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INSIDE

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Ruling opens door for coverage of prescription contraceptives

Advocates move on judicial, legislative fronts following decision

The recent ruling by the Equal Employment Opportunity Commission (EEOC) that employers must provide coverage of prescription contraceptive drugs if their employee health plans include other Rx medications gives fresh impetus to those seeking to establish such coverage for all women.

"An immediate impact is the sense of confirmation many of us feel: The EEOC found that the specific omission of contraceptive prescriptions from prescription health coverage is, as we have argued for years now, sex discrimination," states **Karen Raschke**, a staff attorney with the state program for the New York City-based Center for Reproductive Law and Policy.

The EEOC decision is a response to charges filed by two unnamed registered nurses who claimed that their employers' refusal to cover prescription contraceptives violated the Pregnancy Discrimination Act of 1978. The agency's decision is important because it puts employers on notice of their legal obligation to include contraceptive coverage in their employees' health plans, and also alerts employees to their legal rights to this coverage, observes **Eve Gartner**, senior staff attorney with

EXECUTIVE SUMMARY

More women might obtain insurance coverage for their prescription contraceptives following a recent ruling from the Equal Employment Opportunity Commission (EEOC). The decision calls for employers to cover prescription contraceptive drugs if their employee health plans include other prescription drugs.

- The EEOC ruling might impact a class-action case in Washington state, which alleges it is sex discrimination for an employer to exclude prescription contraception from an employee health plan that covers other prescriptions.
- Women's health advocates will continue to seek federal and state legislation for comprehensive coverage of contraceptives for all women.

the New York City-based Planned Parenthood Federation of America (PPFA).

Although the EEOC ruling technically applies only to the two women who initially filed the complaint, it could open the door to other lawsuits from women whose employers' health care plans exclude prescription contraception. The ruling also could prove helpful in existing suits because agency opinions, while not legally binding, tend to carry a lot of weight in court, according to *The Wall Street Journal*.[1]

Landmark lawsuit filed

The EEOC ruling may indeed impact the outcome of a pending landmark class action lawsuit filed by Seattle-based Planned Parenthood of Western Washington and PPFA on behalf of Jennifer Erickson, RPh, a pharmacist employed by the Seattle-based Bartell Drug Co. Filed in July 2000 in the U.S. District Court in the Western District of Washington, the case alleges it is sex discrimination for an employer to exclude prescription contraception from an employee health plan that covers other prescription drugs.

A class has been certified in the case, meaning that the court has declared the woman who brought the lawsuit serves as a representative of all the other nonunion employees of the drugstore chain. The class certification expands the number of women who would be affected if the case is won, explains Gartner.

"We're hopeful that in the case in Seattle the court will defer to the EEOC's interpretation," states Gartner.

The lawsuit is supported by the Fair Access to Contraception Coalition, which includes Planned Parenthood of Western Washington, PPFA, the Washington, DC-based National Women's Law Center, and the American Civil Liberties Union of Washington and the Northwest Women's Law Center, both based in Seattle. The coalition has set up a Web site, www.covermypills.org, with information to guide women in seeking contraceptive coverage from their employers.

Women who are facing resistance in obtaining such coverage are encouraged to contact the coalition, either through the Web site or by dialing a toll-free number, (800) 727-2996, says Gartner.

Coverage is necessary

Opponents to adding contraceptive coverage have argued such measures would raise insurance costs to employers. In 2000, employer-sponsored health benefit cost rose 8.1% for a third straight year of increases, and the increase was more than double the rate of general inflation, according to a survey of more than 3,300 employers released by William M. Mercer, a New York City-based human resource consulting agency.[2]

Employers are rightfully concerned about the costs of benefit packages, notes **Jacqueline Darroch**, PhD, vice president for research with the New York City-based Alan Guttmacher Institute. Studies have shown that as the cost of health insurance premiums rises, some employers and employees are priced out of the market; thus, businesses scrutinize requests for expanding coverage carefully, says Darroch. However, such concern usually is focused on high-cost services and care that is judged discretionary rather than directly related to a person's health, she observes.

Coverage of contraceptives addresses both of those criteria as well as the one of basic fairness recognized in contraceptive equity legislation and the recent EEOC ruling, states Darroch. "The added cost of including contraceptives is very low, and contraceptives are needed, and used, by almost everyone in the United States during their reproductive years," she says.

A 1998 report issued by the Alan Guttmacher Institute showed that the estimated maximum added cost of covering the full range of Food and Drug Administration-approved reversible medical contraceptives in health plans that do not currently cover them is just $21.40 per employee per year.[3] Of this figure, $17.12 would be employers' costs and $4.28 would be employees' costs. The

COMING IN FUTURE MONTHS

- Review new evidence on DMPA use
- Ads raise emergency contraception awareness
- Sterilization techniques — check new data
- Effective lab model developed for microbicides
- How you can help teens boost 'sex smarts'

added cost for employers amounts to just $1.43 per month per employee, which represents an increase of just 0.6% in employers' costs of providing employees with medical coverage.

"Not only do they [contraceptives] prevent the personal, familial, and social costs of unintended pregnancy and sexually transmitted diseases, but they also prevent health complications from these outcomes," states Darroch. "They are not discretionary, but rather a health necessity for American women and men."

Legislation goes on

The EEOC decision will go a long way toward ensuring that American women have private insurance coverage of contraceptives, states **Cynthia Dailard**, senior public policy associate with the Alan Guttmacher Institute's Washington, DC, bureau. However, it does not extend to all privately insured women, but only to those who fall within the scope of Title VII of the Civil Rights Act. According to information provided by the Fair Access to Contraception project, Title VII prohibits sex discrimination by employers with 15 or more employees. It thus does not protect women who do not have health coverage through their (or their spouse's) employer or women whose employer has fewer than 15 employees.

Thirteen states (California, Connecticut, Delaware, Georgia, Hawaii, Iowa, Maine, Maryland, Nevada, New Hampshire, North Carolina, Rhode Island, and Vermont) have enacted laws requiring health plans with prescription drug coverage to include prescriptive contraceptives.

"While the EEOC decision affects employers, the state mandate laws affect insurers, taking two different approaches to the same problem," notes Dailard. "Ultimately, advocates at the state level will need to continue their work to ensure that all privately insured women have comprehensive coverage of contraceptives."

