Herpes vaccine research may be propelled toward possible candidate

Researchers have designed a new type of vaccine that could be the first for preventing genital herpes. By using a counterintuitive scientific approach, scientists were able to prevent active and latent infections caused by herpes simplex virus type 2 (HSV-2), the virus that causes genital herpes.1 Herpes simplex virus type 2 infection is the leading cause of genital ulcerative disease. It is estimated that more than 500 million people are infected worldwide.2 High prevalence of HSV-2 infection in sub-Saharan Africa contributes significantly to the spread of HIV-1 in the region, say public health officials.3 About one in six adolescents and adults in the United States is infected with the HSV-2 virus, with an estimated 776,000 new cases occurring each year.4

In the past, researchers have focused on HSV-2 glycoprotein D, a component of the outer coating of the virus and required for HSV infection of cells, as the predominant HSV vaccine candidate.5,6 The infection stimulates the immune system to produce predominantly glycoprotein D-specific antibodies, which bind to the virus and block its ability to infect cells. However, outcomes of clinical trials of vaccines based on HSV-2 glycoprotein D have not yielded solid results thus far.7 Results of a Phase III investigational vaccine with such an approach indicated that while it was partially effective at preventing HSV-1, it did not protect women from HSV-2.7

In the current research, scientists at Albert Einstein College of Medicine in the Bronx, NY, took a completely different approach in...
designing a “live” HSV-2 vaccine. Rather than use glycoprotein D to stimulate antibodies, they deleted the gene for glycoprotein D from the virus and, consequently, the protein’s expression on the viral surface. This move weakens the virus, which renders it unable to infect cells or cause disease.

Scientists hypothesized that the altered virus then would stimulate the body to produce different and more effective antibodies. The research team had “a hunch” that glycoprotein D might be masking other viral antigens, said William Jacobs Jr., PhD, the Leo and Julia Forchheimer Chair in Microbiology & Immunology at Einstein in a press statement accompanying the study publication. By removing the dominant protein, scientists would expose those previously masked antigens to the immune system, noted Jacobs, co-leader of the investigation.

When the vaccine was given to mice, the scientists found it provided complete protection against subsequent infection with normal HSV-2, whether animals were challenged intravaginally or through the skin. No virus was detected in vaginal or skin tissue of vaccinated mice or in neural tissue, where HSV-2 often hides in a latent form, only to emerge later to cause disease. When unvaccinated mice were challenged with HSV-2, all showed evidence of the virus in the three tissue sites, and all succumbed to the disease.¹

Scientists observed that the vaccinated mice showed low levels of neutralizing antibodies and high levels of antibodies associated with a different immune response known as antibody-dependent cell-mediated cytotoxicity (ADCC). This observation, coupled with the finding that blood serum from vaccinated mice was able to passively protect unvaccinated mice, demonstrates that ADCC antibodies were responsible for protecting against HSV-2, say researchers.¹

“Why glycoprotein D is not an effective vaccine and why the removal of glycoprotein D from HSV-2 makes an effective vaccine is a puzzle that we may not solve soon,” states a companion piece to the current research article. “Nevertheless, it is indeed a good day in the struggle to develop a vaccine to protect the world’s

EXECUTIVE SUMMARY

Researchers have designed a new type of vaccine that could be the first for preventing genital herpes. By using a counterintuitive scientific approach, scientists were able to prevent active and latent infections caused by herpes simplex virus type 2 (HSV-2) in mice.

• About one in six adolescents and adults in the United States is infected with the HSV-2 virus, with an estimated 776,000 new cases occurring each year.
• In the past, researchers have focused on HSV-2 glycoprotein D, a component of the outer coating of the virus and required for HSV infection of cells, as the predominant HSV vaccine candidate. In early research, scientists deleted the gene for glycoprotein D from the virus and, consequently, the protein’s expression on the viral surface, which stimulated the body to produce different antibodies.
population against the disease burden of HSV infections.\textsuperscript{3}

**The team’s next focus**

What is the next step in research for the Einstein scientific group? The team is focused on completing the work needed to bring the candidate vaccine into the clinic for a Phase 1 study, according to Betsy Herold, MD, the Harold and Muriel Block Chair in Pediatrics at Einstein and chief of the Division of Pediatric Infectious Diseases at the Children’s Hospital at Montefiore and Einstein. Such work requires collaboration with pharmaceutical partners, she notes.

