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Dear ***Contraceptive Technology Update*** Subscriber:

This issue of your newsletter marks the start of a new Continuing Medical Education (CME) semester and provides us with an opportunity to review the procedures.

Contraceptive Technology Update provides you with evidence-based information and best practices that help you make informed decisions concerning treatment options and physician office practices. Our intent is the same as yours: the best possible patient care.

The objectives of ***Contraceptive Technology Update*** are to:
1. **identify** clinical, legal, or scientific issues related to development and provisions of contraceptive technology or other reproductive services;
2. **describe** how those issues affect service delivery and the benefits or problems created in patient care in the participant's practice area;
3. **integrate** practical solutions to problems and information into daily practices, according to advice from nationally recognized family planning experts.

Each issue of your newsletter contains questions relating to the information provided in that issue. After reading the issue, answer the questions at the end of the issue to the best of your ability. You can then compare your answers against the correct answers provided in an answer key in the newsletter. If any of your answers were incorrect, please refer back to the source material to clarify any misunderstanding.

At the end of each semester you will receive an evaluation form to complete and return in an envelope we will provide. Please make sure you sign the attestation verifying that you have completed the activity as designed. Once we have received your completed evaluation form, we will mail you a CME certificate.

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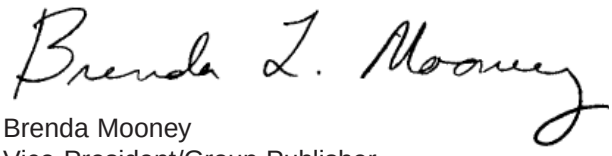

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25th Anniversary

CONTRACEPTIVE TECHNOLOGY UPDATE®

A Monthly Newsletter for Health Professionals

THOMSON AMERICAN HEALTH CONSULTANTS

IN THIS ISSUE

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JULY 2005
VOL. 26, NO. 7 • (pages 77-88)

What will it take for microbicides to go from research to reality?

Science/policy research, public education, advocacy will speed process

The need for female-controlled protection against HIV and sexually transmitted diseases (STDs) has never been greater. While early in the epidemic, HIV infection and AIDS were diagnosed for relatively few women, the HIV/AIDS epidemic now represents a growing and persistent health threat to women in the United States as well as throughout the world.

Check out the most recent statistics from the Centers for Disease Control and Prevention (CDC): In 2001, HIV infection was the leading cause of death for African American women ages 25-34.[1] It was among the four leading causes of death for African American women ages 20-24 and 35-44, as well as Hispanic women ages 35-44.[1] In the same year, HIV infection was the sixth-leading cause of death among all women ages 25-34 and the fourth-leading cause of death among all women ages 35-44.[1] On a global level, of the 14,000 people newly infected with HIV each day, nearly half are women.[2]

Getting a microbicide candidate from test tube to market shelf takes

EXECUTIVE SUMMARY

The HIV/AIDS epidemic now represents a growing and persistent health threat to women in the United States as well as throughout the world. Microbicide advocates are pushing on all fronts to speed the development of microbicides, which provide female-controlled forms of protection.

- Of the 14,000 people around the globe who are newly infected with HIV each day, nearly half are women.
- Microbicides under development generally fall into four categories: vaginal defense enhancers, surfactants, entry and fusion inhibitors, and replication inhibitors.
- Five products have advanced to Phase III clinical trials.

Contraceptive Technology Update® (ISSN 0274-726X), including **STD Quarterly**™, is published monthly by Thomson American Health Consultants, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Periodicals postage paid at Atlanta, GA 30304. POSTMASTER: Send address changes to **Contraceptive Technology Update**®, P.O. Box 740059, Atlanta, GA 30374.

Subscriber Information

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

Subscription rates: U.S.A., one year (12 issues), $449. Outside U.S., add $30 per year, total prepaid in U.S. funds. Discounts are available for multiple subscriptions. For pricing information, call Steve Vance at (404) 262-5511. **Back issues**, when available, are $75 each.(GST registration number R128870672.) **Photocopying:** No part of this newsletter may be reproduced in any form or incorporated into any information retrieval system without the written permission of the copyright owner. For reprint permission, please contact Thomson American Health Consultants. Address: P.O. Box 740056, Atlanta, GA 30374. Telephone: (800) 688-2421. World Wide Web: http://www.ahcpub.com.

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This publication does not receive commercial support.

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Editorial Questions

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time — and money. A 2002 estimate pegged the cost of developing a single microbicide from preclinical research to market registration at about $57 million.[3] No major pharmaceutical company has yet stepped forth to develop a product. Current clinical trials under way are supported almost exclusively by small biotechnology companies, academic centers, nonprofit and government organizations, and private foundations.[3]

Microbicide advocates are pushing on all fronts to speed progress of microbicide development. The Silver Spring, MD-based Alliance for Microbicide Development and the Washington, DC-based Global Campaign for Microbicides have just received grants totaling $5.7 million from the Seattle-based Bill & Melinda Gates Foundation to further their efforts in aiding science and policy research, public education, and advocacy for microbicides.

