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Use contraception management tips for women approaching menopause

Contraception plays key part in health planning during transition

Your next patient is a recently divorced 48-year-old mother of two. Her menstrual periods have become somewhat irregular, and she reports occasional hot flashes and night sweats. Her ex-husband had a vasectomy. She has used condoms with her current boyfriend. What options are available that will address her specific needs?

Perimenopause is the time of transition from normal ovulatory cycles to menopause, with menstrual irregularity as the key marker.[1] No one symptom or test is accurate enough by itself to make a definitive diagnosis. Clinicians should diagnose perimenopause based on menstrual history and age without relying on laboratory test results.[2] (*Editor's note: How is menopause determined? See the story on p. 112.*)

Mean cycle length in the last four years prior to menopause for healthy U.S. women has been reported as 30.48, 35.02, 45.15, and 80.22 days.[3] However, contrary to prevailing opinions, women in the late-menopausal transition group see significantly higher menstrual blood loss after an ovulatory cycle than an anovulatory cycle, recent research indicates.[4]

EXECUTIVE SUMMARY

Perimenopause is the time of transition from normal ovulatory cycles to menopause, with menstrual irregularity as the key marker.

• For perimenopausal women with heavy menstrual bleeding, the levonorgestrel intrauterine system provides effective contraception, as well as prevents erratic perimenopausal bleeding.

• Low-dose combined oral contraceptives can correct irregular bleeding, help with hot flashes and night sweats, and reduce the risk of ovarian and uterine cancer. Low-dose pills, as well as the contraceptive patch and vaginal ring, are appropriate options for healthy, nonsmoking, nonobese perimenopausal women.

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According to the Washington, DC-based Association of Reproductive Health Professionals, most women in their early to mid 40s still ovulate regularly and are at risk for pregnancy.[5] This is evidenced by the latest analysis of U.S. birth trends; the preliminary birth rate for women ages 40-44 in 2008 increased 4%, to 9.9 births per 1,000 women, the highest rate since 1967. The rates for women ages 45-49 years also increased in 2008 from 0.6 births per 1,000 in 2007 to 0.7.[6]

Older maternal age is associated with relatively higher risks of perinatal mortality/morbidity.[7] Medical risks associated with pregnancy in older women include gestational diabetes and pregnancy-induced hypertension.[7] To avoid unintended pregnancy and its complications, contraception is an important part of health planning.

Weigh benefits, risks

What are some of the benefits of using hormonal contraception in women during the "transition years" prior to menopause?

Hormonal contraception provides excellent protection from unintended pregnancy, notes **Nikki Zite**, MD, MPH, assistant professor in the Department of Obstetrics and Gynecology in the University of Tennessee Graduate School of Medicine in Knoxville. Zite will present on contraceptive management for women in the transition years during the October 2010 Contraceptive Technology Quest for Excellence conference in Atlanta.

This protection is extremely important to emphasize to women who might believe they are no longer fertile, says Zite. Fifty-one percent of pregnancies to women over age 40 are unintended, and 60% of pregnancies in women over 40 are terminated.[8]

Hormonal methods of contraception offer numerous non-contraceptive health benefits, such as a decrease in risk of ovarian and endometrial cancer, says Zite. A benefit unique to a "transition years" female is relief from some of the symptoms she is experiencing due to hormonal changes, observes Zite.

"Hormonal contraception can regulate the cycle irregularities that occur as the ovaries less consistently produce follicles and treat the perimenopausal mood issues that often bother women," says Zite.

What conditions may preclude the use of hormonal contraception in women in this age range? Most of the contraindications to the use of hormonal contraception exist regardless of age; however, some of the conditions that are contraindications, such as poorly controlled hypertension, are usually more common as women age, says Zite. Women over age 35 who are smokers, regardless of how much they report they smoke,

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should be advised against estrogen-containing contraceptive options, states Zite. Progestin-only hormonal methods remain safe and effective options for smokers over age 35, she notes.

What are the options?

