CONTRACEPTIVE TECHNOLOGY UPDATE®

A Monthly Newsletter for Health Professionals

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New data emerge from the WHI: How will they impact your practice?

Hormone therapy initiated closest to menopause onset is safest

Has your treatment of menopausal women changed since the initial findings released from the Women's Health Initiative (WHI) randomized, controlled trials of hormone therapy (HT)? Findings from a just-published secondary analysis of data from the WHI indicate that women who initiated HT closer to menopause tended to have reduced risk of coronary heart disease (CHD), while women further from menopause tended to have a slightly higher risk for the disease.[1]

While the news may be seen as reassuring for younger women with moderate to severe menopause symptoms who are considering hormone therapy use, they do not change the current recommendation that hormone therapy should not be used at any age for prevention of CHD, caution scientists involved with the analysis.

Hormone therapy appears to be a reasonable option for the short-term treatment of moderate to severe menopausal symptoms in women who are less than 10 years past the onset of menopause, says **Jacques Rossouw**, MD, lead author of the study and chief of the WHI branch at the National

EXECUTIVE SUMMARY

Findings from a just-published secondary analysis of data from the Women's Health Initiative (WHI) indicate that women who initiated hormone therapy closer to menopause tended to have reduced risk of coronary heart disease, while women further from menopause tended to have a slightly higher risk for the disease.

- While the news may be seen as reassuring for younger women with moderate to severe menopause symptoms who are considering hormone therapy use, they do not change the current recommendation.
- Hormone therapy should not be used at any age for prevention of coronary heart disease, caution scientists involved with the analysis.

Heart, Lung, and Blood Institute of the National Institutes of Health. The therapy does not appear to increase the risk of heart disease in such women, though they should take care of risk factors such as high blood pressure and also have regular mammograms, he observes.

"The average duration of treatment in the trials was four to five years, which is longer than the two to three years most women would need to see them through the initial menopausal symptoms," states Rossouw. "The findings for short-term treatment do not imply that any benefit, or lack of harm, will persist over longer periods of time; therefore, women should use the hormones for the shortest time needed to alleviate their symptoms."

Review the history

The WHI, a long-term national health study, is focused on strategies for preventing heart disease, breast and colorectal cancer, and osteoporotic fractures in postmenopausal women. One component of the study was designed to examine the effects of combined hormones or estrogen alone on the prevention of coronary heart disease and osteoporotic fractures and on associated risk for breast cancer.

The estrogen plus progestin trial was halted early in July 2002 after 5.2 years after researchers found that the therapy's (Prempro, Wyeth; Philadelphia) risks outweighed its benefits.[2] The cessation of the estrogen/progestin therapy set off a flurry of concerned calls from patients and a subsequent drop in use of hormone therapy. **(See the article, "Hormone replacement therapy: Review choices in light of new data," *Contraceptive Technology Update*, September 2002, p. 97.)** Findings from a just-published study indicate that a sharp decline in the rate of new breast cancer cases in 2003 may be related to the decline in the use of hormone therapy.[3] Age-adjusted breast cancer incidence rates in women in the United States fell 6.7% in 2003, according to the study results.

The WHI estrogen-alone study was stopped at the end of February 2004 because results indicated that the drug therapy [combined equine estrogen (CEE), Premarin, Wyeth; Philadelphia] increased the risk of stroke and did not reduce the risk of coronary heart disease, a key question of the trial.[4] The drug did not increase the risk of breast cancer, researchers noted. **(See the article "Estrogen arm of WHI suspended: What next?" *CTU*, May 2004, p. 53.)**

What do new data show?

In the latest WHI analysis, the authors combined data from the estrogen/progestin and estrogen-only trials to explore previously observed trends in hormone effects by distance from the onset of menopause. Differences in hormone therapy effects were examined in three age categories (50 to 59, 60 to 69,

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and 70 to 79) or in years since the onset of menopause (less than 10, 10 to 19, and 20 or more).

