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Interpreting News and Research on Contraceptives and STIs

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Dramatic upswing reported in use of intrauterine devices

National data mirror findings: Over 2 million U.S. women now use IUDs

For the past decade, subscribers to *Contraceptive Technology Update* have been asked questions about their prescribing practices. The question "In the past year, how many IUDs have you personally inserted?" was first included in the 2001 survey in light of the 2000 introduction of the Mirena levonorgestrel IUD (Bayer HealthCare Pharmaceuticals, Wayne, NJ.) In that survey, just 3.4% of 2001 respondents said they inserted 25 or more IUDs, and 9.7% said they inserted 11-25 IUDs.

Look at results from the 2010 survey. A total of 30% of survey respondents said they inserted 25 or more IUDs in the last year, and 12% said they inserted 11-25 IUDs.

The latest installment of the National Survey of Family Growth (NSFG) tracks a similar rise in use. In 1995, just one percent was using the IUD, according to the NSFG. In the latest 2006-2008 NSFG statistics, 5.5% of contraceptors — 2.1 million women — were currently using IUDs.[1]

Planned Parenthood of Illinois in Chicago also has seen a dramatic increase in the use of IUDs, primarily due to provider comfort with the method and staff educating about the benefits of long-acting reversible contraception, says **Kai Tao**, ND, MPH, CNM, vice president of clinical

Contraceptive Technology Update debuts new quarterly OB/GYN supplement

Be sure to check out OB/GYN Quarterly Update, our new quarterly publication inserted in this issue. The supplement is an addition to your existing subscription, and is designed to enhance your clinical skill set with evidence-based information on women's health issues.

operations and associate medical director.

Clinicians at Thomas Jefferson Health District in Charlottesville, VA, are seeing more IUD users, especially Mirena users, says **Leslie Steeves**, CNM, a certified nurse midwife at the facility. Steeves estimates she inserted approximately 40% more Mirena devices this year than in 2009.

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EXECUTIVE SUMMARY

Over the past five years, a review of responses from the *Contraceptive Technology Update* Contraception Survey shows increased use of intrauterine contraception. The number of survey respondents who said they inserted 25 or more devices in the last year rose from 7% in 2005 to 30% in 2010.

- The latest statistics from the National Survey of Family Growth confirm that more women are using the IUD. More than 2 million U.S. contracepting women use the IUD, statistics show.
- The most dramatic increase in IUD use is found in the Contraceptive Choice project in St. Louis, where 56% of women are choosing the IUD.

Providers at Richmond City Health District in Richmond, VA, are inserting more IUDs as a result of a grant from the Community Foundation of Richmond and Central Virginia and the Jenkins Foundation, both of Richmond, that awarded money for long-term contraceptive use, says **Sulola Adekoya**, MD, lead physician at the facility.

While the uptick in use is good, the United States has ground to gain when it comes to use of intrauterine contraception, says **Andrew Kaunitz**, MD, professor and associate chair in the obstetrics and gynecology department at the University of Florida College of Medicine — Jacksonville. Among women in Denmark and Germany who use contraception, 24% and 17%, respectively, use an IUD.[2] In France, 17.3% of married women ages 15-49 rely on the device.[3]

"In parts of Europe, particularly Northern Europe, the prevalence of IUD use is substantially higher than in the U.S. and the rate of unintended pregnancy and induced abortions is lower than in U.S. women," observes Kaunitz. "Our patients will certainly benefit if they become more 'European' in their contraceptive choices by more frequently choosing IUDs."

LARC in focus

Intrauterine device use is being examined as part of the Contraceptive Choice project in St. Louis. The project is designed to promote reversible long-term methods of contraception such as subdermal implants and intrauterine devices and to assess satisfaction and discontinuation rates with various contraceptive methods. *(Read more about the project; see "Check opportunities for long-acting methods," March 2010, p. 27.)*

In preliminary results from the project, almost

70% of the participants chose long-acting methods; 56% chose IUDs and 11% chose implants.[4] A 2010 analysis of data indicates once financial barriers were removed and long-acting reversible methods of contraception were introduced to all potential participants as a first-line contraceptive option, two-thirds of women in the project chose long-acting reversible methods of contraception.[4]

Who can use the IUD?

Two intrauterine contraceptives are available in the U.S.: the ParaGard Copper T 380A IUD (Duramed Pharmaceuticals, Pomona, NY) and the Mirena levonorgestrel intrauterine system (LNG-IUS).

According to *A Pocket Guide to Managing Contraception*, women may use intrauterine contraception if

- they are nulliparous or multiparous,
- are young or older until menopause,
- have had a sexually transmitted infection in the past,
- have had an ectopic pregnancy in the past,
- are not in a monogamous relationship, or
- have fibroids that do not distort the uterine cavity.[5]

In addition, intrauterine contraception may be inserted immediately postpartum in the delivery room. The Copper-T IUD may be used for emergency contraception, while the LNG-IUS may be used to help manage endometriosis, adenomyosis, fibroids, and dysfunctional uterine bleeding.[5]

Counsel women thoroughly about the advantages and disadvantages of both forms of intrauterine contraception. In talking about its effectiveness, help women to think of intrauterine contraception as "reversible sterilization." Women need to know that either intrauterine contraceptive may be removed at any time.[5]

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Which methods are winning in popularity?

More women may be moving toward use of the contraceptive vaginal ring, implant, and intrauterine device (IUD), but combined oral contraceptives (OCs) continue to lead as a top birth control choice. About 42% of respondents to the 2010 *Contraceptive Technology Update* Contraception Survey said more than half of their patients use OCs. While this number reflects a decrease from 2009's 57% level, clinicians say pills remain a popular choice with patients.

The numbers haven't changed much at the Family Planning Center of Ocean County in Lakewood, NJ, says **Chris Ann Lemkan**, APN-C, a nurse practitioner at the facility. If women can use it, the most popular method in still the birth control pill, Lemkan states.

While use of the contraceptive patch Evra (Ortho Evra, Ortho Women's Health & Urology, Raritan, NJ) and the vaginal ring NuvaRing (Merck & Co., Whitehouse Station, NJ) have increased in use in the last year at Casper-Natrona County Health Department in Casper, WY, about 70% of patients still use OCs, says **Tia Hansuld**,

EXECUTIVE SUMMARY

Although combined oral contraceptives (OCs) continue to lead as a top birth control choice, the popularity of pills is decreasing. About 42% of respondents to the 2010 *Contraceptive Technology Update* Contraception Survey said more than half of their patients use OCs. While this number reflects a decrease from 2009's 57% level, clinicians say pills remain a popular choice with patients.

- More than 90% of survey respondents say their facilities are offering the contraceptive vaginal ring. About 57% of survey respondents now offer the implant.
- Less than three-quarter (73%) of survey respondents say their facility now offers the contraceptive patch. This is down from 2009, when 83% of survey respondents indicated their facilities provided the patch.