Progress is being made on the legislative level, as U.S. Senators Jon Corzine (D-NJ), Barack Obama (D-IL), and Olympia Snowe (R-ME) have introduced the Microbicide Development Act of 2005 in the Senate. The bill seeks to establish a microbicide research and development unit at the Bethesda, MD-based National Institutes of Health (NIH) and strengthen microbicide activity at the Washington, DC-based United States Agency for International Development and the CDC. It should be introduced in the second half of 2005 in the House of Representatives, says **Heather Boonstra**, senior public policy associate in the Washington, DC, office of the New York City-based Alan Guttmacher Institute.

Here's how they work

How do microbicides work in warding off infection? Microbicides under development generally fall into four categories:

- **vaginal** defense enhancers, products which boost the body's natural defenses;
- **surfactants**, which rupture the surface membranes of disease pathogens, thereby disabling them and preventing infection;
- **entry and fusion inhibitors**, which bind to disease pathogens or to healthy cells before pathogens have a chance to attack them;
- **replication inhibitors**, formulations that prevent viruses from replicating in invaded cells.[3]

While there are several microbicide candidates in the research pipeline, five are in Phase III clinical status. Of those five, BufferGel (ReProtect,

Baltimore) is a vaginal defense enhancer; Savvy (C31G, Cellegy Pharmaceuticals, Brisbane, CA) is a surfactant; and Carraguard (Population Council, New York City), PRO 2000 (Indevus Pharmaceuticals, Lexington, MA), and Ushercell (cellulose sulfate, Polydex Pharmaceuticals Limited, Toronto) are all entry and fusion inhibitors. No replication inhibitor candidates have reached Phase III testing.[3] Some of the microbicides under development will be able to provide HIV/STD protection and contraception.[3]

Five in advanced trials

Take a closer look at the five microbicides in advanced trials:

• **BufferGel (carbomer 974P).**

BufferGel (carbomer 974P), developed at Baltimore-based Johns Hopkins University and ReProtect, is a gel that reinforces the protective vaginal acidity to kill sperm and inactivate several STD organisms, including HIV.[4,5] It is involved in two advanced trials, one which is looking at its effectiveness as a contraceptive in conjunction with a diaphragm, and the other which is examining its potential in HIV protection. The contraceptive efficacy trial is completed, but it is not yet unblinded, says **Richard Cone**, PhD, ReProtect president. The HIV trial began enrollment in February at sites in Malawi, South Africa, Tanzania, Zambia, Zimbabwe, and the United States, he reports.

• **Carraguard (PC-515).**

Carraguard, formerly known as PC-515, is a gel made from carrageenan, a substance derived from seaweed. In March 2004, the Population Council began a Phase III randomized, double-blind, placebo-controlled, efficacy study of the microbicidal product at three sites in South Africa, reports **Diane Rubino**, Population Council spokeswoman. The council is working with the Gugulethu-based University of Cape Town, the Soshanguve-based Medical University of Southern Africa, and the Isipingo-based Medical Research Council in these studies, says Rubino. Findings from safety and acceptability studies in South Africa and Thailand confirmed the topical safety of the compound.[6]

• **PRO 2000 (polynaphthalene sulphonate).**

PRO 2000 (polynaphthalene sulphonate) is a compound that binds to HIV and other STD pathogens and prevents them from infecting human cells. Phase I testing indicated the product's safety and acceptability,[7] and it now is involved in a Phase II/IIb trial with BufferGel to test its effectiveness in protection against HIV infection in women. The microbicide also is scheduled to undergo Phase III testing in Uganda, South Africa, Tanzania, and Zambia in a study funded by the British government.[8]

• **Savvy (C31G).**

C31G is an antimicrobial and spermicidal agent that contains two surface-active compounds: cetyl betaine and myristamine oxide. Used in a gel formulation, Savvy is being evaluated for its prevention of HIV transmission in two Phase III clinical trials in progress in Africa; it also is being evaluated in Phase III testing for use as a contraceptive.[9]

• **Ushercell (cellulose sulfate).**

Ushercell, a gel formulation of 6% cellulose sulfate, is being tested on a number of fronts, reports **Henry Gabelnick**, PhD, director of the CONRAD program of the Eastern Virginia Medical School in Arlington. CONRAD is working in collaboration with Polydex Pharmaceuticals in developing the compound. CONRAD has just received a $12 million grant from the Bill & Melinda Gates Foundation and matching USAID funds to allow two multicountry Phase III clinical trials to test the product's effectiveness in preventing HIV/AIDS transmission.

