CONTRACEPTIVE TECHNOLOGY UPDATE®

A Monthly Newsletter for Health Professionals

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NOVEMBER 2003
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Move over, Pill: New contraceptives expand acceptance among women

More choosing contraceptive patch and vaginal ring

When discussing contraceptive options with your female patients, what choices are available at your facility? If they include the contraceptive patch (Ortho Evra, Ortho-McNeil Pharmaceutical, Raritan, NJ) and the contraceptive vaginal ring (NuvaRing, Organon, West Orange, NJ), you join the majority of respondents to the 2003 *Contraceptive Technology Update* Contraception Survey.

A total of 88.3% of those surveyed say their facility now offers the contraceptive patch, up from 64.3% in 2002. About 75% say they provide the contraceptive vaginal ring, up from about 58% in 2002.

"We have noticed a decline of about 5% [in the number of oral contraceptive users]," reports **Kimberly Carson**, RN, clinical services supervisor at the Aberdeen, WA-based Grays Harbor County Public Health. "We are seeing a fair amount of users either switching to or trying the patch or the ring."

Evra and NuvaRing have been well received at the Marshfield Clinic, a private, multispecialty group practice in Eau Claire, WI, says **Deborah**

Interest in extended-use contraception to grow

Get ready for a major change to occur in the way birth control pills are prescribed and used with the arrival of Seasonale, the first dedicated extended-regimen oral contraceptive. Shipment of the product, marketed by Barr Laboratories of Pomona, NY, is on its way to retail pharmacy shelves following the Sept. 5, 2003, approval from the Food and Drug Administration (FDA).

(Continued on page 129)

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EXECUTIVE SUMMARY

While oral contraceptives (OCs) continue as a popular form of contraception, providers are seeing women consider other new forms of birth control.

- A total of 88.3% of those participating in the 2003 *Contraceptive Technology Update* Contraception Survey say their facility now offers the contraceptive patch, up from 64.3% in 2002. About 75% say they provide the contraceptive vaginal ring, up from about 58% in 2002.
- About 35% of 2003 survey respondents say half or more of their patients use OCs, which continues a downward trend.

Wright, OGNP, a nurse practitioner at the facility. Several of the clinic's medical assistants use these methods, then tell patients about them, which increases their use, Wright notes.

While oral contraceptives (OCs) continue as a popular form of contraception, providers are seeing women consider other new forms of birth control. Results from the 2003 survey bear this out: About 35% of 2003 survey respondents say half or more of their patients use OCs. This continues a downward trend seen in 2002, when 42% said that 50% or more women used the Pill, and in 2001, when a 53% figure was recorded.

Each Ortho Evra patch contains 150 mcg of the progestin norelgestromin and 20 mcg of the estrogen ethinyl estradiol. Designed to be changed once a week and worn for three weeks, it consists of an adhesive medicated layer worn against the skin, protected by a waterproof polyester layer. Just as pill users take placebos or no pills during the fourth week, patch users go patch-free that week. **(For tips on successful use of the contraceptive patch, see the October 2003 *CTU* article, "Contraceptive patch catches on with women," p. 114.)**

Many of the female patients at the Charlottesville-based University of Virginia have been glad to have another birth control alternative, states **Christine Peterson**, MD, director of gynecology in the department of student health. Most patch users at the student health clinic are enthusiastic about it, though a few have discontinued because of breast tenderness or more breakthrough bleeding than they had experienced on the Pill, she notes.

"It is less popular than the Pill among first-time prescription contraceptive users," she observes. "I suspect this is because they have become more familiar with the Pill than with the patch through secondary school education and mass media,

though I do not have data to support this notion."

Evra is well received at Provo, UT-based Brigham Young University, says **Linda Hale**, MN, APRN, WHNP, ANP, a nurse practitioner at the Student Health Center. "The two most common reasons for discontinuing the patch are breast tenderness/swelling and skin irritation; [however] both of these have occurred only rarely considering how many prescriptions I have written for Evra," she reports.

According to patient information supplied with the method, women can wear an Evra patch on their buttock, abdomen, upper torso (excluding the breasts), or on the outside of the upper arm.[1] A different site may be chosen each week, but whichever place the woman chooses, the patch must remain there for seven days. The patch may be worn in the same location each week; however, women should try to avoid placing it in the same exact spot.