FNP, a nurse practitioner at the facility. Most patients choose the method because it is less expensive, she reports.

Check the options

More women are opting for the contraceptive vaginal ring, say survey respondents. About 92% offer or plan to offer the method, up from 2009's 88% figure.

The clients who like NuvaRing love it, observes **Ingrid Silva**, ANP, a nurse practitioner at El Paso County Department of Health and Environment in Colorado Springs, CO. It was a slower start as a method, but it has gained a positive response, she notes.

What is the best way to initiate contraceptive ring use? According to *A Pocket Guide for Managing Contraception*, teach the woman to insert and remove the ring in the office. Clinicians should ask women if they would like for the clinician to insert a ring following a pelvic exam to demonstrate just how little women will feel an inserted ring.[1]

Women also are choosing longer-acting methods, such as the contraceptive implant Implanon. (Merck & Co.) A single implant inserted under the skin of the upper arm, Implanon releases the progestin etonogestrel at an initial rate of 60 mcg per day, decreasing to 25-30 mcg per day by the end of year three. The method is effective for at least three years.[1] It is considered a top-tier method in contraceptive effectiveness, along with the intrauterine device, female sterilization, and vasectomy.[1] About 57% of survey respondents now offer the implant.

"So far this year, I have inserted 23 Implanons," says **Marnie Schumacher**, ARNP, a nurse practitioner at Grays Harbor County Public Health Department in Aberdeen, WA. "I actually have three clients that are on their second Implanon, the first one being in for three years, and they liked it so much they wanted a second one."

Clinicians at Thomas Jefferson Health District in Charlottesville, VA, also insert Implanons, but that number is not growing, says **Leslie Steeves**, CNM, a certified nurse midwife at the facility. The breakthrough bleeding experienced with the method is a still a significant issue for many women, says Steeves. "Although there are those that I am now taking out at three years and putting in another one, I wish I had a crystal ball to know who would do well on it and who wouldn't," she observes.

Counseling is an important point when it comes to successful use of the progestin-only contraceptive implant, according to **Michael Policar**, MD, MPH, associate clinical professor of obstetrics, gynecology, and reproductive sciences at the University of California, San Francisco (UCSF) School of Medicine and medical director of the UCSF Program Support and Evaluation for the California Family PACT (Planning, Access, Care, and Treatment) Program. Policar presented information on new contraceptive methods in a recent audio conference.[2] Advise women that they will have fewer bleeding episodes, and that they will have the same or fewer bleeding days, said Policar. However, also tell them that their bleeding days/episodes will be unpredictable, and they might have more spotting days than before.[2]

Patch use drops

Use of the Evra contraceptive patch has dropped according to 2010 survey responses. Seventy-three percent say their facility now offers the option, down from 83% of 2009 survey respondents. This statistic continues a trend of decreased use. In 2005, 93% of respondents said their facility provided the method as a contraceptive option.

The Evra product label was revised in 2005, 2006, and 2008 due to the fact that the patch exposes women to higher levels of estrogen than most birth control pills. The 2008 labeling change included the results of an epidemiology study that found that users of the birth control patch were at higher risk of developing venous thromboembolism than women using birth control pills.[3,4] *(*Contraceptive Technology Update *reported on the study; see "FDA updates study data information on Ortho Evra contraceptive patch labeling," April 2008, p. 37.)*

The Evra patch might see competition. Agile Therapeutics of Princeton, NJ, has completed enrollment in its Phase III clinical trial of a transdermal contraceptive containing ethinyl estradiol (EE) and levonorgestrel (LNG). According to a pharmacokinetic study, the estrogen level in the AG200-15 patch EE dose is equivalent to an oral dose of about 30 mcg, while its LNG dose is comparable to approximately 100 mcg of an oral dose.[5]

The company also is developing a progestin-only transdermal contraceptive with an eye toward breastfeeding women who desire birth control, as well as for those women in which estrogen use is contraindicated. The patch under development is designed as a weekly patch using levonorgestrel as

Survey Profile

A total of 103 providers participated in the 2010 *Contraceptive Technology Update* (CTU) Contraception Survey, which monitors contraceptive trends and family planning issues among readers. A total of 767 surveys were mailed, with a response rate of 14.7%. Results were tallied and analyzed by AHC Media in Atlanta, publisher of CTU and more than 60 other medical newsletters and sourcebooks.

About 75% of responses came from nurse practitioners or registered nurses. Physicians represented about 12% of the responses, with health educators/counselors comprising less than 1% of the response group. About 12% listed other professions. About 82% of respondents identified themselves as care providers, with nearly 16% involved in administration and 2% in teaching.

More than half (62%) said they worked in public health facilities, with about 8% employed at private practice settings. About 9% listed student health centers as their place of employment, with about 5% working in hospitals. The remaining 16% reported employment in other settings.

When it comes to location of their employment, about 40% said they worked in an urban location. About 33% said they were employed in a rural area, while about 25% listed a suburban setting. ■

its progestin. Two formulations are being investigated: approximately 75 mcg/day and approximately 40 mcg/day.

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What OCs do clinicians prescribe most often?

The next chart in your inbox is for a healthy 21-year-old nonsmoking woman. She indicates she is interested in using an oral contraceptive (OC) for birth control. What pill do you prescribe?

Ortho Tri-Cyclen Lo (Ortho-McNeil Pharmaceutical; Raritan, NJ) continues as the top pick for young women when no formulary issues dictate pill selections, a spot it has held since 2008. *(See graphic on p. 18.)*

Ortho Tri-Cyclen was named as top pill for this age category when clinicians are bound by available pills in their formulary, changing positions from last year's number two spot. Ortho Tri-Cyclen Lo was the top formulary pill in the 2009 poll.

Ortho Tri-Cyclen Lo is a triphasic pill which contains 25 mcg of ethinyl estradiol for 21 days and three doses of the progestin norgestimate (180 mcg daily/days 1-7; 215 mcg daily/days 8-14; 250 mcg daily/days 15-21). Ortho Tri-Cyclen also is a triphasic pill using the same progestin levels, but with 35 mcg of ethinyl estradiol.