While the EEOC ruling has no immediate legal impact on the movement of state legislation requiring equity for contraceptive prescriptions, it will likely spur such legislation and should decrease the level of opposition to state bills, Raschke observes.

Women's health care advocates look to the reintroduction of the Equity in Prescription Insurance and Contraceptive Coverage Act (EPICC) in the new congressional session. Originally introduced in 1997 in the House of Representatives and Senate, EPICC would mandate that all private insurance plans cover contraception. The EEOC ruling will play an important aspect in the debate over the bill, forecasts Raschke.

"Insurers, usually a powerful lobbying presence in a state capitol, argue that they are responsive to insurance purchasers and they should adopt a similar strategy as the employers," she notes. "While neither employers nor insurers are likely to simply accede to state [or federal] legislation, the EEOC's ruling has surely eliminated much of their fervor in opposing it."

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Internet is new frontier for risky sex activity

Add a new group to those at risk for sexually transmitted diseases (STDs): men and women who use the Internet to make sexual connections.

According to a recent study of clients seeking HIV testing at a Denver HIV counseling and testing site, those who sought sex partners over the Internet reported a higher level of other sexual risk-taking behavior compared with those who did not use the computer for such purposes.[1]

EXECUTIVE SUMMARY

People who look for sex partners on-line may be at higher risk for sexually transmitted diseases (STDs) than those who meet each other in a more conventional way, according to new research findings.

- People who sought Internet sex also were more likely to have other risk factors for getting sexually transmitted disease, the study indicates. For example, they were more likely to have had an STD previously, and they had more partners than people who didn't look for sex on-line.
- Ask your clients if they seek partners on-line and urge them to take additional precautions with those partners to prevent STD transmission.

What does this mean for health care providers?

"The take-home message we would like to see promoted is that Internet sex-partner seeking does appear to be riskier than looking for partners in other venues," says one of the study's co-authors, **Sheana Salyers Bull**, PhD, MPH, former behavioral scientist with the Denver Public Health Department and now an associate scientist with the Denver-based AMC Cancer Research Center. "Practitioners can ask their clients if they do seek partners on-line and urge them to take additional precautions with these partners to prevent STD transmission."

Let patients know that seeking sex partners on the Internet puts them at risk for STDs, HIV, and unintended pregnancy, states lead author **Mary McFarlane**, PhD, a research psychologist at the Atlanta-based Centers for Disease Control and Prevention (CDC) National Center for HIV, STD, and TB Prevention, Division of Sexually Transmitted Disease Prevention.

"Internet-initiated sex can be risky because clients may feel as though they know a great deal about intended partners, when in fact, much of this knowledge may be false," observes McFarlane. "Internet-initiated sex may also put clients at risk for violence, as people can masquerade or misrepresent themselves on the Internet."

Advise patients who intend to meet their Internet contacts face-to-face to do so in a well-lit, well-traveled area, such as a popular coffee shop, says McFarlane. Bring along a friend if possible, and let a third party know about the intended meeting as a safety precaution, she adds.

Cyberseekers take risks

When clients seeking HIV testing at the Denver Public Health Department began telling providers they had met partners on-line through chat rooms and bulletin boards, awareness was raised about this newly emerging risk environment.

"This anecdotal information was interesting, because it appeared that partners could be identified more quickly than through traditional means, e.g., bars or bathhouses," says Bull. "We were interested to learn if this manner of partner-seeking incurred any increased risk for STD transmission."

The Denver cross-sectional study looked at almost 900 clients, the majority of whom were male, heterosexual, and between the ages of 20 and 50. Compared with those who did not use the Internet to make sex connections, cyberseekers were more likely to be male and homosexual and reported more previous STDs, partners, anal sex, and sexual exposure to partners known to be HIV positive.

Researchers are looking at a broader population through an Internet-based self-administered anonymous survey, known as the SexQuiz.[2] More than 4,600 people responded to the survey between April 3, 2000, and Aug. 3, 2000. The survey covered 68 items in an effort to assess sexual risk behaviors with non-Internet and Internet partners.

While substantial information on the likelihood of STD infection from Internet partners is still unknown, and while risks are common, effective strategies for on-line STD prevention are needed, the scientists state. A three-year grant from the Washington, DC-based Association of Teachers of Preventive Medicine and funds from the CDC will allow the researchers to develop and test an on-line STD / HIV prevention intervention targeting men having sex with men, says Bull.

Get message out on Net

The Internet offers fast and efficient encounters resulting in sexual contact, which might translate into more efficient disease transmission, say Bull and McFarlane.[3] However, the Internet also offers many possibilities for innovative technological approaches to promote STD and HIV prevention, they note.

When an outbreak of syphilis occurred in San Francisco among users of an Internet chat room, public health officials were able to alert chat room participants of potential disease exposure, use Internet aliases to contact individuals, and issue Web alerts, rather than direct personal contact, to raise awareness.[4]

The public health establishment should explore the potential value of the Internet as a tool for health communication, according to an editorial by Kathleen Toomey, MD, MPH, director of the Division of Public Health, Georgia Department of Human Resources, and Richard Rothenberg, MD, professor of family and preventive medicine at the Emory University School of Medicine, both in Atlanta.[5]

"Public health systems need to be prepared to deal with the consequences of activities involving these new communication media," observe Toomey and Rothenberg. "The opportunity for STD prevention (at least for this segment of the population, which has grown up using the Internet) will truly become lost in cyberspace unless public health can develop new ways to

better educate sexual risk takers and provide effective interventions with or without the assistance of these new technologies."

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Patch now under regulatory review

Is a contraceptive patch in the near future for American women? The Food and Drug Administration (FDA) is now reviewing the clinical research data on the novel birth control method.

The R.W. Johnson Pharmaceutical Research Institute in Raritan, NJ, under the same Johnson & Johnson corporate umbrella as Ortho-McNeil Pharmaceuticals, has submitted a New Drug Application (NDA) for the Ortho Evra transdermal system, a seven-day contraceptive patch. The application was filed in late December 2000.

Clinical trials for the patch have been completed, according to Mark Monseau, a company spokesman. As with any product under FDA review, the company declined to speculate on the drug's possible approval, other than to note the FDA's standard review period for an NDA is 12 months. If the patch does gain FDA approval, it would be the world's first prescription transdermal contraceptive.