“As initial first steps, we have already begun performing dose range studies to determine the lowest dose needed for complete protection, testing the vaccine against clinical isolates of HSV-1 and HSV-2, and growing the virus on Food and Drug Administration-approved cells,” states Herold.

“At the same time, we are initiating studies to further identify mechanistically why this vaccine provides ‘sterilizing’ immunity, defined as preventing the establishment of latency in the mouse, and why the immune response is different from all prior vaccines tested.”

Glycoprotein candidates with novel platforms still are being explored as potential vaccine candidates. One approach that includes a virus entry molecule with added antigens to block HSV-2 immune evasion has yielded promising results in mice.\textsuperscript{8} Science also is looking at alternative delivery methods of glycoprotein, including lentiviral vectors expressing glycoprotein B and intranasal delivery.\textsuperscript{8}

Research also is evaluating several therapeutic vaccines for genital herpes. Three companies have therapeutic vaccines in United States clinical trials:

- Lexington, MA-based Agenus, which is developing its HerpV recombinant therapeutic vaccine for the treatment of genital herpes caused by HSV-2;
- Genocea Biosciences of Cambridge, MA, which is researching its first-in-class, investigational, protein subunit vaccine, GEN-003;
- Vical of San Diego, which is enrolling patients in its Phase 1/2 trial of its Vaxfectin HSV-2 vaccine.

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**Research eyes use of withdrawal**

Don’t discount withdrawal as a form of contraception. One-third of women at risk of unintended pregnancy used coitus interruptus as a contraceptive method within the past 30 days, often in combination or rotation with more effective methods, according to findings from a new U.S. study.\textsuperscript{1}

The study, which looked at national data from 3,276 women ages 18-39 in 2012, found that among the one-third of women who had used withdrawal in the past 30 days, 12% reported using only withdrawal. Most women who practiced withdrawal also used a hormonal method (13%) or condoms (11%) within that same timeframe.\textsuperscript{1}

What prompted researchers to look into the use of withdrawal? When scientists undertook the study, they wanted to obtain the most accurate measures of recent
contraceptive use available, explains Rachel Jones, PhD, senior research associate at the Guttmacher Institute in New York City. This goal led researchers to do two things differently on their survey, explains Jones, who served as senior author of the paper. “First, we asked about hormonal methods and coital methods separately,” Jones notes. “We adopted this strategy because women and couples use these methods in very different ways and sometimes for reasons unrelated to pregnancy prevention, such as to regulate their periods or to reduce the risk of sexually transmitted infection [STI] transmission.”

The researchers placed withdrawal first on the list of coital methods, states Jones. The researchers suspected that many women don’t consider withdrawal to be a “real” method and, by listing it first, it served as an indication that researchers wanted to know about use of this method as well, she says.

In the national sample of more than 4,500 adult women, researchers found that reliance on withdrawal was as common as reliance on condoms (33% versus 35%, respectively).

“This finding did not necessarily surprise us. We expected we would get higher incidence levels when we placed it first on the list,” observes Jones. “What did surprise us was the fact that most women who reported using withdrawal in the last 30 days also reported using a more effective method, most commonly the condom or the pill.”

Users of withdrawal might fall into two camps, says Jones: women/couples who are not particularly motivated to avoid pregnancy and rely only on withdrawal, and women/couples who are highly motivated to avoid pregnancy and use it as a second or backup method.

**EXECUTIVE SUMMARY**

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- The study, which looked at national data from 3,276 women ages 18-39 in 2012, found that among the one-third of women who had used withdrawal in the past 30 days, 12% reported using only withdrawal. The majority of women who practiced withdrawal also used a hormonal method (13%) or condoms (11%) within that same timeframe.
- Withdrawal has perfect use failure rates (4% of women experiencing unintended pregnancy in first year of use) and typical use failure rates (22% of women experiencing unintended pregnancy in first year of use) that match those for condoms and fertility-awareness based methods.

**What to keep in mind**

Don’t dismiss withdrawal, says Deborah Kowal, MA, PA, executive editor of Contraceptive Technology.

Findings from the National Survey of Family Growth, a national compilation of information on family life, marriage and divorce, pregnancy, infertility, use of contraception, and men’s and women’s health, indicate that half of women report having used withdrawal at some time in their lives. But on closer examination, the extent of use seems greater, notes Kowal. In a study of low-income African-American adolescents, 60% reported having used withdrawal in the previous three months. Withdrawal is “the ever-present backup method,” she states.