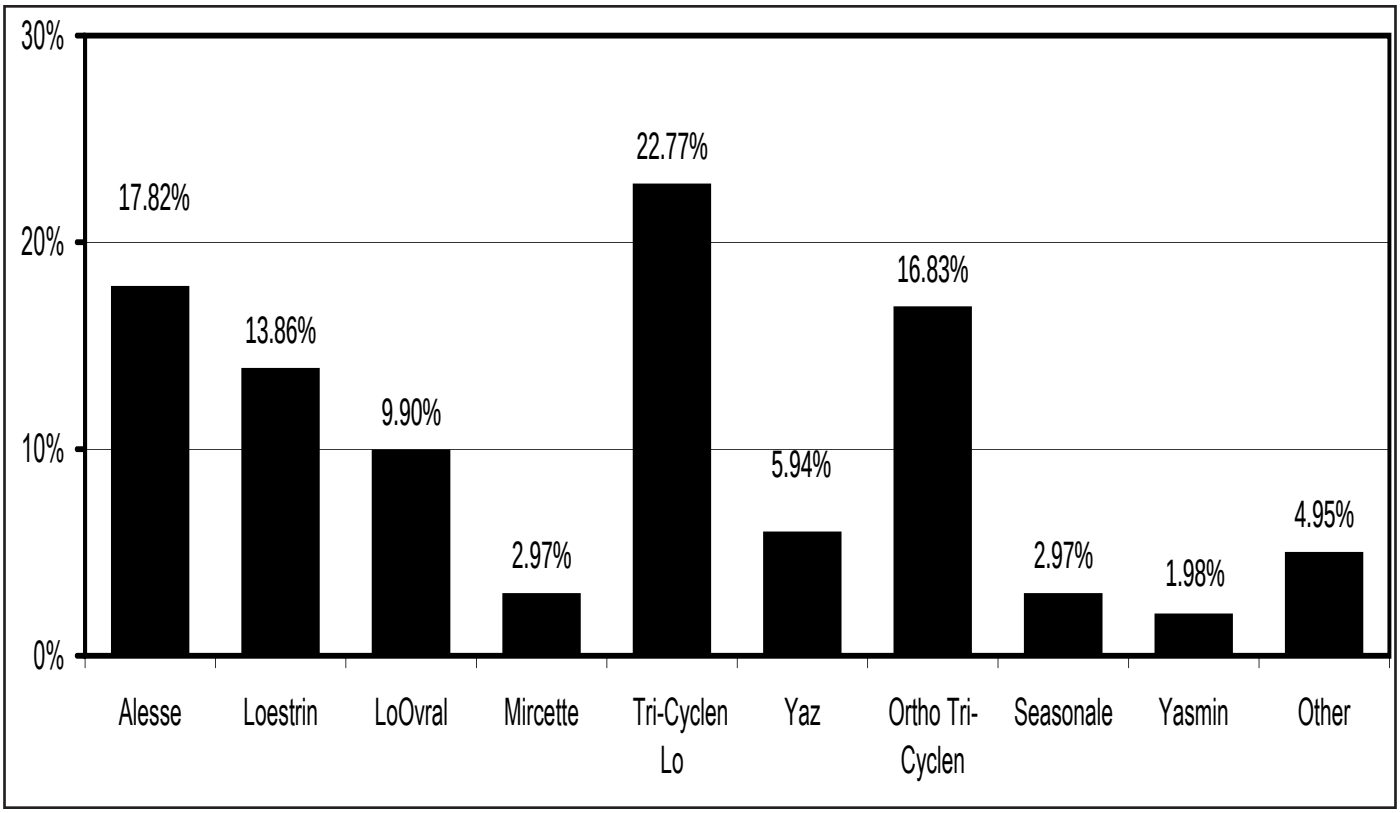
Alesse, a monophasic 20 mcg pill from Wyeth

EXECUTIVE SUMMARY

Ortho Tri-Cyclen Lo continues as the 2010 *Contraceptive Technology Update* Contraception Survey's pick for young women when no formulary issues dictate pill selections, a spot it has held since 2008. When bound by available pills in the formulary, Ortho Tri-Cyclen was named as top pill for this age category.

- Alesse, a monophasic 20 mcg pill, was named the pill of choice for older women, named by 42% of 2010 survey respondents. The pill also continues as the leading option for women who have experienced nausea when using previous pills.
- More than half of survey respondents say their use of generic OC formulations has increased due to budget constraints. About 62% of 2010 respondents say they have increased use of generic brands, as did 68% in 2009.

Assume you could prescribe any pill for a woman initiating combined pills and there were no formulary issues dictating which pills you could prescribe. Which pill would you (or a clinician in your program) prescribe for a 21-year-old nonsmoking woman?



Pharmaceuticals of Collegeville, PA, remains in its top spot as the pill of choice for older women, named by 42% of 2010 survey respondents. *(See graphic on p. 19.)* It is followed by 2009's leader, Loestrin, another 20 mcg pill from Teva Pharmaceuticals USA, North Wales, PA. A total of 17% of respondents named it as first choice for a 42-year-old nonsmoking woman.

Alesse also continues as the leading option for women who have experienced nausea when using previous pills. The pill has been named the top choice in this category since 1999. Ortho Tri-Cyclen Lo was named as the second-choice pill.

Check generic OC use

More than half of survey respondents say their use of generic OC formulations has increased due to budget constraints. About 62% of 2010 respondents say they have increased use of generic brands, as did 68% in 2009.

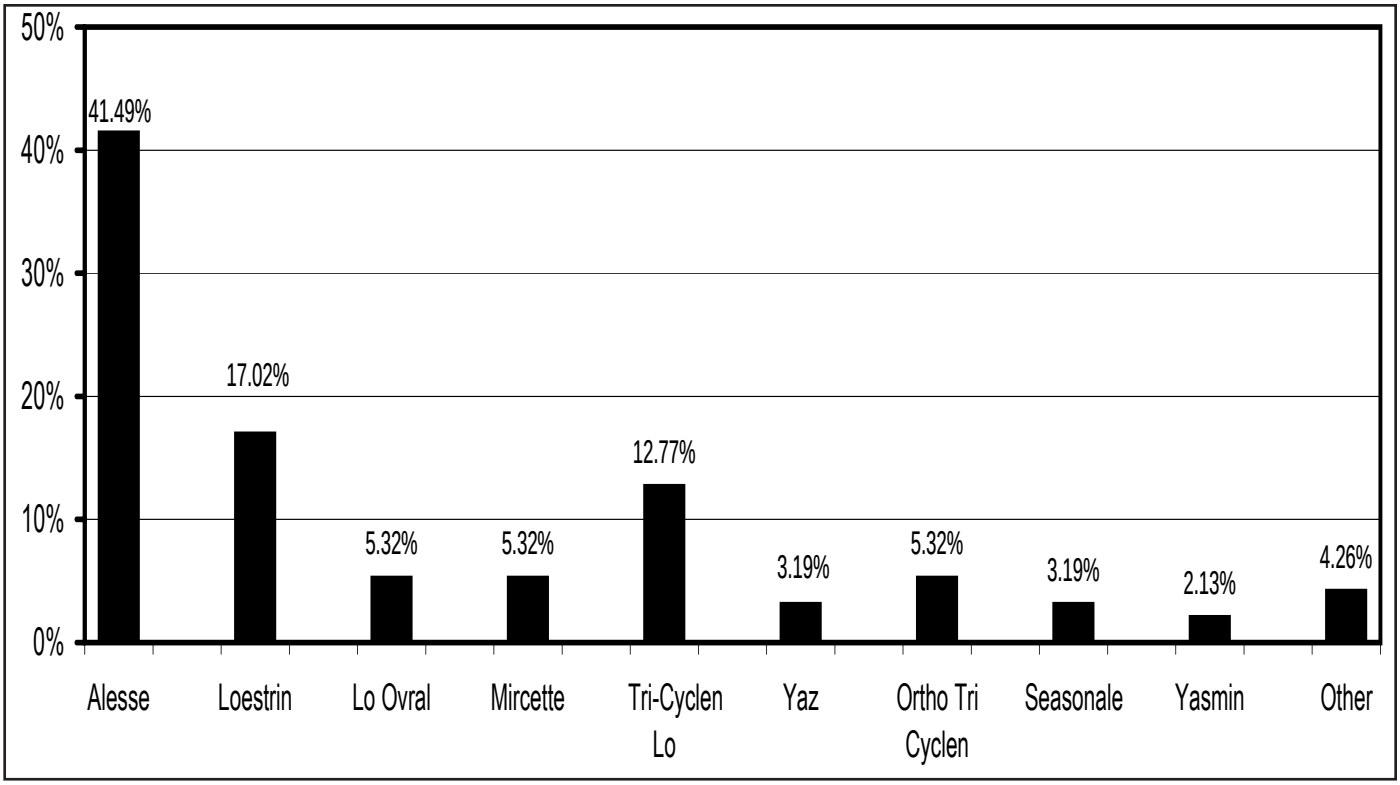
Clinicians at Planned Parenthood of Illinois in Chicago consistently have been using generic oral contraceptives, says **Kai Tao**, ND, MPH, CNM, vice president of clinical operations and associate medical director. "We do lots of education to our patients that 'a pill is a pill, is a pill'," says Tao.