EXECUTIVE SUMMARY

The Ortho Evra, a contraceptive transdermal system developed by R.W. Johnson Pharmaceutical Research Institute in Raritan, NJ, is under review by the Food and Drug Administration. If approved, Evra will be the world's first prescription transdermal contraceptive.

- The patch relies on the progestin/estrogen combination of norelgestromin and ethinyl estradiol. Norelgestromin is the primary active metabolite of norgestimate, which is used in Ortho-Cyclen and Ortho Tri-Cyclen.
- Research indicates that Evra is as effective as oral contraceptives and that patient compliance might be even higher than with the pill.

Two hormones in one patch

The patch relies on the progestin / estrogen combination of norelgestromin and ethinyl estradiol for its contraceptive effectiveness. Norelgestromin is the primary active metabolite of norgestimate, which is the progestin used in two Ortho-McNeil oral contraceptives (OCs): Ortho Tri-Cyclen and Ortho-Cyclen.

Evra can be worn on several areas of a woman's body, but most typically is placed on the lower abdomen or buttocks. The patch is worn for one week at a time and is changed on the same day of the week three times a month. The fourth week is patch-free.

Evra is as effective as oral contraceptives, and patient compliance with the device may be even higher than with the pill, according to poster sessions presented at the May 2000 annual clinical meeting of the Washington, DC-based American College of Obstetricians and Gynecologists (ACOG).[1,2] The first poster, a dosing trial that looked at three sizes of the patch, concluded that the 20 sq. cm patch provides high levels of suppression of ovarian activity and effective cycle control compared with Ortho-Cyclen while providing more complete suppression of follicular development.[1]

Data from the second poster session suggest women are more compliant with the patch than with oral contraceptives. Compliance with the patch was 93%, 94.4%, and 92.7%; whereas compliance with the two oral contraceptive preparations was 87.8% and 78.4%, respectively.[2] Similar data were presented at the October annual meeting of the Washington, DC-based American Society for Reproductive Medicine.

What are the advantages offered by such a transdermal method of contraception? According to **David Archer**, MD, professor of obstetrics and gynecology and director of the Clinical Research

Center at the Eastern Virginia Medical School in Norfolk, there are at least five:

• reduced compliance / motivation, since the transdermal system only has to be changed on a weekly basis;

• improved bleeding profile. According to the information presented at the ACOG meeting, there was little to no breakthrough bleeding associated with use of the Evra patch, notes Archer. He believes this reflects a consistent blood level of the steroid.

• continued contraceptive efficiency due to improved compliance;

• potential for fewer side effects, perhaps due to consistent low blood levels. Archer says he has not seen specific data on this issue;

• acceptance of "new and improved" contraceptives. Consumers like the idea of a new technique or device, so Evra may pique the interest of women who have stopped using OCs for other reasons, states Archer.

"Our patients enjoyed the convenience of once-a-week dosing rather than the daily dosing requirements of the birth control pill," confirms one of the clinical trials' investigators, **Anita Nelson**, MD, professor in the obstetrics and gynecology department at the University of California in Los Angeles (UCLA) and medical director of the women's health care clinic and nurse practitioner training program. "Many of these same women might also be candidates for the once-a-month shot (Lunelle, marketed by Pharmacia Corp. of Peapack, NJ), but they don't like needles." **(For information on the just-released monthly contraceptive injectable, see *Contraceptive Technology Reports*, enclosed in this issue, and *Contraceptive Technology Update*, December 2000, p. 144.)**

The uniqueness of the patch application for contraception makes Evra intriguing, but its visibility might not be optimal for younger women seeking confidentiality, notes Nelson.

Disadvantages include, as with all patch technology, adhesive allergy or reaction, and problems with patch adherence, notes **Sharon Schnare**, RN, FNP, CNM, MSN, women's health consultant and clinician with the Seattle King County Health Department in women's and adolescent health care and the International District Community Health Center in Seattle.

"The contraceptive patch will add an important contraceptive option for women who cannot take pills or remember to take pills, and for women who do not want to have injections or use barrier methods such as diaphragms or cervical caps," observes Schnare. "As with all contraceptive methods, women should be encouraged to use condoms" for protection against sexually transmitted diseases, she says.

A big challenge for some women is the need for daily pill taking, reflects **Andrew Kaunitz**, MD, professor and assistant chair in the obstetrics and gynecology department at the University of Florida Health Science Center / Jacksonville. Even women who are excellent and consistent pill takers might live with a certain apprehension over what might happen if they miss pills and experience an unintended pregnancy.

"From this perspective, a weekly patch, which uses the same familiar hormones as are in contemporary OCs, is appealing indeed," says Kaunitz. "I believe the availability of Evra will increase the number of U.S. women who use modern effective methods of birth control."

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Sterilization not the cause of menstrual problems

Concerns over the existence of post-tubal ligation syndrome, characterized by dysmenorrhea, heavy bleeding, or spotting, have been eased with the recent publication from a large prospective comparative study.[1]

Researchers used data from the U.S. Collaborative Review of Sterilization (CREST) to determine whether the likelihood of persistent menstrual abnormalities was greater among women who had undergone tubal sterilization than among women who had not. No other study of the potential for post-tubal ligation syndrome offers prospective data acquired in repeated interviews from such a large cohort over such a long period, notes a companion editorial published with the new study.[2]

The findings indicate that women who have undergone tubal sterilization are no more likely than other women to have menstrual abnormalities. Concerns that sterilization causes menstrual

EXECUTIVE SUMMARY

The recent findings from a large prospective study indicate that women who have undergone tubal sterilization are no more likely than other women to have menstrual abnormalities.

- The new study followed the experiences of 9,514 women who underwent tubal sterilization and 573 women whose partners underwent vasectomy for up to five years.
- Scientists found no differences in intermenstrual bleeding or length of menstrual cycles, but the women who underwent tubal sterilization were more likely to have shorter menstrual periods, less bleeding, and more irregular cycles than the women whose partners underwent vasectomy.

problems remain common among women and clinicians. Against this backdrop, the recent reassuring data from the study are particularly welcome, states **Andrew Kaunitz**, MD, professor and assistant chair in the obstetrics and gynecology department at the University of Florida Health Science Center / Jacksonville.

The chief reason for the new report was to attempt to resolve a longstanding debate regarding whether tubal sterilization causes menstrual abnormalities, says **Herbert Peterson**, MD, principal investigator of the U.S. Collaborative Review of Sterilization Working Group.