Take the initiative in asking patients whether they sometimes rely on withdrawal, because many women won’t otherwise volunteer that they use it, notes Kowal. Since withdrawal falls on the bottom tier of effectiveness, couples need to be prepared for a potential failure. The method can effectively prevent pregnancy. Withdrawal has perfect use failure rates (4% of women experiencing unintended pregnancy in first year of use) and typical-use failure rates (22% of women experiencing unintended pregnancy in first year of use) that match those for condoms and fertility-awareness based methods.

When used with a hormonal method, withdrawal adds protection, notes Kowal. When it is used with condoms or with fertility-awareness based methods during the fertile days, withdrawal doesn’t give added protection; it’s just a substitute for correct use or abstinence, she states.

If a patient says she uses condoms, it might not be the case, says Kowal. If her partner places the condom on after he’s already had vaginal penetration, then it is really withdrawal, she notes. Correct condom use requires that the condom be placed on the penis before any penile-vaginal contact. In one study of college males, 43% reported using withdrawal during initial phases of intercourse, then applying a condom for intravaginal ejaculation.

Remind women that pre-ejaculate can contain sperm, though generally less than 23 million, says Kowal. The risk of pregnancy is still low, but it is not zero. Also counsel that withdrawal does not protect against
It is not helpful to tell women that withdrawal doesn’t work, says Susan Wysocki, WHNP-BC, FAANP, president & chief executive officer of iWomansHealth in Washington, DC, which focuses on information on women’s health issues for clinicians and consumers. “It’s much better than nothing,” states Wysocki. “It’s the one method you don’t leave home without.”

Using withdrawal as a method is a sign that the woman/couple is motivated to prevent pregnancy, states Wysocki. Clinicians can help by offering methods with a higher rate of effectiveness with a script such as, “I can see you are motivated not to become pregnant. I can provide you with other methods that are much more effective for preventing pregnancy.”

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With the trend toward increased use of long-acting reversible contraceptives (LARCs) such as the intrauterine device and contraceptive implant, science is looking at development of longer-acting injectable contraceptives. More than 40 million women worldwide use injectable contraceptives to prevent pregnancy.2

While LARCs offer top-tier effectiveness, for many women around the world, they are unaffordable or don’t meet individual needs or preferences.3 New reversible injectable products with durations between the three-month injectable contraceptives and the contraceptive implants and intrauterine devices would fill an important gap in the existing contraceptive method mix and would increase choices for women, say researchers.1

Injectables on the global market are effective for 1-3 months, depending on the formulation. These injectables therefore require women to return to providers 4-12 times per year. An important reason for discontinuation of the method is missed reinjections, says Vera Halpern, MD, scientist at FHI 360 in Durham, NC.

“Women find it difficult to comply with reinjection schedules whether it is difficult because they forget or it is difficult for them to get to the clinical facility in time, especially in areas where the access is not simple or easy,” notes Halpern, who served as the lead author of a current analysis on development of longer-acting injectables. “An injection that would last longer and require less frequent visits for reinjection seems like a very good
option to have in the method mix, and it does not exist.”

According to the table of U.S. contraceptive effectiveness/continuation rates in Contraceptive Technology, depot medroxyprogesterone acetate (DMPA, Depo Provera, Pfizer, New York City) has the lowest continuation rate of all modern contraceptives; 56% of women continue use of the method at the end of the first year.4

**Research in the pipeline**

With funding from the Bill & Melinda Gates Foundation of Seattle, FHI 360 has launched a project to support early testing of innovative approaches toward the goal of developing an injectable contraceptive that would last for six months. This project is a first step toward bringing a game-changing injectable contraceptive to market, says FHI 360.

In 2012, FHI 360 issued a Request for Proposals for proof-of-concept testing of candidates that have the potential to be developed into a longer-acting injectable. Proposals were received from lead drug delivery research groups in the United States, Europe, India, and China, and represented a wide range of innovative approaches. (Contraceptive Technology Update reported on the search. See “Longer-acting method that is injectable probed,” March 2013, p. 28, and “The search has begun for long-acting contraceptives,” December 2013, p. 137.)