Using generic pills has not impacted practice for **Marnie Schumacher**, ARNP, a nurse practitioner at Grays Harbor County Public Health Department in Aberdeen, WA. "Our clients are very accepting of generic brands, and if they prefer the brand name, I can always write a prescription with a 'do not substitute,'" says Schumacher.

Patients are pleased to find that generic pills are available when they are beginning use of oral contraceptives, says **Susan Krasner**, CNM, MS, APRN, a certified nurse midwife at Dartmouth-Hitchcock Nashua Obstetrics and Gynecology in Nashua, NH. "We also have many patients who take advantage of Wal-Mart discounted pharmacy products," says Krasner. "Many patients will call the office to be changed to a generic formula if copayment is too high on brand name OCs."

Insurance formularies can influence what pill is prescribed, says **Donna Price**, ARNP, a nurse practitioner at Duval County Health Department in Jacksonville, FL. "I find that I am ordering pills to meet the requirements of the insurance that they are on rather than the pill I would like to order," says Price.

Assume you could prescribe any pill for a woman initiating combined pills and there were no formulary issues dictating which pills you could prescribe. Which pill would you (or a clinician in your program) prescribe for a 42-year-old nonsmoking woman who wants to use combined pills?



Can smokers use OCs?

If a healthy patient who is 23 years old and smokes 10 cigarettes a day says she would like to use the Pill, would you write a prescription? Almost 100% of 2010 survey respondents said they would. Ninety-nine percent checked "yes" for prescribing pills to women ages 20-24 who smoke 10 cigarettes per day.

The U.S. Medical Eligibility Criteria for Contraceptive Use rates use of combined hormonal contraceptives for smokers under age 35 as a 2 — a condition for which the advantages of using the method generally outweigh the theoretical or proven risks.[1]

However, when it comes to a 40-year-old woman who smokes 10 cigarettes a day, clinicians are just as emphatic in not providing pills. A total of 96% of 2010 survey respondents said they would not write a pill prescription for such women. The U.S. eligibility guidelines rank combined hormonal contraceptive use for women age 35 or older who smoke less than 15 cigarettes per day as a 3 — a condition for which the theoretical or proven risks usually outweigh the advantages of using the method. For women in the same age range who smoke 15 cigarettes or more per day, the guidelines rank combined hormonal contraceptive use as a 4 — where the condition represents an unacceptable health risk if the method is used.[1]

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Clinicians reveal strategies on OC use

When it comes to providing oral contraceptives (OCs) to patients for the first time, 87% of respondents to the 2010 *Contraceptive Technology Update* Contraception Survey say they choose Quick Start, the immediate initiation of the hormonal method in the office. The figure is in line with 2009 statistics, which underlines clinicians' confidence in the practice.

Using Quick Start has improved the number of women initiating birth control on the first visit, says **Sulola Adekoya**, MD, lead physician at Richmond City Health District, Richmond, VA.

Quick Start eliminates the gap between decision and implementation, said **Alison Edelman**, MD, MPH, associate professor in the department of obstetrics and gynecology and assistant director of the Family Planning Fellowship at Oregon Health and Science University in Portland. Edelman presented on the topic at the 2010 Contraceptive Technology conference.[1] The practice is endorsed by the World Health Association, Edelman noted. When used with the contraceptive pill, vaginal ring (NuvaRing, Merck & Co., Whitehouse Station, NJ) and the contraceptive injection depot medroxyprogesterone acetate (Depo-Provera, Pfizer, New York City; Medroxyprogesterone Acetate Injectable Suspension, USP, Teva Pharmaceuticals USA, North Wales, PA), research suggests the practice can lead to higher initiation rates, higher short-term continuation rates (in the pill only), and lower pregnancy rates.[2] Using Quick Start is acceptable to women, Edelman stated.

If a clinician is reasonably certain that a woman is not pregnant, Quick Start of contraception can begin. Provide emergency contraception (EC) if indicated, and advise backup contraception for seven days.[1]

Yes to extended regimen

Kim Burtle, CMN, director of the Women's Health Care Clinic in Torrance, CA, says prescription of extended or continuous regimen oral contraceptives has increased in the last year. What has led to the increase? Patient requests, she reports. *[Help patients understand menstrual suppression. Use the Association of Reproductive Health Professionals patient handout, "Understanding Menstrual Suppression," available with the online issue. For assistance, contact customer service at customerservice@ahcmedia.com or (800) 688-2421.]*

About 53% of 2010 Contraception Survey respondents say they increased use of such pill regimens in the last year, down slightly from 2009's 59% percentage.

Extended use of pills might mean one of four strategies, according to *A Pocket Guide to Managing Contraception*:

- manipulation of a cycle to delay one period for a trip, honeymoon, or a sporting event;
- use of active hormonal pills for more than 21 consecutive days followed by 2-7 days hormone-free days;
- continuous daily OCs for at least 21 pills, but after that, may break for two to seven days if spotting or breakthrough bleeding is bothersome; or
- use of a monophasic pill indefinitely.[3]

Pills in postpartum?