What did the analysis discover? The increased risk in heart disease due to hormone therapy in older women is primarily in those who also have hot flashes and night sweats. Women in the study who had these symptoms were more likely to have risk factors for CHD such as high blood pressure or high blood cholesterol. Researchers could not determine whether this finding explained their higher risk on hormone therapy.[1]

Other findings from the analysis include:

- confirmation that hormone therapy increases the risk of stroke and that this risk does not appear to be influenced by age or time since the onset of menopause;
- even in women within 10 years of the onset of menopause, there appears to be an increased risk of breast cancer in women taking estrogen with a progestin;
- a trend, while not statistically significant, toward reduced risk for death associated with hormone use in younger compared to older women.[1]

What is your approach?

Most women requesting treatment of vasomotor and related symptoms are patients in their late perimenopausal years and young postmenopausal women — those whose last period was less than one decade prior, observes **Andrew Kaunitz**, MD, professor and assistant chairman of the Department of Obstetrics and Gynecology at the University of Florida Health Science Center in Jacksonville. Unfortunately, the use of complementary approaches, such as soy supplements and black cohosh, and nonhormonal prescription therapies, such as antidepressants, have not consistently proved more effective than placebo in treatment of such symptoms,[5] says Kaunitz.

"In looking both at relative and absolute benefits and risks from WHI and other evidence, hormone therapy represents a reasonable approach to treatment of bothersome symptoms in late perimenopausal and young postmenopausal women," says Kaunitz. "After initiation of treatment, clinicians and their patients can consider reducing the dose of hormone therapy gradually, over a number of years."

Some women ultimately may choose to discontinue therapy when symptoms are no longer bothersome, while others — particularly those in whom skeletal health concerns are present — may choose to continue a low dose of hormone therapy indefinitely, says Kaunitz. When vasomotor symptoms are not a concern and symptoms of genital atrophy are bothersome, vaginal rather than systemic therapy is appropriate, he states.

The North American Menopause Society (NAMS) recently released an updated position paper on use of hormone therapy.[6] Current evidence supports the use of estrogen/progestin or estrogen-alone therapy for menopause-related symptoms and disease prevention in appropriate populations of peri- and postmenopausal women, the position paper states.[6] *(Access the statement at the NAMS web site, www.menopause.org. Click on "Other Healthcare Professionals," then "NAMS Estrogen and Progestogen Position Statement," to download the statement.)*

Clinicians should use the new WHI data to talk to women in both relative and absolute terms, help them understand what risks are involved, and discuss the "considerable" benefits offered by hormone therapy, says **Lee Shulman**, MD, distinguished physician and professor in the Department of Obstetrics and Gynecology at Northwestern University's Feinberg School of Medicine in Chicago. Shulman presented information on hormone therapy at the recent *Contraceptive Technology* conference in Washington, DC.

In randomized trials and observational studies, estrogen/progestin and estrogen-alone therapies have been shown to be effective in treating and preventing vasomotor symptoms, vulvovaginal atrophy, urinary symptoms of dysuria, frequency and nocturia, as well as preventing osteoporotic fractures of the hip and spine,[7] says Shulman. "While hormone therapy is not for everyone, it is clearly an important component of menopausal management for the majority of women who are seeking relief from menopausal symptoms," Shulman states.

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New recommendations out for gonorrhea treatment

Update your practice when it comes to treatment of gonorrhea: The Centers for Disease Control and Prevention (CDC) no longer recommends the fluoroquinolone antibiotics ciprofloxacin, ofloxacin, and levofloxacin as a treatment for gonorrhea in the United States.[1]

The change comes on the heels of the release of the agency's updated *Sexually Transmitted Diseases Treatment Guidelines*.[2] **(*Contraceptive Technology Update* reported on the original recommendations for gonorrhea in the *STD Quarterly* article, "Stay vigilant in stemming gonorrhea," inserted in the October 2006 issue, supplement, p. 3.)**

What led to the revision? Publication of just-released data indicates that fluoroquinolone-resistant gonorrhea is now widespread in the United States among heterosexuals and men who have sex with men (MSM).[1] According to the new report, the proportion of drug-resistant cases among heterosexuals has risen above the recognized threshold of 5% for changing treatment recommendations. The CDC took similar measures in 2004, when officials stated that fluoroquinolones should no longer be used to treat gonorrhea in MSM. **(See the *STD Quarterly* article, "Gonorrhea rates drop; stay focused on spread," inserted in the March 2005 issue, supplement, p. 2.)**

In the new report, derived from the CDC's Gonococcal Isolate Surveillance Project (GISP) in 26 U.S. cities, data showed that among heterosexual men, the proportion of gonorrhea cases classified as fluoroquinolone-resistant *Neisseria gonorrhoeae* (QRNG) reached 6.7% in the first half of 2006, which represented an 11-fold increase from 0.6% in 2001.