Four proposals were selected to move forward for proof-of-concept testing and are collecting data in support of this initiative:

• poly(lactide) and poly-lactic-co-glycolic acid microspheres releasing levonorgestrel, (Shanghai [China] Institute of Planned Parenthood Research);

• poly-lactic-co-glycolic acid microspheres releasing etonogestrel, (Orbis Biosciences in Kansas City);

• nanostructured porous silicon microparticles releasing various contraceptive steroids, (University of California, San Diego in La Jolla);

• a biodegradable polymeric gel formulation releasing levonorgestrel, (University of Tennessee Health Science Center in Memphis).

The goal is to develop and bring to market a six-month injectable within 10-15 years and possibly sooner, say researchers.1

**Longer duration desired**

Previous investigations have shown that injectable contraceptives with a longer interval between injections lead to better adherence and continuation rates when compared to those with shorter intervals, notes Halpern.

A study that looked at the three-month injectable depot medroxyprogesterone acetate and one-month injectable medroxyprogesterone acetate/estradiol cypionate (Cyclofem, not available in the United States) found that the one-year continuation rate was higher for the longer-acting drug.2 The main difference stated by study participants was logistical difficulty in making frequent clinic visits. In a study comparing DMPA 150 mg given every three months versus DMPA 450 mg given every six months, findings indicate a significantly better acceptability of the six-month regimen, primarily due to convenience and reduced travel costs.3 Research on the acceptability of longer-acting injectables in other therapeutic areas also points to acceptability of a longer-acting shot, notes Halpern.4

“Thats our main rationale and reason for investing in developing a longer-acting injectable contraceptive,” says Halpern. “We think that compliance will be better and, therefore, the effectiveness will be better.”

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New data indicate insurance is important in implementing over-the-counter OC

Just-published research finds that insurance coverage of a future over-the-counter (OTC) birth control pill would result in more widespread use by women and would be cost effective for health insurance plans. Findings suggest use of an OTC birth control pill would be highest among low-income women, and would therefore have the biggest impact on unintended pregnancy, if it were fully covered by insurance.¹

Researchers from the University of California, San Francisco (UCSF) and Ibis Reproductive Health in Oakland, CA, used data from published surveys on contraceptive use and women’s interest in an OTC pill to perform the analysis. Findings indicate that if the pill were fully covered by insurance, there would be an increase of 11%-21% in the number of low-income women using the birth control pill. Most new users would be previous users of a birth control method less effective than the pill or those using no method at all, which would result in a reduction of unintended pregnancy by 7%-25%, findings suggest.¹

Making the pill available without a prescription has the potential to make a large impact on unintended pregnancy rates, says Diana Greene Foster, PhD, associate professor in the UCSF Department of Obstetrics, Gynecology and Reproductive Sciences and director of research of UCSF’s Advancing New Standards in Reproductive Health at the Bixby Center for Global Reproductive Health.

Birth control pills are the most commonly used reversible method of contraception in the United States,² but it isn’t easy to obtain

EXECUTIVE SUMMARY

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• Findings indicate that if the pill were fully covered by insurance, there would be an increase of 11%-21% in the number of low-income women using the birth control pill.
• Most new users would be previous users of a birth control method less effective than the pill or those using no method at all, which would result in a reduction of unintended pregnancy by 7% to 25%.
Access to contraception and school-based health — One strategy for preventing teen pregnancy

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School-based health centers (SBHCs) are unique in that they can provide care to adolescents in a setting that is trusted, familiar, immediately accessible, and in their own school. Such centers exist in urban, rural, and suburban communities. They can be found in all but four states: Idaho, Montana, North Dakota, and Wyoming.

School-based health centers provide a wide range of services to students as well as to parents, school faculty, and staff, and sometimes the wider community. According to the 2010-2011 School-Based Health Alliance Census Report, there are 1,930 SBHCs in the United States, 340 more than the previous census report. With expanded funding for these centers provided through the Affordable Care Act (ACA), such centers are likely to expand even further in coming years.1

More than 80% of school-based health centers provide some kind of reproductive health services. However, which specific services are offered vary widely from one center to another, as well as by state and region. The most commonly offered services are counseling on abstinence (82%) and pregnancy testing (81%). Most (69%) also offer diagnosis and treatment for sexually transmitted infections (STIs) and reproductive health services, such as testicular exams for young men (69%), gynecological exams (59%), and contraceptive counseling (64%).1

While contraceptive counseling is reported to be available in two-thirds of centers, dispensing contraceptive methods is less common. In fact, 50% of centers report that they are prohibited from dispensing contraceptives.1

While state laws or regulations prevent contraceptive access for about one-third of SBHCs, a more common barrier is having a restrictive policy at the school or at the district level. School-based health centers in the 2010-2011 census reported having a school district policy that blocked contraceptive dispensing at 76% of centers. Individual school policies
also were a barrier in 54% of centers, according to that census report.¹

**Centers the right venue?**

Are school-based health centers the right venue for dispensing contraception?