After what period of time postpartum do most clinicians recommend pill initiation? About 38% of 2009 survey respondents say they would start combined pills in new moms who are not breastfeeding from three weeks to three weeks and six days postpartum, with about 14% indicating initiation from one week to two weeks and six days postpartum, and 17% stating pill starts upon hospital discharge.

When it comes to use of progestin-only pills in breastfeeding women, 29% said they would issue the pills on hospital discharge. A total of 28% said they would start progestin-only pills from three weeks to three weeks and six days postpartum, and 14% indicated start dates from one week to two weeks and six days postpartum.

If a new mother is not breastfeeding, the U.S. Medical Eligibility Criteria for Contraceptive Use rates use of combined hormonal contraceptives in two time increments:

- less than 21 days postpartum: 3 (a condition for which the theoretical or proven risks usually outweigh the advantages of using the method);
- 21 or more days: 1 (a condition for which there is no restriction for the use of the contraceptive method).

In the case of progestin-only pills for breastfeeding mothers, the criteria offer three time segments:

EXECUTIVE SUMMARY

When it comes to providing oral contraceptives (OCs) to patients for the first time, 87% of respondents to the 2010 *Contraceptive Technology Update* Contraception Survey say they choose Quick Start, the immediate initiation of the hormonal method in the office.

- About 53% of 2010 Contraception Survey respondents say they increased use of extended pill regimens in the last year.
- While emergency contraceptive pills (ECPs) can be provided from behind the counter for people ages 17 and older, many clinicians continue to provide ECPs in advance for their patients. A total of 67% say they offer advance EC provision.

• less than one month postpartum: 2 (a condition for which the advantages of using the method generally outweigh the theoretical or proven risks);
• one month to less than six months postpartum: 1;
• six months or more postpartum: 1.[4]

How to provide EC?

While emergency contraceptive pills (ECPs) can be provided from behind the counter for people ages 17 and older, many clinicians continue to provide ECPs in advance for their patients. More than two out of three (67%) say they offer advance EC provision.

Clinicians at Comprecare Clinic in San Jose, CA, continue to prescribe Plan B (Teva Pharmaceuticals USA) because patients can't afford it to purchase it over the counter (OTC), says **Lisa Friedrichs-Sherard**, OB-GYN NP, a nurse practitioner at the facility.

Nora Lewis, CNM, a certified nurse midwife with Santa Barbara County Public Health Department in Santa Maria, CA, reports a similar situation. Lewis says that clinicians provide advance prescriptions for EC or provide Next Choice (Watson Pharmaceuticals) in the clinic since the drug is covered by the state family planning program. The OTC version would be an out-of-pocket expense for the client, notes Lewis.

Tia Hansuld, FNP, a nurse practitioner at Casper-Natrona County Health Department in Casper, WY, says, "We don't often write advance prescriptions for ECP, but will provide a package of Plan B for them to keep at home if the need arises, especially if they do not want contraception other than condoms."

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TEEN TOPIC

Emergency contraception changes may benefit teens

By **Anita Brakman**, MS
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Physicians for Reproductive Choice and Health
New York City
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Clinical Professor of Pediatrics
University of Pittsburgh School of Medicine
Staff Physician
University of Pittsburgh Student Health Service

An important change might be on the horizon for adolescents seeking emergency contraception (EC). On Nov. 16, 2010, the Center for Reproductive Rights filed a motion charging the United States Food and Drug Administration (FDA) of being in contempt for ignoring a March 2009 court order to end age restrictions of the EC product, Plan B.

Women ages 16 years of age and younger are required to get a prescription, while older women can access this medication over the counter (OTC) in pharmacies. The court recognized that there are no medical contraindications to EC use in female adolescents.[1] Additionally, recent studies agree that females under age 17 are clearly able to comprehend EC labeling in order to use the medication appropriately and effectively.[2,3] Finally, the decision reflects professional consensus among organizations including the American Congress of Obstetricians and Gynecologists, American Academy of Pediatrics, and Society for Adolescent Health and Medicine, which have all recommended OTC access regardless of age.[4-6]

This potential change in EC access is one of many changes that have occurred in relation to this important medication for pregnancy prevention after unprotected sex or contraceptive failure. First, the very product that this lawsuit centers on has undergone a change in name and formulation. When Plan B was first marketed in the United States, it consisted of two tablets each containing 0.75mg of levonorgestrel. After research showed that taking the two tablets at one time was just as safe and effective as the FDA-approved regimen of

taking the two tablets 12 hours apart,[7] it became common practice for clinicians to recommend a single-dose regimen.

In July 2009, the FDA approved Plan B One-Step, a single tablet EC containing 1.5mg of levonorgestrel that has now replaced the original Plan B on the market. In June 2009, the first generic EC was approved by the FDA. NextChoice is a generic version of the original Plan B including two tablets, each containing 0.75mg levonorgestrel. Similar to all Plan B branded products, NextChoice is available OTC for women ages 17 years and older, but younger adolescents still require a prescription.

While safety and efficacy profiles are the same between the two products, the generic might be more desirable for adolescents who are paying for the medications out of pocket or using insurance, which often provides better coverage for generic medications. Plan B One-Step ranges in price from $35-60, while NextChoice is generally priced about 10% less.[8]

Yet another change is the entrance of a new form of EC on the market, ella. Ella consists of one 30mg tablet of ulipristal acetate, a progesterone receptor modulator that works primarily by inhibiting or delaying ovulation. Ella is available by prescription only to all women regardless of age, and it costs about $55.[8] While increased cost might be a barrier for women, especially teens, the fact that it maintains consistent efficacy for 120 hours, rather than declining over this time period compared to levonorgestrel, offers women a longer window with which to access highly effective EC.[7,9,10]

Continue advance Rxs

The prescription requirements for all of the EC products described above make it essential that clinicians continue to provide advance prescriptions for EC products to patients, especially those ages 16 years and younger. Contrary to critics' claims that advance provision will lead to increased risk taking, research has shown advance provision among adolescents increases use and decreases delays in taking the medication, but not does increase the likelihood they will engage in unprotected sex.[11]

To reduce the lengthy process that prescription requirements create, ella has integrated an online prescription service into its web site that allows users to submit medical information to physicians electronically and receive the medication overnight by mail. *(See resource box, p. 23.)* Unfortunately, many adolescents will not have access to a credit card necessary to use the online service. Also, service and shipping costs for online ordering bring the cost up to $77.[8]

Clinicians can stay updated on prescription requirements and age restrictions for EC by visiting the Emergency Contraception Website, not-2-late.com. Patients also can visit the site to get more information on the whole range of EC products, as well as referrals to local clinicians who can provide EC.

COMING IN FUTURE MONTHS

- Science eyes pill for HIV prevention
- News from the front: chlamydia, syphilis rates increase
- Update your EC information database
- Research investigates vaginal contraceptive
- What works for urinary tract infections?