For example, if a woman prefers to wear it on her abdomen, on her next patch change day, she should switch to the opposite side. The patch should not be applied to skin that is red, irritated, or cut.[1]

NuvaRing releases a continuous low dose of the estrogen ethinyl estradiol and the progestin etonogestrel at an average rate of 0.120 mg etonogestrel and 0.015 mg ethinyl estradiol per day over a 21-day period of use. **(Review recent research on NuvaRing; see "New research confirms efficacy of NuvaRing," *CTU*, June 2003, p. 68.)**

The method was slow to take off at the University of Wisconsin-La Crosse Student Health Center, but it was helpful to give a month free, says **Carol Burgmeier**, MSN, FNP, a family nurse practitioner at the facility.

"Students would at least try it, and then found that they liked it," she notes. "That seems to be the fastest growing form of hormonal contraceptive."

NuvaRing now is available at the Klickitat County Health Department in White Salmon, WA, reports **Theresa Rundell**, ARNP, a nurse practitioner at the facility. Acceptance of the method was slow in starting, but now it is catching on, she states.

The contraceptive vaginal ring is a little more difficult to sell to patients, says Hale. Two recent patients have started the ring and "love" it, she says; both of these women started with OCs, had nausea, and were motivated to try another monthly contraceptive, she notes.

Samples of the contraceptive ring and patch are very helpful with women considering these newer methods, says **Sharon Schnare**, RN, FNP, CNM, MSN, clinician at South Kitsap Family Care Clinic in Port Orchard, WA.

"I find that having a woman insert the ring in the office increases her success with this method; once she inserts the ring or applies the patch in the office, I provide a prescription for that method," she notes. "This style of active engagement significantly improves success."

Reference

1. Ortho-McNeil Pharmaceutical. *What You Should Know About Ortho Evra.* Accessed at www.orthoevra.com. ■

Survey profile

A total of 215 providers participated in the 2003 *Contraceptive Technology Update* Contraception Survey, which monitors contraceptive trends and family planning issues among readers. Surveys were sent to subscribers of *CTU, Alternative Therapies in Women's Health*, and *OB/ GYN Clinical Alert.*

Results were tallied and analyzed by Thomson American Health Consultants in Atlanta, publisher of *CTU* and more than 100 other resources.

About 52% of responses came from physicians. Nurse practitioners or registered nurses represented about 40% of the responses, with allied health professionals and health educators comprising about 2% of total responses. About 6% listed other professions. About 80% of respondents identified themselves as care providers, with about 12% involved in administration.

About one-third of the respondents said they were employed at public health facilities, with about 44% working in private practice settings. About 10% listed student health centers as their place of employment, with some 5% working in hospitals. The remaining 10% reported employment in other settings.

When it comes to location of their employment, about 34% said they worked in an urban setting. Another 34% said they were employed in a suburban facility, while 30% listed a rural location. ■

Readers rank top oral contraceptives

While new birth control methods are attracting attention from new and established contraceptive users, family planning clinicians say many women continue to choose combined oral contraceptives (OCs) for safe,

EXECUTIVE SUMMARY

Many women continue to choose combined oral contraceptives (OCs) for safe, reliable pregnancy prevention.

- Ortho Tri-Cyclen, a 35-mcg ethinyl estradiol phasic pill marketed by Ortho-McNeil Pharmaceuticals, continues its sixth year in the Contraceptive Survey as the top nonformulary and formulary selection for a 21-year-old nonsmoking woman.
- Alesse, a monophasic 20-mcg pill from Wyeth-Ayerst Laboratories, is the leading choice for a 42-year-old nonsmoking woman.

reliable pregnancy prevention.

There has been no change at the St. Clair County Health Department in Port Huron, MI; most of its clients request OCs, says **Ruth Napolitan**, RNC, BSN, WHNP, a nurse practitioner at the facility.

Cost can be a factor for many women when making a contraceptive choice, explains **Linda Hale**, MN, APRN, WHNP, ANP, a nurse practitioner at the Provo, UT-based Brigham Young University Student Health Center.

"We sell NuvaRing [the contraceptive vaginal ring marketed by Organon, West Orange, NJ] for $34, Evra [the transdermal contraceptive marketed by Ortho-McNeil Pharmaceutical, Raritan, NJ] for $22, and many of the OCs for $12," she reports. "That is often the biggest factor when a woman chooses her contraceptive here."

