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INSIDE

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Are Norplant's days numbered in the U.S.? Test results could decide its fate

Use contraceptive backup for women with suspect implants

Look for the outcome of tests on suspect lots of Norplant implants to play a major role in the availability of the contraceptive method in the United States. Because the arsenal of contraceptives in the nation is already limited, compared with contraceptives available internationally, some family planning experts have expressed dismay at the possibility that Norplant might be removed from the market.

"Norplant is very popular in other parts of the world and widely used; it must be given more time to gain a market niche. I hope the company has the courage to continue supplying Norplant to American women," observes **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. Some of Schnare's patients are waiting for a shipment of Norplant for insertion.

EXECUTIVE SUMMARY

Product stability tests on suspect lots of Norplant contraceptive implants in the United States should be completed by late October. Until then, women who have Norplant implants from lots distributed on or after Oct. 20, 1999, should use an additional nonhormonal method of contraception, states the manufacturer, Wyeth-Ayerst Laboratories in Philadelphia.

- All women with implants from the suspect lots should use condoms, spermicide, diaphragms, or intrauterine devices until the tests are completed, according to a Sept. 13 letter from the manufacturer. A letter issued Aug. 10 advised backup contraception for those women who would be considered at high risk if they became pregnant. When Wyeth-Ayerst officials realized the results of the tests would be unavailable until late October, they issued the second letter as a precaution.
- Counsel women with the suspect implants about backup contraception. Upon request, the company will cover the costs of backup birth control and reimburse those who want the suspect implants removed.

Manufacturer Wyeth-Ayerst Laboratories in Philadelphia has been working with the Food and Drug Administration (FDA) to ensure that patients who may have the implants from the suspect lots are aware of the potential reduction in contraceptive protection.

Routine laboratory tests of the product's shelf-life stability indicated lower-than-expected release rates of levonorgestrel in recently manufactured implants. The tests showed that implants from certain specified lots might not release enough levonorgestrel to deliver effective ongoing contraception. **(*Contraceptive Technology Update* reported on Wyeth-Ayerst's initial findings in its October 2000 issue, p. 117.)** Some 22,000 kits were contained in the suspect lots, according to company estimates.

The investigation is expected to conclude in late October, reports company spokeswoman **Audrey Ashby**. Until that time, there are no additional Norplant system kits available for reinsertion, she says. "The resolution of this situation will have a significant impact on the decision of whether Wyeth will continue to market Norplant,'' says Ashby.

Implant provides choice

Use of the implant lags behind other contraceptive methods in the United States. An analysis of a national survey indicates fewer than 2% of American women at risk of an unintended pregnancy rely on the implant for birth control.[1]

CTU readers also report low levels of Norplant use: More than 70% of those responding to the 2000 Contraception Survey said they had not performed any Norplant insertions in the last year, comparable to 1999 statistics. **(See *CTU,* September 2000, for complete survey results.)** The number of Norplant removals also remained consistent with 1999 figures; about 72% reported no removals, compared with 69.3% in 1999.

The number of women nationwide currently requesting Norplant implants is limited, agrees **Andrew Kaunitz**, MD, professor and assistant chair in the obstetrics and gynecology department at the University of Florida Health Science Center / Jacksonville and director of menopause and gynecology services at the Medicus Women's Diagnostic Center in Jacksonville. However, providers are continuing to insert implants regularly at his institution, particularly in postpartum patients, he reports.

"If Norplant is removed from the U.S. market, the impact may not be great," says Kaunitz. "Nonetheless, Norplant is currently meeting the needs of certain women."

For many women, Norplant is the long-term solution when they want reliable, reversible contraception, says **Susan Wysocki**, RNC, NP, president and chief executive officer of the National Association of Nurse Practitioners in Women's Health, based in Washington, DC. It would be unfortunate if Norplant were unavailable to women who want it, she notes.

Norplant was a very exciting product when first introduced, and the Population Council in New York City had worked long and hard on its development, reflects **Allan Rosenfield**, MD, dean of the Mailman School of Public Health, DeLamar Professor of Public Health, and professor of obstetrics / gynecology at Columbia University in New York City. The issue of removal, however, was never given the attention it needed, he notes. In 1994, complicated implant removals were the basis of the first lawsuit involving Norplant and the flood of media coverage and litigation that followed.[2]

After Norplant's initial takeoff, when problems hit, the market for the method fell dramatically, states Rosenfield, who led a national committee on contraceptive research and development that examined the U.S. experience with Norplant. At this point, Norplant's removal from the U.S. market would be unfortunate, but it probably would not have had a significant effect on contraceptive practice, he notes.

"There are a number of lessons to be learned, but it is most unfortunate that a major innovative and effective new approach to hormonal contraception may be lost to American women, despite

COMING IN FUTURE MONTHS

- Review male contraceptives in research
- Target heart disease in menopausal women
- Review the use of the intrauterine device
- Learn how to use the combined injectable
- Scan advances in early abortion methods

the fact that it really is safe and equal to sterilization in effectiveness," Rosenfield asserts. "This latest blow probably will make it difficult for the company to continue its distribution."

Kaunitz says he looks forward to the availability of second-generation implants, including the single-rod Implanon, to become available in the United States. "Given the simplicity and insertion, the availability of easier-to-insert-and-remove systems like Implanon could perhaps increase patient and provider interest in contraceptive implants," he says. **(See *CTU*, August 1999, p. 87, for information on Implanon, a 3-keto-desogestrel progestin product manufactured by Organon NV; Wyeth-Ayerst's two-rod levonorgestrel implant; and the Population Council's Nestorone subdermal contraceptive.)**

Second advisory issued

Providers moved quickly to contact women with suspect implants after Wyeth-Ayerst distributed a second advisory Sept. 13. The letter recommended that all women who have suspect implants use an additional nonhormonal method of contraception until the company can determine the product's effectiveness. The guidance is stronger than Wyeth-Ayerst's initial letter issued Aug. 10, which advised backup contraception for those women with the suspect implants who would be considered at high risk if they became pregnant. When company officials realized the test results would be unavailable until late October, it issued the second letter as a precaution.

The FDA also issued an advisory "talk paper" on the subject that called for nonhormonal backup contraception for those with the suspect implants.[3]

All affiliates of New York City-based Planned Parenthood Federation of America were alerted of the second advisory letter the day it was issued, says organization spokeswoman **Adina Wingate Quijada**. "We've been following right along with the information that was directed from the first letter, and the second letter is just an amplification of the first letter," she notes.

How have affiliates dealt with the patient notification process? "The information we have received indicates that it has been absolutely consistent, smooth, and routine," she says.

Check your patient files for records of implant insertions beginning Oct. 20, 1999, to determine if any women received a kit from the specified lots of Norplant. If you are unable to ascertain the lot number, assume that any insertions performed on or after that date are from the suspect lots, Wyeth-Ayerst advises. If patients have implants that were inserted by another provider, contact them for the lot number and insertion date, the company instructs. Women who began using Norplant before Oct. 20, 1999, are not affected, and their Norplant implants remain effective, long-term contraceptives.