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SOURCE

To access ella's integrated online prescription service, go to www.ella-rx.com. Click on "Where do I get ella," then "Need a prescription for ella?"

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CTUPDATES

News ■ Resources ■ Events

New publication to focus on STD statistics, trends

The Centers for Disease Control and Prevention has just released Sexually Transmitted Disease Surveillance, 2009. The report presents statistics and trends for sexually transmitted diseases (STDs) in the United States through 2009.

This annual publication, designed as a reference document for policy makers, program man-

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 June issue, you must complete the evaluation form provided and return it in the reply envelope provided in that issue to receive a letter of credit. When your evaluation is received, a letter 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.

5. The contraceptive implant Implanon releases the progestin etonogestrel at an initial rate of:
A. 60 mcg per day.
B. 80 mcg per day.
C. 100 mcg per day.
D. 150 mcg per day.

6. The U.S. Medical Eligibility Criteria for Contraceptive Use rates use of combined hormonal contraceptives for smokers under age 35 as a:
A. 1 — no restrictions on use.
B. 2 — a condition for which the advantages of using the method generally outweigh the theoretical or proven risks.
C. 3 — a condition for which the theoretical or proven risks usually outweigh the advantages of using the method.
D. 4 — where the condition represents an unacceptable health risk if the method is used.

7. If a new mother is not breastfeeding, the U.S. Medical Eligibility Criteria for Contraceptive Use rates use of combined hormonal contraceptives after 21 or more days postpartum as:
A. 1
B. 2
C. 3
D. 4

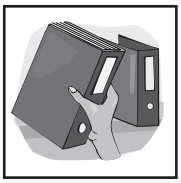
8. According to A Pocket Guide to Managing Contraception, which of the following women may NOT use intrauterine contraception?
A. Those who have had a sexually transmitted infection in the past.
B. Those who have had an ectopic pregnancy in the past.
C. Those who are not in a monogamous relationship.
D. Those who have fibroids that distort the uterine cavity.

Answers: 5. A; 6. B; 7. A; 8. D

agers, health planners, and researchers, presents information in four sections. The national profile section provides an overview of STD morbidity in the United States, with accompanying text identifying major findings and trends for selected STDs. The special focus profiles section looks at selected subgroups and populations, such as women and infants, adolescents and young people, and men who have sex with men. The tables section offers statistical information about STDs at county, metropolitan statistical area, regional, state, and national levels.

View the document at the CDC web link, http://www.cdc.gov/std/stats09/default.htm. ■

BINDERS AVAILABLE



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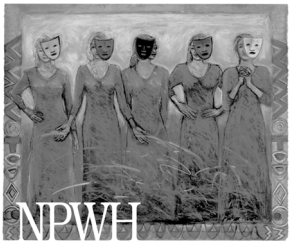

OB/GYN
QUARTERLY UPDATE

Does availability of screening mammography significantly reduce breast cancer mortality?

Abstract & Commentary

By **Jeffrey T. Jensen**, MD, MPH, Editor, *OB/GYN Clinical Alert*, also published by AHC Media, and **Leon Speroff**, Professor and Vice Chair for Research, Department of Obstetrics and Gynecology, Oregon Health & Science University, Portland.

Synopsis: The availability of screening mammography in Norway did not result in a significant reduction in breast cancer mortality after subtracting the effect of improved cancer treatment.

Source: Kalager M, Zelen M, Langmark F, et al. Effect of screening mammography on breast-cancer mortality in Norway. *N Engl J Med* 2010; 363:1203-1210.

To assess the effect of screening mammography on breast cancer mortality, the authors used data from the Norwegian Breast Cancer Screening Program to observe chronologic trends associated with screening as well as advances in breast cancer awareness and treatment. The Norwegian Breast Cancer Screening Program offered women between the ages of 50 and 69 years screening mammography every two years. The authors compared the incidence-based rates of death from breast cancer in four groups: two groups of women that from 1996 through 2005 were living in counties with screening (screening group) or without screening (nonscreening group); and two historical comparison groups that from 1986 through 1995 mirrored the current groups.

Analyzing data from 40,075 women with breast cancer, the death rate was reduced by 7.2 deaths per 100,000 person-years in the screening group as compared with the historical screening group (rate ratio [RR], 0.72; 95% confidence interval [CI], 0.63-0.81) and by 4.8 deaths per 100,000 person-years in the nonscreening group as compared with the historical nonscreening group (RR, 0.82; 95% CI, 0.71-0.93). This yielded a nonsignificant relative reduction in mortality of 10% in the screening group. The difference in the reduction in mortality between the current and historical groups that could be attributed to screening alone was 2.4 deaths per 100,000 person-years, or a third of the total reduction of 7.2 deaths. The authors concluded that the implementation of a screening mammography program explained only one-third of the reduction in breast cancer mortality.

Commentary

Whether routine screening mammography results in a clinically important reduction in the risk of breast cancer mortality remains a hotly contested issue. In November 2009, the U.S. Preventive Services Task Force (USPSTF) released revised recommendations for breast cancer screening.[1] The USPSTF recommended

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against routine screening mammography in women ages 40-49 years and concluded that the risk of harm attributable to screening exceeds the potential benefit for low-risk women. Mammography was recommended for women ages 50-74 years, but only every two years, and the USPSTF concluded that the evidence of additional benefits and harms of screening mammography in women 75 years or older was inconclusive. The task force also found the evidence insufficient to recommend clinical breast examination in women age 40 or older that undergo mammography and determined that teaching breast self-examination (BSE) is not longer recommended.

I reviewed these guidelines and background information including positions from ACOG and the American Cancer Society (both recommend annual mammograms starting at age 40) in the January 2010 issue of *OB/GYN Clinical Alert*.[2] The primary benefit of screening at an earlier age is a reduction in mortality and the risk is unnecessary interventions; annual mammograms starting at age 40 instead of age 50 and continued to age 69 will prevent one additional cancer death (8.3 vs 7.3) for every 1,000 women screened at the expense of 63 unnecessary biopsies. In other words, 10 additional years of mammogram screening yields a 6% chance of getting a biopsy but only a 0.1% chance of avoiding cancer mortality. If women are screened every other year starting at age 40 until age 69, there will be 70 fewer biopsies per 1000 women, but two additional women/1,000 will die from breast cancer.[3]

While we should not dismiss the burden of screening, most of us consider death an even less desirable outcome. However, if the observed reduction in breast cancer mortality is not associated with mammography screening, but is instead due to other factors, mammogram screening should be abandoned. The recent publication of data from the Norwegian Breast Cancer Screening Program put this issue back in the public eye again, so prepare for more calls from patients.

