

# CONTRACEPTIVE TECHNOLOGY

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## Lower unintended pregnancy rates: Use IUD for emergency contraception

*Copper-T IUD most effective form of EC, but use remains low*

Women seeking emergency contraception (EC) are at high risk of unintended pregnancy. To counter this possibility, family planning providers often issue advance supply of emergency contraceptive pills (ECPs). But is this practice effective in addressing the problem?

Analysis of all available data to date indicates that efficacy of advance provision compared with standard provision of ECPs in reducing unintended pregnancy rates at the population level has not been demonstrated.<sup>1</sup> Data show that while any use of ECPs was two to seven times greater among women who received an advanced supply of pills, there was no significant reduction in unintended pregnancy (relative risk 0.90, 95% confidence interval 0.69-1.18) over 12 months when advance provision was compared with standard provision of ECPs.

The copper-T intrauterine device (ParaGard IUD, Teva Women's Health, North Wales, PA) is the most effective method of EC with a failure rate of less than 0.1%, yet few family planning providers offer EC IUD insertions. Results of a survey of 1,246 clinicians in a California state family planning program, where contraceptives approved by the Food and Drug Administration are

## EXECUTIVE SUMMARY

Women seeking emergency contraception (EC) are at high risk of unintended pregnancy. Family planning providers often issue advance supply of emergency contraceptive pills (ECPs).

- Analysis of all available data to date indicates that efficacy of advance provision compared with standard provision of ECPs in reducing unintended pregnancy rates at the population level has not been demonstrated.
- The copper-T intrauterine device (ParaGard IUD) is the most effective method of EC with a failure rate of less than 0.1%, yet few family planning providers offer EC IUD insertions. Results of a survey among 1,246 California state family planning program clinicians indicate 85% never recommended the copper IUD for EC and 93% required two or more visits for an IUD insertion.

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available at no cost to low-income women, show most clinicians (85%) never recommended the copper IUD for emergency contraception, and most (93%) required two or more visits for an IUD insertion.<sup>2</sup>

Why are providers hesitant when it comes to inserting IUDs for EC? **David Turok**, MD, associate professor in the University of Utah Department of Obstetrics and Gynecology in Salt Lake City, hears

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Editor: **Rebecca Bowers**.

Executive Editor: **Joy Daughtery Dickinson** (404) 262-5410  
([joy.dickinson@ahcmedia.com](mailto:joy.dickinson@ahcmedia.com)).

Production Editor: **Kristen Ramsey**.

Interim Editorial Director: **Lee Landenberger**.

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### Editorial Questions

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several explanations when he speaks to family planning groups. Providers say their clinics don't have the financial resources to stock devices, don't have the time to obtain preapprovals for insertions, or don't have the flexibility in scheduling time for EC insertions, he says. Such practices need to change, he says.

"We need to have the ability to view these things as true contraceptive emergencies, just like cardiologists and emergency room physicians view chest pain as a cardiac emergency," explains **Eleanor Bimla Schwarz**, MD, MS, director of the Women's Health Services Research Unit and associate professor of medicine, epidemiology, and obstetrics, gynecology, and reproductive sciences at the University of Pittsburgh. "In those cases, we're not telling people 'come back tomorrow or some other day.' We see them on the spot, and that's the shift that we need to make in order to make it happen."

Schwarz and Turok led a session at the recent Reproductive Health 2013 national conference in Denver to optimize chances for women seeking EC to initiate a highly effective method of contraception before leaving the clinic.<sup>3</sup> Participants were asked to reflect on challenges that might arise in their own clinical settings when trying to offer emergency IUD placement and to brainstorm potential solutions. The session also focused on helping women who opt for ECPs to transition to other highly effective methods of contraception, such as the contraceptive implant (Nexplanon, Merck & Co., Whitehouse Station, NJ) or the levonorgestrel IUD (Mirena, Bayer HealthCare Pharmaceuticals, Wayne, NJ), before leaving the clinic.

## What did Pittsburgh do?

Researchers at the University of Pittsburgh have developed a program to ensure that all women who seek EC or walk in pregnancy (WIP) testing are equipped with the knowledge and services they need to avoid unintended pregnancy.

The researchers explored how often women seeking clinic-based pregnancy testing who don't desire pregnancy might benefit from EC, as well as examined variables associated with patients asking for EC when use is indicated. They invited women seeking pregnancy testing or EC from a Pittsburgh inner-city Title-X-funded family planning clinic to complete surveys. Twenty-seven percent of women were seeking EC, and 73% were seeking pregnancy testing. Of those seeking pregnancy testing, 39% might have benefited from same-day use of EC pills.

Researchers found that women who had never used EC and who had more than one episode of

unprotected sex within the past month were less likely to request EC when use was indicated, while single women were more likely to request EC. Counseling regarding EC options is important for women seeking same-day pregnancy testing who don't desire pregnancy, researchers conclude.<sup>4</sup>

The Pittsburgh researchers then looked at what it would take for a Title X clinic to routinely offer women seeking EC or WIP same-day placement of highly effective reversible contraception. They also looked at the impact of brief structured counseling about long-acting reversible contraception (LARC), combined with the offer of same-day placement, on women's knowledge of IUDs and implants and contraceptive use. (*See the brief scripted counseling message on this page.*)

Of women who came into the Pittsburgh clinic for EC, 29% received an IUD within five days, and 34% had an IUD within three months. These women represent an additional 5% of women who received an IUD more than five days after their EC visit. About 19% of women reported the counseling prompted their switch to an IUD.<sup>3</sup>

During the baseline period, no women received an IUD on the day of their clinic visit, Schwarz noted. After researchers implemented the brief counseling script, 10.5% of women had an EC IUD inserted.