The company continues to recommend that there be no new insertions of Norplant implants from the following lots, which have expiration dates in January or February 2004:

- 3990729;
- 3990775;
- 3990776;
- 3993006;
- 3003127;
- 3003166;
- 3003355.

Facilities may return remaining implants from those lots to Wyeth-Ayerst. Providers may call the Norplant System Information Line at (800) 364-9809 for more on returning the product.

Patients with the suspect implants should be informed that they need to use a backup nonhormonal method of contraception until the company's investigation is complete. Such types of backup contraception include condoms, spermicides, diaphragms, and intrauterine devices. Women who wish to receive financial assistance for backup contraception should call the Norplant System Information Line, which also is available to answer questions from health care providers, says Ashby.

Ashby says the company will pay up to $100 to women who request financial assistance for backup contraception. In addition, the company will reimburse women $700 if they wish to have the suspect Norplant removed, although Wyeth-Ayerst is not recommending removal yet, and the company says it has no reports of increased pregnancy rates among Norplant users.

References

1. Tanfer K, Wierzbicki S, Payn B. Why are U.S. women not using long-acting contraceptives? *Fam Plann Perspect* 2000; 32:176-183, 191.

2. Harrison PF, Rosenfield A, eds. *Contraceptive Research, Introduction, and Use. Lessons from Norplant.* Washington, DC: National Academy Press; 1998.

3. Food and Drug Administration. Talk Paper. *Update of Advisory for Several Lots of Norplant Contraceptive Kits.* Bethesda, MD: Sept. 13, 2000; T00-42. ■

Third-generation OCs don't increase VTE risk

A just-released study indicates that "third-generation" pills — combined oral contraceptives (OCs) with a gestodene or desogestrel progestin component — do not put women at increased risk of developing clots in the veins.[1]

The new research may put to rest epidemiological questions that have surrounded OC progestins and venous thromboembolism (VTE) risk, says **Andrew Kaunitz**, MD, professor and assistant chair in the obstetrics and gynecology department at the University of Florida Health Science Center in Jacksonville and director of menopause and gynecology services at the Medicus Women's Diagnostic Center, also in Jacksonville.

"Whether formulated with newer or older progestins, all combination OCs increase the risk of thromboembolism," he says. "From an absolute perspective, this elevated risk is small indeed; nonetheless, this observation underscores the importance of not prescribing combination OCs to high-risk women, particularly those with a prior history, unless they are chronically anticoagulated."

Pills with a gestodene or desogestrel component have been the focus of multiple investigations in the aftermath of what has been termed the British "pill scare." **(See *Contraceptive Technology Update*, January 1996, p. 6, for details on the 1995 pill scare that arose following a warning from Britain's Committee on the Safety of Medicines.)**

EXECUTIVE SUMMARY

"Third-generation" oral contraceptives (OCs) containing the progestins gestodene or desogestrel don't put women at increased risk of clots in the veins, according to a recently published investigation. Concern over use of the pills arose from earlier findings that indicated up to a twofold increase in the risk of venous clotting compared with older combined formulations.

- The new study compared the incidence of venous clots in women in the three years before and after the 1995 British "pill scare," when use of such OCs fell from 54% to 14% in women ages 15 to 49 taking combined pills.
- The results show that although the use of third-generation OCs fell during the period after 1995, the rates of venous clots among women taking the pill did not change significantly.

Concern over use of the pills arose from findings that indicated up to a twofold increase in risk of venous clotting compared with older combined formulations.[2-4]

No pills in the United States contain gestodene; only two contain desogestrel: Ortho-Cept from Ortho-McNeil Pharmaceuticals in Raritan, NJ, and Desogen from Organon in West Orange, NJ. Although the Food and Drug Administration was quick to issue a statement following the British alert to affirm the safety of desogestrel pills, use of such OCs fell in the United States.

Ortho-Cept dropped from its leading position in the 1995 *CTU* Contraception Survey to fifth place in 1996, with Desogen falling from sixth place in 1995 to ninth place in 1996. Ortho-Cept remained at fifth place as a first-choice pill for a 21-year-old nonsmoker in *CTU*'s 2000 Contraception Survey; Desogen was not among the top nine pills named in the survey. **(For complete results of the survey, see *CTU*, September 2000, pp. 101-114.)**

Several subsequent studies have found no risk difference between the older and newer pills,[5-9] while others have shown an increased risk.[10-12] After weighing the evidence, Britain's Medicines Commission, a government advisory body, issued a national statement in April 1999 saying doctors can prescribe the third-generation pills as a first-line form of contraception. The government again affirmed the safety of the pills after publication of a Danish study showing an increased risk of VTE in users of the third-generation pills.[12] **(For full study results, see *CTU*, December 1999, p. 140.)**

A look at the new study

The new study examines the incidence of venous clots in British women in the three years before and after the 1995 pill scare, when use of third-generation OCs fell from 54% to 14% in women ages 15 to 49 who take combined pills. Researchers analyzed information from the General Practice Research Database, which pulled data from 304 general practices throughout Great Britain. Women who were at risk of clots for other reasons were not included in the study.

The results show that although the use of third-generation OCs fell during the period after 1995, the rates of venous clots among women taking the pill did not change significantly. Therefore, the findings are not compatible with the assertion that third-generation OCs are associated with a twofold increase in risk of VTE compared with older progestins, the authors conclude.

Most of the studies have been case-control investigations, which are fairly fragile, observes **Richard Farmer**, MRCGP, FFPHM, PhD, professor at the postgraduate medical school of the University of Surrey in Guildford and lead author of the new analysis. "You have to be sure that the controls you identify genuinely represent the population," he notes. "And they are even more fragile when you are talking about the sort of very low frequency as [is associated] with VTE."

Farmer says only three studies — none of which was adjusted for duration of use — have shown an increased risk with the third-generation pills.[2,3,4] The new study can be classified as an intervention study, because the entire pattern of OC use had changed, he says. "If there was genuinely an increase in risk in the so-called third-generation pills, you would expect there to be a fall, and there wasn't a fall. I think that there is very strong evidence to support the notion that there are no differences between the different types of pills."