Providers now are down to a single class of antibiotics known as cephalosporins when it comes to recommended options for treating gonorrhea. The lack of treatment options calls for accelerated research into new drugs, as well as increased monitoring for emerging drug resistance, especially to cephalosporins, say CDC officials. The agency is working with the World Health Organization to strengthen international efforts to monitor emergence of cephalosporin resistance and is communicating with government and industry partners to identify and evaluate promising new drug regimens.

"We are running out of options to treat this serious disease," said **Kevin Fenton**, MD, PhD, director of the agency's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, in a press statement on the revised recommendations. "Increased vigilance in monitoring for resistance to all available drugs is essential."

The Infectious Diseases Society of America (IDSA) also is raising the flag for new antibiotics. In a prepared statement issued following the CDC recommendations, the professional society called on the U.S. Congress to address the issue.[2] The Food and Drug Administration Revitalization Act now under consideration by the Senate provides an opportunity to expand existing incentives for so-called orphan drugs and specifically targets antibiotics, states the IDSA.

Henry Masur, MD, IDSA president, in the issued statement said, "Gonorrhea has now joined the list of other superbugs for which treatment options have become dangerously few. To make a bad problem even worse, we're also seeing a decline in the development of new antibiotics to treat these infections."

Gonorrhea is the second most commonly

EXECUTIVE SUMMARY

The Centers for Disease Control and Prevention (CDC) no longer recommends the fluoroquinolone antibiotics ciprofloxacin, ofloxacin, and levofloxacin as a treatment for gonorrhea in the United States.

- New data indicate that fluoroquinolone-resistant gonorrhea now is widespread in the United States among heterosexuals and men who have sex with men. The proportion of drug-resistant cases among heterosexuals has risen above the recognized threshold of 5% for changing treatment recommendations.
- New data from the CDC's Gonococcal Isolate Surveillance Project show that the proportion of gonorrhea cases classified as fluoroquinolone-resistant among heterosexual men reached 6.7% in the first half of 2006, an 11-fold increase from 2001.

reported infectious disease in the United States after chlamydia, according to the CDC. In 2005, there were 339,593 cases reported nationwide, although experts believe the actual number of cases may be twice that amount. While national gonorrhea rates recorded a substantial decline from 1975 to 1997, overall rates appear to have leveled off in recent years, the agency states.

Oral fluoroquinolones were recommended as first-line treatments for gonorrhea in 1993. When drug-resistant cases increased in recent years, the CDC began to modify its approach. In 2002, the agency recommended that fluoroquinolones no longer be used for gonorrhea infections acquired in California and Hawaii, followed by the change in treatment for MSM in 2004. **(See the article, "Ciprofloxacin-resistant gonorrhea on the rise," *CTU*, June 2002, p. 64.)**

25 of 26 cities have resistance

According to the new CDC analysis, fluoroquinolone resistance now is widespread. Resistant cases were seen in 25 of the 26 cities included in the analysis. Sharp increases occurred from 2004 to 2006 in several cities including Philadelphia — spiking from 1.2% to 26.6 % of gonorrhea cases — and Miami, rising from 2.1% to 15.3% of cases. Resistant cases continued to increase in the MSM population; 38% of MSM gonorrhea cases were fluoroquinolone-resistant in the first half of 2006, compared to 1.6% in 2001.[1]

What is your first-line defense against the STD? Within the class of cephalosporins, CDC now recommends ceftriaxone, available as an injection, as the preferred treatment for genital, anal, and throat gonorrheal infection. While there are some alternative oral cephalosporin treatments for genital and anal gonorrhea, there currently are no recommended alternatives for pharyngeal infection. Clinicians can review additional information on available gonorrhea treatments at: www.cdc.gov/std/gonorrhea/arg.

