditionally at risk, including heterosexual and minority populations, as well as increased efforts among men who have sex with men, says Berman. *(Editor's note: To review the CDC's updated plan, go to the CDC Syphilis Elimination Effort site, www.cdc.gov/stopsyphilis. Under "Plans," click on "National." Also, click on "SEE Toolkit" and then "Health Care Provider Materials" for free resources, such as a physician pocket guide on syphilis.)*

"This plan will improve surveillance data and increase local capacity to respond to new outbreaks. Additionally, it will prioritize and target innovative interventions for populations at risk," notes Berman. "Finally, the National Plan will improve accountability and outcomes of syphilis elimination efforts with evidence-based approaches, training, and research to enhance prevention and control efforts."

Get a grip on gonorrhea

Public health officials also are keeping a watchful eye on the spread of gonorrhea, the second most commonly reported infectious disease in the United States. According to the CDC, 358,366 cases were reported in 2006. Following a 74% decline in the rate of reported gonorrhea from 1975 through 1997, overall gonorrhea rates plateaued, then increased for the past two years, the agency reports.[1] In 2006, the gonorrhea rate

was 120.9 cases per 100,000 population, which represented an increase of 5.5% since 2005.

The racial disparities in diagnoses of gonorrhea are stark, says Douglas. In 2006, African-Americans accounted for more than two-thirds (69%) of reported cases. American Indians and Alaskan Natives had the second highest rate of infection, followed by Hispanics. In June 2007, the CDC convened a consultation to address STD disparities in African-American communities as part of its accelerated efforts to bring community leaders and other partners together to address racial and ethnic disparities in STD rates.[1]

The South continues to record the highest gonorrhea rate among the four regions of the country, according to the CDC.[1] Infection rates rose in the region for the first time in eight years, increasing 12.3% between 2005 and 2006 from 141.8 to 159.2 per 100,000 population. Researchers also are concerned about continued increases in the West, where the rate of reported gonorrhea cases rose 2.9% between 2005 and 2006, from 80.5 to 82.8 per 100,000.

Based on preliminary 2006 data that showed widespread fluoroquinolone-resistance among heterosexual and MSM populations, the CDC revised its gonorrhea treatment guidelines in April 2007. **(See the *CTU* article, "New recommendations out for gonorrhea treatment," June 2007, p. 64.)** The agency no longer recommends that the fluoroquinolone class of antibiotics be used to treat any cases of gonorrhea in the United States.

With the loss of fluoroquinolones, recommended gonorrhea treatments are limited to a single class of antibiotics — cephalosporins. Although 2006 data show no indication of cephalosporin resistance, increased monitoring for emerging resistance and accelerated research into new treatments are needed to continue the nation's progress in stemming the spread of STDs, the CDC states.

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New research focuses on rapid chlamydia test

New research indicates that a rapid test that uses self-collected vaginal swabs may be effective in diagnosing chlamydia.[1] With its ability to deliver results in less than 30 minutes, the test, now in development, would give clinicians a same-day diagnostic and screening tool for chlamydial infection.

Clinicians need effective tools to battle chlamydia's spread. *Chlamydia trachomatis* infection is the most prevalent sexually transmitted bacterial infection worldwide. Common among sexually active young women, undiagnosed and untreated chlamydial infection can result in complications such as pelvic inflammatory disease, ectopic pregnancy, and infertility.[2]

According to the Centers for Disease Control and Prevention (CDC), 1,030,911 chlamydia diagnoses were reported in 2006 in the United States, up from 976,445 in 2005.[3] Under-reporting of the infection is substantial because most people with chlamydia are not aware of their infections and

EXECUTIVE SUMMARY

New research indicates that a rapid test that uses self-collected vaginal swabs may be effective in diagnosing chlamydia. With its ability to deliver results in less than 30 minutes, the test, now in development, would give clinicians a same-day diagnostic and screening tool for chlamydial infection.

- Scientists at the University of Cambridge in the UK have formed a spin-out company to seek marketing approval for the test. The company plans to seek marketing approval in the United States.
- *Chlamydia trachomatis* infection is the most prevalent sexually transmitted bacterial infection worldwide. Undiagnosed, untreated chlamydial infection can result in complications such as pelvic inflammatory disease, ectopic pregnancy, and infertility.

do not seek testing. Women are frequently re-infected if their sex partners are not treated.

Scientists who have developed the test at the University of Cambridge in the UK have formed a spin-out company, Diagnostics for the Real World, to seek marketing approval for it. The company does plan to seek approval for the test to be marketed in the United States, confirms **Helen Lee**, PhD, head of the research team. **(See *CTU* article on rapid test research, "Research eyes rapid testing of chlamydia," March 2004, p. 31.)**

Check the results

The Chlamydia Rapid Test is an immunoassay-based test that detects chlamydial lipopolysaccharide. The published study is an evaluation of the sensitivity, specificity, and predictive values of the rapid test in comparison with polymerase chain reaction and strand displacement amplification assay. A total of 1,349 women, ages 16 to 54, participated in the trial, held at three United Kingdom clinics.

Polymerase chain reaction assay, considered the reference standard for chlamydial testing, tested positive for *C. trachomatis* in 8.4%, 9.4%, and 6% of specimens evaluated at the three clinics. In comparison, the rapid test had a positive predictive value of 86.7% and a negative predictive value of 98.6%. Comparison with the strand displacement assay demonstrated a sensitivity of 81.6% and specificity of 98.3% for the rapid test.

The Chlamydia Rapid Test is based on a signal amplification system that greatly improves the sensitivity of rapid tests, explains Lee.

"Because of this improved sensitivity, unlike other existing rapid tests, which require the difficult-to-collect cervical swabs, ours is the only one able to use self-collected vaginal swabs," states Lee. "In 1,063 young women surveyed, 99.4% found the instructions easy to understand, and 95.9% felt comfortable collecting their own vaginal swab specimens."

The Chlamydia Rapid Test is about more than speed of treatment for positive clients, says **Penny Barber**, chief executive of Brook in Birmingham, one of the clinics that participated in the clinical trial.

"All clients, anxious about having chlamydia, benefit from the relief a rapid result gives," says Barber. "For clinics, there is a strong business case for a method that cuts out the logistics and cost of transporting samples, sending results back, and then contacting clients."

The availability of the Chlamydia Rapid Test results within 30 minutes allows for immediate treatment and contact tracing, potentially reducing the risks of persistent infection and onward transmission, say the research scientists. It also could provide a simple and reliable alternative to nucleic acid amplification tests in chlamydia screening programs, they conclude.

The U.S. National Institutes of Health and the Wellcome Trust, a UK-based charity, provided funding for the research. Pivotal to the Wellcome Trust's decision to fund the program was endorsement from health care professionals that a rapid point-of-care test, based on a non-invasive sample, would transform the acceptability of chlamydia screening in the target population, says **Richard Seabrook**, head of business development of its Technology Transfer Division. Additional evaluation from diagnostic experts, which shows that the technology will deliver the required sensitivity and will be sufficiently robust for a resource-poor setting, led the charity to support the research, says Seabrook.

What is the next step in research for the chlamydia test? Lee says the scientists are moving forward on several fronts. The research team recently was awarded $50,000 for development of the signal amplification system during the 2007 Tech Museum Awards. The international program honors innovators who are applying technology to benefit humanity.

"Having now developed the platform technology of a simple, rapid, and sensitive test format, we will continue to develop tests for the detection of other sexually transmitted diseases such as gonorrhea," Lee states. "Our next product is a duplex test that would simultaneously detect chlamydia and gonorrhea from the same self-collected sample."

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