Since 1951, when Williams and colleagues first reported a higher than expected number of sterilized women with abnormal menstrual bleeding,[3] the question, "Is there a post-tubal ligation syndrome of menstrual abnormalities?" has persisted, Peterson states. When sterilization became prevalent in the 1970s, concerns were heightened, with increased or abnormal menstrual bleeding with consequent hysterectomy reported in uncontrolled case series.[4]

In the United States, 11 million women rely on tubal sterilization to prevent pregnancy.[5] With such great numbers of women involved, it was important to resolve the issue, says Peterson.

Investigators followed the experiences of 9,514 women who underwent tubal sterilization and 573 women whose partners underwent vasectomy for up to five years by means of annual telephone interviews. All women were asked the same questions about six characteristics of their menstrual cycles in the presterilization and follow-up interviews. Multiple logistic-regression analysis was used to assess the risk of persistent menstrual changes.

Researchers found that the women who had undergone sterilization were no more likely than those who had not been sterilized to report persistent changes in intermenstrual bleeding or the length of the menstrual cycle.

There were no differences in intermenstrual bleeding or length of menstrual cycles, but the women who underwent tubal sterilization were more likely to have shorter menstrual periods, less bleeding, and more irregular cycles than the women whose partners underwent vasectomy, according to the findings.

Add data to counseling

Providers can counsel patients prior to sterilization that the procedure does not appear to cause menstrual abnormalities, states Peterson.

"Menstrual abnormalities are common in sterilized and nonsterilized women," he observes. "When menstrual abnormalities occur after sterilization, women should determine with their providers whether treatment is necessary and, if so, whether medical or surgical therapy is most appropriate."

In general, the indications for hysterectomy for sterilized women should be the same as those for nonsterilized women, states Peterson.

If women have been using combination oral contraceptives (OCs) or depot medroxyprogesterone acetate (DMPA) contraceptive injections prior to sterilization, Kaunitz says he prepares them for potential changes following the procedure.

"I advise such women that if they notice heavy flow, cramps, or unpredictable bleeding, it will not be caused by the tubal sterilization procedure, but rather will represent that they have discontinued their hormonal contraception which was causing light regular cycles [with OCs] or amenorrhea [with DMPA]," states Kaunitz.

Kaunitz says he tells women scheduling sterilization that it is not unusual or inappropriate for those going off hormonal contraception after their sterilization to restart hormonal treatment later, to address unpleasant menstrual periods.

"Giving women and their partners relevant information about risks, benefits, and alternatives is central to family planning," states **Carolyn Westhoff**, MD, professor of obstetrics, gynecology, and public health at Columbia University in New York City, in the editorial accompanying the new CREST data. "Such informed consent is most important for sterilization — both tubal ligation

and vasectomy — because these methods are permanent."

The CREST investigation has yielded several important findings supporting the safety and efficacy of sterilization. What will be the next installment from this large body of research?

"Upcoming reports from CREST include an evaluation of regret after vasectomy as compared with regret after tubal sterilization," says Peterson.

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Raise EC awareness by training providers

Before women can obtain emergency contraception (EC), their health care providers must know about the method and be willing to prescribe it. Two West Coast projects coordinated by Population Services International (PSI), a Washington, DC-based nonprofit group, have focused on provider training as part of their strategy in improving EC access.

The projects, based in Sacramento, CA, and Portland, OR, have used different training models in educating providers about EC, but they are employing the same media campaign to raise awareness among their target audience: sexually active young women between the ages of 15 and 24. The programs began formative research and provider training in early 2000 and kicked off their media campaigns in November. While it is too early to access their impact, those involved with the program say they have had excellent response from providers and the community at large.

"Although our official evaluation data are not yet in, we do know that some of the major health care systems in the area who participated in the training are in the process of revising their protocols to facilitate easier access to EC," says **Lorrie Harris-Sagaribay**, MPH, project manager in Sacramento.

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Two emergency contraception projects sponsored by the Washington, DC-based Population Services International reach a similar target audience: sexually active young women between the ages of 15 and 24.

- The Sacramento-based "train-the-trainer" program prepares providers and community organizers, while the Portland-based program employs a "master-trainer" approach.
- The media campaign is based on the theme that "Accidents happen — Pregnancy doesn't have to." Radio ads, posters, and trifold wallet cards promote emergency contraception.

The Sacramento project is collaborating with the Los Angeles-based Pacific Institute for Women's Health (PIWH) for its provider training. Led by PIWH consultant **Debbie Postlethwaite**, MPH, RNP, the program conducted six "train-the-trainer" workshops for 67 participants, including physicians, nurse practitioners, nurses, and health educators. The curriculum was designed to foster sensitivity about unintended pregnancy and also to focus on issues that were the most relevant for the providers, says Harris-Sagaribay.

Master trainers present material

The Portland project has worked with Seattle-based Program for Appropriate Technology in Health in developing its "master-trainer" provider education model. The core of the educational model relies on a one-hour Microsoft PowerPoint computer program presentation, offered to clinical and nonclinical providers by a set of "master trainers." According to Portland project manager **Alexandra Lowell**, MPH, more than 500 have received education from the master trainers since the project began last year.

Research conducted prior to the program showed that while providers were eager to learn more about EC, they had busy schedules that often precluded training outside their normal business hours. The solution? PSI sets up the trainings so they coincide with facilities' regular inservice sessions. By presenting the material in a time-effective

manner at no cost to the organization, the organizations obtain free education, and more numbers are added to the pool of knowledgeable EC providers.

With providers prepared, the Sacramento and Portland projects have moved ahead with their media campaigns. The heart of the campaigns relies on radio advertisements, posters, and trifold wallet cards, all reinforcing the message, "Accidents happen — Pregnancy doesn't have to." The wallet cards, printed in eye-catching pink and orange, are available in English and Spanish versions.

The material, developed by Slingshot Productions, an Oakland-based creative firm, answers women's basic questions about ECPs and encourages them to talk with their health care providers or call the national Emergency Contraception Hotline [(888) NOT-2-LATE] for more information. By sharing the media development costs, the programs have been able to maximize their individual $75,000 budgets.

In addition to placing the material in such traditional areas as health care clinics and physicians' offices, the programs also are putting material in neighborhood job training centers and other areas where young women congregate. The Portland program enlisted a local company, Water Closet Media, to place the posters in restrooms around the city, including those at a popular ski resort.