The copper-bearing intrauterine device (ParaGard IUD, Teva Women's Health) provides convenient and excellent long-term pregnancy prevention without hormones. For perimenopausal women with heavy menstrual bleeding, the levonorgestrel intrauterine system (Mirena LNG IUS, Bayer HealthCare Pharmaceuticals, Wayne, NJ) provides effective contraception, as well as prevents erratic perimenopausal bleeding. The Food and Drug Administration gave approval in October 2009 for use of the Mirena for heavy menstrual bleeding in women who desire contraception.

The LNG IUS is the most effective medical treatment of heavy menstrual bleeding. In clinical trials, 85% of women with idiopathic heavy menstrual blood had normalization of menses. Women had a 71% reduction in median blood loss by six months. Longer use of the method is associated with increasing rates of amenorrhea.[9] By five years of use, 50% of users had no spotting or bleeding.

How about use of the contraceptive injection [depot medroxyprogesterone acetate (DMPA), Depo Provera, Pfizer, New York City; Medroxyprogesterone Acetate Injectable Suspension, USP, Teva Pharmaceuticals USA, North Wales, PA]? Use of DMPA in women ages 18-45 is classed by the US Medical Eligibility Criteria for Contraceptive Use as a "1," a condition for which there is no restriction for the use of the contraceptive method.[10] Use in women above age 45 is classed as a "2," a condition for which the advantages of using the method generally outweigh the theoretical or proven risks.[10]

Most studies have found that women lose bone mineral density (BMD) while using DMPA, but regain BMD after discontinuing the method, the criteria note. However, it is not known whether adult women with long duration of DMPA use can regain BMD to baseline levels before entering menopause, it states. The relation between DMPA-associated changes in BMD during the reproductive years and future fracture risk is unknown.[10]

For perimenopausal women who have contraindications to the pharmacologic doses of estrogen in combined hormonal methods, progestin-only pills may also be considered for contraception.[11]

Pill, patch, or ring?

Low-dose birth control pills represent another possible option for women during perimenopause. Low-dose combined oral contraceptives (OCs) can correct irregular bleeding, help with hot flashes and night sweats, and reduce the risk of ovarian and uterine cancer. Low-dose pills, as well as the contraceptive patch (Ortho Evra, Ortho Women's Health and Urology, Raritan, NJ) and the contraceptive vaginal ring (NuvaRing, Merck & Co., Whitehouse Station, NJ) are appropriate options for healthy, nonsmoking, nonobese perimenopausal women.[11]

How long can women take the Pill? According to information presented at the 2010 Contraceptive Technology conference, combined oral contraceptives may be used up until age 50.[12]

What about the risk for breast cancer? Many of your patients may overestimate their risk for breast cancer. In a 2009 national survey, 40% of women ages 35 to 75 estimated that a 40-year-old's chance of developing breast cancer over the next decade is 20% to 50%. The real risk is 1.4%, according to the National Cancer Institute.[13]

In the wake of the Women's Health Initiative (WHI) studies, women might be confused by information they hear about hormones. According to *Contraceptive Technology*, healthy reproductive-aged women are not affected by low-dose OCs because they already are exposed to endogenous hormones.[11]

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Exactly when is menopause?

According to *Contraceptive Technology*, menopause can be diagnosed in women in the following circumstances:[1]

- Women who have had surgical removal of their ovaries.
- Women with intact ovaries who have been amenorrheic for one year with no other cause.
- Women who had a hysterectomy with ovarian presentation when ovarian estradiol production has decreased to a menopausal level.

The median age of menopause is 51.3 years, according to *Contraceptive Technology*. Approximately 1% of women undergo menopause before age 40; 2% of women still are not menopausal at age 55, it says. Menopause before 30 can be associated with chromosomal abnormalities. A genetic evaluation is indicated, according to *Contraceptive Technology*. Premature menopause (less than 40 years old) and early menopause (less than 45 years old) are strongly influenced by family history; however, age of menopause does not follow a clear familial pattern and therefore is not predictable, it says.

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Add ella to options for emergency contraception

(*Editor's note: This story discusses off-label use of emergency contraception.*)

Get ready to add another option to the list of emergency contraception (EC) methods. The Food and Drug Administration has approved ella (ulipristal acetate, UPA) tablets. The drug, which will be available by prescription only, prevents pregnancy when taken orally within 120 hours (five days) after a contraceptive failure or unprotected intercourse.