One trial is a randomized, placebo-controlled Phase III study to determine the effectiveness of Ushercell to prevent HIV transmission when used vaginally in the same manner as a spermicide, says Gabelnick. Studies sites are located in Benin, Burkina Faso, Uganda, and South Africa.

A similar trial is being conducted in Nigeria by the Research Triangle Park, NC-based research organization Family Health International (FHI), with the drug supplies provided by CONRAD, says Gabelnick. FHI is providing statistical, monitoring, and social and behavioral science support for the multicountry trial, he states.

Moving forward on the microbicide front poses unique difficulties, observes **Michael Rosenberg**, MD, MPH, clinical professor of obstetrics and gynecology and adjunct professor of epidemiology at the University of North Carolina at Chapel Hill and president of Health Decisions, a private research firm specializing in reproductive health.

"The intensive search for a microbicide has been under way for more than a decade, with little to show for the modestly funded efforts to date," states Rosenberg, whose firm has been involved in microbicide testing. "This type of research is difficult because of the difficulty of enrolling and retaining large numbers of women using vaginal preparations for an extended time."

While one study of vaginal preparations recently was terminated because of inadequate enrollment, another study being conducted by Health Decisions under NIH contract has enrolled at a record rate, says Rosenberg. Lessons from this effort are being distilled in order to facilitate similar studies elsewhere, he adds.

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Does contraception affect HIV treatment?

EXECUTIVE SUMMARY

Just-published research indicates that the hormones in birth control do not influence the effectiveness of highly active antiretroviral therapy (HAART), now used to treat HIV infection.

- The drug interactions between oral contraceptives and many drugs used in HIV disease make an additional means of contraception advisable in many cases. Adding condoms also aids in protecting against disease transmission.
- Clinicians should cover all possible side effects associated with the various hormonal methods and their HAART regimen.

Is your family planning facility seeing more women who are HIV-positive? Statistics point to a "yes." In 2003, women accounted for 27% of the estimated 32,048 diagnoses of HIV infection in the United States, according to statistics from the Atlanta-based Divisions of HIV/AIDS Prevention of the Centers for Disease Control and Prevention (CDC).[1]

Antiretroviral (ARV) drugs are an important first-line defense in treating HIV infection. Clinicians now use combinations of ARV drugs, known as highly active antiretroviral therapy or HAART, to suppress HIV replication. When it comes to birth control, women are concerned about potential interactions between hormonal therapies and HAART, particularly if the interactions may affect the efficacy of the birth control method or how well they may respond to their HAART therapy, says **Rebecca Clark**, MD, PhD, associate professor of medicine at Louisiana State University Health Sciences Center and maternal/child director of the HIV outpatient program of the Medical Center of Louisiana, all based in New Orleans.

Just-published research indicates that the hormones in birth control do not influence the effectiveness of HAART.[2] Until recently, there has been no information regarding the hormonal contraceptive influence on HAART effectiveness, she notes. Findings from the new study are reassuring that such drugs do not affect response to HAART, Clark adds.

Focus on the findings

Findings from the latest paper come from the Women's Interagency HIV Study, a long-term, ongoing comprehensive cohort study of HIV-infected and at-risk women, explains co-author **Stephen Gange**, PhD, associate professor in the Department of Epidemiology at Bloomberg School of Public Health, Johns Hopkins University in Baltimore. The study was begun in 1993, prior to the advent of HAARTs introduced in the mid 1990s. Since anti-HIV therapy now is so widespread, study investigators have many initiatives evaluating factors that may affect the response to HAART, he explains.

To conduct the current analysis, the study authors matched hormonal contraceptive users with nonusers, according to age, race/ethnicity, pre-HAART CD4+ T-lymphocyte counts, and viral load. They focused on effects on the two

RESOURCE

- **To get the latest guidelines on use of antiretroviral agents in HIV treatment**, visit the National Institutes of Health web site, aidsinfo.nih.gov. Click on "Guidelines," "Adult and Adolescent Guidelines," then *"Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents* — April 07, 2005." The guidelines are available in Adobe PDF and Personal Digital Assistant (PDA) versions.

main markers of HIV disease progression: CD4 cell count and viral load.

No association was found between hormonal contraceptive use and changes in CD4+ cell count or time to viral load suppression after initiation of HAART. There was also no relationship between those outcomes and the duration of hormonal contraception use before HAART initiation.[2]

Counsel on methods

While women undergoing HAART are concerned about the effectiveness of their HIV treatment, they also look to the efficacy of their chosen birth control method to protect against unplanned pregnancy. Clinicians should cover all possible side effects associated with the various hormonal methods and their HAART regimen, says Clark, coauthor of *A Woman's Guide to Living with HIV Infection*, a book aimed at helping women deal with the medical, emotional, and social issues surrounding HIV infection (Johns Hopkins Press; 2004).