A total of 95 women came to the clinic for EC and left with levonorgestrel ECPs; seven of those women were pregnant by three months. Ten women who presented for EC left with ulipristal acetate pills; three of them were pregnant by three months. In contrast, none of the women who requested EC and had a copper-T IUD inserted same-day (25 women) were pregnant at three months.<sup>3</sup>

## Look at opportunities

When can a copper-T IUD be placed for EC? According to the recently released U.S. Selected Practice Recommendations for Contraceptive Use, it can be inserted within five days of unprotected intercourse, but can be inserted six or more days after unprotected sex if the day of ovulation can be estimated and not more than five days have passed since ovulation, says Schwarz.<sup>5</sup>

What can be gained from the results of the Pittsburgh project? Schwarz says it is possible for a Title X clinic to routinely inform women about the option of EC IUD. As only 10-20% of women might opt for same-day intrauterine contraception, this practice will not flood most clinic schedules, she notes. Clinics must have IUDs in their stock cabinet prior to establishing same-day EC IUD insertion

## Same-day placement uses counseling script

Looking for a quick way to counsel on long-acting reversible contraception (LARC) for same-day placement? Here is a brief counseling script, used by researchers at the University of Pittsburgh:

- “The birth control methods that work best to prevent pregnancy are the implant and the IUD. These methods are more effective than condoms, pills, or the Depo shot. The implant and IUD are as effective as having your tubes tied, but they can be reversed at any time if you decide to become pregnant or want to switch to a different method.

- The birth control implant is called Nexplanon. It is a small flexible rod that is placed under the skin of the upper arm and can be used for three years.

- An IUD is a small, flexible, T-shaped device that is slid into the uterus and can be used for at least five years. There are two types that you might have heard of: the Mirena IUD and the copper IUD, sometimes called ParaGard.

- If you have had sex without a condom or other type of birth control in the last seven days and don't want to become pregnant, the copper IUD might be your best option today because it is more effective than emergency contraceptive pills.

- Do you have any questions about implants, IUDs, or any other types of birth control?” ■

services, Schwarz says. (*To read about Utah clinics' experience with IUD EC insertions, see the story on p. 136.*)

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## IUD for EC: Check the Utah experience

*New research to emerge*

Can increased use of the copper T intrauterine device (ParaGard IUD, Teva Women's Health, North Wales, PA) for emergency contraception (EC) make an impact on the rate of unplanned pregnancy at your clinic? Take a look at results from a study of two Utah family planning clinics.<sup>1</sup>

Researchers with the University of Utah in Salt Lake City designed the prospective cohort study to follow women who chose the copper IUD or oral levonorgestrel emergency contraceptive pills for emergency contraception at Planned Parenthood Association of Utah clinics in Salt Lake City and West Valley City. The primary outcome was unplanned pregnancy 12 months after presenting for EC. Analysis was by intent to treat.

Of the 548 women who presented for EC and agreed to participate in the trial, 218 women (39.7%) chose the copper IUD and 331 (60.3%) chose oral levonorgestrel (LNG) pills. More than half (58.7%) of the women had never been pregnant; 16% had had a prior abortion.

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### EXECUTIVE SUMMARY

Study results indicate that 12 months after presenting for emergency contraception (EC), women selecting the copper T intrauterine device (IUD) for EC were more likely to be using an effective method of contraception and less likely to have had an unplanned pregnancy than those who chose EC pills.

- In the prospective cohort study, 40% chose the copper IUD, with the remainder choosing EC pills. More than half (58.7%) had never been pregnant; 16% had had a prior abortion.
- Among nulliparous women, 27 of 138 (19.6%) IUD insertions were unsuccessful. Results of a subsequent intervention that provided best practices education and trained all providers to do paracervical blocks and cervical dilation are forthcoming.

Twelve months after presenting for EC, use of an effective method of contraception (typical use failure rate 8% or less) was greater in the IUD group (125/183 [68%]) than the oral LNG group (106/257 [41%],  $p < 0.0001$ ). The 12-month cumulative pregnancy rate in the IUD group (6.5%) was less than that in the oral LNG group (12.2%) (hazard ratio 0.53 [95% confidence interval, 0.29-0.97],  $p = 0.041$ ).<sup>1</sup>

Twelve months after presenting for emergency contraception, women selecting the copper IUD for EC were more likely to be using an effective method of contraception and less likely to have had an unplanned pregnancy than those who chose oral levonorgestrel, researchers conclude.

### Failed IUD insertions?

In the Utah study, a total of six nurse practitioners performed 197 EC IUD insertion attempts. These providers had a mean of 14.1 years of experience (range 1-27, standard deviation  $\pm 12.5$ ).

Patients included in the trial presented as walk-ins and, thus, were not scheduled into IUD insertion time slots. Providers inserted EC IUDs in the following standard fashion: after bimanual exam and placement of speculum, the cervix was prepped with betadine and a tenaculum was placed on the anterior lip of the cervix. The uterus then was sounded using a 4-mm stainless steel sound, and IUD insertion was attempted. Adjuvant measures to facilitate difficult IUD insertions, such as cervical anesthesia, dilation, pain medication, and use of ultrasound guidance, were not used, the researchers note. Data from providers performing less than five insertions during the study period were excluded.

In an already published analysis of the IUD insertion failures, 27 of 138 (19.6%) nulliparous women had unsuccessful IUD insertions. In parous women, eight of 59 IUD insertions were unsuccessful (13.6%). The adjusted odds ratio (aOR) showed that IUD insertion failure was more likely in nulliparous women compared to parous women (aOR=2.31, 95% CI 0.90-6.52,  $p = .09$ ).<sup>2</sup>

Women who presented at the clinics for EC did not come in expecting an IUD insertion, so they might have experienced anxiety in placement, researchers note. However, patient anxiety was not assessed in the study, so the role it might have played on insertion success is not clear. Previous research indicates that women with anxiety over the procedure have higher level of perceived pain, which potentially contributes to a more difficult insertion.<sup>3</sup>

Intrauterine devices are safe, effective choices for women of all ages who have never given birth. In

2012, the American College of Obstetricians and Gynecologists (ACOG) issued a committee opinion stating that long-acting reversible contraceptives such as the IUD and the contraceptive implant are safe, effective, and appropriate options for adolescents.<sup>4</sup> (To read more about the opinion, see the Contraceptive Technology Update article, “Long-acting methods safe for teens: include options in your counseling,” December 2012, p. 133; also review research covered in “Old myth debunked: data show IUD is safe birth control option for teens,” July 2013, p. 73.)