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What is next on the HPV vaccine horizon?

As clinicians begin to integrate use of the first cervical cancer vaccine (Gardasil, Merck & Co.; Whitehouse Station, NJ), the Food and Drug Administration (FDA) is set to review the application for a second vaccine.

GlaxoSmithKline USA, of Philadelphia, submitted the application for Cervarix, its human papillomavirus (HPV) vaccine candidate, in March 2007. If licensed, the vaccine will be indicated for the prevention of cervical cancer and precancerous lesions associated with the most common cancer-causing HPV types. The application includes a "considerable amount" of data for virus types 16 and 18 that cause 70% of cervical cancer cases worldwide, as well as data for other virus types that can lead to cervical cancer, says **Barbara Howe**, MD, vice president and director of GlaxoSmithKline's North American vaccine development organization.

Research details protection

Published research indicates that the vaccine demonstrated protection up to 4.5 years against persistent infection with HPV 16 and HPV 18 and protection from precancerous lesions.[1] Protection also was demonstrated against infection with the third and fourth most prevalent cancer-causing types of HPV, types 45 and 31.[1] More recent findings show that the cervical candidate vaccine, formulated with its proprietary adjuvant system, AS04, induced higher antibody levels and immune memory

EXECUTIVE SUMMARY

GlaxoSmithKline USA has submitted an application for Cervarix, its human papillomavirus (HPV) vaccine candidate, to the Food and Drug Administration. If licensed, the vaccine will be for the prevention of cervical cancer and precancerous lesions associated with the most common cancer-causing HPV types.

- While one in four U.S. females between the ages of 14 and 59 may have HPV, more information is needed on male infection.
- Scientists are looking at men's roles in spreading HPV, with research to determine the incidence and persistence of type-specific penile HPV infections.

response compared to a similar HPV vaccine composition formulated with an aluminum hydroxide adjuvant.[2]

What about men?

Gardasil, which was approved in June 2006, targets four types of HPV: types 6, 11, 16, and 18. Guidance from the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) states that the vaccine be routinely given to girls when they are 11-12 years old.[3] According to the ACIP recommendation, three doses of the new vaccine should be routinely given to girls when they are ages 11 to 12; however, the vaccination series can be started as early as age 9 at the discretion of the health care provider. Females ages 13-26 also may receive the vaccine, according to the ACIP recommendation. **(Read more about the ACIP recommendation in the article "HPV vaccine, with nod from FDA, is first one approved to prevent cervical cancer," *CTU*, September 2006, p. 97.)**

About one in four U.S. females between the ages of 14 and 59 may have HPV, according to results of the first national estimate of the infection.[4] But what about men? HPV infection is highly prevalent in sexually active men as well, according to a systematic literature review.[5]

Tampa researchers eye male role

Researchers at the Lee Moffitt Cancer Center & Research Institute, with headquarters at the University of South Florida in Tampa, are looking at men's roles in spreading HPV. The four-year study, funded by the National Institutes of Health, is designed to determine the incidence and persistence of type-specific penile HPV infections, measure the humoral immune response to HPV infection, and assess the factors independently associated with acquisition, persistence, and clearance of type-specific HPV infections in men. Soon-to-be published data indicate a high HPV prevalence in men, with little change in prevalence across the age span.[6]

To date, vaccine research information only is available on antibody levels in boys, which are similar to those seen in their female counterparts, says **Khalil Ghanem**, MD, assistant professor of medicine and associate fellowship program director in the Division of Infectious Diseases at Johns Hopkins University School of Medicine in Baltimore. Ghanem presented information on HPV vaccines at the recent *Contraceptive Technology* conference in Washington, DC.

HPV studies continue

Efficacy studies of the quadrivalent vaccine in men are ongoing, Ghanem says. They include a heterosexual male cohort evaluating the efficacy of the quadrivalent vaccine for preventing genital warts and a gay male cohort in evaluating the efficacy of the quadrivalent vaccine in preventing anal carcinoma. With no data yet available, the Gardasil vaccine is not currently recommended for males, he notes. "If the quadrivalent vaccine lives up to expectations in men, it will provide direct benefit against genital warts and against anal cancer," says Ghanem. "In addition, it will likely provide indirect benefit to unvaccinated women by decreasing their likelihood of exposure to HPV 6, 11, 16, and 18 if they come into contact with a man who has been vaccinated."