HAART regimens may include combinations of nucleoside reverse transcriptase inhibitors such as zidovudine (AZT), lamivudine (3TC), and abacavir, all of which may slow the spread of HIV in the body and delay the start of opportunistic infections; non-nucleoside reverse transcriptase inhibitors such as nevirapine and efavirenz; and protease inhibitors such as indinavir, ritonavir, and lopinavir, which interrupt the virus from making copies of itself at a later step in its life cycle.[3,4] The drug interactions between oral contraceptives and many drugs used in HIV disease make an additional means of contraception advisable in many cases.[5]

"We do know that protease inhibitors and nonnucleoside reverse transcriptase inhibitors may have significant pharmacokinetic interactions with oral contraceptive pills, which will result in affecting hormonal levels and potentially efficacy," states Clark. "Therefore, a second form of birth control is recommended to be used concurrently for most HAART regimens, as outlined in Department of Health and Human Services guidelines.[6] **(See the resource guide, left, for information on accessing the guidelines.)**

According to information from the Department of Health and Human Services, oral contraceptives significantly interact with amprenavir/fosamprenavir, efavirenz, lopinavir, nelfinavir, nevirapine, and ritonavir (RTV).[5] An additional method of contraception, such as condoms, is recommended.[5]

"I think it is important to continue counseling HIV-infected women in the use of contraception [e.g., barrier methods] that reduce the chance of transmitting the virus," observes Gange. "Needless to say, further research in microbicides and other compounds to reduce the chance of HIV transmission is critical."

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Research moves HPV vaccines within view

When discussing sexually transmitted diseases (STDs) with your patients, what do you tell them about human papillomavirus (HPV)? Exposure to HPV can have significant health implications, particularly for women. Some strains of the virus, including HPV-16 and HPV-18, can trigger cancers of the cervix.

About 10,370 cases of invasive cervical cancer will be diagnosed in the United States in 2005, according to the American Cancer Society (ACS).[1] About 3,710 women will die from the disease in

EXECUTIVE SUMMARY

Two potential vaccine candidates against human papillomavirus (HPV) are in advanced trials. Some strains of the virus, including HPV-16 and HPV-18, can trigger cancers of the cervix.

- Findings from a recent study indicate that a trial quadrivalent vaccine, Gardasil, reduced the combined incidence of persistent HPV 6, 11, 16, or 18 infection and related diseases, including new cervical pre-cancers and genital warts.
- Initial findings indicate an experimental bivalent vaccine, Cervarix, also may provide cross-protection against strains 31, 45, and 52.

2005, the ACS estimates.[1]

You soon may be able to tell women about a vaccine against HPV if scientists are able to deliver a product that is safe and effective. Merck & Co. in Whitehouse Station, NJ, and GSK Biologicals in Rixensart, Belgium, have vaccines in advanced clinical trials.

In just-published research, scientists report Merck's trial HPV vaccine reduced the combined incidence of persistent HPV 6, 11, 16, and 18 infection and related diseases, including new cervical pre-cancers and genital warts.[2] The quadrivalent vaccine, under development as Gardasil, is in Phase III clinical trials in the United States, Canada, Europe, and Latin America, says **Kelley Dougherty**, spokeswoman for Merck & Co. The company plans to file for Food and Drug Administration approval in the second half of 2005, with subsequent filings in Canada and Europe, she states.

Information presented at the recent International Papillomavirus Conference and Clinical Workshop in Vancouver, British Columbia, indicates that GSK's Cervarix bivalent vaccine, targeting strains 16 and 18, also may provide cross-protection against strains 31, 45, and 52.[3,4] GSK began a Phase III trial of the vaccine in 2004. It is scheduled to run for four years.[5]

Findings from the Gardasil study, a Phase II randomized, double-blind, placebo-controlled trial, indicate the quadrivalent HPV vaccine reduced the incidence of HPV infection and any HPV-related diseases by 90% compared with placebo.[2]

The trial evaluated 552 women ages 16-23 from the United States, Europe, and Brazil, who were randomized to receive the vaccine or a placebo three times over six months. The women were followed for 2.5 years, with a primary endpoint of reduction in the combined incidence of persistent HPV types 6, 11, 16, and 18 infections and related diseases, including precancerous conditions such as cervical intraepithelial neoplasia.

Thirty-six cases of disease, persistent infection, or detection of HPV on the last visit on record were seen in the placebo group compared to four in the group who received the vaccine. Of the four cases in the vaccine group, one was confirmed as persistent infection. In the other three cases, HPV was detected on the last study visit but was not later confirmed as a persistent infection.

How will vaccine be used?