Look to new research to emerge from the Utah clinic experience, says **David Turok**, MD, associate professor in the University of Utah Department of Obstetrics and Gynecology in Salt Lake City. Following the initial study, fellow researcher Amna Dermish, MD directed an intervention, training all providers to do paracervical blocks and cervical dilation, as well as presenting education on best practices. Dermish then observed providers performing a few blocks and dilations. Forthcoming research will be published.

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## The search has begun for long-acting contraceptives

With funding from the Bill & Melinda Gates Foundation of Seattle, Durham, NC-based FHI 360 has launched its Contraceptive Technology Innovation Initiative to develop innovative, long-acting contraceptives to help expand choice and access for women most in need in low-income countries. The Initiative will expand current work to develop a longer-acting injectable contraceptive and

research funded by the U.S. Agency for International Development to develop a new biodegradable contraceptive implant.

It is estimated that 222 million women around the world have an unmet need for modern contraception.<sup>1</sup> Since long-acting forms of contraception don't require regular resupply from a provider or action from users, they are ideal in settings where access to healthcare services is limited. While existing long-acting methods have better continuation and adherence rates than shorter-acting methods and are cost-effective, they might be unaffordable for women in resource-challenged countries, or they might not meet women's needs or preferences.

There is a need for new long-acting contraceptive options that will fill existing gaps and increase choices for women, notes **Laneta Dorflinger**, PhD, Initiative director. “In recent decades, there has been limited investment in contraceptive research and development,” noted Dorflinger in a statement accompanying the project launch. “We applaud the Gates Foundation's long-term vision, which looks not only to meet the needs of women today through efforts such as FP 2020 (a global partnership of governments, non-profit organizations, and the private sector to enable 120 million more women and girls to use contraceptives by 2020) but also to ensure that we can meet the needs of women tomorrow by making longer-term investments in innovative product development.”

## A biodegradable implant?

With research funded by the US Agency for International Development (USAID), FHI 360 is pressing forwarding in developing a highly effective biodegradable contraceptive implant. Prototypes are being designed now to last approximately 18 months, and have a short “tail” — the time between when the

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## EXECUTIVE SUMMARY

FHI 360 has launched its Contraceptive Technology Innovation Initiative to develop innovative, long-acting contraceptives to help expand choice and access for women most in need in low-income countries. The Initiative will expand current work to develop a longer-acting injectable contraceptive and research funded by the U.S. Agency for International Development to develop a new biodegradable contraceptive implant.

- Research on biodegradable implants is focused on developing prototypes that will last about 18 months and ensure rapid return of fertility thereafter.
- Four research groups are involved in the development of a longer-acting injectable contraceptive.

method becomes less effective and when blood levels of the progestin (contraceptive hormone) decline to undetectable, says Dorflinger. This characteristic is important to ensure a rapid and predictable return to fertility, she explains.

“During the period of effectiveness, ideally the progestin release from the implant will be ‘zero order,’ so that blood levels are quite constant, but remain above a threshold to ensure high effectiveness,” states Dorflinger. “Finally, the implant should be easily removable for at least some period of time in the event that a woman has unwanted and intolerable side effects.”

With such a target product profile in mind, a substantial technological challenge will be to develop a drug delivery system that will provide constant release for the intended duration, but then have release rates drop to zero quite quickly, observes Dorflinger.

“Formulating this drug delivery in a way that allows for removal, if desired, without the implant fragmenting will be a second challenge,” she notes. “Advances in sustained release delivery systems and biodegradable polymer technology make us optimistic that we will be able to reach these two goals.”

## 2-rod implant progresses

FHI 360 continues to work with Sino-implant (II), a highly effective, low-cost, subdermal contraceptive implant composed of two thin, flexible, silicone rods, each containing 75 mg of levonorgestrel. The two rods are inserted under the skin of a woman’s arm by a trained healthcare provider and are labeled for four years of use, at which point they have to be removed. The annual pregnancy rate for the Chinese-manufactured implant method is listed below 1%. It is not available in the United States.

FHI 360 is providing technical assistance to facilitate the device’s global introduction, including conducting independent quality testing, negotiating public-sector price-ceiling agreements, supporting the World Health Organization prequalification application process, and working with distributors to secure national regulatory approvals. It also is leading a new clinical trial in the Dominican Republic, which will supplement existing clinical evidence, and is collaborating on post-marketing surveillance studies in four countries with support from the Gates Foundation and USAID.

## A longer-acting shot?

FHI 360 is continuing its work on the development of a longer-acting injectable contraceptive, says Vera

Halpern, MD, FHI 360 scientist. (To read about its efforts, see the *Contraceptive Technology Update* article, “Longer-acting method that is injectable probed,” March 2013, p. 28.)

Since mid-2013, an additional research project has been selected for proof-of-concept testing under the initiative, says Halpern. Researchers at Orbis Biosciences of Kansas City, KS, led by principal investigator Nathan Dormer, PhD, are evaluating poly(lactic-co-glycolic) microspheres manufactured using Orbis Biosciences’ proprietary Precision Particle Fabrication technology and releasing etonogestrel. Orbis Biosciences’ technology allows for a linear increase in concentration to therapeutic levels, followed by a steady-state, sustained release for desired length of time. The goal is to reduce the number of injections and improve patient compliance.

“All four subcontracts have been executed, and all four research sites have started collecting the data,” states Halpern.

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# Help women lower risks for gynecologic cancers

*Being overweight is a risk factor*

As a healthcare provider, there are several things you can do to help women lower their risks for gynecologic cancer. From getting vaccinations, losing weight, and knowing their family history, women can lower their risk of developing certain types of cancer and improve their chances for survival if they do develop one of them.