References

1. Farmer RDT, Williams TJ, Simpson EL, et al. Effect of 1995 pill scare on rates of venous thromboembolism among women taking combined oral contraceptives: Analysis of General Practice Research Database. *BMJ* 2000; 321:477-479.
2. World Health Organisation Collaborative Study on Cardiovascular Disease and Steroid Hormone Contraception. Venous thromboembolic disease and combined oral contraceptives: Results of international multicentre case-control study. *Lancet* 1995; 346:1,575-1,582.
3. Jick H, Jick SS, Gurewich V, et al. Risk of idiopathic cardiovascular death and nonfatal venous thromboembolism in women using oral contraceptives with differing progestogen components. *Lancet* 1995; 346:1,589-1,593.
4. Spitzer WO, Lewis MA, Heinemann LAJ, et al. Third generation oral contraceptives and risk of venous thromboembolic disorders: An international case-control study. *BMJ* 1996; 312:83-88.
5. Suissa S, Blais L, Spitzer WO, et al. First-time use of newer oral contraceptives and the risk of venous thromboembolism. *Contraception* 1998; 57:61-65.
6. Lidegaard O, Edstrom B, Kreiner S. Oral contraceptives and venous thromboembolism: A case-control study. *Contraception* 1998; 57:291-301.
7. Lewis MA, MacRae KD, Kuhl-Habichl D, et al. The differential risk of oral contraceptives: The impact of full exposure history. *Hum Reprod* 1999; 14:1,493-1,499.
8. Farmer RDT, Lawrenson RA, Thompson CR, et al. Population-based study of risk of venous thromboembolism associated with various oral contraceptives. *Lancet* 1997; 349:83-88.
9. Farmer RDT, Lawrenson RA, Todd J-C, et al. A comparison of the risks of venous thromboembolic disease in association with different combined oral contraceptives. *Br J Clin Pharmacol* 2000; 49:580-590.
10. Parkin L, Skegg DCG, Wilson M, et al. Oral contraceptives and fatal pulmonary embolism. *Lancet* 2000; 355:2,133-2,134.
11. Bloemenkamp KW, Rosendaal FR, Buller HR, et al. Risk of venous thrombosis with use of current low-dose oral contraceptives is not explained by diagnostic suspicion and referral bias. *Arch Int Med* 1999; 159:65-70.
12. Mellemkjaer L, Sorenson HT, Dreyer L, et al. Admission for and mortality from primary venous thromboembolism in women of fertile age in Denmark, 1977-95. *BMJ* 1999; 319:820-821. ■

Teens waiting longer, using better protection

Good news: A shift toward safer, more protective sexual behavior among teens has been confirmed by an analysis of findings from four national surveys.[1] This confidence-booster comes on the heels of new statistics from the Hyattsville, MD-based National Center for Health Statistics (NCHS), which show that the birth rate for teenagers declined 3% between 1998 and 1999 to reach a rate of 49.6 births per 1,000 women ages 15 to 19 — the lowest teen birth rate in the 60 years of recorded data.[2]

The trends in the 1990s toward later first intercourse and increased condom use are real, conclude researchers who analyzed data from four national surveys:

- National Survey of Family Growth (NSFG), administered by the NCHS to provide comprehensive data on fertility, contraception, marriage, and cohabitation;
- Youth Risk Behavior Surveillance System

EXECUTIVE SUMMARY

Reports on adolescents' shift toward safer, more protective sexual behavior have been confirmed by a new analysis of four national surveys.

- The news comes on the heels of the federal government's announcement that the birth rate for teen-agers declined 3% between 1998 and 1999, reaching the lowest rate in the 60 years since data on teen births have been recorded.
- The new analysis verifies trends in the 1990s toward later first intercourse and increased condom use. More data are needed to compare the impact of rising condom use with the drop in oral contraceptive use and to confirm the trend toward long-acting methods such as the contraceptive injectable.

(YRBS), administered by the Atlanta-based Centers for Disease Control and Prevention (CDC) to help states monitor critical health risk behaviors among teen-agers;

• National Survey of Adolescent Males (NSAM), supported by the Department of Health and Human Services agencies to provide information on the behavior of young men;

• National Longitudinal Study of Adolescent Health, funded by the National Institute of Child Health and Human Development of the National Institutes of Health and other Health and Human Service agencies to provide data on risky behaviors and resiliency factors in adolescents.

Tracking trends, gender differences

Each survey differs in purpose, methodology, and sample, so the researchers focused on a common subset of high school students ages 15 to 17. They examined trends and gender differences in six behaviors:

• ever having had sexual intercourse;

• having had sexual intercourse in the last three months;

• pill use at last intercourse;

• condom use at last intercourse;

• number of partners in the last three months;

• number of lifetime partners.

In both the NSAM and YRBS, researchers found decreases in the proportion of all males and of white males who reported ever having had sexual intercourse and increases in condom use among all males.

A second group of trends reveals a significant finding in one survey with a parallel but insignificant change in another, the researchers state. The YRBS indicates a significant decrease in the proportion of black females who reported ever having had intercourse, with the same finding a suggested trend in the NSFG. A decline in the proportion of Hispanic males reporting ever having had intercourse is significant in the YRBS and insignificant in the NSAM. The decrease in the proportion of white males who reported having had four or more lifetime sexual partners is significant in the YRBS and is suggested in the NSAM, researchers report. The variations in data may be related to survey design and implementation, they note.

Nonetheless, the declines in sexual experience and the increases in condom use reported in these data indicate shifts toward safer and more self-protective behaviors among adolescents, the researchers conclude. The fact that several surveys show these changes increases confidence that the trends are real, they state.

Trying to understand how the methodological differences in the surveys may affect results might be confusing to the casual reader, says **John Santelli**, MD, MPH, assistant director for science in the CDC's Division of Reproductive Health and lead author of the paper. What is reassuring is that the trends are consistent, he notes.

While the just-published analysis offers good news, there are some qualifications, says **Susheela Singh**, PhD, director of research at the New York City-based Alan Guttmacher Institute (AGI). The findings related to increased condom use and decline in sexual activity among adolescent males are indeed positive, she notes. However, there was much less change in female adolescents, she says.

While the movement toward increased condom use is a welcome one in light of the need for protection against sexually transmitted infections, it is coupled with a decrease in use of oral contraceptives, Singh says. This same finding was recorded in a 1999 paper issued by AGI.[3] Increased use of long-acting contraceptives, such as depot medroxyprogesterone acetate (DMPA or Depo-Provera, manufactured by Pharmacia Corp. in Peapack, NJ) and Norplant levonorgestrel implants (manufactured by Wyeth-Ayerst Laboratories in Philadelphia) may be helping protect teens against pregnancy.

"Primarily because of this shift to long-acting methods, overall contraceptive effectiveness among teen-agers improved between 1988 and 1995 — or, put another way, teen-age contraceptive users grew less likely to become pregnant," the AGI paper notes.[3]

While anecdotal reports signal that use of injectables continues to climb, it will take new data to confirm those findings, says Singh. AGI researchers also are reviewing data to see if adolescents are resorting to noncoital sexual activities instead of intercourse to see if such a switch is contributing to the decline in teen pregnancies.

References

1. Santelli JS, Lindberg LD, Abma J, et al. Adolescent sexual behavior: Estimates and trends from four nationally representative surveys. *Fam Plann Perspect* 2000; 32:156-165, 194.