If a vaccine is approved, successful implementation will require definition of the vaccine's public health impact, cost effectiveness, the optimal age for vaccination, and the duration of protection, says **Luisa Villa**, PhD, head of the virology group at the Ludwig Institute for Cancer Research, São Paulo, Brazil. Villa served as lead author of the Gardasil research paper.

Lack of effective means to prevent HPV infection in sexually active adolescents and adults supports the value of vaccinating preadolescents; however, this may prove difficult because there are no systematic vaccination programs now in place for adolescents and young adults, she says.

"Ideally, this could be envisaged as a good opportunity to establish programs that would deliver contraception and STD information as well as vaccination against HPV and other diseases," Villa observes. "Besides infrastructure aspects, the physicians that will see adolescents and potentially deliver the HPV vaccine — most probably pediatricians — do not seem to be fully aware of the situation and soon-availability of the vaccine."

Another important aspect of setting up an immunization program will relate to the durability of vaccine's induced immune responses, she says.

Thus far, the longest follow-up for the quadrivalent vaccine was 30 months after vaccination. Extension of this and other trials are under way to better assess the efficacy of the vaccine along time, Villa states. "Certainly this is one of the most important aspects that will define policies for vaccine implementation," she notes. "There is no a priori reason to think that the observed waning of antibody titers will pose a problem, but one has to show that a vaccine administered four to 10 years prior to onset of sexual activity will still be protective."

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Sole U.S. distributor of cap closes business

EXECUTIVE SUMMARY

The sole U.S. distributor of the Prentif Cavity-Rim Cervical Cap has announced it has dissolved its business, with the barrier contraceptive no longer available to women in the United States.

- The Prentif cervical cap was approved for U.S. use in 1988. Other available barrier options include the diaphragm, female condom, FemCap, Lea's Shield, and the Today contraceptive sponge.
- Vaginal barrier methods are simple to use and noninvasive and may be used intermittently with little advanced planning; however, consistent and correct use is essential for their effectiveness.

The options in barrier contraceptives for American women have been reduced as the sole U.S. company distributing the Prentif Cavity-Rim Cervical Cap has announced its dissolution and the device is no longer available in the United States.

The move to dissolve the distribution company, Cervical Cap (CxC) Ltd. of Los Gatos, CA, was made after it was advised that the manufacturer of the device, Lamberts (Dalston) Ltd. of Luton, England, would no longer carry product liability insurance, says **Liz Summerhayes**, RN, NP, CxC's chief executive officer. In addition, the manufacturer announced a considerable increase in the cost of the cap and closure of its United Kingdom manufacturing plant, she adds.

Summerhayes, who has been involved with use of the barrier device since its initial U.S. testing in 1981 and approval in 1988 by the Food and Drug Administration, says that while there has been a decline in the interest in the Prentif cap over the years, those who have supported its use have been passionate in advocating the barrier method.

"For women who have really wanted a barrier method, there have been very few options," she notes. The company's web site, www.cervcap.com, will remain active as a source of product support, she states.

Katy Backes, MPA, executive director of the Cambridge, MA-based Cervical Barrier Advancement Society (CBAS), a nonprofit advocacy group, echoes similar disappointment in the announcement.

"The Prentif Cervical Cap is a safe, effective, female-controlled contraceptive with a long history of use in the U.S., and this product, as well as other cervical barrier methods, offer important contraceptive options to women who prefer a method they can control and those who cannot or choose not to use hormonal methods," she says. "There is an urgent need for more contraceptive and HIV/STI [sexually transmitted infection] prevention options that meet women's needs, and we regret that American women will no longer have access to this safe, effective contraceptive option."

Look for options

What other female-controlled barrier options are available for American women? Choices include:

- the diaphragm, Ortho All-Flex Arcing Spring Diaphragm and the Ortho Coil Spring Diaphragm, both manufactured by Ortho-McNeil Pharmaceutical, Raritan, NJ, and the Milex Wide Seal Diaphragm, Milex Products, Chicago;
- the FemCap cervical cap, FemCap, Del Mar, CA;
- Lea's Shield, Yama, Union, NJ;
- the female condom, FC Female Condom, Female Health Co., Chicago;
- the Today contraceptive sponge, Allendale (NJ) Pharmaceuticals.

The diaphragm, FemCap and Lea's Shield are prescription-only devices; the FC female condom

(formerly known in the United States as the Reality Female Condom) and the Today sponge are over-the-counter products. **(Get more information on these methods; see the resource box, below.)**

While diaphragms must be fitted by the clinician, the FemCap and Lea's Shield do not require custom fitting. The FemCap is available in three sizes: 22 mm, for women who have never been pregnant; 26 mm for women who have miscarried or had cesareans, and 30 mm for women who have vaginally delivered a full-term baby. Lea's Shield is a "one-size-fits-all" vaginal barrier contraceptive device.