Break down barriers

While their respective communities have accepted both programs, those involved say there is more work to be done in breaking down the barriers to emergency contraception. For example, the Portland project is working toward increasing the number of pharmacies stocking Plan B, the progestin-only ECP marketed by the Women's Capital Corp. of Bellevue, WA. Also, both programs are encouraging providers to consider prophylactic prescription of ECPs.

"That is one of the key messages we try to say, to [get providers to] talk about it now, rather than after the fact when a woman is fearing a risk of potential pregnancy and is in more of a crisis mode," says Lowell.

Organizations continue to impose barriers to EC by insisting on pregnancy testing and pelvic exams prior to EC provision, says Postlethwaite. Such restrictions not only make the service more difficult to deliver from a staff position, but are unnecessary, she states. The PSI program has made an impact, though, she contends.

"Providers have done trainings, changed guidelines, and changed protocols — we're seeing that now," says Postlethwaite. "When we do the evaluation, we'll see if provider practice has changed. I'm sure it has." ■

Research supports use of misoprostol

With publication of a review article that identifies more than 200 studies involving more than 16,000 women who have used misoprostol, health care providers hope the evidence supporting the safe use of the drug in women at various stages of pregnancy will prompt a change in the medication's labeling.[1]

The Washington, DC-based American College of Obstetricians and Gynecologists (ACOG) has filed a citizen's petition with the Food and Drug Administration (FDA) outlining the reasons justifying the continued use of misoprostol and requesting a change in the drug's current labeling. Other groups and individuals have a similar right to file petitions, states **Stanley Zinberg**, MD, vice president of practice activities at ACOG.

"We think the most important uses of misoprostol are one, facilitating delivery in post dates and high-risk pregnancies; two, increasing access to safe abortion; three, controlling uterine hemorrhage where access to other drugs is limited," states **Philip Darney**, MD, MSc, professor at the University of California, San Francisco, and

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Providers who use the drug misoprostol in women's health care point to the publication of evidence affirming the safe use of the drug as the basis for its continued use.

- Marketed as Cytotec by G.D. Searle & Co., the drug carries one indication: prevention of gastric ulcers associated with nonsteroidal anti-inflammatory medications. However, misoprostol also has been used for cervical ripening as a prelude to labor and a component to early medical abortions using mifepristone.
- Controversy arose following an August letter from Searle that warned of possible safety issues surrounding off-label use of the drug. Many hospitals removed misoprostol from their pharmacies.

OB/GYN department chief at San Francisco General Hospital Medical Center. Darney served as a co-author of the review article, which concludes that "misoprostol is one of the most important medications in obstetrical practice."

Misoprostol, marketed in the United States as Cytotec by G.D. Searle & Co. of Skokie, IL, was approved by the FDA in 1988 for the prevention of gastric ulcers associated with the use of nonsteroidal anti-inflammatory drugs. Since that time, however, the drug has been used on an off-label basis, particularly for cervical ripening as a prelude to induction of labor and as the second component to early medical abortions using mifepristone.

The 'treatment of choice'

Indeed, use of the drug for cervical ripening prior to labor induction has been used so frequently and effectively that it has become the "treatment of choice," wrote Zinberg and Ralph Hale, MD, ACOG executive vice president, in an editorial accompanying the recently published review article.[2] ACOG published a committee opinion and a practice bulletin in November 1999 as guidelines for appropriate use of misoprostol.[3,4]

However, Searle issued a letter to providers on Aug. 23, 2000 that cautioned that "Cytotec administration by any route is contraindicated in women who are pregnant because it can cause abortion."[5] ***(Contraceptive Technology Update* included information on the Searle letter in its December 2000 report of the FDA's approval of mifepristone; see p. 141.)** Many women's health care advocates questioned the timing of the letter, issued about one month prior to the FDA's approval of mifepristone (Mifeprex, marketed by Danco Laboratories of New York City).

Letter impacts care

Following the Searle letter, many hospitals, often on the advice of their legal counsel, removed misoprostol from their hospital pharmacies, states Zinberg.

"As a result, the best drug for cervical ripening prior to induction in full-term pregnancies was unavailable in these institutions," says Zinberg.

ACOG issued responses affirming the use of misoprostol for induction of labor and for medical abortion in combination with mifepristone.[6,7]

"Some hospitals restored misoprostol to their formularies after ACOG's published reports supporting its continued off-label use," states Zinberg. "However, many have not done so."

Searle has issued a response defending its issuance of the provider warning letter, which states that it "resulted from lengthy discussions between Searle and the FDA after reports were received of uterine rupture in connection with the off-label use of Cytotec in pregnant women."[8]

In the response, **Michael Friedman**, MD, senior vice president for research and development at Searle, states "the FDA requested that Searle make a labeling change to clarify further the serious risks and to consider sending a letter to health care professionals." The timing of the provider letter was coincidental, he adds.

"We fully support the role of physicians, using their professional judgment, to prescribe an approved pharmaceutical product for a use outside of its FDA-approved indication in the best interest of their patients, on the basis of published research, expert clinical opinion, or their own clinical experience," notes the response.

The company says it is looking for a better dialogue with providers in the misoprostol issue. That sentiment is shared by ACOG, which seeks continued use of misoprostol in women's health care.

"It is our hope that further evaluation by Searle and the FDA will result in a retraction of the letter of Aug. 23, 2000, and a recognition of the beneficial roles misoprostol can have during and after pregnancy," write Zinberg and Hale in their editorial. "Women in the United States should not be deprived of access to misoprostol."[2]

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Web offers coverage of midlife information

As more women enter perimenopause, they raise health questions that must be addressed by health care providers. The following sites are representative of the broad array of resources now available on the Internet:

1. North American Menopause Society: www.menopause.org. The Cleveland-based society is the leading nonprofit scientific organization devoted to promoting understanding of menopause. Its site offers basic information about menopause, as well as gives answers to frequently asked questions, such as how to deal with common hormonal replacement side effects.

2. National Women's Health Resource Center: www.healthywomen.org. The New Brunswick, NJ-based National Women's Health Resource Center is a nonprofit organization that serves as a national clearinghouse for women's health information. The Health Center section of its Web site offers information on a variety of subjects from breast cancer to osteoporosis. Sections include a discussion forum, a news center, and a library, which offers ordering information on newsletters, magazines, and books. Click on "Menopause — Take Charge" in the Health Center to view the site's designated area on menopause material.