Ella is a progesterone agonist/antagonist whose likely main effect is to inhibit or delay ovulation. Since May 2009, the prescription product has been available in Europe through Paris-based HRA Pharma under the brand name ellaOne. Ella will be launched and marketed in the United States later in 2010 by HRA Pharma's partner Watson Pharma of Morristown, NJ.

"Ella, or UPA, is safe and effective at preventing ovulation and therefore pregnancy in the five days after unprotected intercourse," said **Vanessa Cullins**, MD, MPH, vice president for medical affairs at the New York City-based Planned Parenthood Federation of America in a statement following the Aug. 13, 2010, regulatory approval.[1] "Given the fact that half of all pregnancies in the U.S. are unintended, it is vital that women have an array of choices available to prevent unplanned pregnancy," Cullins said. "Ella will become an important option for women."

Check the science

Two multicenter clinical studies were used to evaluate ella's efficacy and safety. An open-label study provided the primary data to support the

use of the drug when taken 48-120 hours after unprotected intercourse. A single-blind comparative study looked at use of the drug when taken 0-72 hours after unprotected intercourse, as well as provided supportive data for drug use when it is taken more than 72-120 hours after unprotected intercourse. Women in both studies were required to have a negative pregnancy test prior to receiving emergency contraception.

The open-label study was a multicenter open-label trial conducted at 40 U.S. family planning clinics. Participants in the trial included healthy women with a mean age of 24 who requested emergency contraception 48-120 hours after unprotected intercourse. The median body mass index (BMI) for the study participants was 25.3 and ranged from 16.1 to 61.3 kg/m.[2]

Twenty-seven pregnancies occurred in 1,242 women ages 18-35 who were evaluated for efficacy. The number of pregnancies expected without emergency contraception was calculated based on the timing of intercourse with regard to each woman's menstrual cycle. Ella reduced the pregnancy rate from an expected rate of 5.5% to an observed rate of 2.2%, when taken 48-120 hours after unprotected intercourse.

The second study was designed as a multicenter, single-blind, randomized comparison of the efficacy and safety of 30 mg ulipristal acetate to levonorgestrel. Study participants were enrolled at 35 sites in the United States, the United Kingdom, and Ireland, with most (66%) in the United States. Healthy women with a mean age of 25 who requested emergency contraception within 120 hours of unprotected intercourse were enrolled and randomly allocated to receive ella or 1.5 mg of levonorgestrel. Median BMI for the study subjects was 25.3 and ranged from 14.9 to 70.0 kg/m.[2]

A total of 16 pregnancies occurred in 844 women ages 16 to 35 years in the ella group when the drug was taken 0-72 hours after unprotected intercourse. The number of pregnancies expected without emergency contraception was calculated based on the timing of intercourse with regard to each woman's menstrual cycle. Ella reduced the pregnancy rate from an expected 5.6% to an observed 1.9%, when taken within 72 hours after unprotected intercourse. Researchers report no pregnancies were observed in the women who were administered ella more than 72 hours after unprotected intercourse (10% of women who received ella).[2]

Scientists pooled data from the two studies to calculate a total efficacy population of women treated with ulipristal acetate up to 120 hours after unprotected intercourse. Analysis for the five 24-hour intervals from 0-120 hours between unprotected intercourse and treatment was conducted. There were no significant differences in the observed pregnancy rates across the five time intervals, researchers report.[2]

Subgroup analysis of the pooled data by BMI showed that for women with BMI of more than 30 kg/m^2 (16% of all subjects), the observed pregnancy rate was 3.1% [95% confidence interval (CI): 1.7, 5.7], which was not significantly reduced compared to the expected pregnancy rate of 4.5% in the absence of emergency contraception taken within 120 hours after unprotected intercourse. In the comparative study, a similar effect was seen for the levonorgestrel comparator emergency contraception drug. For levonorgestrel, when used by women with BMI more than 30 kg/m^2, the observed pregnancy rate was 7.4% (95% CI: 3.9, 13.4), compared to the expected pregnancy rate of 4.4% in the absence of emergency contraception taken within 72 hours after unprotected intercourse.[2]

EXECUTIVE SUMMARY

The Food and Drug Administration has approved ella (ulipristal acetate, UPA) tablets. The drug, which will be available by prescription only, prevents pregnancy when taken orally within 120 hours (five days) after a contraceptive failure or unprotected intercourse.