Vaginal barrier methods are simple to use, non-invasive, and may be used intermittently with little advanced planning, according to the authors of *Contraceptive Technology*. However, consistent and correct use is essential for their effectiveness. Most pregnancies occur because the method is not used.[1]

As the search continues for female-controlled protection against pregnancy and STI/HIV, renewed focus is being aimed at barrier methods. CBAS, formed in June 2004, is a new initiative stimulated by an emerging global interest in cervical barriers, reports Backes.

"CBAS is an international, professional networking organization including clinical and social science researchers, academic institutions, policy and advocacy groups, program managers, pharmaceutical, biotech, and medical device companies, health care providers, and consumers," she says. "Membership is free and open to all who are interested in joining." **(See the resource box, left, for contact information.)**

Reference

1. Hatcher RA, Trussell J, Stewart F, et al. *Contraceptive Technology*. 18th revised edition. New York City: Ardent Media; 2004. ■

RESOURCES

For more information on the Cervical Barrier Advancement Society, contact:

- **Katy Backes**, Cervical Barrier Advancement Society, P.O. Box 382031, Cambridge, MA 02238-2031. Telephone: (617) 349-0025. Fax: (617) 349-0041. E-mail: info@cervicalbarriers.org. Web: www.cervicalbarriers.org. The CBAS web site contains information about cervical barriers, research updates, downloadable materials, and images of cervical barriers. The CBAS web site offers a cervical barrier methods poster, depicting available options. CBAS members and others who are interested can receive free full-size copies of the poster by emailing info@cervicalbarriers.org with a shipping address and the number of desired posters.

For more information on barrier options, contact:

- **Ortho-McNeil Pharmaceutical**. Telephone: (800) 682-6532. Web: www.orthowomenshealth.com.
- **Milex Products**, 4311 N. Normandy Ave., Chicago, IL 60634. Telephone: (800) 621-1278. Fax: (800) 972-0696. E-mail: customerservice@milexproducts.com. Web: www.milexproducts.com.
- **FemCap**, 14058 Mira Montana Drive, Del Mar, CA 92014. Fax: (858) 792-2624. E-mail: femcap@yahoo.com. Web: www.femcap.com.
- **Yama**, 650 Liberty Ave., Union, NJ 07083. Telephone: (800) 699-8130. Fax: (908) 206-8725. E-mail: info@leasshield.com. Web: www.leasshield.com.
- **Female Health Co.**, 515 N. State St., Suite 2225, Chicago, IL 60610. Telephone: (312) 595-9123. Fax: (312) 595-9122. E-mail: info@femalehealth.com. Web: www.femalehealth.com.
- **Allendale Pharmaceuticals**, 73 Franklin Turnpike, Allendale, NJ 07401. Telephone: (888) 343-4499. E-mail: questions@todaysponge.com. Web: www.todaysponge.com.

Research hones in on EC mechanism of action

The young woman in your examination room has questions about how emergency contraception pills (ECPs) works. How do you explain the method's mechanism of action?

Recent research from members of the New York City-based Population Council's International Committee for Contraception Research indicates that levonorgestrel-only ECPs (Plan B, Barr Pharmaceuticals, Pomona, NY) appear to

EXECUTIVE SUMMARY

Recent research indicates that levonorgestrel-only emergency contraceptive pills (ECPs) appear to work by interfering with ovulation, thus preventing fertilization of the egg. The pills do not appear to disrupt post-fertilization events, such as the implantation of a fertilized egg in the uterus, which has been a point of contention among ECP opponents.

- Canadian regulatory authorities have just approved over-the-counter (OTC) sales of the drug.
- A similar request for OTC access in the United States continues to be reviewed by the Food and Drug Administration.

work by interfering with ovulation, thus preventing fertilization of the egg.[1,2] The pills do not appear to disrupt post-fertilization events, such as the implantation of a fertilized egg in the uterus, which has been a point of contention among EC opponents.

Further research needs to be done to accrue more indirect evidence to help settle the issue, at least at the technical level, says **Horacio Croxatto**, MD, a reproductive physiologist at the Chilean Institute for Reproductive Medicine in Santiago, Chile, and co-author of the recent research. This evidence can be obtained when funding for this type of research becomes available, he notes.

Plan B now is available at Canadian pharmacies without a prescription following the April 2005 approval by Canadian regulatory authorities. The drug is distributed in Canada by Montreal-based Paladin Labs. EC proponents continue to await word from the Food and Drug Administration regarding the pending U.S. application for over-the-counter (OTC) status of the drug.