According to the Centers for Disease Control and Prevention (CDC), five main types of cancer can affect a woman’s reproductive organs: cervical, ovarian, uterine, vaginal, and vulvar. The five cancer types are collectively referred to as gynecologic cancer; a sixth type of gynecologic cancer is fallopian tube cancer, which is very rare. According to CDC statistics, 84,155 women in the United States were diagnosed with a gynecologic cancer in 2009; 27,813 died from the disease.<sup>1</sup>

To help women be proactive against gynecologic cancer, share the following recommendations from the Society of Gynecologic Oncology:

Providers now have a valuable prevention tool against cervical cancer in vaccines against human papillomavirus (HPV), the virus responsible for most cervical cancer. (*Who should be vaccinated? See box on p. 140.*)

According to the CDC, HPV is the main cause of cervical cancer in women, with about 12,000 new cervical cancer cases each year in the United States. About 4,000 deaths in women each year in the United States are attributed to cervical cancer.<sup>2</sup>

The CDC estimates there are about 15,000 HPV-associated cancers in the United States that might be prevented by vaccines each year in women, including cervical, anal, vaginal, vulvar, and oropharyngeal cancers. About 7,000 HPV-associated cancers might be prevented by vaccine each year in men; oropharyngeal cancers are the most common.<sup>2</sup>

## Know family history

It is extremely important that providers talk to women about their potential increased genetic risk for cancer, says **Stephanie Blank**, MD, associate professor and director of the Gynecologic Oncology Fellowship at the New York (City) University School of Medicine.

“If a woman has a personal or strong family history of cancer, she may be at increased risk for gynecologic cancer,” observes Blank. “Knowledge about this risk can allow patient and her doctor to look into potentially life-saving prevention strategies.”

It is also important that a provider speaks to a patient with ovarian cancer about the role genetics might play in the course of her disease and how a genetic predisposition to cancer might affect her prognosis, treatment, and her family’s future, says Blank.

Each year, about 35,000 women in the United States obtain uterine cancer, according to the CDC.

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## EXECUTIVE SUMMARY

Help women lower their risks for gynecologic cancer. From getting vaccinations, losing weight, and knowing their family history, women can lower their risk of developing certain types of cancer and improve their chances for survival if they do develop one.

- According to the Centers for Disease Control and Prevention (CDC), five main types of cancer can affect a woman’s reproductive organs: cervical, ovarian, uterine, vaginal, and vulvar. The five cancer types are collectively referred to as gynecologic cancer. A sixth type of gynecologic cancer is fallopian tube cancer, which is very rare.

- According to CDC statistics, 84,155 women in the United States were diagnosed with a gynecologic cancer in 2009, and 27,813 died from the disease.

Being overweight is a major risk factor for developing the disease.

Counsel women that losing weight might significantly reduce their risk and might help improve survival rates if cancer does develop. In a 2013 report, three of five new cases of endometrial cancer in the United States could be prevented if women maintain a healthy weight and are physically active.

According to the analysis, 59% of cases, or about 29,500 annually, could be prevented if women were physically active for a minimum of 30 minutes per day and maintained a healthy body weight (body mass index from 18.5 to 25.0 kg/m<sup>2</sup>).<sup>3</sup>

## Detection in research

All women are at risk for gynecologic cancers, and risk increases with age. When gynecologic cancers are found early, treatment is most effective. What might providers see from current clinical trials for detection of gynecological malignancies?

Look at new findings of a prospective single-arm study led by the Houston-based University of Texas MD Anderson Cancer Center. For the 11-year study, 4,051 women were enrolled from seven sites across the country, with MD Anderson serving as the lead site. All were healthy, post-menopausal women, ages 50-74, with no strong family history of breast or ovarian cancer. The study’s primary endpoint was specificity, or few false positives. In addition, the study looked at the positive predictive value, or the number of operations required to detect a case of ovarian cancer.

Each woman received a baseline CA-125 blood-test. Using the Risk of Ovarian Cancer Algorithm (ROCA), a mathematical model based on the patient’s age and CA-125 score, women were assigned to one of three risks groups, with the respective follow-up:

- Women determined to be “low” came back in a year for a follow-up blood test.
- Those classed as “intermediate” received further monitoring with repeat CA-125 blood testing in three months.
- Those determined to be “high” were referred to receive transvaginal sonography and see a gynecologic oncologist.

Findings indicate that based on the women’s CA-125 change over time, the average annual rate of referral to the intermediate and high groups were 5.8% and .9%, respectively. A total of 117 women (2.9%) were determined to be high risk, and they received a sonography and a specialist referral. Of those women, 10 underwent surgery: four had inva-

## Who should receive HPV vaccination?

The Centers for Disease Control and Prevention (CDC) recommends that all girls ages 11 or 12 receive the three doses of either brand of HPV vaccine (Gardasil, manufactured by Merck, or Cervarix, manufactured by GlaxoSmithKline) to protect against cervical cancer. Girls and young women ages 13-26 should receive the HPV vaccine if they have not received any or all doses when they were younger.

Gardasil also is licensed, safe, and effective for males ages 9-26 years. CDC recommends Gardasil for all boys ages 11 or 12, and it recommends Gardasil for males ages 13-21 who did not get any or all of the three recommended doses when they were younger. All men may receive the vaccine through age 26, and they should speak with their provider to find out if getting vaccinated is right for them.

The vaccine also is recommended for any man who has sex with men and men with compromised immune systems, including those with HIV, through age 26, if they did not get fully vaccinated when they were younger. ■

sive ovarian cancer, two had borderline disease, one had endometrial cancer, and three had benign ovarian tumors. There was a positive predictive value of 40%, which greatly surpasses the clinical benchmark of 10%. The specificity of the test was 99.9; the screening failed to detect two borderline ovarian cancers.<sup>4</sup>

Evaluation of changes in CA-125 over time are likely to be the most successful strategies in terms of early detection of ovarian cancer, says **Barbara Goff, MD**, director of gynecologic oncology at the University of Washington, Seattle and president of the Society of Gynecologic Oncology. Scientists await further answers on CA-125 testing from the United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS), a similarly designed study.

“I think we are on the verge of having an effective test for screening for ovarian cancer,” says Goff. “The question is, will we able to make it cost-effective so it could be used in a large population of people?”