Ortho Tri-Cyclen, a 35-mcg ethinyl estradiol phasic pill marketed by Ortho-McNeil Pharmaceuticals, continues its sixth year in the *Contraceptive Technology Update* Contraceptive Survey as the top nonformulary and formulary selection for a 21-year-old nonsmoking woman. About 29% of respondents in the 2003 survey say Tri-Cyclen is their top nonformulary choice, and when bound by program formularies, 23% of 2003 responses list the OC as the No. 1 choice.

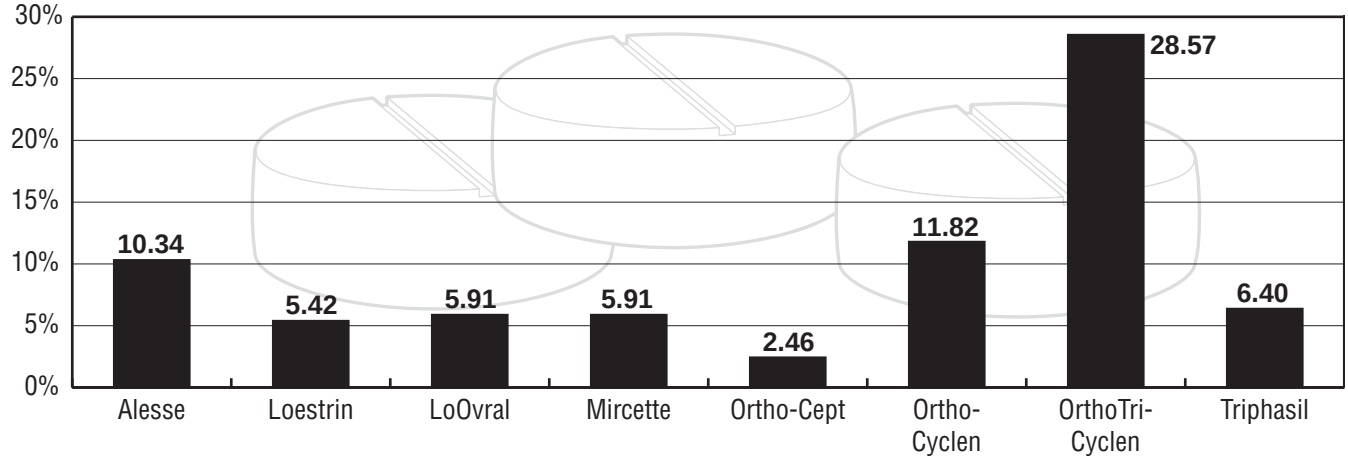
These figures, however, show a decline from 2002's responses, when about 36% of survey respondents named the pill as the top nonformulary OC, and 37% picked it as the No. 1 formulary pill.

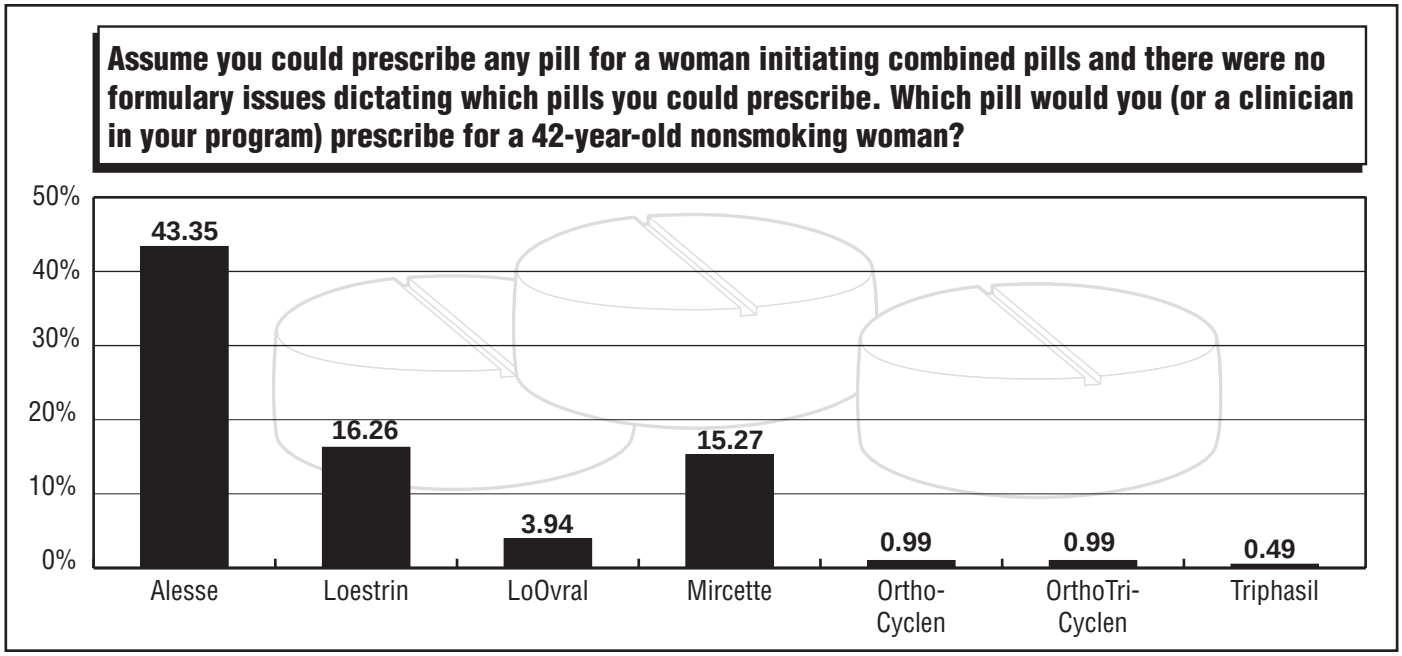
"We began using this tablet as a first choice three to four months ago; it has had a great response with little to no initial use side effects, and many of our clients, new and returning, are requesting it." says Napolitan.