It will be virtually impossible to guarantee 100% vaccine uptake in women, says Ghanem. This fact makes it imperative that men be vaccinated to increase the likelihood that the unvaccinated women will not be exposed. "However, all of this is dependent on the vaccine being efficacious in men," Ghanem states. "We await the data." **(See the *Contraceptive Technology Update* article "Men next target in HPV research drive," April 2005, p. 46.)**

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New recommendations out on HIV & circumcision

Global policies are being updated with the recent issuance of recommendations from an expert consultation on male circumcision for HIV prevention.[1] But what impact do the recommendations have on your practice?

An international expert consultation convened in March 2007 by the World Health Organization (WHO) and the UNAIDS Secretariat issued a recommendation that male circumcision now be recognized as an additional important intervention to reduce the risk of heterosexually acquired HIV infection in men. The consultation was held following publication of evidence from three randomized, controlled trials undertaken in Kisumu, Kenya; Rakai District, Uganda; and Orange Farm, South Africa, show that male circumcision reduces the risk of heterosexually acquired HIV infection in men by approximately 60%.[2-4] ***(Contraceptive Technology Update* reported on the data in the articles "Adult male circumcision reduces risk for HIV," March 2007, p. 30, and "Male circumcision and HIV prevention: Method can dramatically reduce risk, study says," *STD Quarterly*, October 2005, supplement p. 1.)**

In making the recommendations, global experts noted that male circumcision should be part of a comprehensive HIV prevention package that includes the provision of HIV testing and counseling services, treatment for sexually transmitted infections, the promotion of safer sex practices, and the provision of male and female condoms and promotion of their correct and consistent use.

EXECUTIVE SUMMARY

An international expert consultation recommends that male circumcision be recognized as an additional important intervention to reduce the risk of heterosexually acquired HIV infection in men.

- The consultation looked at results from three randomized, controlled trials in Africa that suggest that male circumcision reduces the risk of heterosexually acquired HIV infection in men by about 60%.
- Male circumcision should be part of a comprehensive HIV prevention package that includes the provision of HIV testing and counseling services, treatment for sexually transmitted infections, the promotion of safer sex practices, and the provision of male and female condoms and promotion of their correct and consistent use.

Being able to recommend an additional HIV prevention method is a significant step toward getting ahead of the HIV epidemic, said **Catherine Hankins**, associate director of UNAID's Department of Policy, Evidence, and Partnerships, in a joint statement on the new recommendations at a WHO/UNAIDS press conference. However, the message must be clear that male circumcision does not provide complete protection against HIV, she states. **(Download the expert consultation at www.who.int/entity/hiv/mediacentre/MCrecommendations_en.pdf.)**

What is the U.S. impact?

What are the implications of the global guidance for the U.S. population? At press time, the Centers for Disease Control and Prevention (CDC) was scheduled to hold a consultation in late April to begin developing U.S. recommendations and outline research needs, states **Jennifer Ruth**, CDC spokeswoman.

There are significant differences in the United States to be considered before recommendations can be made, explains Ruth. Africa and the United States are experiencing very different HIV epidemics. Africa has a generalized epidemic with most transmission through heterosexual sex, while in the United States, the epidemic is primarily among men who have sex with men (MSM), she notes. The African trials do not provide data on how circumcision affects the most common routes of transmission in the United States: male-to-male and male-to-female, observes Ruth.

"CDC will be evaluating the potential role of circumcision in the U.S. as we continue to support a combination of evidence-based HIV prevention strategies," she says. "We are currently working with our public health partners to evaluate the potential value, risks, and feasibility of circumcision to prevent HIV in the U.S."

Ward Cates, MD, MPH, president of research at Family Health International in Research Triangle Park, NC, presented information on the male circumcision studies during his talk on new approaches to HIV prevention at the recent *Contraceptive Technology* conference in Washington, DC.[5] There is a different situation in this country compared to the settings where the three African randomized, controlled trials occurred, he says. "First, most men in this country are circumcised," Cates observes. "Second, the overall incidence of HIV in

the U.S. is quite low in the general population; however, it is higher in selected populations."