2. National Center for Health Statistics. *Births: Preliminary Data for 1999.* Hyattsville, MD; 2000. (PHS) 2000-1120.

3. Darroch JE, Singh S. *Why is Teenage Pregnancy Declining? The Roles of Abstinence, Sexual Activity, and Contraceptive Use.* New York: Alan Guttmacher Institute; Occasional Report No. 1, December 1999. ■

Tucson teens urged to 'Use Condom Sense'

As a family planning provider, you want to reach teens who are sexually active and are not practicing safer sex. While your clinic makes condoms readily available, teens either don't take advantage of them or are unaware that such programs exist. What can you do?

Take a look at Tucson's "Protection Connection." Managed by Planned Parenthood of Southern Arizona, the program operates 19 condom vending machines in high-traffic areas frequented by adolescents. For 50 cents, they can obtain a condom and a friendly reminder to "Use Condom Sense" to reduce the risk of pregnancy and the spread of sexually transmitted infections.

The program allows the condoms to be distributed to youth who really need them: sexually active teens under age 17 who don't normally access local reproductive health services, says **Patti Caldwell**, MSW, senior vice president of Planned Parenthood of Southern Arizona. Most of those adolescents obtain their condoms from drugstores, rely on friends for supplies, or wait until they are a little older to visit reproductive health clinics.

"We don't see the majority of these teens, so it is important to us that we don't make access to what they need conditional on walking into a clinic," notes Caldwell.

Protection Connection is a social marketing campaign focused on changing the social norm among sexually active youth to consistent condom use, according to Caldwell. Its approach was inspired by programs such as Portland's "Project ACTION," administered by Population Services International, a nonprofit health organization in Washington, DC. **(*Contraceptive Technology Update* offered an overview of Project ACTION in *STD Quarterly* in June 1997, p. 72.)**

EXECUTIVE SUMMARY

Sexually active youth in Tucson are getting the message about condom use, thanks to the "Protection Connection," managed by Planned Parenthood of Southern Arizona.

- This marketing campaign focused on changing the social norm among sexually active youth to consistent condom use. Targeted for sexually active teens under 17 who don't normally access reproductive health services, the program operates 19 condom vending machines in high-traffic areas frequented by adolescents.
- More than half of young people surveyed by an independent research firm say they now associate condoms with safer sex, compared with 39% in 1998. Use of the condom machines rose to 57%, up from 42% the previous year.

Teen focus groups help design program

Training and technical assistance from Population Services International began in late 1997, with 1998 devoted to developing a community advisory board and raising funds for the project. The program also contracted with market research firm Behavior Research Center of Phoenix for baseline research with local teens, including 12 focus groups of young people and a convenience sample of 300 young people under age 17. This initial research, as well as pretesting, guided the development of media images and messages.

The youth identified city park and recreation centers, coffee houses, and night clubs featuring teen nights as potential vending machine locations. Program staff installed the machines and kicked off a media campaign in midsummer 1999. Bus benches, advertising placards in local transit buses, and radio spots were used to heighten awareness of the program. This year has seen the addition of a teen advisory board, a part-time teen coordinator, and six part-time outreach workers. The program costs about $100,000 per year, Caldwell estimates.

The machines are stocked with Ansell LifeStyles condoms from Ansell Personal Products of Red Bank, NJ. The program has hired one person to install the machines and perform regular maintenance every two weeks to keep them clean and functional, says Caldwell.

Behavior, attitudes shift

A second convenience sample was performed this spring to check on project recognition and impact. More than half of young people now associate condoms with safer sex, compared with 39% in 1998. Use of the condom machines rose to 57%, up from 42% the previous year.

The simple message of "Use Condom Sense" has been heard by the target audience. About three-quarter of teens surveyed said they were

aware of the media campaign. More than 90% of teens say the campaign has made them very or somewhat likely to use condoms when they have sex.

The ads seen on the bus benches and placards feature one of four images of a young man or woman holding a condom, along with the words "Use Condom Sense — a friendly reminder from Planned Parenthood," and the message, "Although no contraceptive or prophylactic can guarantee 100% effectiveness, condoms, when properly used, reduce the risk of pregnancy and the spread of sexually transmitted infections, including HIV." The same images are used on the condom vending machines.

To advertise the location of the machines, Planned Parenthood has printed wallet-size cards with the "Use Condom Sense" logo and a listing of all machine locations. Included inside the cards is an illustration of how to use a condom, because the 2000 convenience survey indicated a decline in the number of teens who said they knew correct condom usage.

Repeating the message

Planned Parenthood of Southern Arizona is committing to the condom awareness program for the long haul, says Caldwell.

"We want to continue to evolve the media campaign and get enough money to keep funding it," she notes. "Keeping the message out there is really important, since teen-agers are only teen-agers for awhile, then there are new teen-agers."

Such a continued commitment is needed, says **Cynthia Mick**, FNP, BSN, MSN, primary nurse practitioner at Planned Parenthood's Jean Hoffman Center in Tucson. The clinic sees a large number of teen- and college-age patients.

"I think teen-agers are beginning to use condoms more often, although I think it is still a significant problem," observes Mick. "I think that it is a difficult group, and it's going to take more time." ■

RESOURCE

For more information on the Protection Connection campaign, contact:

- **Patti Caldwell**, MSW, Planned Parenthood of Southern Arizona, 127 S. Fifth Ave., Tucson, AZ 85701. Telephone: (520) 624-1761, ext. 211. E-mail: patti.caldwell@ppfa.org.

Fund established in memory of Burnhill

A memorial fund has been established at the New York City-based Planned Parenthood Federation of America for family planning pioneer, innovator, and advocate **Michael Burnhill**, MD. Burnhill, who died unexpectedly of natural causes Aug. 4, served as the federation's vice president of medical affairs.

Burnhill wrote more than 110 scientific publications, books, chapters, and monographs and was a prolific inventor who held several U.S. patents, including one for the "Birnberg Bow," an early intrauterine device.

Burnhill began his career at Planned Parenthood of New York City in 1972, when that agency became the second Planned Parenthood affiliate in the nation to offer abortion services. In 1991, Burnhill received the Christopher Tietze Humanitarian Award from the Washington, DC-based National Abortion Federation, and he was awarded the Alan Guttmacher Lectureship in 1995. From 1977 until 1999, Burnhill was a faculty member at the Robert Wood Johnson Medical School of the University of Medicine and Dentistry of New Jersey in New Brunswick.

> "Michael Burnhill was at the forefront of caring for the health and well-being of women, both here in the United States and abroad."

"During his long productive career, Michael Burnhill was at the forefront of caring for the health and well-being of women, both here in the United States and abroad," said **Allan Rosenfield**, MD, dean of Columbia University's Mailman School of Public Health in New York City and a former chair of the board of Planned Parenthood Federation of America. "He will be sorely missed by his many patients, colleagues, family, and friends."

Donations to the memorial fund may be sent to Planned Parenthood Federation of America Inc., 810 Seventh Ave., New York, NY 10019. To post a special memory of the physician, visit the Web site of the Association of Reproductive Health Professionals: www.arhp.org. ■

Join global forces on World AIDS Day

What is your facility planning for Dec. 1, World AIDS Day? Since the first event was held in 1988, observances have been broadened into a year-round campaign, with events culminating on Dec. 1.