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### RESOURCE

• The Centers for Disease Control and Prevention has developed a campaign, “**The Inside Knowledge: Get the Facts About Gynecologic Cancer**” to raise awareness of the five main types of gynecologic cancer: cervical, ovarian, uterine, vaginal, and vulvar. The campaign encourages women to pay attention to their bodies and know what is normal for them, so they can recognize the warning signs of gynecologic cancers and seek medical care. Materials available for free download include fact sheets, a brochure, symptom wallet card, and more. Go the campaign website, <http://1.usa.gov/OKTlt1>, and follow links to access the print materials. ■



## Postpartum LARCs help avert repeat pregnancy

By **Anita Brakman, MS**  
Director of Education, Research & Training  
Physicians for Reproductive Health  
New York City

**Melanie Gold, DO, FAAP**  
Clinical Professor of Pediatrics  
University of Pittsburgh School of Medicine  
Staff Physician  
University of Pittsburgh Student Health Service

The Colorado Department of Health Care Policy and Financing recently issued a bulletin notifying healthcare providers that hospitals can be reimbursed for the devices and placement of long-acting reversible contraceptive (LARC) methods inserted immediately postpartum while women are in the hospital following

deliveries. Previously, this cost could not be billed separately from a global labor and delivery expense, and hospitals wishing to insert LARC methods postpartum would have to cover the upfront costs of methods such as intrauterine contraception (IUC) and implants with no option for reimbursement. Implementation of this new policy began on Oct. 1, 2013, and is sure to benefit hospitals and patients throughout the state, especially adolescent mothers wishing to delay repeat pregnancy.

Adolescent mothers are at especially high risk of rapid repeat pregnancy, with 20% giving birth again within two years of delivery.<sup>1</sup> These additional births make it extremely difficult for young mothers to achieve their educational goals and economic self-sufficiency, even when compared to peers who experienced only one birth before age 20.<sup>2</sup>

A recent analysis of data from the Pregnancy Risk Assessment and Monitoring System found a lack of consistent use of highly effective contraception puts young mothers at particular risk for repeat pregnancy. An examination of data across seven states demonstrated that at four months postpartum, 20% of respondents ages 15-19 were not using any contraception, while 14% relied solely on condoms or withdrawal. Use of LARCs was reported by only 12% of respondents, with the preponderance (11%) using IUC and only 1% using implants.<sup>3</sup>

## Why LARC methods?

Why are LARC methods better for adolescent mothers compared to other contraceptives? In addition to high levels of efficacy, discontinuation rates are lower among adolescent mothers using LARCs than other hormonal methods including depot medroxy-progesterone.<sup>4</sup> The US Medical Eligibility Criteria for Contraceptive Use gives IUC and implants a category 1 for postpartum adolescent women, which affirms these as safe choices. For breastfeeding mothers, the US MEC give hormonal LARCs a category 2, indicating that the benefit of the method outweighs potential risk.<sup>5</sup>

The American College of Obstetricians and Gynecologists' 2012 Committee Opinion on adolescents and LARCs also recommends implants and IUC as first-line options for postpartum adolescents. The opinion emphasizes that the slightly higher risk for expulsion of an IUC does not outweigh the benefit of exceptional prevention of unintended pregnancy for youth who might not be able to access these methods in a timely way.<sup>6</sup>

Unfortunately many barriers block adolescent mothers, even those who planned to use a LARC post-

partum, from successful initiation of LARC in a timely way. A study by Tocce et al found that even when adolescents intended to obtain an implant within two weeks of delivery, only two-thirds had received the implant by 14 weeks postpartum.<sup>7</sup> Even when women are able to attend a six-week postpartum visit and discuss contraceptive options, by that time they are likely to have already resumed sexual activity.

## Eliminate protection gap

Inserting a LARC immediately postpartum helps women initiate a highly effective method and eliminates gaps in protection, just as Quick Start does for routine contraceptive initiation. Tocce and her co-authors have published several recent studies indicating that inserting LARCs, especially implants, on the labor and delivery floor can make a huge impact on decreasing rapid repeat pregnancy among adolescents.

One study of adolescent mothers in Colorado assessed pregnancy rates among those receiving an immediate postpartum implant compared to a control group. Data indicates 10% of the control group were pregnant six months postpartum, and 19% were pregnant within a year. No women who received implants were pregnant within six months. Within a year, there were four pregnancies among the group. Three of these pregnancies occurred in women who had the implant removed, and the other was a patient using another medication that might have reduced the implant's efficacy.<sup>8</sup> This data was crucial to convincing the state to make the administrative changes necessary to allow hospitals to bill for LARC devices separately from the global labor and delivery charges.

## Time for a change

Policy changes such as those implemented in Colorado need to occur at the state level. South Carolina and New Mexico also have improved access to immediate postpartum LARC devices. While state departments of health, hospitals, and LARC advocates work together to improve immediate postpartum access for adolescents and all women, women in states without these policies might find relief from improvements in contraceptive coverage through the federal Affordable Care Act (ACA).

Under the ACA, insurers are required to cover all Food and Drug Administration-approved contraceptives without any patient cost-sharing.<sup>9</sup> For women who are motivated and have timely access to a health-care provider, this new policy might allow them to obtain a LARC at a six-week postpartum check-up or any other time they wish to initiate.

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## Attacks continue on family planning funds

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

The last several years have brought unprecedented attacks on the publicly supported family planning effort in the United States.

At the federal level, the House of Representatives voted in 2011 and 2012 to eliminate all funding for

the Title X family planning program, the first such successful votes in the program's history.<sup>1</sup> The same legislation included a separate provision that would have barred Planned Parenthood affiliates from receiving any federal funds, including reimbursement for services provided to women and men insured through Medicaid. Both provisions were rejected by the Senate and by President Obama. Nevertheless, funding for Title X has dropped by \$36 million, more than 11%, between FY 2010 and FY 2013.<sup>2</sup>

Social conservatives' efforts have been more successful at the state level. Between 2010 and 2013, 13 states enacted laws attacking family planning programs or providers, by disproportionately slashing family planning funding, barring or disfavoring certain types of health centers in eligibility for family planning grants, or barring such health centers from receiving reimbursement under Medicaid.<sup>3</sup> Many of these laws have been challenged in court, and the Obama administration has interceded to protect the right of Medicaid enrollees to receive services from the family planning provider of their choice.