To determine whether the results of the Norwegian study provide guidance to U.S. clinicians, let's look at the screening program itself. Norway has a population of 4.8 million and a public health care system. Patients generally receive treatment in their county of residence, and there is no private primary care (e.g., mammograms) for breast cancer. The Breast Cancer Screening Program (BCSP) began as a pilot project in four of the 19 Norwegian counties in 1996, but it was expanded to the remaining 15 counties over the next nine years, and it has offered screening mammography to all women between the ages of 50 and 69 since 2005.

Women receive an invitation by mail to participate in screening, and 77% of all women who are invited participate in the program and obtain a standard two-view film mammogram. Breast cancer specialty services are centralized for all residents within each county; establishing these specialty teams was a prerequisite to participation in the BCSP.

In an attempt to avoid confounding due to improvements in treatment and heightened awareness due to the establishment of the breast specialty services, the authors compared death rates in counties with and without screening before and after the introduction of the BCSP. They first compared women in the nonscreening group with their historical counterparts to determine the temporal change in mortality that was not attributable to the introduction of the screening program (reflecting improved treatment and earlier clinical diagnosis) and then compared women in the screening group with their historical counterparts to determine the change in mortality after implementation of the screening program (attributable to both the screening program as well as temporal trends in mortality that were unrelated to the screening program). They then calculated the reduction in mortality that was related to the screening program as the difference between the rate ratio for death among women in the screening group as compared with their historical counterparts, and the rate ratio for death among women in the nonscreening group as compared with their historical counterparts.

Simple enough for a statistician, but what does this mean to patients and clinicians in the Unites States where screening is much more widely established?

The overall crude death rate from breast cancer in U.S. women ages 50-65 in 2005 was about 21.4/100,000.[4] This rate is comparable to the rate seen among nonscreened women of the same age in Norway (21.2/100,000). The prevalence of mammography screening in the United States among women ages 50-64 in 2005 varied from 50% in poor women to 77% among well off women,[5] while in Norway this was more than 70% for everyone. As the proportion of women screened with mammography has increased, the death rate from breast cancer in the United States has declined 3.2% in women younger than age 50 and 2% in women older than age 50.[4] This decline in breast cancer mortality has been attributed to both improvements in breast cancer treatment and early detection, and it is difficult to tease out these effects.

The Norwegian paper suggests that mammography results in a nonsignificant reduction of only 2.4 deaths among 100,000 screened women ages

50-69. Most of the reduction in mortality was attributed to better care once cancer is diagnosed. Adding weight to the argument are data that demonstrated a similar reduction in mortality among older and younger age groups that did not undergo screening mammography that was attributable entirely to better treatment.

Before abandoning mammography, it is important to consider that we start screening earlier in the United States, and screen annually rather than every two years. Annual screening may be of particular benefit to younger women who are more likely to develop fast growing tumors.[1] Data from U.S. studies do demonstrate a small but real reduction in mortality with annual screening. These reductions in mortality may only be one case per 1,000 women screened, but women are highly motivated to avoid that statistic.

A logical and rational distribution of health care resources requires us not to hold on to any sacred cows. However, more data will be needed to determine if routine mammography is ready to be sacrificed. In my opinion, it is premature to abandon our current screening practices on the basis of the data in the Kalager paper. At the same time, we should continue to evaluate this important topic as more data become available.

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New biological agents for cervical cancer treatment

Abstract & Commentary

By **Robert L. Coleman**, MD, Professor, University of Texas; M.D. Anderson Cancer Center, Houston; Associate Editor for *OB/GYN Clinical Alert*, also published by AHC Media

Synopsis: Pazopanib, an orally administered tyrosine kinase inhibitor of vascular endothelial growth factor receptor (VEGFR), demonstrated superior clinical efficacy to lapatinib, a tyrosine kinase inhibitor (TKI) of the epidermal growth factor receptor (EGFR) and human epidermal growth factor 2 (HER2/neu), in women with advanced stage or recurrent cervical cancer. A planned futility analysis deemed the combination was unlikely to be superior to single agent pazopanib.

Source: Monk BJ, Mas Lopez L, Zarba JJ, et al. Phase II, open-label study of pazopanib or lapatinib monotherapy compared with pazo-panib plus lapatinib combination therapy in patients with advanced and recurrent cervical cancer. *J Clin Oncol* 2010; 28:3562-3569.

Previous investigation of cervical cancer biology has revealed a dependence on VEGF, among other factors, for growth and metastases. This dependence is mediated by HPV infection and by ubiquitous hypoxia, which is also recognized as a poor prognostic factor. It also has been demonstrated that cellular growth signaling through the ErbB receptors is prevalent in cervical cancer. These observations underscore the study's rationale and hypotheses.

Pazopanib, an oral TKI targeting VEGFR, cKit, and platelet-derived growth factor receptor (PDGFR), and lapatinib, an oral TKI targeting EGFR and HER2/neu, were used in this three-arm study as monotherapy or in combination. All patients were required to have measurable disease and to have been treated at least once with systemic chemotherapy. Of the 230 enrolled patients, 152 were randomly assigned to one of the monotherapy arms. Overall, approximately 70% had squamous cell histology and 62% had recurrent disease.

A planned interim futility analysis assessed the performance of the combination arm against lapatinib monotherapy. This analysis demonstrated increased toxicity and a low likelihood that the combination would exceed efficacy of lapatinib, which resulted in discontinuation of the combination therapy arm. Relative to lapatinib, pazopanib increased progression-free survival (hazard rate [HR], 0.66; P = 0.013) and overall survival (OS; HR, 0.67; P = 0.045). Median OS for pazopanib or lapatinib was 51 weeks vs 39 weeks, and response rates were 9% and 5%, respectively. Grade 3 and 4 toxicities were infrequent with either compound (diarrhea: 11% pazopanib, 13% lapatinib). The authors conclude that anti-angio-

genesis targeting is a viable approach in women with advanced and recurrent cervical cancer, with pazopanib being a well-tolerated and active agent worthy of further investigation.

Commentary

Patients with advanced stage cervical cancer not amenable to curative therapy and those with recurrent disease have few therapeutic options. While most will receive systemic chemotherapy, the majority ultimately will progress on treatment or within a short duration of completing treatment.

Since many of these patients will receive our most active agents in first recurrence, the options upon progression are extremely limited and define a clear unmet medical need. Unfortunately, the rarity of the disease in the United States and the difficulty of clearing an efficacy benchmark generally have tempered enthusiasm for drug development. Nevertheless, there are clear "druggable" targets, upon which modulation appears to hold some promise for subsequent clinical development.

Bevacizumab, a monoclonal antibody to VEGF, also has been evaluated in this setting and demonstrated similar efficacy to pazopanib. Those promising results prompted the development of an ongoing randomized phase III study addressing the utility of adding bevacizumab to one of two chemotherapy backbones in women with advanced or recurrent cervical cancer who have not received previous systemic chemotherapy (GOG 240). However, what is striking in this report is the continued apparent disconnect between EGFR targeting and efficacy. The experience with lapatinib joins several EGFR-targeted agents assessed in this disease, each with disappointing results. Most squamous cell cervical cancers overexpress this target, and its presence is a poor prognostic factor.