The theme for the 2000 observance is "AIDS: Men Make a Difference." Men tend to have more sex partners than women, including more extramarital partners, thereby increasing their own and their primary partners' risk of contracting HIV, according to the Geneva-based Joint United Nations Programme on HIV / AIDS (UNAIDS), lead organization for the annual event. That risk is compounded by the secrecy, stigma, and shame surrounding HIV, which keeps men and women from acknowledging their HIV status. Focusing the campaign on men also acknowledges the fact that men are often less likely to seek health care than women, says UNAIDS.

Learning about prevention, treatment

Following are some Web resources to help you and your patients focus on prevention and treatment of HIV:

1. Joint United Nations Programme on HIV/AIDS (UNAIDS): www.unaids.org/wac/2000/index.html.

This section of the UNAIDS Web site deals specifically with the World AIDS Campaign. It offers two posters in Adobe Acrobat format that may be downloaded for use. Also available is information from past campaigns that may provide insight for designing present and future campaigns.

2. National Center for HIV, STD, and TB Prevention, Divisions of HIV/AIDS Prevention: www.cdc.gov/hiv/wad.htm.

The Atlanta-based Centers for Disease Control and Prevention's National Center for HIV, STD, and TB Prevention, Divisions of HIV / AIDS Prevention has a wealth of patient and provider information at its World AIDS Day site. While the site still contains information on the 1999 campaign, it offers many brochures and fact sheets in both HTML and Adobe Acrobat format that can be downloaded for use for general education on HIV / AIDS. Click on "World AIDS Day Activities" to see a state-by-state breakdown of 1999 activities to get ideas for your 2000 observance.

3. National Institute of Allergy and Infectious Diseases: www.niaid.nih.gov/publications.

The National Institute of Allergy and Infectious Diseases offers several brochures and fact sheets on HIV / AIDS. Click on "AIDS," then "General," then "How to Help Yourself" to view handouts written in an easy-to-read format in English and Spanish on such subjects as "Taking the HIV Test" and "Testing Positive for HIV."

4. The Body: www.thebody.com.

The Body Web site, which is operated by Body Health Resources Corp. in New York City, defines itself as a Web tool "to lower barriers between patients and clinicians; demystify HIV / AIDS and its treatment; improve patients' quality of life; and foster community through human connection." It offers forums on such topics as treatment regimens, side effects management, and diet and exercise. Search more than 250 topic areas of HIV / AIDS information through the site's search engine.

5. HIV InSite: hivinsite.ucsf.edu/social/un/3098.0041.html.

HIV InSite is a project of the University of California at San Francisco (UCSF) Positive Health Program at San Francisco General Hospital Medical Center and the UCSF Center for AIDS Prevention Studies, which are programs of the UCSF AIDS Research Institute. The project offers a link to "Fact Sheets on HIV / AIDS for Nurses and Midwives," developed by the World Health Organization and the Joint United Nations Programme on HIV / AIDS. Providers may choose from 13 fact sheets that cover the care of people living with HIV / AIDS.

While the fact sheets are written in an easy-to-understand style, they are designed for nurses and midwives and contain detailed information about nursing care and medical matters. The fact sheets are available in Adobe Acrobat format. ■

CTUPDATES

News ■ Resources ■ Events

Contraceptives are focus of new ACOG bulletin

Is combination oral contraceptive (OC) use safe for women with chronic hypertension? What hormonal contraceptive options are available for women with benign breast disease?

A new practice bulletin on hormonal contraception from the American College of Obstetricians and Gynecologists (ACOG) in Washington, DC, answers these and other questions surrounding use of hormonal contraception in women with coexisting medical conditions.

The bulletin offers ACOG's recommendations on the use of OCs, implants, and injections in women with hypertension, diabetes, migraine headaches, fibrocystic breast changes, or a history of breast cancer, uterine fibroids, or high cholesterol. The publication was developed by the ACOG Committee on Practice Bulletins with the assistance of Andrew Kaunitz, MD, professor and assistant chair in the obstetrics and gynecology department at the University of Florida Health Science Center in Jacksonville and director of menopause and gynecology services at the Medicus Women's Diagnostic Center, also in Jacksonville.

Examples of the ACOG recommendations include the following:

• Women with fibroadenoma (benign breast disease) or a family history of breast cancer are at little or no additional risk of breast cancer because of OC use. Therefore, OCs can be prescribed for those women if they are otherwise appropriate candidates.

• Combination OCs should be prescribed with caution, if ever, to smokers over 35. Women smokers younger than 30 who are otherwise healthy generally can be prescribed combination OCs.

• Women ages 35 and younger who have well-controlled and monitored hypertension are appropriate candidates for a trial combination OC formulated with 35 mcg or less of estrogen, provided they are otherwise healthy nonsmokers with no evidence of end organ vascular disease. If blood pressure remains well-controlled several months after beginning OCs, use can be continued.

• Use of combination OCs by diabetic women should be limited to those who do not smoke, are younger than 35, and are otherwise healthy with no evidence of hypertension, nephropathy, retinopathy, or other vascular diseases.

• Progestin-only contraceptives might be appropriate for women with coronary artery disease, congestive heart failure, or cerebrovascular disease. However, combination OCs are not recommended for these women.

• Birth control injections or implants are safer alternatives than combination OCs in women with one or more of the following conditions: migraine headaches, lupus, sickle cell anemia, and hypertension, diabetes with vascular disease, or age greater than 35.

The bulletin "The Use of Hormonal Contraception in Women With Coexisting Medical Conditions" is available in packs of 25; cost is $20 per pack of 25 for ACOG members and $30 per pack for nonmembers, plus shipping. Bulk discounts are offered beginning at the 10-pack order level. To order, contact: American College of Obstetricians & Gynecologists, 409 12th St. S.W., P.O. Box 96920, Washington, DC 20090-6920. Telephone: (800) 762-2264 or (202) 863-2535. Fax: (202) 554-3490. E-mail: sales@acog.com. ▼

LifeStyles Condoms offers new flavors

LifeStyles Condoms, manufactured by Ansell Healthcare's personal products division in Red Bank, NJ, has added three popular flavors — banana, strawberry, and vanilla — to its Condom Discs product line.

Condom Discs' unique, user-friendly packaging, inspired by restaurant single-serving butter packs, makes it nearly impossible for consumers to put the condom on incorrectly or to damage it while opening the package, according to the company. The flavored Condom Discs are available in the flared condom shape in five colors: red, pink, yellow, blue, and green.