### Cuts undermine care

When successful, these attacks have undermined women's health and state budgets. In Texas, for example, the state in 2011 enacted severe family planning budget cuts and restrictions on providers' eligibility for public funds. The result has been closed health centers, reduced access to affordable and confidential care, government savings from family planning services being cut by more than half, and an estimated 30,000 additional unintended pregnancies in 2012. Indeed, the consequences have led the legislature to reverse course and restore some of the cut funding.<sup>4,5</sup>

All of these attacks are shortsighted and counterproductive when it comes to reducing the need for abortion or saving government funds. The latest evidence comes from a Guttmacher Institute report estimating the need for, extent of, and benefits from the U.S. publicly funded family planning effort in 2010.<sup>6</sup> That year, a total of 8.9 million women received publicly supported contraceptive services, including 6.7 million women served by health centers and 2.2 million receiving Medicaid-funded care from private doctors.

The contraceptive services provided to these women helped them prevent 2.2 million unintended pregnancies in 2010, which would have resulted in 1.1 million unplanned births and 760,000 abortions.<sup>6</sup> Without publicly funded contraceptive services, the rate of unintended pregnancies, unplanned births, and abortions in the United States would all be 66% higher.

The rates for teens would be 73% higher. By helping women avoid unintended pregnancies and the maternity and infant costs that would have followed, public funding for contraceptive services in 2010 resulted in net public savings of \$10.5 billion, or \$5.68 for every dollar spent providing contraceptive care.

## Title X is crucial

The Title X program was central to this effort, with Title X-supported health centers serving 4.7 million women in 2010. Those services helped women avert 1.2 million unintended pregnancies, 590,000 unplanned births, and 400,000 abortions, and they resulted in \$5.3 billion in net savings.<sup>6</sup> In addition, according to the Title X program's 2011 annual report, these health centers tested 2.5 million clients for chlamydia and provided 2.7 million tests for gonorrhea, 744,000 for syphilis, and 1.3 million for HIV.<sup>7</sup> They also provided 1.4 million clients with Pap tests to detect early signs of cervical cancer and 1.9 million women with breast exams to detect warning signs of breast cancer.

Despite the objections of social conservatives, Title X and other sources of public funding for family planning services will be just as critical in the years to come. The network of safety-net health centers, and the grant funding to support that network, will be needed to ensure that women and men newly insured under healthcare reform have a place to go for high-quality care. Moreover, many of these providers are well-situated to connect the uninsured to healthcare coverage and to care for the people who are left out of healthcare reform's coverage expansions.

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## COMING IN FUTURE MONTHS

- Long-acting reversible contraception — first line, single visit
- Screen for sexual violence in young adults under age 21
- Determine cause of irregular menses in teens
- Review options for permanent birth control

## CNE/CME QUESTIONS

1. What is the most effective method of emergency contraception?  
A. Levonorgestrel pills  
B. Ulipristal acetate pills  
C. Combined oral contraceptives containing ethinyl estradiol and levonorgestrel or norgestrel, used in the Yuzpe regimen  
D. Copper T intrauterine device
2. What is the name of the low-cost, subdermal contraceptive implant composed of two thin, flexible, silicone rods, each containing 75 mg of levonorgestrel?  
A. Sino-implant (II)  
B. Norplant  
C. Nexplanon  
D. Implanon
3. Which of the following is a major risk factor for uterine cancer?  
A. Younger than age 50  
B. Have an abnormally high, unhealthy amount of body fat  
C. Multiparous  
D. Excessive alcohol intake
4. What is the name of the class of immune cells that reside long-term in the genital skin and mucosa and are believed to be responsible for suppressing recurring outbreaks of genital herpes?  
A. CD8B1 T-cells  
B. CD8B T-cells  
C. CD8aa+ T-cells  
D. CD8A T-cells

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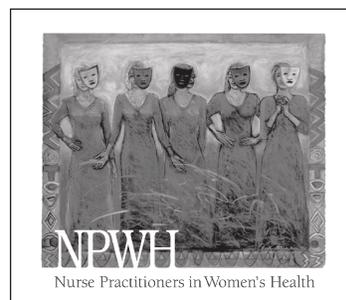
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# S · T · I

## Q U A R T E R L Y

## Initial positive results reported on herpes vaccine — What's next?

*More than 775,000 new herpes infections in U.S. each year, and no cure available*

Some 776,000 people in the United States incur new genital herpes infections each year. There is no current cure for such infections. Initial, positive results have just been reported for a therapeutic vaccine candidate for treating patients with genital herpes.<sup>1</sup>

The seven trial sites are: Birmingham-based University of Alabama Vaccine Research Unit; Cincinnati (OH) Children's Hospital Medical Center; Houston-based Center for Clinical Studies; Indianapolis-based Indiana University Infectious Disease Research; Portland, OR-based Westover Heights Clinic; Seattle-based University of Washington Virology Research Clinic; and Webster, TX-based Center for Clinical Studies. They are participating in the double-blind, placebo-controlled dose escalation Phase 1/2a clinical trial to evaluate the safety and immunogenicity of GEN-003, a vaccine candidate under development by Genocea Biosciences of Cambridge, MA.

The vaccine candidate is a T cell vaccine designed to reduce the transmission risk and clinical symptoms of herpes simplex virus type 2 (HSV-2). Its chemistry is designed to induce a balanced B cell and T cell immune response. It includes fragments of ICP4 and gD2 antigens, as well as a proprietary adjuvant, Matrix-M, licensed from Novavax of Rockville, MD.

The study enrolled 143 volunteers with a history of moderate-to-severe recurrent HSV-2 infection. Patients were sequentially enrolled into one of three

dose cohorts (10, 30, or 100 mcg of each protein) and randomized within cohorts to receive GEN-003, vaccine antigens without adjuvant, or placebo. Patients received three injections of the assigned treatment into an arm muscle at 21-day intervals. Antibody (B cell) and T cell immune responses to the two protein antigens contained in the vaccine were measured. A secondary objective of the study was to compare the quantitative presence of HSV-2, known as shedding, before and after the treatments.

Interim data presented at the 2013 Interscience Conference on Antimicrobial Agents and Chemotherapy indicate that patients who received three doses of GEN-003 had reductions in the frequency of viral shedding of up to 51% ( $p < 0.001$ ).