Adolescents can certainly benefit from access to reproductive healthcare in a variety of settings, and evidence is growing that SBHCs that dispense contraceptives can have a significant impact on increasing the likelihood of students’ using contraception to avoid unintended pregnancy.

A 2011 study of two SBHCs in two demographically similar southwestern U.S. high schools, one that dispensed contraceptives on site and one offering referrals for contraception off site, found a significant impact on teen pregnancy, even among motivated students who requested contraception.²

After 16 months, the school with on-site dispensing found 6% of student who requested contraception became pregnant. At the comparison school, 20% of those referred for contraception became pregnant during the follow-up period.²

More recently, an examination looked at reproductive health behaviors among students at two New York City high schools, of which only one had a school-based health center that dispensed contraception on-site.³ Researchers found students at the school with a school-based health center to be more likely to report using condoms at first intercourse and using hormonal contraception at last intercourse. The students at the school with a health center also were more likely to report receiving education in the classroom on STIs, HIV, and abstinence, as well as higher rates of counseling about contraception and emergency contraception in the last 12 months. However, students at both schools had similar rates of reporting that they ever accessed reproductive health services.³

Additionally, some research indicates SBHCs can have a positive impact on teens who already are pregnant or parenting. Such centers have demonstrated positive effects on pregnant and parenting teens in regard to their educational outcomes, their decisions to use contraception to prevent future unintended pregnancy, as well as in the health and developmental outcomes of their infants.⁴

Such positive findings have contributed to organizations such as the American Academy of Pediatrics and Society for Adolescent Health and Medicine publishing position statements supporting the school-based health centers model of care and specifically recognizing their role in providing confidential reproductive and sexual health services.⁵,⁶

The research to date has not all been positive. In 2011, the “Journal of Adolescent Health” published a study of 12 California high schools, six with school-based health centers.⁷ Findings indicate that female students at schools with a school-based health center reported higher use of hormonal contraceptive at last intercourse compared to those students at schools without a center. Nevertheless, the group of female students at schools with an SBHC still reported low use (less than one-third) of a hormonal method or condoms at last intercourse. Also, no increase in condom or contraceptive use was found among male students, regardless of school, and students at SBHC and non-SBHC schools reported equal rates of ever accessing reproductive health services.⁷

Even among schools with school-based health centers where dispensing is available, many students remain at risk of unintended pregnancy. While expansion of SBHCs through ACA funding might positively impact the ability of centers to meet students’ needs for contraception, this is only one of many strategies to help adolescents prevent unintended pregnancies.

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HPV vaccination — Urging male vaccination might protect more young people at same price

Public health programs that devote a portion of their funding to encourage more boys to be vaccinated against human papillomavirus (HPV), rather than merely attempting to raise coverage among girls, ultimately might protect more people for the same price, a new analysis indicates.¹

The incidence of new HPV-related cancer cases in the United States in 2009 exceeded 35,000, with more than one-third of cases occurring in the male population.² It is estimated that almost all cervical cancers, up to 90% of anal cancers, and up to 60% of oropharyngeal cancers are caused by HPV.³ While screening has led to a significant decrease in cervical cancer incidence and mortality in developed countries, there has been an increase in other HPV-related cancers for which population screening is not performed.⁴

Many HPV cancers could be prevented with vaccination. However, even with the Centers for Disease Control and Prevention’s recommendations that boys and girls ages 11 to 12 should receive the HPV vaccine, just 37% of girls and 14% of boys in the United States have received all three shots in the HPV vaccine series.⁵ (Contraceptive Technology Update reported on the statistics. See the article, “HPV vaccine continues to be underutilized,” October 2014, p. 117.)

Analysis eyes strategies

It remains debated among experts whether HPV vaccination programs should focus on girls only or whether boys and girls should be targeted simultaneously, says Marc Ryser, PhD, a mathematician at Durham, NC-based Duke University. Previous modeling studies that addressed this question deemed it more effective to focus on females only, notes Ryser.

One common assumption among these modeling studies was that it would be possible to vaccinate a large fraction of females, says Ryser, who served as lead author of the current analysis. However, although high uptake among girls has been achieved in other countries such as the United Kingdom, the HPV vaccine has only had limited success in the United States, he notes.