LifeStyles Condom Discs, in thin and lubricated styles with the spermicide nonoxynol-9 in both three- and six-packs, are available at retail stores around the country. For more information, visit the Web at www.lifestyles.com or write to 200 Schulz Drive, Red Bank, NJ 07701. ▼

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 "Are Norplant's days numbered in the U.S.? Test results could decide its fate," on the cover.)**

• 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. ■

New formulation cuts BV course of treatment

Cleocin vaginal cream, which debuted as a bacterial vaginosis (BV) treatment in 1992, is now available in a convenient, nonmessy, easy-to-take ovule (vaginal suppository) application from Pharmacia Corp. in Peapack, NJ. The new clindamycin phosphate formulation reduces the course of treatment to three days instead of five or seven days, a convenience that may enhance patient compliance, say Pharmacia officials.

While about half of women with BV do not experience symptoms, symptoms normally include a dull or dark gray watery vaginal discharge with a strong, fishy odor that may be especially noticeable after sexual intercourse. Other organisms associated with vaginitis, such as those that cause yeast infections, should be ruled out before treating with Cleocin Vaginal Ovules.

The ovules should not be used in women with a hypersensitivity to clindamycin, lincomycin, or any of the components of the vaginal cream or suppository or a history of regional enteritis, ulcerative colitis, or antibiotic-associated colitis. Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clindamycin.

About 30% of the clindamycin dose is systemically absorbed; such information should be considered in diagnosing patients who experience diarrhea following the use of Cleocin Vaginal Ovules.

Prescribing information is available on the company's Web site (www.pnu.com). Click on "Pharmacia & Upjohn," "Product Information," "Physicians," "Additional Products," then "Cleocin Vaginal Ovules." ■

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13th International AIDS Conference report: Complacency eroding gains in war on epidemic

Some are dropping guard against infection

Antiretroviral drugs are creating complacency in some developed countries and reversing gains in the AIDS epidemic, said **Roy Anderson**, FRS, of Wellcome Trust Centre for the Epidemiology of Infectious Disease at the University of Oxford in Oxford, England.

Addressing attendees at the recent 13th International AIDS Conference in Durban, South Africa, Anderson said, "Complacency is the main worry in many Western countries for the coming decade with increases in risk behavior already apparent in young gay men, as reflected, for example, in the rise in the incidences of various sexually transmitted diseases [STDs] such as rectal gonorrhea in San Francisco and a concomitant recent rise in the incidence of HIV."

Success creates its own challenges

Anderson attributed the problem partly to the perception that AIDS is a treatable condition. That idea has arisen from the advent and success of combination drug therapies. The slow and steady increase in the incidence of HIV among heterosexuals and the explosive epidemic of AIDS in many Eastern European countries such as Russia also are of major concern, he said.

Public health authorities, therefore, face many challenges in the coming decade, Anderson noted. They include:

- intensifying AIDS educational campaigns for the young;
- combating the spread of drug-resistant strains of the virus;
- promoting good adherence to recommended drug regimens for those infected and on combination drug therapy;
- finding the necessary resources for enhanced surveillance to detect a higher percentage of infections early on;
- stimulating more research in the development of vaccines.

Successful public health campaigns have reduced the impact and spread of HIV, but that progress varies in different countries, Anderson

EXECUTIVE SUMMARY

The reports in this supplement come from the recent 13th International AIDS Conference in Durban, South Africa.

- While progress is being made in the war on AIDS, more effective drugs are creating complacency, states the lead conference report. While vaccines hold promise in clinical trials, efforts must not waver in presenting a comprehensive global strategy to fight the disease.
- Current drug treatments don't hold the key to eradicating the AIDS virus. The future will see a re-evaluation of less potent regimens for battling the virus.
- Many vaccines are now under investigation. Researchers are cautioned from searching for the "perfect" vaccine, because the virus represents such a complex immunological challenge.

said. While Sweden has made remarkable progress in limiting the spread, countries such as Spain and certain areas of the United States have achieved much less success, he said. "Each country has a unique epidemic formed from varying contributions by infections in gay men, IV drug users, and heterosexuals."

While little variability has occurred in general patterns of the distribution of age-related sexual partner acquisition, much heterogeneity exists in patterns of mixing within and between major risk groups and the degree to which educational messages have penetrated certain sectors of society in industrialized countries, Anderson said.

Successes on record

Many success stories have been recorded, including effective needle exchange programs, reports of frequent use of condoms, and a reduction in the number of new sexual partners for those at risk for HIV, Anderson noted. Drug therapy also has significantly reduced the likelihood of vertical transmission of the virus.

"What typifies the most convincing cases is the quantitative study of behavior change, concomitant with the monitoring of HIV incidence and seroprevalence," he said.

The widespread use of highly active antiretroviral therapy during the past five years in developed countries has greatly reduced the incidence of AIDS, Anderson said. That change is concomitant with an increase in the pool of HIV-infected persons, as combination therapy has prolonged the lives of those infected, he stated. However, it also brings the associated risks of an enhanced net rate of transmission, Anderson observed.

And while aggressive drug therapy could lower viremia to undetectable levels and create improvements in immune status, even the combination of five drugs doesn't seem to eliminate the virus from the host, he pointed out. Cessation of therapy, therefore, typically results in rapid growth of the virus and associated diseases while poor adherence to treatment has created multidrug-resistant strains that are difficult to treat, Anderson said.

"Tight adherence to prescribed drug regimens is key to long-term suppression of viral load," said Anderson. "Since the net rate of viral evolution is proportional to total viral load, poor adherence early on post the initiation of combination therapy [when viral load is declining from high levels] carries the greatest risk of the evolution of resistance."

Once viral load is very low, a short period of poor adherence is less serious, he said. However, the general messages for those on treatment are that good adherence is vital, as is the adoption of safe sex practices at all times, he added.

Need for action is now

The development of vaccines, the focus of much attention at the conference, is seen as a long-term solution to the epidemic. Anderson cautioned, however, that the path to this goal will be difficult, largely due to the great genetic diversity of the virus and its propensity for rapid evolution.

"The clear need is for action now, at a scale and degree of international collaboration not seen before in the history of the fight against infectious disease," he said. "International collaboration and political leadership are key ingredients for promoting this goal." ■

Experts say current drugs won't kill virus

The pendulum will swing back toward later treatment of HIV-infected patients, and the definition of failure of clinical trials will be revisited, predicted **Mauro Schechter**, MD, PhD, professor of infectious diseases at the Hospital Universitario Clementino Fraga Filho at Federal University of Rio de Janeiro in Rio de Janeiro, Brazil.

Speaking at the 13th International AIDS Conference in Durban, South Africa, Schechter offered predictions about what would happen by the time the international conference reconvenes in 2002 in Barcelona. He foresaw a greater emphasis on "delta viral load," the renaissance of CD4 count as a guide to therapy, and the availability of simpler drug regimens. He also addressed a renewal of interest in the prevention of opportunistic infections, which in turn will take into consideration local epidemiological conditions.

Schechter's address re-emphasized the point

made by Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health in Bethesda, MD, that eradication of the virus with currently available drugs is unlikely.