### EXECUTIVE SUMMARY

Some 776,000 U.S. residents incur new genital herpes infections annually. There is no cure. Initial, positive results are reported for a therapeutic vaccine candidate for treating genital herpes.

- Interim results from a double-blind, placebo-controlled dose escalation Phase 1/2a clinical trial of GEN-003, a vaccine candidate under development by Genocea Biosciences, show effectiveness against viral shedding.
- Washington state researchers identified a class of immune cells that reside long-term in the genital skin and mucosa and are believed to be responsible for suppressing recurring outbreaks of genital herpes.

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

Patients who received a placebo vaccine had no decline in viral shedding. Scientists also looked at T cell immune responses, which are believed to be important for the control of HSV-2 infection; they increased more than twentyfold to the ICP4 vaccine antigen and more than tenfold to the gD2 vaccine antigen. The vaccine candidate also increased neutralizing antibodies to the HSV-2 virus fivefold, on average, compared to baseline values.

The ability to reduce viral shedding is “critical,” says **Anna Wald, MD, MPH**, the study’s principal investigator and professor of medicine, epidemiology, and laboratory medicine at University of Washington. Viral shedding is the main driver of transmission of HSV-2 to sexual partners and infants. “These are the first data that provide compelling evidence that a vaccine administered to people with genital herpes can affect their infection,” said Wald in a statement accompanying the presentation. “We are excited that GEN-003 reduced viral shedding, as this finding paves the way for future trials that will measure the impact on clinical outbreaks.”

### What’s next step?

There are several steps that will need to be taken before scientists will know if the promising early results will hold up, says study co-investigator **Kenneth Fife, MD**, professor of medicine and of microbiology and immunology at Indiana University. The number of volunteers in the study is small, Fife notes. While researchers do statistical analysis to determine if the results are significant, the real test is whether the positive result can be reproduced in a larger number of research subjects that might be more representative of the overall population of people with genital herpes, he states. There also might be trials of different doses, different numbers of injections, or a different dosing schedule in determining the optimal dose of vaccine, Fife observes.

“One of the big unanswered questions is the durability of the effect. Will this last for six months or a year or five years?” asks Fife. “In other words, will booster immunizations be required and, if so, how often?”

The current study looked at the impact of the vaccine on viral shedding, but scientists also will want to know the impact on clinical recurrences, Fife states. Such a study will require additional subjects.

“The bottom line is that we are years away from having a product that will be available for use in practice, or the vaccine could fail at one of the additional steps and never come to market,” says Fife. “Despite all of these caveats, our group is still very excited by the results, and we hope to

be involved in additional studies that will be conducted in the future.”

### Immune cells identified

Earlier in 2013, researchers at the at the Seattle-based Fred Hutchinson Cancer Center and the University of Washington were able to identify a class of immune cells that reside long-term in the genital skin and mucosa and are believed to be responsible for suppressing recurring outbreaks of genital herpes.<sup>2</sup>

The discovery of this subtype of CD8+ immune cells, called CD8aa+ T-cells, might expand avenues to develop a vaccine to prevent and treat HSV-2. Identifying these T-cells’ specific molecular targets, called epitopes, is the next step in developing a vaccine.

For the first time, researchers know the type of immune cells that the body uses to prevent outbreaks, said **Lawrence Corey, MD**, virologist and president of the Fred Hutchinson Cancer Center in a statement accompanying the published results of the discovery. Scientists also know these cells are quite effective in containing most reactivations of HSV-2, he stated.

“If we can boost the effectiveness of these immune cells, we are likely to be able to contain this infection at the point of attack and stop the virus from spreading,” he said.

Scientists think the presence of CD8aa+ T-cells where initial infection occurs might be a factor in why there are asymptomatic recurrences of genital herpes. The cells constantly recognize and eliminate the virus.

### What’s in pipeline?

Vical, a San Diego company, is planning to start an early-stage study of a vaccine against HSV-2 before the end of 2013, enlisting approximately 150 HSV-2 positive adults with a history of symptomatic genital herpes lesions.

The road to an effective vaccine has been a rocky one. GlaxoSmithKline Biological of London ceased investigation of its HSV-2 vaccine candidate after Phase III study, data indicates an investigational vaccine, Simplirix, protected some women against infection from one of the two types of herpes simplex viruses that cause genital herpes. While the vaccine was partially effective at preventing HSV-1, data indicate it did not protect women from HSV-2.<sup>3</sup> (*To read more about the trial, see “New approaches eyed to herpes simplex virus,” STI Quarterly supplement, March 2012, p. 3.*)

Until a vaccine is developed, patients can reduce the risk of genital herpes through correct and consistent use of latex condoms. However, outbreaks can

occur in areas not covered by a condom. According to the Centers for Disease Control and Prevention, the surest way to avoid transmission of sexually transmitted diseases, including genital herpes, is to abstain from sexual contact, or to be in a long-term mutually monogamous relationship with a partner who has been tested and is known to be uninfected.

For patients with herpes, talk with them about abstaining from sexual activity with partners when sores or other symptoms of herpes are present. Emphasize the fact that even if a person does not have any symptoms, he or she can still infect sex partners. (See resource listing below for a patient handout on genital herpes from the Centers for Disease Control and Prevention.)

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## RESOURCE

The Centers for Disease Control and Prevention offers a freely reproducible **fact sheet on genital herpes**. Go to <http://1.usa.gov/17GISlr> to download the printable version. ■

# HPV linked to rise in oropharyngeal cancer

A new analysis of national data shows human papillomavirus (HPV) might be to blame for the rise of young adults with oropharyngeal cancer. Data indicate an overall 60% increase from 1973 and 2009 in cancers of the base of tongue, tonsils, soft palate, and pharynx in people younger than 45.<sup>1</sup>

To perform the analysis, a research team used the Surveillance Epidemiology and End Results (SEER) database maintained by the National Cancer Institute to gather information about U.S. adults younger than 45 who had been diagnosed with invasive squamous cell oropharyngeal cancer between 1973 and 2009. The team was led by Farzan Siddiqui, MD, PhD, director of the Head & Neck Radiation Therapy Program in the Department of Radiation Oncology at Henry Ford Hospital in Detroit. Because the SEER database does not record HPV information, the researchers used tumor grade as a surrogate indicator of HPV infection.