If Ortho Tri-Cyclen is seeing competition, some of it may be coming from its lower-dose version, Ortho Tri-Cyclen Lo, a triphasic pill introduced at the end of 2002. When breaking down the selections named in the "other" category in formulary and nonformulary pills, Ortho Tri-Cyclen Lo led the pills listed in that category. Ortho Tri-Cyclen Lo provides a daily dose of 25 mcg estrogen for 21 days and three different doses of the progestin norgestimate (180 mcg daily/days 1-7; 215 mcg daily/days 8-14; and 250 mcg daily/days 15-21). The last seven days contain no active ingredients. **(Read more about the pill in the December 2002 article "Pill options expand with new, generic OCs," p. 140.)**

Ortho Tri-Cyclen Lo represents the first-choice

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





nonformulary and formulary OC for 21-year-old nonsmokers, says **Patricia Bauer**, MSN, RNC, a nurse practitioner at the Benzie Leelanau District Health Department in Benzonia, MI. The pill is an inexpensive one that many people request, she reports.

What pill would you prescribe for a 42-year-old nonsmoking woman? Once again, CTU survey respondents named Alesse as their preferred OC. About 43% of responses listed the pill as their leading choice, an increase from its 39% ranking in 2002.

Loestrin, a monophasic 20 mcg pill from Pfizer of New York City, fell from its 2002 No. 2 position; while it was named by almost 26% as their leading choice in the 2002 poll, about 16% chose it in 2003. Competition again came from Ortho Tri-Cyclen Lo, which was the leading write-in choice in the "other" category. It was selected by 6.6% of survey respondents as their No. 2 choice in 2002 and 14.29% in 2003.

When you review the Pill's advantages and disadvantages, do you talk about its noncontraceptive benefits?

According to the 2003 *CTU* Contraception Survey, more providers say they are recommending pills to women specifically to reduce their risk of cancer of the ovary. A total of 40% of survey respondents indicated they prescribed pills based on patient history of ovarian cancer risk, up from 2002's 36% figure.

How do you approach women with information on the noncontraceptive benefits of OCs?

According to **Christine Peterson**, MD, director of gynecology in the department of student health at the Charlottesville-based University of Virginia, the student health center's in-house handout contains information on the noncontraceptive benefits of OCs, including the reduction in risk for ovarian and endometrial cancer.

Peer health educators provide the handout to the students with whom they discuss contraception, as well as by clinicians to all OC users, she notes.

"Only the most medically savvy medical and nursing students indicate to us that this [benefit] is important for them," says Peterson. ■

Readers share views on common OC challenges

The next patient on your schedule is a 41-year-old woman who smokes 12-15 cigarettes a day. She would like to use combined oral contraceptives (OCs). Will she leave your office with a prescription for the Pill?