Since the Geneva conference two years ago, data indicate that virologic failures are more common in practice than in trials and that opportunistic infections occur at similar CD4 cell counts in patients on therapy and patients who are not, Schechter said. Although many patients did not achieve full immune recovery in those studies, a large proportion did achieve a "safe" level of immune competence, he added. On a more cautionary note, he said antiretroviral therapy was associated with potentially serious side effects, some of which might be time-dependent.

The treatment timing debate

These newly acquired data have led to renewed debate on the optimum time to treat, the choice of initial drug regimens, when to change and how to sequence them, and how to simplify existing regimens, Schechter said. Emphasis has shifted to the role of new drugs, pharmacological enhancement in extending treatment benefits, and management and prevention of opportunistic infections.

Schechter reviewed recent data on a wide range of issues related to HIV / AIDS treatment, making reference, among others, to the contested debate about what is considered to be the optimal time to initiate therapy, particularly in connection with threshold values of viral load and CD4 cells.

With regard to viral load, two recently published reports demonstrated a direct association between the slope of the increase of plasma viral load in the first few years after seroconversion and the probability of progressing to AIDS, said Schechter.[1,2]

"It was also shown that for those who progressed to AIDS, the slope of viral load increase in the three years preceding progression to AIDS was similar, regardless of prior AIDS-free time," he noted.

Those observations argue against a blanket concept of a fixed set point, he observed. They also suggest that it may be more appropriate to measure viral load in a serial fashion, rather than rely on one or two measurements to make therapeutic decisions. Schechter referred to a report presented at the conference by Julio Montaner, MD, national co-director of the Canadian HIV Trials Network in Ottawa, Ontario, on a population based cohort analysis of antiretroviral naive patients in British Columbia who started highly-active antiretroviral therapy between August 1996 and September 1999.

Results from the study, which involved 1,200 eligible participants, showed that effectiveness of therapy is dependent on baseline CD4 count, not on age, gender, viral load, prior AIDS diagnosis, or protease inhibitor use.

"Furthermore, few patients with baseline CD4 > 200 cells / mm^3 experienced clinical progression, and progression rates were similar for patients with CD4 counts of 200-350 or 350-500 cells / mm^3," Schechter noted.

The study also showed that it is probably correct to postpone treatment initiation provided therapy is started while immune recovery to "safe" levels is still possible. However, the question of how to define that moment precisely remains unanswered, he said.

More progress needed

While progress has been made in the past two years, Schechter emphasized that many earlier conclusions have yet to be revisited. The future will see a re-evaluation of "less potent" regimens, particularly of their cost effectiveness in resource-limited settings, he predicted.

Structured treatment interruptions will be discussed as a means of making treatment less toxic and more affordable, and pressure on industry and governments will increase to ensure equal and universal access to antiretroviral therapy, Schechter forecasted. That approach is still not available to the majority of those infected with HIV in the developing world, he observed.

References

1. Lyles RH, Munoz A, Yamashita TE, et al. Natural history of human immunodeficiency virus type 1 viremia after seroconversion and proximal to AIDS in a large cohort of homosexual men. Multicenter AIDS Cohort Study. *J Infect Dis* 2000; 181:872-880.

2. Lyles RH, Xu J. Classifying individuals based on predictors of random effects. Multicenter AIDS Cohort Study. *Stat Med* 1999; 18:35-52. ■

Don't look for the perfect HIV vaccine

The clinical goal of an HIV vaccine differs from other such projects because of the urgent need to make an impact on the global pandemic. Unlike traditional vaccines that prevent infection, an approach that would prevent AIDS or even delay the progression of the disease would be a tremendous achievement in the case of HIV, said **Margaret Liu**, MD, vice president for vaccines research and gene therapy at Chiron Corp., an Emeryville, CA-based biotechnology company.

Liu, who addressed attendants at the 13th International AIDS Conference in Durban, South Africa, cautioned scientists against setting their sights on the "perfect" vaccine. "For a pathogen such as HIV that is capable of entering the genome of cells, the challenge to make a vaccine that would prevent any infection at all is indeed great and may be too big a first step," she said.

At the start of the epidemic, no one even knew enough about the virus or its immunology to know what questions to ask, Liu said. Advances in the fields of virology, immunology, and cell biology during the past two decades have added impetus and knowledge to the vaccine effort, she said. "Although we don't fully understand correlates of immunity or how and where to generate immune responses, we have gained many insights from animal studies and human populations," she explained. "These inform and guide our vaccine development efforts."

While scientists have accumulated more knowledge in such areas as the genotype of different strains, there is still much to learn, Liu observed. Because of that, she cautioned that researchers should not be dogmatic and should always be guided by the proof provided by scientific data.

"We must be careful to not make any assumptions, for example, about which strains to use for vaccines that would hinder the development of an effective candidate," she noted.

Advances made so far are encouraging, Liu said. They include the elucidation of immune responses in highly exposed uninfected individuals, such as commercial sex workers, and in patients whose disease did not progress as rapidly as expected, the so-called "long-term nonprogressors."

"These individuals provide evidence for the power of the immune response to contain and restrain the viral infection," Liu observed. "Likewise, their immune responses provide clues as to what a vaccine should elicit."

Progress also has been made in illuminating the structure of HIV, as well as in understanding what processes and structures need to be altered to prevent infection or its spread, Liu said. "Given the types of immune responses that are thought necessary for an HIV vaccine, the novel and dramatic advances in vaccine technologies promise to provide the means for making an HIV vaccine."

Candidates in the wings

Several vaccine candidates are in the early stages of development, reported Liu. These include live virus vaccines, viral vectors, and gene-based vaccines such as plasmid DNA vaccines. Others in evaluation are vaccines combining more than one type of entity (known as "mixed-modality" vaccines), protein-based vaccines utilizing other forms of envelope or other viral proteins, and recombinant envelope glycoproteins, now in phase III efficacy trials.

There have been increased efforts in vaccine research to induce cellular responses instead of or in addition to antibody response, Liu said. Because T lymphocytes appear to recognize pieces of the virus displayed on the surface of infected cells, the T-cell responses can be directed against conserved regions of the virus, she explained.

As one way to make a vaccine with broad efficacy against different strains of the virus, Liu said, scientists might be able to take advantage of the conservation of certain proteins or regions of proteins between different strains, even if the protein is on the viral surface.

The ability of cytolytic T lymphocytes (CTL) to kill HIV-infected cells is not the only mechanism for cellular immunity, she observed. "The multiple mechanisms of cellular immunity provide another reason for efforts to induce cellular responses. In addition to killing virus-infected cells, CTLs release molecules that may play a crucial role for a preventive or therapeutic AIDS vaccine." ■

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Exclusive News Bulletin

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Monthly combined injectable becomes first new method of U.S. contraceptive since '93

FDA approves Lunelle from Pharmacia Corp.

By **Rebecca Bowers**
Editor, *Contraceptive Technology Update*
Atlanta

The cafeteria of contraceptive choices just expanded in the United States with the regulatory approval of Lunelle, a monthly combined injectable from Pharmacia Corp. in Peapack, NJ. The drug, approved Oct. 5 by the Food and Drug Administration, represents the first new method of birth control in the United States since 1993, when the Reality female condom was introduced by Female Health Co. of Chicago.