However, whether administered alone or in combination with chemotherapy, EGFR-targeted monoclonal antibodies and small molecule inhibitors have produced limited signs of efficacy. In the current trial, EGFR or HER2/neu overexpression was not an eligibility requirement, and tissue was not procured for assessment of expression, gain-of-function mutations, or the presence of ras/raf activation. Based on results with other solid tumors, such information could have brought clarity to the clinical observations and should be the focus of future work in this disease.

Additional Reading

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Antivirals not linked with birth defects

By **William T. Elliott**, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division, Assistant Clinical Professor of Medicine, University of California-San Francisco

Young women with herpes infections often are treated with the oral antivirals acyclovir, valacyclovir, or famciclovir. A recent study suggests that these drugs are relatively safe when taken in the first trimester of pregnancy (*JAMA* 2010;304:859-866).

A population-based historical cohort study was performed reviewing the records of more than 800,000 liveborn infants in Denmark who had no diagnosis of chromosomal aberrations, genetic syndromes, birth defects syndromes with known causes, or congenital viral infections. There were 1,804 pregnancies exposed to acyclovir, valacyclovir, or famciclovir in the first trimester. Of those, 40 infants (2.2%) were diagnosed with major birth defects compared with 19,920 (2.4%) among the unexposed infants (adjusted POR, 0.89; 95% CI, 0.65-1.22).

Broken down by drug, major birth defects were seen with 2% of infants exposed to acyclovir and 3.1% exposed to valacyclovir; exposure to famciclovir was uncommon. There was no association between antiviral drugs and specific types of birth defects. The authors conclude that exposure to acyclovir or valacyclovir in the first trimester of pregnancy was not associated with an increased risk of major birth defects. ■

Association of Reproductive Health Professionals

HEALTH MATTERS
Understanding Menstrual Suppression

www.arhp.org/healthmatters

What is menstrual suppression?

Menstrual suppression, sometimes called "skipping your period," is a way of using certain types of hormonal birth control to avoid having monthly bleeding. With many birth control pills, women take three weeks of pills containing active hormones, which prevent pregnancy by stopping ovulation (when an egg is released from a woman's ovaries) and keeping the uterine lining thin. During the fourth week of their cycle, women take pills that do not contain active hormones; this is the time when they experience bleeding. This monthly bleeding is not a "true" period; instead, this is withdrawal bleeding – the body's reaction to not having the hormones it gets the other three weeks of the cycle. For this reason, this fact sheet will use the term "monthly withdrawal bleeding" rather than "period."

Hormonal contraceptives can be used by women to decide when, or if, they get their monthly withdrawal bleeding. Women may choose to have shorter or less frequent withdrawal bleeding, skip bleeding when it's inconvenient, or eliminate bleeding completely for up to a year or more. Menstrual suppression also helps women cope with or get rid of uncomfortable side effects or conditions that are connected to their bleeding. For years, women have suppressed their periods for things like honeymoons or vacations, and new surveys show that many women are interested in bleeding less than once a month, or not at all.[1,2,3]

Do I have to bleed every month?

There is no evidence that shows women need monthly withdrawal bleeding, and no health problems are linked to skipping or eliminating bleeding. Studies have found that using the pill continuously for two or more cycles before having withdrawal bleeding is as safe and effective at preventing pregnancy as a traditional regimen.[4]

Am I a good candidate for menstrual suppression?

Any woman who wants to bleed less frequently, or not at all, can try menstrual suppression, and it may be especially appealing to women who are already on hormonal contraception. Women who may be good candidates for menstrual suppression include: women who have serious symptoms around the time of monthly withdrawal bleeding, like premenstrual syndrome (PMS); young women and adolescents; women who are perimenopausal; women in the military; athletes; or developmentally delayed women. Women who like getting monthly withdrawal bleeding for whatever reason, including to feel sure they are not pregnant, may not be interested in menstrual suppression.

What are the benefits of menstrual suppression?

Women may enjoy many benefits from skipping monthly bleeding. Some of these benefits include[5]:

- Less pain with monthly bleeding
- Less heavy bleeding

Health Matters is a publication of ARHP for the general public that provides a brief overview of existing facts and data on various topics related to reproductive health.

- Fewer PMS symptoms
- Fewer perimenopausal symptoms (hot flashes, night sweats, and irregular monthly periods, etc)
- Reduced menstrual migraines, endometriosis, and acne
- An increased feeling of well-being

In the United States, 2.5 million women aged 18–50 years have menstrual disorders. Of these women, 31 percent report spending an average of 9.6 days in bed each year.[6] By reducing the symptoms that often happen around the time of their monthly bleeding, menstrual suppression may help women feel better and have more flexibility in their lifestyle.

What are the side effects or disadvantages of suppressing bleeding?

The most common side effect of menstrual suppression is that many women have breakthrough bleeding or spotting in the first few months.[7] This is less common once your body has gotten used to the new routine. Blood from spotting may be dark brown from being in the uterus longer. You should contact a clinician if you experience ACHES—Abdominal pain, Chest pain, Heavy bleeding, Eyesight or vision changes, or Severe leg pain.

How can I suppress monthly bleeding?

Oral Contraceptives

The easiest way is to change the way you take your birth control pills. Birth control pills contain the hormones estrogen and progestin, which regulate your cycle, and are taken every day at the same time to prevent pregnancy. A traditional schedule is 21 days of active pills (which contain hormones), followed by 7 days of placebo pills (which are hormone-free). During the placebo week, women go through withdrawal bleeding, which will look and feel much like a period. To suppress bleeding, a woman simply skips her 7 days of placebo pills and starts the new pill pack right away. By doing so, she skips the withdrawal bleeding entirely.

Women can suppress their withdrawal bleeding for two or more months (called extended use) or even up to a year or more (called continuous use).

Some birth control pills are specifically designed to be used for extended use. For example, Seasonale® is designed so that a woman takes 84 days (3 months) of pills containing hormones, followed by one week of placebo pills to bring on withdrawal bleeding. Using this pill, a woman would only bleed four times a year.

With a continuous use schedule, a woman might choose to bleed only once a year, or not at all. Lybrel™is a birth control pill made specifically for continuous use and packaged with an entire year of active pills.

Other Hormonal Methods

In a similar way to the pill, other birth control methods can be used to suppress monthly bleeding. The birth control injection (Depo-Provera®), one type of intrauterine device (Mirena®), and a birth control implant (Implanon™) also eliminate monthly bleeding, although breakthrough bleeding and spotting are still likely.[8] There have been a few studies that looked at extended use with the vaginal ring (NuvaRing®) and the contraceptive patch (Ortho Evra®). While the studies found similar results as when using the pill, the FDA has not yet approved the ring and the patch for extended use.[9,10]

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