- Ella is a progesterone agonist/antagonist whose likely main effect is to inhibit or delay ovulation.
- This prescription product has been available in Europe through HRA Pharma under the brand name ellaOne since May 2009. Ella will be launched and marketed in the United States later in 2010 by HRA Pharma's partner, Watson Pharma.

More time for action

There are many reasons that women do not make it into a pharmacy immediately for EC after unprotected sex, said **Aimee Gallagher**, MPH, director of communications and policy of the Washington, DC-based National Association of Nurse Practitioners in Women's Health, in a statement during the FDA's July 2010 reproductive health committee.[3] Adding ella increases women's options for dealing with the possibility that they might have been exposed to an unintended pregnancy, she noted.

Ulipristal acetate has been shown to be effective for up to five days, versus 72 hours with the current method of emergency contraception, said Gallagher. Both Plan B One-Step (Teva Women's Health, Woodcliff Lake, NJ) and Next Choice (Watson Pharmaceuticals) are indicated to be taken as soon as possible within 72 hours after unprotected intercourse.

"Perhaps this product will take some of the 'emergency' out of emergency contraception and allow more access to women in this situation," said Gallagher.

According to **Robert Hatcher**, MD, MPH, professor of gynecology and obstetrics at Emory University School of Medicine in Atlanta, the labeling of ella for use up to 120 hours is no advantage over the currently available EC pills, except it is directly stated in the labeling. As noted in the chapter on emergency contraception in the current edition of *Contraceptive Technology*, treatment effectiveness of EC pills has been documented through 120 hours.[4-8]

Emergency insertion of a copper T intrauterine device (ParaGard IUD, Teva Women's Health) is significantly more effective than use of EC pills, reducing the risk of pregnancy following unprotected intercourse by as much as 99%.[9-10]

According to *Contraceptive Technology*, the copper-bearing intrauterine device as emergency contraception can be inserted up to five days after ovulation. Most family planning providers, however, limit insertion to the first five days after intercourse because it is difficult to reliably estimate the day of ovulation. If emergency IUD insertion is planned, but cannot be carried out immediately, provide EC in pill form when the woman is initially evaluated.[4]

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HIV breakthrough: Trial results offer promise

The search for a female-controlled form of HIV prevention just took a giant step. Results of a Phase IIB trial of a tenofovir gel indicate that use of the gel before and after sex provided moderate protection against sexually transmitted HIV.[1]

The study, known as CAPRISA 004, was conducted to establish whether the vaginal use of a gel containing tenofovir, an antiretroviral drug, is safe and whether it can prevent male-to-female sexual transmission of HIV. Results of the study, announced at the July 2010 XVIII International AIDS Conference in Vienna, Austria, indicate that use of the vaginal gel reduced a woman's chance of becoming infected with HIV during sex by 39% compared with a control group that used a placebo gel.[1]

The study also showed that the gel was effective in preventing transmission of genital herpes simplex virus (HSV-2). The women using the tenofovir gel had 51% fewer cases of HSV-2 infection than the control group.[1]

The CAPRISA 004 trial was conducted by a team of South African and American researchers headquartered at the Centre for AIDS Programme of Research in South Africa (CAPRISA) at the

University of KwaZulu — Natal in Durban. Funds were provided by the United States Agency for International Development (USAID) and South Africa's Technology Innovation Agency, with product supplied by CONRAD in Arlington, VA, and collaborating support from Family Health International (FHI) in Research Triangle Park, NC. Principal investigators for the study were Salim Abdool Karim, MD, MPH, and Quarraisha Abdool Karim, PhD, director and associate director of CAPRISA and both professors of clinical epidemiology at the Mailman School of Public Health at Columbia University in New York City.