Croxatto and colleagues at the Chilean Institute have studied the effects of levonorgestrel (LNG) on the reproductive cycles of female rats, monkeys, and humans. In one study, performed in female rat subjects, the scientists exposed the rats to very high doses of LNG at various stages of their reproductive cycles.[1] LNG appeared to inhibit ovulation completely or partially, depending on the timing of treatment and the dose administered; however, it had no effect on fertilization or implantation.[1]

Next, the scientists looked at the effects of LNG given to monkeys before ovulation or after intercourse.[2] When given before ovulation, LNG was able to inhibit or postpone ovulation but when administered after mating, researchers found that pregnancy rates were identical in cycles treated with LNG or with a placebo. Such findings indicate that the drug did not interfere with any post-fertilization process required for embryo implantation, scientists conclude.[2]

Ten original research papers focusing on the mechanism of action of LNG have been published from 2001-2004, Croxatto points out.[1-10] He offers the following explanation of the published work:

- Five of the studies provide evidence that the drug interferes with ovulation.[3-5, 9-10]
- Two studies find no alteration in the endometrium that would support the hypothesis that LNG prevents implantation.[4,5]
- Two studies document, in two animal models, that the drug does not interfere with any of the processes that take place after fertilization, which are necessary for the establishment of pregnancy.[1,2]
- Two other studies report minimal if any direct effect of LNG upon human spermatozoa *in vitro*.[7,8]
- One paper reports effects of LNG on the endometrium in three women who took doses severalfold higher than used for EC[6]; therefore the findings reported do not apply to the current regimen.

Why then do misconceptions persist that emergency contraception is an abortifacient?

"Some people received the message that this was not a hypothesis, but a proven fact, and for different reasons they have not updated their knowledge on this issue," states Croxatto. "Others have the same concept, but emotionally rooted and are reluctant to accept the contrary, even when they are faced with the evidence."

The political question is not how often ECPs may work after fertilization, but whether they ever work in this way, states **James Trussell**, PhD, professor of economics and public affairs and director of the Office of Population Research at Princeton (NJ) University.

"Croxotto's excellent work has shown that Plan B does work in many cases by causing dysfunctional ovulation where the result is a short luteal phase; however, it is possible that even with dysfunctional ovulation that fertilization does occur and not possible to prove that fertilization never occurs," he states.

While the mechanism of action for emergency contraception is not known with certainty, it is believed EC combines delay of ovulation with a local effect on the endometrium and prevention of fertilization, according to a recent commentary by **Leon Speroff**, MD, professor of obstetrics and gynecology at Oregon Health Sciences University in Portland.[11] How much a post-fertilization effect contributes to efficacy is not known, but it is not believed to be the primary mechanism, he notes.

"I would just emphasize that all the evidence that exists has failed to indicate an abortifacient effect; indeed, when pregnancy is established, EC does not work," states Speroff. "We should emphasize, to patients, pharmacists, and colleagues that the evidence is consistent with prevention of implantation."

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Touchscreen technology — Coming to your clinic?

EXECUTIVE SUMMARY

Two programs are making it easier for women to get contraception information through touchscreen technology.
- Family Planning Health Services of Wausau, WI, has installed computer touchscreen kiosks at three college campuses in an effort to widen access to enrollment in the state's Medicaid family planning waiver.
- Planned Parenthood of North Texas in Dallas has installed interactive media screens at several of its clinics to better educate its patients and to obtain patient feedback.

How do you broaden access to family planning services? Some family planning agencies are looking to touchscreen technology to get information front and center to those who may need their services.

Family Planning Health Services (FPHS) of Wausau, WI, has developed and installed mobile touch-screen computer kiosks at three Wisconsin college campuses in an effort to help women enroll in the state's Medicaid family planning waiver program.

According to **Lon Newman**, FPHS executive director, several reasons led FPHS to locate the kiosks at the college sites. Their student populations are primarily made up of reproductive-age people at risk of unintended pregnancy and sexually transmitted diseases. None of the facilities, which are two-year campuses, offer student health services. Also, student status generally reduces earning potential and income, which in turn impacts ability to pay for care.

The state waiver program took effect in January 2003. The most recent estimates indicate that 320,422 Wisconsin women are eligible for services under the program, says Newman. The kiosks were developed to help women enroll in the program as quickly and conveniently as possible.

"Many of those 320,422 women don't know that the waiver is available," he explains. Because of the mobility of the kiosk, it can be placed it in easily accessible locations, such as businesses and college campuses, Newman adds. "It is a visible and interactive way of promoting waiver participation."

FPHS, which offers reproductive health care, contraceptive services, and education at seven clinics in a seven-county area of central Wisconsin, has fielded questions from other agencies about use of kiosks in their organizations, says Newman. "The kiosk is a work in progress and not quite ready for mass distribution, but we are ready to work with providers on a site-by-site basis so a kiosk could serve the women in their location."