What can U.S. clinicians do now? Cates encourages clinicians to follow CDC guidelines in assisting patients to find out their HIV infection status. The CDC issued recommendations in late 2006 that voluntary HIV screening become a routine part of medical care for all patients ages 13 to 64.[6] **(See the *CTU* article, "New HIV screening guidelines issued — How will they impact your practice?" December 2006, p. 133.)** Patients should be encouraged to learn the infection status of their sexual partners as well, he suggests.

If you are using the "A-B-C approach" (Abstain, Be faithful, and use Condoms) when talking about HIV risk reduction, expand your alphabet to include the full A to Z of risk reduction strategies, says Cates.

CDC continues to support a combination of approaches to reduce HIV infection, supported by the best available science, states Ruth. As the agency proceeds with the development of public health recommendations for the role of circumcision in preventing HIV transmission in the United States, Ruth says individual men may wish to consider circumcision as an additional HIV prevention measure, but must recognize that circumcision:

- has only proved effective in reducing HIV risk of infection through insertive vaginal sex;
- confers only partial protection and should be considered only with other proven prevention measures;
- does carry risks and costs that must be considered in addition to potential benefits.

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Face facts about effectiveness of ECPs

In 1992, reproductive health advocates estimated that emergency contraceptive pills (ECPs) could prevent half of all unintended pregnancies and abortions in the United States each year.[1] Today, two analyses of available data show that advance provision of emergency contraceptive pills enhances use but has not been shown to reduce unintended pregnancy rates.[2-3] This finding comes in light of the fact that one demonstration project[4] and three clinical trials[5-7] were specifically designed to address this issue.

What do the new analyses mean for family planners?

"Be honest with women when discussing ECPs: Do not oversell by implying Plan B will reduce unintended pregnancy," says **James Trussell**, PhD, professor of economics and public affairs and director of the Office of Population Research at Princeton (NJ) University and a co-author of one of the current analyses. Trussell presented data on the subject at the recent *Contraceptive Technology* conference in San Francisco and Washington, DC.

However, clinicians should not give up on the method, because ECPs do work, he says. While advance provision of ECPs does not reduce unintended pregnancy on a population level, it does not have any harmful effects. Analyses of the research

EXECUTIVE SUMMARY

Two current analyses of available data show that advance provision of emergency contraceptive pills (ECPs) enhances use but has not been shown to reduce unintended pregnancy rates.

- Increased access does not increase rates of sexually transmitted infections, decrease condom use, encourage adoption of less reliable contraceptive methods, or otherwise negatively impact sexual and reproductive behavior, according to the two analyses.
- Women should be given information on and easy access to emergency contraception because individual women can decrease their chances of pregnancy by using the method.

show that increased access does not:

• increase rates of sexually transmitted infections;

• decrease condom use;

• encourage adoption of less reliable contraceptive methods;

• otherwise negatively affect sexual and reproductive behavior.[2]

"Conclusions about population-level effects should not impede efforts to ensure all women have access to emergency contraception when they need it," states one of the analyses.[3] "Women should be given information on and easy access to emergency contraception because individual women can decrease their chances of pregnancy by using the method."

Why didn't pregnancies decrease with advance provision? Trussell points to three examples:

• In a San Francisco study, almost half of the women in the advance provision group who had unprotected intercourse did not use ECPs.[5]

• In a Chinese study, 30 of the 38 pregnancies in the advance provision group occurred in women who did not use ECPs in that cycle.[6]

• In a Nevada/North Carolina study, 57 of the 74 pregnancies in the advance provision group occurred in women who did not use ECPs in that cycle.[7]

The lesson? "ECPs are not used frequently enough," Trussell says.

Check ABCs of ECPs

There are two types of emergency contraceptive pills: combined ECPs, which are ordinary birth control pills containing estrogen and progestin, and progestin-only pills. The hormones that have been studied the most in clinical trials of ECPs are ethinyl estradiol and levonorgestrel or norgestrel.[8] Such hormone combinations are found in 22 brands of combined oral contraceptives available in the United States.