In fact, the fraction of girls who have received all three doses has stagnated around 37%, and the fraction of fully vaccinated boys remains low at about 14%. At the same time, parental opposition to getting their children vaccinated against HPV has increased to about 44%.⁶

“Together, stagnating vaccine uptake at low levels and increasing parental opposition seem to suggest that a further increase in uptake may require costly outreach and education programs to raise awareness and acceptability of the vaccine,” says Ryser. “In addition, we expect that it is more expensive to raise the uptake from 37% to 38% than from 14% to 15%. The higher the uptake, the harder it is to find additional parents who are willing to vaccinate their child. In other words, educational costs are expected to be coverage-dependent.”

To find out whether different strategies for allocating public funds might protect more people, Ryser, Duke mathematician Kevin McGoff, PhD, obstetrician/gynecologist Evan Myers, MD, MPH, and colleagues developed a mathematical model of HPV transmission among sexually active 14-18 year olds. The goal of the study was to assess the impact of education and outreach costs on the optimal vaccination strategy.

The findings suggest that public health officials might be able to protect more people for the same price by shifting some funds to encourage vaccination of boys, since the fraction of parents willing to vaccinate has yet to be exhausted among boys.¹

What’s the next step?

What do the Duke analysts see as the next step in research in determining real-world data on actual patient costs? The costs, and how to measure them, will depend based on the intervention, says Myers.

If the intervention involves providers spending a little bit more time with parents, there are ways to measure the actual time being spent discussing vaccines, Myers states. Measuring such methods might be
difficult, with data relying on provider self-report or having someone sitting in the office with a stopwatch, he observes.

“If it’s a specific advertising/outreach campaign, the costs of designing and implementing those types of interventions are measurable and would be part of the budgeting process for any study,” says Myers.

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The latest addition to the video library is “Risk Perception.” Many women discontinue contraceptive use over concerns about side effects without considering the health risks of pregnancy. Because risk is such a complex concept to effectively convey to patients, this new video includes two case studies. One focuses on helping patient Maggie understand the risks of using (or not using) hormonal contraception and find the method that is best for her. The other looks at educating patient Jessica on permanent contraceptive options while counseling to minimize the risk of decision regret.

Other video titles include such topics as “Applying Cervical Cancer Screening Guidelines to Clinical Practice,” “Improving HPV Vaccine Uptake and Compliance,” and “Discovering the Barrier Methods: Female Condom, Diaphragm, and Cervical Cap.”

Explore the full collection of “Clinical Minute” activities at http://bit.ly/1EuXyIL.

Special focus issue coming: Patient-centered care
Patient-centered care is more than a buzzword. It’s a key part of the “Triple Aim” of healthcare reform. Look to the July 2015 issue of *Contraceptive Technology Update* to get ideas on how to take a more patient-centered approach, as opposed to a medical condition approach. We will share tips from national experts and talk with programs who have successfully integrated patient-centered care.

Explore new online videos from ARHP
Check out the “Clinical Minutes” online videos from the Association of Reproductive Health Professionals. These short video case studies are designed to deliver the key points for practice in 15 minutes or less.

Free continuing education credit is available for physicians, nurse midwives, nurse practitioners, pharmacists, physician assistants, students, educators, and researchers who focus on reproductive health, family practice, or internal medicine.

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CNE/CME QUESTIONS

1. What is a component of the outer coating of the herpes simplex virus type 2 (HSV-2) virus and one that is required for HSV infection of cells?

A. Glycoprotein D  
B. Eukaryote  
C. Bacteriophage  
D. Thymidine kinase

2. What is an important reason for discontinuation of contraceptive injections?

A. Increase in menstrual symptoms  
B. Missed reinjections  
C. Heavier periods  
D. Weight loss

3. What is the typical use failure rate for the withdrawal method of contraception?

A. 50%  
B. 37%  
C. 22%  
D. 18%

4. What percentage of boys in the United States have received all three shots in the HPV vaccine series?

A. 45%  
B. 35%  
C. 22%  
D. 14%

CNE/CME OBJECTIVES

After reading Contraceptive Technology Update, the participant will be able 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 services and patient care;
3. Integrate practical solutions to problems and information into daily practices, according to advice from nationally recognized family planning experts;
4. Provide practical information that is evidence-based to help clinicians deliver contraceptives sensitively and effectively.