The results of the CAPRISA 004 trial were an HIV prevention "first" in many ways, says **Willard Cates Jr.**, MD, MPH, director of research at FHI. The trial represents the first microbicide proof-of-concept, the first antiretroviral-based pre-exposure regimen, and the first vaginal gel effective for women, says Cates. In addition, the research represents the first in-country investigator-led trial, supported by U.S. technical expertise; the first study jointly funded by the United States and South Africa; and the first to secure voluntary product license for Africa upfront, Cates notes.

Look at the science

The CAPRISA 004 study was designed as a two-group, double-blind, randomized, controlled trial to assess the safety and effectiveness of 1% tenofovir gel in 889 sexually active HIV-uninfected urban and rural women at risk for HIV infection in South Africa. After undergoing the informed-consent process, each participant was randomly assigned to one of the two study groups: tenofovir gel or placebo. All women were provided with a supply of single-use, pre-filled gel applicators and were counseled to apply a first dose of the assigned study product within 12 hours prior to sexual intercourse and to insert a second dose as soon as possible within 12 hours after sex. Women were counseled to use no more than two doses of gel in a 24-hour period. Participants in both gel groups also received condoms, extensive risk-reduction counseling, and treatment of symptomatic sexually transmitted infections.

After 12 months, researchers found 50% fewer instances of HIV infection among women who used the gel compared with the placebo group. After two and a half years, there were 39% fewer cases among those using the tenofovir gel. The degree of protection was proportional to the degree to which the women complied with the instructions. Women who reported using the gel more than 80% of the time they engaged in sexual relations had a 54% reduction in HIV infection, whereas those who used the gel less than half the time had a 28% reduction.[2]

EXECUTIVE SUMMARY

Results of a Phase IIB trial of a tenofovir gel indicate that use of the gel before and after sex provided moderate protection against sexually transmitted HIV.

- The CAPRISA 004 study was conducted to establish whether the vaginal use of a gel containing tenofovir, an antiretroviral drug, is safe and whether it can prevent male-to-female sexual transmission of HIV.
- Results of the study indicate that use of the vaginal gel reduced a woman's chance of becoming infected with HIV during sex by 39% compared with a control group that used a placebo gel. The study also showed that the gel was effective in preventing transmission of genital herpes simplex virus; the women using the tenofovir gel had 51% fewer cases of HSV-2 infection than the control group.

More research needed

While the results of the CAPRISA 004 trial are encouraging, more research is needed. The trial was designed as a proof-of-concept study; a larger Phase III trial would provide more conclusive data regarding the gel's potential effectiveness for preventing the sexual transmission of HIV.

"We need studies now to be done in other settings, in other countries in Africa, to see if they can also find this protective effect, so that we know that the effect is much more broadly present and not unique to just one setting," says **Salim Abdool Karim**, MD, MPH, one of the study's principal investigators.

If adequate confirmatory data becomes available through additional studies, the CAPRISA 004 consortium of investigators would then work with manufacturers and sponsors to gain regulatory approval of the product by relevant drug regulatory authorities.

The results of CAPRISA 004 can be considered a "game changer" in HIV prevention research, says Cates. Since the trial established proof-of-concept for a topical antiretroviral regimen, used intermittently, the finding might throw many

in the HIV-prevention field into a spin, Cates observes. Some scientists had questioned whether a topical microbicide would ever be effective in preventing HIV acquisition, notes Cates. Now their thinking may be changed.

The belief structure was that the oral regimen, used daily, would have the greatest likelihood of demonstrating proof-of-concept. As a result, most of the prevention trials of pre-exposure prophylaxis with antiretrovirals were oriented toward the oral daily regimen, explains Cates. The theory was that the daily oral approach would produce better adherence and higher concentrations of drug in tissues, thus it represented the best first step, says Cates. Only after success with the daily oral regimen, the other approaches, such as intermittent topical and oral dosing, could be evaluated for their relative effectiveness, he says.

"However, CAPRISA 004 has leapfrogged this projected development timeline," says Cates. "We need to go back to the drawing board."

More information on tenofovir will come from the VOICE (Vaginal and Oral Interventions to Control the Epidemic) trial, an ongoing study evaluating daily use of tenofovir gel, regardless of when participants have sex. The trial also is testing daily use of oral antiretroviral tablets (tenofovir alone or tenofovir plus emtricitabine). The trial should help determine how well each product works compared to its control (placebo gel or placebo tablet) and which approach — gel or tablet — women prefer to use. Investigators plan to enroll about 5,000 women at sites in four countries in southern Africa. About 1,000 women are enrolled in the study so far.