3. Power Surge: www.power-surge.com. Power Surge is an on-line support community for women at midlife. It was created in 1994 by Alice Lotto Stamm of New York City, better known by her America Online persona, "Dearest." This on-line resource sprang from Stamm's own frustrations with the limited information available about menopause. The site offers its own on-line newsletter, transcripts of discussion sessions with medical experts, and message boards.

4. Medem: www.medem.com. The nation's leading medical societies, including the Washington, DC-based American College of Obstetricians and Gynecologists, have joined forces to create Medem, an e-health network. Click on the Medical Library icon, then "Women's Health," then "Menopause" to view a variety of information on midlife subjects, including hormone replacement therapy.

5. Mayo Health: www.mayohealth.org. The "Life Stages" section of this Web site offers concise, easy-to-read articles on midlife issues, including "Perimenopause — A Period before Your Period Ends" and "Phytoestrogens — Hormones from Plants." Click on "Women's Health" under "Healthy Living Centers," then "Life Stages" to access midlife articles. ■

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Editor: **Rebecca Bowers**.
Vice President/Group Publisher: **Brenda Mooney**, (404) 262-5403, (brenda.mooney@ahcpub.com).
Editorial Group Head: **Valerie Loner**, (404) 262-5475, (valerie.loner@ahcpub.com).
Managing Editor: **Joy Daughtery Dickinson**, (229) 377-8044, (joy.dickinson@ahcpub.com).
Production Editor: **Nancy McCreary**.

Editorial Questions

Questions or comments?
Call **Joy Daughtery Dickinson** (229) 377-8044.

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CTUPDATES
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Cervical cancer meeting scheduled for April

The Baltimore-based Johns Hopkins University School of Medicine, the Bethesda, MD-based National Cancer Institute, and Houston-based University of Texas MD Anderson Cancer Center will co-sponsor the first International Cervical Cancer Meeting April 6-8 in Baltimore.

The meeting will cover issues of etiology, screening, vaccines, and quality of life. Presentations will include the role of human papillomavirus in cervical carcinogenesis, sexual practices and cervical neoplasia, and reaching the unscreened.

For additional information, contact Johns Hopkins Office of Continuing Medical Education, Johns Hopkins University School of Medicine, Turner 20, 720 Rutland Ave., Baltimore, MD 21205-2195. Telephone: (410) 955-2959. Fax: (410) 955-0807. E-mail: cmenet@jhmi.edu. Web: ww2.med.jhu.edu/cme; search "cervical cancer." ■

CE objectives

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

• Identify clinical, legal, or scientific issues related to development and provisions of contraceptive technology or other reproductive services. **(See "Patch now under regulatory review," p. 29; and "Research supports use of misoprostol," p. 33.)**

• Describe how those issues affect service delivery and note the benefits or problems created in patient care in the participant's practice area.

• Cite practical solutions to problems and integrate information into daily practices, according to advice from nationally recognized family planning experts. **(See "Internet new frontier for risky sex activity," p. 27; and "Sterilization not the cause of menstrual problems," p. 30.)** ■

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Contraceptive Technology Reports

A supplement to *Contraceptive Technology Update* **March 2001**

Lunelle: Evaluation of a New Monthly Contraceptive Injection for U.S. Women

Author: **Andrew M. Kaunitz, MD**, Professor and Assistant Chair, Department of Obstetrics and Gynecology, University of Florida Health Science Center, Jacksonville.

Peer Reviewer: **Daniel R. Mishell Jr., MD,** Professor, Department of Obstetrics and Gynecology, University of Southern California School of Medicine, Los Angeles.

Introduction

In October 2000, the Food and Drug Administration approved the monthly combination hormone injection Lunelle for contraception. This method, the first new contraceptive to be approved in the United States since 1993, is safe, quickly reversible, and extremely effective in preventing pregnancy.

Some clinicians were skeptical that American women would want to receive a monthly birth control injection. However, researchers were pleasantly surprised to learn that many subjects were enthusiastic about the use of Lunelle — in fact, they preferred to try that method over the Pill when given a choice at the start of the trial — and did not find the prospect of an injection or a monthly visit a deterrent to use.

Mechanism of Action

Lunelle contains 25 mg of medroxyprogesterone acetate (MPA) and 5 mg of estradiol cypionate (E_2C), and has been studied clinically for the past 35 years and tested in more than 12,000 women worldwide.[1] MPA is the same progestin used in the three-month depot medroxyprogesterone acetate (DMPA or Depo-Provera) contraceptive injection. The estradiol released from Lunelle's injection site is not the synthetic ethinyl estradiol used in birth control pills, but rather the natural hormone 17-beta estradiol produced by the ovaries. The primary mechanism of action for prevention of pregnancy is inhibition of ovulation.[2]

Effectiveness

The World Health Organization (WHO) performed a pilot study of Lunelle in 1981 and several multinational pharmacological and dose-ranging studies between 1984 and 1990.[1] These studies led to the selection of 25 mg of MPA and 5 mg of E_2C as the optimal doses for suppressing ovulation and producing the lowest rate of menstrual pattern disturbances.

In Phase III clinical trials conducted by the WHO in various parts of the world, the injectable combination alternately was compared with Mesigyna, another injectable product containing 50 mg of norethisterone enanthate and 5 mg of estradiol valerate, DMPA, and oral contraceptives (OCs).[1]

Pregnancy Rate. In comparison with Mesigyna, Lunelle had an annual pregnancy rate of 0.2% vs. 0.4%, respectively.[1] Overall, five pregnancies in 44,160 woman-months of exposure were reported for Lunelle vs. 12 pregnancies in 41,329 woman-months of exposure for Mesigyna.[1]

Adverse Events and Coagulation Impact. In studies conducted by the WHO, no clotting, cardiovascular, or other serious events have been attributed to use of Lunelle. In a prospective clinical trial, an OC containing 35 mcg of ethinyl estradiol and 1 mg norethindrone was compared with Lunelle.[3] Lunelle had a minimal effect on clotting parameters: Its use produced slight decreases in factors VII and X, an increase in tissue plasminogen factor, and minor decreases in antithrombin III activity and protein C levels. In contrast, the oral contraceptive increased factors VII and X and plasminogen, shortening the activated partial thromboplastin time. In addition, protein C increased by nearly 10%. These changes indicated a mild procoagulant effect associated with OC use.[3]