If results of *Contraceptive Technology Update's* 2003 Contraception Survey are any indication, she'll be offered another form of birth control. The majority of 2003 survey respondents say they will not provide pill prescriptions for older women who smoke 10 cigarettes a day. For women ages 35-39, about 76% say they will not supply OCs, and for women ages 40 and older, the number climbs to almost 90%. These findings closely follow those found in the 2002 survey responses.

EXECUTIVE SUMMARY

Participants in the 2003 Contraception Survey face common challenges regarding oral contraceptives (OCs): women who smoke, nursing mothers, and those who have experienced nausea during previous pill use.

- Most 2003 respondents say they won't provide pill prescriptions for older women who smoke 10 cigarettes a day. For women ages 35-39, about 76% say they will not supply OCs, and for women ages 40 and older, the number climbs to almost 90%.
- About 39% of 2003 respondents say they would prescribe OCs four to six weeks postpartum to a new mother who chooses not to breast-feed. For new mothers who wish to breast-feed, about 36% of respondents say they would begin progestin-only pills at four to six weeks postpartum.
- For women who have experienced nausea on previous pills, more than half of survey respondents chose Alesse, a monophasic 20 mcg pill.

Use the "4 As" in your clinical approach when it comes to smoking:

- **Ask** all patients about smoking.
- **Advise** all patients to quit.
- **Assist** with motivation and assess nicotine dependence.
- **Arrange** for a follow-up appointment.[1]

When talking with patients, find out how much they smoke, how ready they are for a change, whether they have tried to quit in the past, and their motivation for smoking cessation. For women who continue to smoke, counsel on use of intrauterine devices or progestin-only methods.[2]

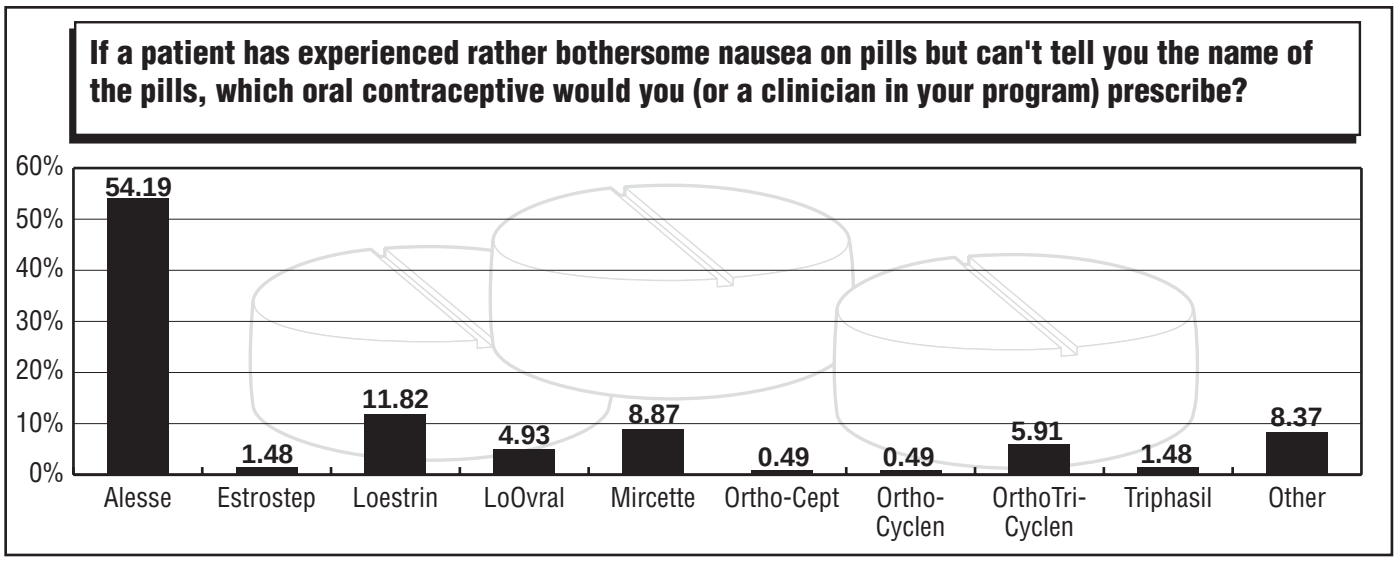
What is your approach to providing combined pills for a new mother who chooses not to breast-feed? About 39% of 2003 *CTU* survey respondents say they would prescribe OCs four to six weeks postpartum, a decrease from 2002's 46% level. About 29% say they would initiate OCs one to three weeks postpartum, with 10% providing pills upon hospital discharge. About 10% would start pills at first menses, with about 7% using other approaches. These views are consistent with those reported in the 2002 survey.