Among the study group of more than 1,600 patients, 90% were ages 36-44; 73% were identified as Caucasian. During the 36-year period, most patients (50-65%) underwent surgical resection for their tumors. Patients who had surgery and radiation therapy had the highest five-year survival rate.

Among Caucasians, there was a 113% increase in cancers of the base of tongue, tonsils, soft palate, and pharynx. Among African-Americans, the rate of these cancers declined by 52% during the same period of time.<sup>1</sup>

What factors might have led to the increase and decline? One factor might lie in sexual practices. Oropharyngeal cancer has been linked to an increase in the number of people who perform oral-genital sex.<sup>2</sup> An analysis of the National Survey of Adolescent Males indicates that white males were 2.7 times more likely to engage in oral sexual activity with a female and were 1.4 times more likely to receive oral sex from a female, compared to black males. Compared with white males, black males were 1.35 times more likely to engage in genital-to-genital sex with a female.<sup>3</sup>

For the current analysis, the five-year survival rate for the study group was 54. African Americans, however, had significantly poor survival rates compared to other races, researchers note.<sup>1</sup> Previous research indicates that compared with Caucasians, African Americans are more likely to have an advanced stage of disease at diagnosis and to have inferior outcomes (shorter survival) within the same stage.<sup>4</sup>

## Look for signs

What are the signs and symptoms of oropharyngeal cancer? According to the Centers for Disease Control and Prevention, they might include persistent sore throat, earaches, hoarseness, enlarged lymph nodes, pain when swallowing, and unexplained weight loss. Some persons have no signs or symptoms.

How common is oral HPV? Data indicate about

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## EXECUTIVE SUMMARY

Human papillomavirus (HPV) might be to blame for the rise of young adults with oropharyngeal cancer. Data indicate an overall 60% increase from 1973 and 2009 in cancers of the base of tongue, tonsils, soft palate, and pharynx in people younger than 45.

- Signs and symptoms include persistent sore throat, earaches, hoarseness, enlarged lymph nodes, pain when swallowing, and unexplained weight loss. Some persons have no symptoms.
- Data indicate about 7% of people in the United States have oral HPV, but only 1% of people have the type that is found in oropharyngeal cancers (HPV type 16). Oral HPV is about three times more common in men than in women.

7% of people in the United States have oral HPV, but only 1% of people have the type of oral HPV that is found in oropharyngeal cancers (HPV type 16). Oral HPV is about three times more common in men than in women.<sup>5</sup> There is no Food and Drug Administration-approved test to detect oropharyngeal cancer.

## Cancer on the rise

Oropharyngeal squamous cell cancer has attained “epidemic” proportions in the past few years, says Siddiqui. The incidence has increased significantly in the 50- to 60-year-old age group, and this increase has been attributed to the rising rates of HPV infection, which has a sexual mode of transmission, he notes.

“It has been postulated that the sexual revolution of the 1960s and 70s led to increased transmission and infection of high-risk HPV, and people who were probably exposed as teenagers at that time are now presenting with HPV-positive oropharyngeal cancers,” says Siddiqui.

Researchers at Henry Ford Hospital were interested in examining what is happening in the people who were born during that time or later, says Siddiqui. The database analysis was carried out to see if the incidence of oropharyngeal cancers is rising in these younger individuals also, he states. Scientists also wanted to see if there is a difference between race and gender in the incidence of these cancers over the past few decades from 1973 to 2009, states Siddiqui.

“These young individuals are in the prime of their lives and in their most productive phases,” says Siddiqui. “The diagnosis of cancer is very devastating for them, and they have to undergo cancer therapy and live with the side effects of the cancer therapy — radiation, chemotherapy, surgery — for the rest of their lives.”

It remains a mystery why vaccination of men against HPV is not more widely encouraged, says Robert Hatcher, MD, MPH, professor emeritus of gynecology and obstetrics at Emory University School of Medicine in Atlanta.

“Equally disappointing is our failure to achieve close to 100% vaccination of women by age 26,” says Hatcher.

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## CDC launches STD treatment mobile app

The Centers for Disease Control and Prevention (CDC) recently launched a free STD Treatment Guidelines mobile app for healthcare providers called STD Tx Guide.

By using this app, providers will have quick access to current information about the diagnosis and treatment of 21 sexually transmitted diseases (STDs) and the useful booklet, “A Guide to Taking a Sexual History.”

The app is available for Apple and Android devices, and may be downloaded from the iTunes and Google Playstores. Learn more about the app by visiting the STD Tx Guide webpage, <http://1.usa.gov/1eQgpzx>. ■

## New report issued on antibiotic resistance

A new report, “Antibiotic Resistance Threats in the United States, 2013,” gives a first-ever snapshot of the burden and threats posed by the antibiotic-resistant germs having the most impact on human health. The report is available at the Centers for Disease Control and Prevention (CDC) web site. Go to <http://1.usa.gov/1aHZij4> to access it.

Each year in the U.S., the CDC estimates at least 2 million people become infected with bacteria that are resistant to antibiotics and at least 23,000 people die each year as a direct result of these infections. Many more people die from other conditions that were complicated by an antibiotic-resistant infection, the CDC states.

Antibiotic-resistant infections can happen anywhere, according to the CDC. Data show that while most happen in the general community, the majority of deaths related to antibiotic resistance occur in healthcare settings such as hospitals and nursing homes. ■

# CONTRACEPTIVE TECHNOLOGY

U P D A T E<sup>®</sup>

A Monthly Update on Contraception and Sexually Transmitted Diseases

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When looking for information on a specific topic, back issues of *Contraceptive Technology Update* might be useful. If you haven't already activated your online subscription so that you can access the newsletter archives through the company web site, go to [www.ahcmedia.com](http://www.ahcmedia.com) and click on "Access Your Newsletters" on the right side of the page. Or contact our customer service department at P.O. Box 550669, Atlanta, GA 30355. Phone: (800) 688-2421 or (404) 262-5476. Fax: (800) 284-3291 or (404) 262-5560. E-mail: [customerservice@ahcmedia.com](mailto:customerservice@ahcmedia.com).

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