The only progestin-only product available in the United States is Plan B (marketed by Duramed, a subsidiary of Barr Pharmaceuticals; Pomona, NY). It was originally approved by the Food and Drug Administration (FDA) in July 1999 as a prescription-only drug; on Aug. 24, 2006, the FDA approved the nonprescription sale of Plan B for women and men 18 and older. Younger women still need a prescription to buy the drug, and it is sold from behind the pharmacy counter, not the shelf. ***(Contraceptive Technology Update* reported on the nonprescription sale approval in the article "Finally! Emergency contraception given approval by FDA for nonprescription sale," October 2006, p. 109.)**

Use of Plan B continues to climb. Barr Labs sold $11.8 million in Plan B prescriptions in the first six months of 2006, up 41% from the previous year, according to IMS Health, a health care information company.[9]

What about use of the intrauterine device (IUD) for emergency contraception? The copper-T IUD (ParaGard, marketed by Duramed, a subsidiary of Barr Pharmaceuticals; Pomona, NY) can be inserted up to the time of implantation — five to seven days after ovulation — to prevent pregnancy.[8] Due to the difficulty in determining the day of ovulation, many protocols allow insertion up to only five days after unprotected intercourse.[8]

Much more emphasis should be placed on the EC use of the IUD, says **Robert Hatcher**, MD, MPH, professor of obstetrics and gynecology at Emory University in Atlanta. Not only does the woman avoid unintended pregnancy, but she is protected against such risks for up to 10 years, he notes.

According to Hatcher, two important conclusions may be drawn from the recent analyses:

• When a woman and a man do not want to become pregnant, they must make a commitment to never have intercourse without contraception. "This commitment is an 'inside job'; no contraceptive delivery system is as important as a commitment from individuals not to take chances," Hatcher observes.

• All providers of emergency contraception must begin to stress that insertion of a copper-T IUD as an emergency contraceptive is preferable for most women than use of ECPs.

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Update your practice when it comes to IUDs

EXECUTIVE SUMMARY

Updated medical eligibility criteria from the World Health Organization (WHO) and revised product labeling now make the intrauterine device (IUD) available to a wider patient population.

- In a recent survey of young pregnant women ages 14-25, while half of the women said they had heard of the IUD, 71% did not know about its safety, and 58% did not know about its efficacy.
- The WHO eligibility criteria classifies use of IUDs in young women ages 20 and younger, as well as for nulliparous women, as a "2" — situations in which the advantages of using the method generally outweigh the theoretical or proven risks.

Consider the following patients: a 15-year-old young mother, a 30-year-old married woman with no previous pregnancies, a 30-year-old single woman with no children, and a 30-year-old HIV-positive woman with three children. When discussing contraceptive options, do you include intrauterine contraception in talking with these women?

If not, it may be time to rethink your approach. Updated medical eligibility criteria from the World Health Organization (WHO) and revised product labeling now make the intrauterine device (IUD) available to a wider patient population, says **Bryna Harwood**, MD, assistant professor of obstetrics and gynecology and director of family planning at the University of Illinois at Chicago. Harwood reviewed patient guidelines at the recent *Contraceptive Technology* conference in Washington, DC.

The expanded eligibility criteria have not yet translated into increased use, notes Harwood. Take a look at the statistics: Just 2.1% of U.S. women use IUDs.[1] In a recent survey of young pregnant women ages 14-25, while half of the women said they had heard of the IUD, 71% did not know about its safety, and 58% did not know about its efficacy.[1]

Two intrauterine contraceptives are available in the United States: the Mirena levonorgestrel intrauterine system (Mirena LNG IUS, Berlex; Wayne, NJ) and the Copper T 380A intrauterine device (ParaGard IUD, Duramed, a subsidiary of Barr Pharmaceuticals; Pomona, NY). The ParaGard IUD is approved for 10 years of contraception; the Mirena is approved for five years of birth control.[2]

The ParaGard IUD is approved for use for nulliparous women in stable relationships from age 16 through menopause. ***(Contraceptive Technology Update* reported on the labeling change in the article "Intrauterine method sees upswing in use," November 2005, p. 131.)** Women with a history of sexually transmitted diseases or pelvic inflammatory disease (PID) are no longer contraindicated for use of ParaGard, unless a patient currently has acute PID or engages in sexual behavior suggesting a high risk for the disease, the labeling states.