Bleeding patterns. Overall, 70% of the subjects in the WHO

trials had predictable, regular menstrual cycles after one year on the combination injectable, compared with only 8% of DMPA injectable users. Predictability of cycles increased with time among the combination injectable users.[1]

Amenorrhea was substantially less common among Lunelle users than among DMPA users and untreated controls.[1]

Discontinuation Rates. Discontinuations for bleeding-related problems occurred in approximately 8% of subjects overall (although rates varied widely from country to country). There were no discontinuations for serious adverse events.[1]

Return to Fertility. After a Lunelle injection, follicular activity resumed 41-49 days later, and luteal activity initially occurred 59-87 days post-injection.[1] When 70 South American women who used Lunelle for 1-19 cycles were followed after they discontinued the injections because they wished to conceive, Bahamondes et al found that the return to fertility rate at the end of the first month was 1.4 per 100 women and 82.9 per 100 women at one year.[4] Fifty-one pregnancies recorded in this study ended in a live birth, two ended in a spontaneous abortion, and one was a hydatidiform mole pregnancy. No congenital anomalies in pregnancies were associated with use of Lunelle.[4]

U.S. Trial Confirms High Patient Satisfaction

Study Protocol. A Phase III study comparing Lunelle to the OC Ortho-Novum 7/7/7 (0.035 mcg ethinyl estradiol, 0.5/0.75/1 mg norethindrone) was conducted in the United States at 42 investigational sites.[5] The trial was open-label, controlled, and nonrandomized. All subjects were sexually active and desired contraception, aged 18 to 49 years, and nonlactating. Recent use of hormonal contraception, including OCs, was permitted with the exception of DMPA injections.

Participants were allowed to choose the contraceptive method they would use during the study. Lunelle was chosen by 782 women, and 321 patients chose the OC. The baseline demographics between the two groups were similar, except for a slightly higher proportion of Hispanic women and a lower proportion of white women in the Lunelle vs. OC group. As has been found in other U.S. trials of long-acting contraceptive methods, women who chose the injectable tended to be more likely to have used a nonhormonal method of contraception in the past and have given birth compared with women who chose OCs.

The first injection of Lunelle was given within five days of the onset of menses. Subsequent injections were repeated every 28 days + 5 days.

Pregnancy Rate. There were no pregnancies in the Lunelle group and two in the OC group over the two years of the trial, for a life table pregnancy rate for the injectable of 0% vs. 0.3% for the OC.[5]

Bleeding Patterns. Irregular bleeding occurred in both groups during the first few months of treatment. However, most women receiving Lunelle had regular menses by the end of the third month of use; indeed, by that time, 80% of Lunelle users vs. 87% of OC users were having a single withdrawal bleed per cycle without any breakthrough bleeding or spotting.[5,6]

The average cycle interval was 28 days among Lunelle users vs. 27 days among OC users, with a five- to six-day bleeding episode for both types of contraceptives. Mean onset of bleeding occurred on day 22 of the cycle for Lunelle subjects vs. day 24 for OC users (with day 1 being the day of the injection or start of a pill pack). Women who received all injections at regularly spaced intervals had more predictable bleeding patterns.[5,6]

Breakthrough bleeding and spotting rates decreased after several months of use in both groups, from 8% to 4% in the Lunelle group and from 11% to 6% in the OC group.[6]

Amenorrhea was experienced by 1% to 4% of the injectable users during the course of the study, compared with 1% of OC users. During cycles 2-12, 15% of Lunelle users and 3% of OC users experienced a missed period.[6]

Lunelle users (5-6 days) had one more bleeding day per cycle than did OC users (4-5 days); however, when compared with untreated women (6 days) enrolled in the WHO trials, injectable users had somewhat fewer bleeding days.[5]

Women with a body mass index (BMI) lower than 27.3 were more likely to have a single withdrawal bleed in cycle 13 than were women with a BMI higher than 27.3 (80% vs. 64%, respectively) and less likely to be amenorrheic (11% vs 24%, respectively) during a single month.[6]

Adverse Events. Eighty-nine percent of injection users and 84% of OC users reported an adverse event. Serious adverse events occurred in only 1.9% of injectable users and 1.3% of OC users.[5]

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VICE PRESIDENT/GROUP PUBLISHER: Brenda Mooney.
EDITORIAL GROUP HEAD: Valerie Loner.
MANAGING EDITOR: Joy Daugherty Dickinson.
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To reveal any potential bias in this publication, we disclose the following: Dr. Kaunitz (author) participated in the clinical trials for Lunelle, which is marketed by Pharmacia-Upjohn of Peapack, NJ. He also is a consultant for Pharmacia and does continuing medical education presentations and publications. Dr. Kaunitz has participated in clinical trials for Berlex, Galen, Lilly, National Institutes of Health, Parke Davis, Pfizer, R.W. Johnson Pharmaceutical Research Institute, and Solvay. He has participated in clinical trials and done CME presentations and publications for Merck and Organon. He has done CME presentations and publications for Ortho-McNeil and Wyeth-Ayerst. He is a consultant for the American College of Obstetricians and Gynecologists, Association of Professors of Obstetrics and Gynecology, Association of Reproductive Health Professionals, Barr Laboratories, Organon, Ortho-McNeil, Parke Davis, Pharmacia & Upjohn, Procter and Gamble, and Rhone-Poulenc Rorer. He is a stockholder in Johnson and Johnson and Ostex International. Dr. Mishell (peer reviewer) is a consultant for Organon, Warner-Chilcott and Pharmacia & Upjohn. He is on the speaker's bureau for Wyeth Ayerst, Organon, and OrthoMcNeil. He has performed research for Pharmacia-Upjohn and Berlax. Dr. Mishell (peer reviewer) performs research for Pharmacia-Upjohn and Berlax. He is a consultant for Organon, Warner-Chilcott and Pharmacia & Upjohn. He is on the speaker's bureau for Wyeth Ayerst, Organon, and OrthoMcNeil.