The VOICE trial will provide not only the essential evidence to support or challenge the CAPRISA 004 findings, but also will contribute to understanding the relative value of the oral versus topical regimens in preventing HIV acquisition in women, says Cates.

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Managing recurrent vaginitis: What works?

While vaginitis usually is considered a minor nuisance, many women experience chronic symptoms that persist or recur after treatment. What can clinicians do?

Recurrent vaginitis encompasses a broad array of problems, which include vaginal infections, vulvar skin disorders, and vulvovaginal atrophy, says **Paul Nyirjesy**, MD, professor of obstetrics and gynecology and director of the Drexel University Vaginitis Center in the Drexel University College of Medicine in Philadelphia.

What is vaginitis? The condition is defined as inflammation of the vagina marked by pain, itching, and/or a purulent discharge. The most common causes of infectious vaginitis are (depending on the population):

- bacterial vaginosis (BV) (22%–50% of symptomatic women);
- vulvovaginal candidiasis (VVC) (17%–39%);
- trichomoniasis (4%–35%).[1]

"In women with recurrent symptoms, obtaining an accurate diagnosis is crucial," says Nyirjesy. "For women where they have been told they have yeast infections, a yeast culture will confirm the diagnosis and allow proper selection of antifungal therapy."

Check self-treatment

The trend in the last 15 years has been for women to diagnose and treat themselves for VVC.[2] Patients with recurrent symptoms should

EXECUTIVE SUMMARY

Vaginitis is defined as inflammation of the vagina marked by pain, itching, and/or a purulent discharge. Recurrent vaginitis encompasses a broad array of problems, which include vaginal infections, vulvar skin disorders, and vulvovaginal atrophy.

- Resist the urge to use a telephone diagnosis. Research findings indicate that diagnosis of vaginal symptoms by telephone often result in misdiagnosis.
- At a minimum, women with vaginitis should undergo office testing, which consists of a vaginal ph, amine or whiff test, wet mount, and 10% potassium hydroxide test. The right test matters when it comes to successfully treating vaginitis. Look at new point-of-care tests.

avoid self-treatment, as treating themselves might interfere with obtaining the correct diagnosis and might exacerbate symptoms, says Nyirjesy.

Women who have had prior yeast infections or bacterial vaginosis might think the source of their current discharge is similar to a previous condition and will self-medicate with an over-the-counter yeast medication, says **Kimberly Workowski**, MD, professor of medicine in the Division of Infectious Disease at Emory University and team leader of the Guidelines Unit in the Centers for Disease Control and Prevention's (CDC) Division of STD Prevention, both in Atlanta. The problem with self-medication is that other types of infectious vaginitis are not affected by the over-the-counter antifungal drug, Workowski notes.

All vaginal discharge doesn't mean vaginitis. It could indicate that some of the discharge is coming from the cervix or higher up in the female genital tract, says Workowski. Patients need to be counseled not to assume that all vaginal infection is due to what has been experienced before, especially if the patient has been sexually active and has been using non-barrier methods of protection, she advises.

Test before treating

While patients with recurrent vaginitis might represent a large portion of the daily calls into your facility, resist the urge to use a telephone diagnosis.[2] Research findings indicate that diagnosis of vaginal symptoms by telephone often result in misdiagnosis.[3]

At a minimum, women with vaginitis should undergo office testing, which consists of a vaginal ph, amine or whiff test, wet mount, and 10% potassium hydroxide (KOH) test, says Nyirjesy.