The WHO eligibility criteria classes use of IUDs in young women age 20 and younger, as well as for nulliparous women, as a "2" — situations in which the advantages of using the method generally outweigh the theoretical or proven risks.[3] Clinicians may hesitate to place an IUD in these women due to unfounded concerns about potential increased risk of PID leading to increased risk for tubal infertility. Findings from a case-control study should alleviate such concerns, notes Harwood. Research indicates that the previous use of a copper IUD is not associated with an increased risk of tubal occlusion among nulligravid women.[4]

For HIV-positive women, the WHO gives a classification of "3"— a situation in which the

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theoretical or proven risks usually outweigh the advantages of using the method.[3] Results from a prospective cohort study of HIV-infected and noninfected women in Nairobi, Kenya, suggest, however, that the IUD may be an appropriate contraceptive method for HIV-infected women with ongoing access to medical services.[5]

For women with a Copper T 380A IUD, should there be concerns about use of magnetic resonance imaging (MRI)? Many people have questioned whether it was safe to undergo an MRI exam with a ParaGard in place, now that MRI units have increased Tesla strengths, observes **Miriam Zieman**, MD, adjunct associate professor of obstetrics and gynecology at Emory University in Atlanta. In performing an in-vitro examination of a ParaGard in a 3.0 Tesla MRI unit, the outcomes measured revealed no safety concerns for the use of the device, she notes.[6]

Despite recent changes in the labeling of intrauterine devices, clinicians commonly restrict use of the method.[7] This may be particularly true in the case of nulliparous women, observes Harwood. In researching an IUD checklist screening tool based on the WHO contraceptive eligibility criteria, scientists found that some providers were concerned about placing an IUD in nulliparous women. Why? If conception proved difficult in the future, the IUD and the provider would be blamed for these difficulties.[8]

"I think we have very good evidence to back up the use of the IUD in nulliparous women and not having it increase the risk of tubal infertility," says Harwood.

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. **The semester ends with this issue. You must complete the evaluation form included in this issue and return it in the provided reply envelope that is addressed "Education Department" to receive a certificate of completion.** When your evaluation is received, a certificate will be mailed to you. ■

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.
- **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.

21. According to the Centers for Disease Control and Prevention, the following antibiotics are no longer recommended for treatment of gonorrhea:
A. Ciprofloxacin, ofloxacin, and levofloxacin
B. Ciprofloxacin, ofloxacin, and ceftriaxone
C. Ceftriaxone, ofloxacin, and levofloxacin
D. Ciprofloxacin, ofloxacin, and cefixime

22. Research indicates that the human papillomavirus (HPV) vaccine candidate Cervarix provides protection against _____.
A. HPV 6 and HPV 11
B. HPV 16 and HPV 18
C. HPV 6 and HPV 16
D. HPV 11 and HPV 18

23. Results from three randomized, controlled trials suggest that male circumcision reduces the risk of heterosexually acquired HIV infection in men by approximately _____.
A. 20%
B. 40%
C. 60%
D. 80%

24. Medical eligibility criteria from the World Health Organization classes use of intrauterine devices in young women ages 20 and younger, as well as for nulliparous women, as
A. 1 — Can use the method. No restriction on use.
B. 3 — Should not use the method unless clinician makes clinical judgment that the patient can safely use it. Theoretical or proven risks usually outweigh the advantages of method.
C. Should not use the method. Condition represents an unacceptable health risk if method is used.
D. 2 — Can use the method. Advantages generally outweigh theoretical or proven risks.

Answers: 21. A; 22. B; 23. C; 24. D.

Why do family planners look to intrauterine contraception? Consider the following four reasons, says Harwood:

- It has the highest efficacy possible.
- It is safer than tubal sterilization.
- It is the second most long-acting method.
- It requires attention only at insertion and removal.[9]

What is the trouble with IUDs? "More women don't have one," says Harwood.

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