Lunelle will be available later this fall, according to **Kristin Elliott**, Pharmacia spokeswoman. Lunelle's cost, including cost of the injection, will be comparable to the monthly cost of birth control pills, she says. **[Providers who would like more details on Lunelle should contact Pharmacia at (800) 253-8600, ext. 38244 or visit the company's Web site at www.pharmacia.com.]**

Developed in the late 1960s, this combination injectable has been widely tested. More than 17,000 women have participated in controlled trials worldwide, and the drug is in routine use in several countries. The drug is marketed in other countries under the brand names Cyclofem and Cyclo-Provera. **(Read more about the drug's history in *CTU*, June 1996, p. 71, and November 1999, p. 125.)**

Who can use Lunelle? *A Personal Guide for Managing Contraception for Women and Men* notes that suitable candidates include those who have no medical contraindications to combined pills, desire a highly effective reversible method, want to have a child in one or two years, and do not want to take pills every day.[1]

As with other hormonal contraceptives, Lunelle is not appropriate for women with known or suspected pregnancies; thrombophlebitis or thromboembolic disorders; a past history of deep-vein thrombophlebitis or thromboembolic disorders, cerebral vascular, or coronary artery disease; or undiagnosed abnormal genital bleeding. As with other hormonal contraceptives, menstrual bleeding patterns might be disrupted with initial use of Lunelle. In addition, the method does not protect against HIV and other sexually transmitted diseases.

Once-a-month dosing offers convenience

Lunelle offers women a reliable form of birth control that prevents unintended pregnancy with the convenience of once-a-month dosing, notes **Andrew Kaunitz**, MD, professor and assistant chair in the obstetrics and gynecology department at the University of Florida Health Science Center/Jacksonville. Kaunitz served as an investigator for the U.S. clinical trial.[2] Monthly estrogen/progestin contraception, he says, combines the high effectiveness of long-acting methods with the regular cycles and easy return to fertility characteristic of oral contraceptives.

"At our University of Florida/Jacksonville site, some of our original research participants have chosen, almost two years after the initial 60-week comparative component was completed, to continue their monthly injections," he reports. "Their preference for Lunelle speaks to the advantage and security of not having to worry about missing a pill and the [attending] consequences."

Each 0.5 cc aqueous solution of Lunelle contains 5 mg estradiol cypionate (E2C) and 25

mg medroxyprogesterone acetate (MPA). The intramuscular injection is commonly administered to the gluteus or deltoid muscles, but it can be administered safely and effectively in the anterior thigh. Ideally, it is administered every 28 to 30 days, but effective contraception is maintained with a 10-day reinjection window (at least 23 days and no more than 33).

According to two studies based on the U.S. clinical trial, Lunelle is highly effective, safe, and well-accepted among women.[2,3] In the Phase III 60-week trial, which compared Lunelle with Ortho-Novum 7/7/7, an oral contraceptive manufactured by Ortho-McNeil Pharmaceuticals of Raritan, NJ, the data showed two unintended pregnancies in the oral contraceptive group and none in the Lunelle group.

Compared with the progestin-only injectable, depot medroxyprogesterone acetate (DMPA or Depo-Provera, also manufactured by Pharmacia Corp.), Lunelle offers a more regular bleeding pattern, and women using Lunelle maintain estrogen levels normal for ovulatory women.[1] Another advantage of Lunelle is that its effects are reversed relatively rapidly. MPA is cleared within 60 to 90 days, restoring ovulation. This return to fertility is about twice as fast as that achieved after the last progesterone-only injection.[4]

The most common adverse events leading to discontinuation of Lunelle in the clinical trial were hormone-related. Complaints of excessive bleeding were recorded in 2.5%, breast pain in 1.8%, menorrhagia in 1.5%, and dysmenorrhea in 1.2%. The study found that discontinuation rates for any adverse event were low in the injectable and pill study groups.[2]

Family planners hail the expansion of contraceptive choices represented by Lunelle's introduction. "I think Lunelle can be a worthwhile addition for women who need less structure in their lives," says **David Archer**, MD, professor of obstetrics and gynecology and director of the Clinical Research Center at the Eastern Virginia Medical School in Norfolk. "Remembering to take a pill a day can be difficult; a monthly reminder for an injection could be easier with the reduction in need for motivation."

While providers like the advantages of the new method, they note the need for monthly injections as a potential disadvantage.

"The major problem is the monthly injection," says Archer. "A technique that could allow the recipient to self-inject is sorely needed."

Research of such auto-injection is proceeding, says **Sharon Schnare**, RN, FNP, CNM, MSN, women's health consultant and clinician with the Seattle King County Health Department and the International District Community Health Center in Seattle. A Brazilian study indicates that women can be trained to self-administer the monthly injectable contraceptive and generally respond positively to the auto-injection device.[5]

To enhance success with Lunelle, providers should discuss all of the method's benefits and side effects, says Schnare. Prepare patients to deal with side effects, and be prepared to manage such side effects with them, she advises.

"When patients know what to expect and know that providers are available to help them if side effects occur, they tolerate side effects much better," she says.

In addition, with the advent of two injectable contraceptives in the U.S. market, when patients present for their "birth control shot," it will be important to determine which one is used.

Help patients plan how they will return for reinjections and discuss scheduling issues, Schnare suggests. Most women who participated in the clinical trial found the monthly treatment schedule easy to comply with and would recommend this form of contraception to others.[3]

"In my judgment, Lunelle will prove to be a popular choice," says Kaunitz. "Clinicians and facilities that provide easy injection access will find this to be an attractive method for many women."

References

1. Hatcher RA, Pluhar E, Zieman M, et al. *A Personal Guide to Managing Contraception for Women and Men*. Decatur, GA: Bridging the Gap Communications; 2000.

2. Kaunitz AM, Garceau RJ, Cromie MA. Comparative safety, efficacy, and cycle control of Lunelle monthly contraceptive injection (medroxyprogesterone acetate and estradiol cypionate injectable suspension) and Ortho-Novum 7/7/7 oral contraceptive (norethindrone/ethinyl estradiol triphasic). *Contraception* 1999; 60:179-187.

3. Shulman LP, Oleen-Burkey M, Willke RJ. Patient acceptability and satisfaction with Lunelle monthly contraceptive injection (medroxyprogesterone acetate and estradiol cypionate injectable suspension). *Contraception* 1999; 60:215-222.

4. Thompson S. *New Developments in Contraception Featuring Monthly Combination Injectables*. Washington, DC: Association of Reproductive Health Professionals; 2000.

5. Bahamondes L, Marchi NM, Nakagava HM, et al. Self-administration with UniJect of the once-a-month injectable contraceptive Cyclofem. *Contraception* 1997; 56:301-304. ■