For bacterial vaginosis, diagnosis can be obtained by using clinical criteria or Gram stain.[4] Diagnosis by clinical criteria require three of the following symptoms or signs:

- homogeneous, thin, white discharge that smoothly coats the vaginal walls;
- presence of clue cells on microscopic examination;
- pH of vaginal fluid more than 4.5;
- a fishy odor of vaginal discharge before or after addition of 10% KOH.[4]

When using a Gram stain, determining the relative concentration of lactobacilli (long Gram-positive rods), Gram-negative and Gram-variable rods and cocci (i.e., G. vaginalis, Prevotella, Porphyromonas, and peptostreptococci), and curved Gram-negative rods (Mobiluncus) characteristic of BV is considered the gold standard laboratory method for diagnosing BV, according to the CDC. Clinicians also might look at the use of such rapid tests as the Affirm VP III test (BD Diagnostics, Sparks, MD), OSOM BV Blue (Genzyme Diagnostics, Framingham, MA), and the QuickVue Advance G. vaginalis (Quidel Corp., San Diego, CA).[5]

The right test matters when it comes to successfully treating vaginitis. Yeast cultures used to detect VVC increase sensitivity and allow for speciation of the organism. This detection is crucial to choosing the proper antifungal drug. Non-albicans species of Candida are less likely to respond to standard azole therapy.[2]

Many clinicians might resort to using the microscope to detect trichomoniasis, but such practice might not be successful, says Workowski. "The traditional approach has been to look at the secretions under the microscope, but we know that for some of these infections, using those traditional approaches can be insensitive, particularly with trichomoniasis, where you can only diagnose kind of up to 60% of patients who have trichomoniasis," she says.[4]

Culture can be used to test for infection, as well as two point-of-care tests: the OSOM Trichomonas Rapid Test (Genzyme Diagnostics) and the Affirm VP III (BD Diagnostics).

Continuing education is an important part of staying on top of current strategies to detect and treat vaginitis, says Workowski. The CDC offers free continuing medical education credits on vaginitis through its Self-Study STD Curriculum Modules for Clinicians, available on the CDC web site. (**See resource box below for access information.**)

RESOURCE

Earn free continuing medical/nursing education credit through the Centers for Disease Control and Prevention's (CDC's) Self-Study STD Curriculum Modules for Clinicians, available on the agency's web site. To access the modules, go to the STD portal of CDC, www.cdc.gov/std. Under "Key Resources," select "Training." Next, select "Continuing Education Online," then "STD Curriculum Self-Study Modules." Click on "Vaginitis" for the self-study module.

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New research may boost AIDS vaccine search

EXECUTIVE SUMMARY

Scientists at the National Institute of Allergy and Infectious Diseases Vaccine Research Center have discovered two potent human antibodies that can neutralize more than 90% of known global HIV strains from infecting human cells in the laboratory.
• They have demonstrated how one of these disease-fighting proteins achieves this action.
• By using their knowledge of the structure of the outer surface of HIV to refine molecular tools to pinpoint the vulnerable spot on the virus, scientists can now use the antibodies that attach to this spot to block the virus from infecting cells.

Good news! Scientists have discovered two potent human antibodies that can neutralize more than 90% of known global HIV strains from infecting human cells in the laboratory, and they have demonstrated how one of these disease-fighting proteins achieves this action.[1,2] Such antibodies might be used to design improved HIV vaccines, researchers say.

Finding individual antibodies that can neutralize HIV strains anywhere in the world has been difficult due to the virus' capability to develop surface proteins to evade recognition by the immune system. As a result, several HIV variants exist worldwide.

However, researchers have identified a few areas on HIV's surface that remain nearly constant across all variants. One such area, called the CD4 binding site, is located on the surface spikes used by HIV to attach to immune system cells and infect them. By using their knowledge of the structure of the outer surface of HIV to refine molecular tools to pinpoint the vulnerable spot on the virus, scientists now can use the antibodies that attach to this spot to block the virus from infecting cells.

Led by a team from the National Institutes of Health's National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center, scientists have discovered two naturally occurring antibodies, named VRC01 and VRC02, in an HIV-infected individual's blood. The two antibodies were detected by a center-designed molecular device to look specifically at those cells that make antibodies against HIV. The device is a modified HIV protein that is engineered to react only with antibodies specific to the site where the virus binds to infected cells. VRC01 and VRC02 block HIV infection by attaching to the CD4 binding site, which prevents the virus from latching onto immune cells.