FPHS has worked with the three colleges — University of Wisconsin Marathon County and Northcentral Technical College, both in Wausau, and Mid-State Technical College in Stevens Point

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- ■ Review midlife contraceptive options

— to determine the most appropriate kiosk location for students, says Newman. On one campus, the kiosk is located in a hall in the student union. On another campus, where the students were more concerned about privacy, it is located in a corner of the library. The third campus has a kiosk placed in a computer lab.

The touch screens are used to conduct presumptive eligibility enrollment for the family planning waiver program, as well as to submit orders for ongoing prescription and nonprescription contraceptive supplies for existing FPHS clients, says Newman.

If a woman wants to see if she is eligible for the waiver program, she uses the kiosk to answer a series of Medicaid eligibility questions and options. As the user enters information on the screen, the computer automatically prompts her through the questions.

"Initially, there were some concerns about personal information being read from the screen from a distance, which we overcame by encoding information, such as Social Security numbers, that appears on the screen," explains Newman. "This is comparable to the way a PIN [personal identification number] appears on an ATM machine."

The information from the kiosk is submitted via the Internet to the FPHS clinic, where a nurse can call to follow up on the request, whether it is to enroll in the waiver program or to reorder contraceptive supplies. Appointments for annual exams and sexually transmitted disease (STD) screenings also may be made at this time.

Many women feel comfortable using the kiosk to enroll in the waiver or to reorder supplies, says Newman. It is particularly convenient for women who do not have Internet access and would otherwise need to enroll in person during regular business hours, he states. The kiosk works well for the FPHS staff because it saves them the time and labor required to fill out the forms, and they receive complete information via the web before interacting with a client, says Newman.

"When a staff member contacts a client, she already knows whether or not the client is eligible for the waiver and what services the client can receive at no charge," he explains. "Because the client indicates contraceptive method preferences on the kiosk, the nurse is prepared to discuss the appropriateness of the method and alternatives when she is reviewing the client's medical information."

In-house developments costs have been approximately $40,000, says Newman. Hardware/software costs for one machine are less than $10,000, he estimates. Currently, the kiosks display and 'speak' information in English only.

Touchscreen technology is on the move in Texas, where Dallas-based Planned Parenthood of North Texas (PPNT) is installing interactive media terminals in 16 of its 28 clinics.

The kiosks are being installed to enhance

Corrections

The February 2005 article, "Hormonal-based male contraceptive moves ahead," p. 20, contained inaccurate information on an upcoming male contraception study.

According to **Diana Blithe**, PhD, program director of the Contraceptive Clinical Trials Network at the National Institute of Child Health and Human Development (NICHD) within the National Institutes of Health, the study is being conducted by the NICHD at two clinical sites: one headed by Christina Wang, MD, at Harbor-UCLA Medical Center in Torrance, CA, and the other headed by William Bremner, MD, PhD, at the University of Washington in Seattle. Scientists will be testing a combination of testosterone gel and Nestorone gel. The Nestorone gel will be prepared and supplied by the Population Council, a New York City-based research organization.

The May 2005 article, "Bacterial vaginosis is focus of new research," p. 58, contained an error in the dosing regimen for metronidazole gel. The correct regimen is once a day for five days. ■

CE/CME Instructions

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

patient education and obtain patient feedback, says **Emily Snooks**, PPNT director of media relations and communications. The kiosks eventually will add information in Spanish — about a fourth of PPNT's patient base is Hispanic, she reports.

Estimated cost for the project is $120,000, adds Snooks. ■

CE/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. (See **"What will it take for microbicides to go from research to reality?"** and **"Research moves HPV vaccines within view."**)
- **Describe** how those issues affect service delivery and the benefits or problems created in patient care in the participant's practice area.
- **Integrate** practical solutions to problems and information into daily practices, according to advice from nationally recognized family planning experts. (See **"Does contraception affect HIV treatment?"** and **"Sole U.S. distributor of cap closes business."**)

1. What is BufferGel?
A. A vaginal defense enhancer
B. A surfactant
C. An entry and fusion inhibitor
D. A replication inhibitor

2. What is zidovudine?
A. A non-nucleoside reverse transcriptase inhibitor
B. A nucleoside reverse transcriptase inhibitor
C. A protease inhibitor
D. An antidepressant

3. The Gardasil vaccine now under investigation is designed to target which types of HPV?
A. HPV 6, 11
B. HPV 6, 11, 16, 52
C. HPV 6, 11, 16, 18
D. HPV 6, 11, 16, 31

4. Which contraceptive barrier device is available in three sizes?
A. Lea's Shield
B. Today Contraceptive Sponge
C. Filshie Clip
D. FemCap

Answers: 1. A; 2. B; 3. C; 4. D.

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.*