Weight Gain. Although mean body weight was unchanged for OC users during the course of the study, injection users experienced a median increase of four pounds during seven months of use, and five pounds over 15 months of use. Women weighing more than 150 pounds tended to gain more weight than women weighing fewer than 150 pounds. This finding differed from the results of the WHO trials.[1,6]

Laboratory Tests and Metabolic Impact. Laboratory parameters of glucose, hepatic, and renal function and hematologic indices were unaffected by either treatment.[5] Laboratory parameters included blood sugar, hematocrit, hemoglobin, creatinine, alanine aminotransferase or asparate aminotransferase and bilirubin were unaffected by either treatment. Coagulation parameters were not assessed in this study.

Discontinuations. The most common reasons for discontinuations in the Lunelle and OC groups were weight gain (5.7% and 0.9%, respectively), metrorrhagia (2.5% and 0.9%), emotional liability (2.5% and 1.6%), and acne (1.9% and 0.9%).[5]

Patient Compliance. Ninety-seven percent of Lunelle users received at least one subsequent injection between 23 and 33 days after prior injections; 70% had all of their injections within this time frame. Fourteen percent missed two or more pills per cycle.[5]

Patient Satisfaction. Satisfaction with the monthly injectable method was high and similar between groups, as assessed by questionnaires administered to participants during the trial. Ninety percent of the injectable users reported they would recommend the method to a friend, and 90% said they experienced no difficulties returning to their clinician's office for the monthly injections.[7]

Eighty-one percent of Lunelle users said they were very comfortable or comfortable with the route of administration for the contraceptive, compared with 88% and 87% of new and prior OC users, respectively. Ninety-one percent of Lunelle users said they were not bothered by the injections. In contrast, 97% of new OC users and 99% of prior OC users said they were not bothered by having to take a daily pill. Also, 79% of Lunelle users and 90% of all OC users said the methods they were using did not interfere with daily activities, and 86% of Lunelle users and 95% of all OC users said their methods did not interfere with social activities.

Comparison to Depo-Provera and the Pill

Irregular menstrual patterns and amenorrhea are common with Depo-Provera use (with the latter occurring in more than one-half of users by the end of one year), and return of fertility may be delayed for 10-18 months after a final injection. In contrast, Lunelle injections confer regular menstrual cycles, little amenorrhea, and a rapid return to fertility after discontinuation of the method.[5,8,9]

Both methods require a visit to a provider to initiate and continue use, with Depo-Provera requiring visits every three months and Lunelle monthly. Neither method necessitates a visit or consultation with a provider for discontinuation. Because it contains estrogen, the monthly injection is not appropriate for lactating women or others in whom estrogen use is contraindicated. These women are, however, candidates for Depo-Provera.[5, 8,9]

Both methods are extremely efficacious, with Lunelle demonstrating a zero failure rate in the U.S. trial.[5] With typical use, the failure rate for Depo-Provera is 0.3%.[8]

Side effects associated with Depo-Provera may include irregular bleeding/spotting, amenorrhea, weight gain, and transient decreases in bone density.[8] Side effects of the combination monthly injectable may include menstrual bleeding changes, breast tenderness, and weight gain.[5]

In comparison to OCs, Lunelle confers comparable efficacy and safety, a more convenient dosing schedule (eliminating the need to take a daily pill), and a similar menstrual pattern and side effect profile.[5] In the U.S. trial, the failure rate was zero for Lunelle vs. 0.3% for the OC.[10]

Further study is needed to adequately characterize the potential noncontraceptive benefits of Lunelle. Like the Pill, it is likely that Lunelle will have bone-protective effects and might prevent ovarian cancer. Like both OCs and the progestin-only injection, it also might reduce the risk of endometrial cancer, iron-deficiency anemia, pelvic inflammatory disease, and ectopic pregnancy.[9]

Neither Lunelle, Depo-Provera, nor the Pill provide protection against sexually transmitted infections.

Suitable Candidates

Based on currently available data, women of all reproductive ages and socioeconomic strata who are candidates for the Pill are also candidates for Lunelle. Because Lunelle contains estrogen and requires monthly administration, many Depo-Provera candidates may not find Lunelle to be a suitable choice.

Contraindications to Lunelle use are the same as those observed for combination OCs. For instance, the method is not recommended for women with known or suspected pregnancy, a past or present history of thrombophlebitis or thromboembolic disorders, cerebral vascular or coronary artery disease, undiagnosed abnormal genital bleeding, liver dysfunction or disease, or carcinoma of the endometrium or breast.[8]

Administration Basics

Injection Technique. Lunelle is provided in the unit dose formulation and may be administered intramuscularly into the deltoid, quadriceps, or gluteus maximus muscle using a 1- to 1.5-inch needle no thinner than a 23-gauge. The solution must be gently shaken prior to aspiration into the syringe to ensure uniform suspension of the hormone crystals.[8,9]

Injection Schedule. The initial injection should be given within five days of the onset of a normal menstrual period. It also may be administered within seven days following a first-trimester abortion or between three and six weeks postpartum.[8]

Subsequent injections should be given within 28-30 days of the preceding injection, although they may be administered as early as 23 days and as late as 33 days.[8]

Counseling. Patients should be counseled to expect irregular bleeding, particularly during the first three months of use, and instructed to return for repeat injections on as regular a schedule

as possible.[8] They should be advised to expect cyclic withdrawal bleeding to occur approximately 2-3 weeks after each injection.[5]

Summary

The monthly combination injection Lunelle offers comparable efficacy to that of OCs and DMPA, is quickly reversible with a rapid return of fertility, and has a minimal impact on laboratory and clotting parameters. After three injections, it usually confers a regular menstrual pattern, particularly when the contraceptive is received on a regular schedule, and is well-accepted by patients. The advent of a self-administered subcutaneous formulation, currently in development by Pharmacia Corp. of Peapack, NJ, may make Lunelle even more accessible and convenient for women looking for extremely effective contraception that is not linked to coitus or daily administration.

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CME Question

To earn CME credit for this issue of Contraceptive Technology Reports*, please refer to the enclosed Scantron form for directions on taking the test and submitting your answers.*

1. The estradiol released from Lunelle's injection site is:
   - A. the synthetic ethinyl estradiol used in birth control pills
   - B. 17-beta estradiol, identical to the hormone produced by the ovaries
   - C. neither of the above

2. The return to fertility rate with Lunelle is comparable to that seen with:
   - A. Depo-Provera
   - B. oral contraceptives
   - C. neither of the above

In Future Issues: Mirena IUS