Scientists now will use their new understanding of the structure of the precise place where VRC01 binds to HIV to design immunogens that will elicit VRC01-like antibodies when administered through a vaccine, says **Gary Nabel**, MD, PhD, director of the NIAID Vaccine Research Center. Nabel outlines the following possibilities in the research of VRC01 and VRC02:

- Determine whether VRC01 confers protection in macaques from a non-human primate form of HIV.
- Develop immunogens for a vaccine designed to elicit VRC01-like antibodies.
- Make preparations to study the safety and potential protective effects of VRC01 in humans.
- Develop the VRC01 antibody for other HIV prevention strategies, such a microbicides and pas-

COMING IN FUTURE MONTHS

- Is the Pill protective against brain aneurysms?
- Science looks at HPV microbicide
- Check care of HIV-positive women
- Research: Oral sex becoming more common
- Some clinicians not strongly encouraging HPV vaccine

sive immune protection.

Scientists also are generating more broadly neutralizing HIV antibodies based on structural design and are testing combinations of antibodies to protect against HIV resistance mutations, says Nabel.

Facebook new tool?

Such new developments in science can only boost HIV vaccine research. At the present time, the Seattle-based HIV Vaccine Trials Network (HVTN) lists no studies in Phase III clinical trials, says organization spokesperson Sarah Alexander. However, there are several Phase I trials, and two Phase II trials, in the field, Alexander reports.

The HVTN 505 study is using social media to engage potential study participants, says Alexander. The study is enrolling men and transwomen in Boston; New York City; Philadelphia; Washington, DC; Atlanta; Rochester, NY; Nashville, TN; Birmingham, AL; Chicago; Seattle; San Francisco; and Los Angeles. The Phase II study is looking at a prime-boost strategy of two investigational vaccines developed by scientists at NIAID's Vaccine Research Center. The two vaccines are three immunizations with recombinant DNA-based vaccine (the primer vaccine) over eight weeks followed by a single immunization with a recombinant vaccine (the boosting vaccine) based on a weakened adenovirus type 5 that carries the vaccine contents and helps stimulate the immune system.

The HVTN is running ads on Facebook that seek men who are having sex with men and who live in or near one of the cities with clinics. It also is employing a much edgier and more provocative

CNE/CME INSTRUCTIONS

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

CNE QUESTIONS

After reading Contraceptive Technology Update, the participant will be able to:

- identify clinical, legal, or scientific issues related to development and provisions of contraceptive technology or other reproductive services;
- describe how those issues affect services and patient care;
- integrate practical solutions to problems and information into daily practices, according to advice from nationally recognized family planning experts;
- provide practical information that is evidence-based to help clinicians deliver contraceptives sensitively and effectively.

13. What is the key marker of perimenopause?
A. Menstrual irregularity
B. Hypoestrogenemic amenorrhea
C. Hyperandrogenemia
D. Mood swings

14. What was the active agent in the gel used in the CAPRISA 004 microbicide trial?
A. Carrageenan
B. Tenofovir
C. Dapivirine
D. Sodium lauryl sulfate

15. Which is NOT one of the most common causes of infectious vaginitis?
A. Bacterial vaginosis
B. Vulvovaginal candidiasis
C. Desquamative inflammatory vaginitis
D. Trichomoniasis

16. Research conducted by the National Institute of Allergy and Infectious Diseases Vaccine Research Center shows that VRC01 and VRC02 attach to which site on the HIV virus?
A. CCR5
B. CXCR4
C. CD8
D. CD4 binding site

Answers: 13. A;14. B; 15. C; 16. D

ad, which is being placed on online gay hook-up sites to help bring in interested individuals networkwide to a web site for more information. These online ads are designed to integrate with other outreach tools such as transit ads, posters, and giveaways, including palm cards, yo-yos, and coasters.

One of the HVTN trial sites, the Fenway Health Vaccine Studies clinic in Boston, is using the popular internet site Craigslist to recruit potential study participants. By reading personal ads on Craigslist, clinic recruiters can invite individuals who appear to fit the target profile to consider participating in the trial. Such approaches use language approved by the clinic's Institutional Review Board to invite advertisers to learn more about HIV vaccine clinical trials at the clinic. These invitations include the clinic's web address for the clinic and an e-mail address to be used for response.

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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.