For new mothers who wish to breast-feed, about 36% of respondents say they would begin progestin-only pills (POPs) at four to six weeks postpartum, a slight decline from 2002's 44.4% figure. A total of 26% note they would initiate POPs at one to three weeks postpartum. About 20% would initiate POP use at hospital discharge, with about 2% starting minipills at first menses. About 7% say they would use other approaches.

Review the stance of the Elk Grove Village, IL-based American Academy of Pediatrics about OC use in breast-feeding women, advises **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 at Harbor-UCLA Medical Center in Torrance.[3] The AAP is comfortable with combined OC use once women have introduced another source of calories into the infant's diet, she notes.

Which OC for nausea?

For women who have experienced bothersome nausea on previous OCs, but can't remember the brand name of the pill used, clinicians continue to



use Alesse, a monophasic 20-mcg pill from Wyeth-Ayerst Laboratories of Philadelphia. About 54% named the pill as their first choice in this category, and the percent was up from 2002's 49.7% figure.

Alesse is the first-choice OC for patients who have experienced nausea with previous pills, reports **Patricia Bauer**, MSN, RNC, a nurse practitioner at the Benzie Leelanau District Health Department in Benzonia, MI. The pill is the lowest estrogen effect pill that the agency carries, she notes.

Other pills named as first choices in the 2003 survey include Loestrin 1/20, a 20-mcg monophasic pill from Pfizer of New York City, and Mircette from Organon of West Orange, NJ, a pill with a unique dosing schedule (21 days of 150 mcg desogestrel/20 mcg ethinyl estradiol, two days of placebo pill, followed by five days of 10 mcg ethinyl estradiol). About 12% of 2003 survey respondents chose Loestrin, compared to 20.2% in 2002, while about 9% named Mircette, compared to 10.2% in 2002.

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Emergency contraception provision catches on

EXECUTIVE SUMMARY

More than 84% of respondents to the 2003 Contraception Survey report their facility prescribes emergency contraception (EC) on site and provides emergency contraceptive pills at any time, continuing an upward trend.

- The majority of respondents to the 2003 survey say they use Plan B, the levonorgestrel regimen.
- Just-published results of a randomized trial indicate that advance provision of EC significantly increased use without adversely affecting use of routine contraception.

Just six years ago, a national report asked, "Is the secret getting out?" when it comes to emergency contraception (EC).[1] If results of the 2003 *Contraceptive Technology Update* Contraception Survey are any indication, EC's message now is being heard loud and clear.

More than 84% of survey respondents said their facility prescribes EC on site and provides emergency contraceptive pills (ECPs) at any time, continuing an upward trend from 2001's 81% mark. In 1997, just 54% of survey participants indicated such full access to the method.

Use of EC has grown at the University of Wisconsin-La Crosse, observes **Carol Burgmeier**, MSN, FNP, a family nurse practitioner at the university's Student Health Center. Fliers advertising the availability of EC are placed in the dorm rooms for incoming freshmen, she notes.

"Our number of requests for ECPs a little more than doubled last year," says **Ruth Napolitan**, RNC, BSN, WHNP, a nurse practitioner at the St. Clair County Health Department in Port Huron, MI. "Because we live in a small, extremely conservative community, we do not advertise; word of mouth historically has been our way of advertising."

Benzie Leelanau District Health Department in Benzonia, MI, provides EC in advance, says **Patricia Bauer**, MSN, RNC, a nurse practitioner. Posters are placed in the clinic to advertise the availability of the method, and clinicians counsel on it during patient education sessions, she reports.

Just-published results of a randomized trial indicate that advance provision of EC significantly increased use without adversely affecting use of routine contraception.[2] The trial compared advance provision of EC with usual care in 370 postpartum women from an inner-city public hospital. All participants received routine contraceptive education, with the intervention group receiving a supply of EC and a five-minute educational session on its use. Women provided with ECP were four times as likely to have used emergency contraception as women in the control group over the course of the year, but they were no more likely to have changed to a less effective method of birth control or to use contraception less consistently.[2]

Reinforce the standard of advance prescription, says **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 at Harbor-UCLA Medical Center in Torrance. The Washington, DC-based American College of Obstetricians and

Gynecologists urged its members in March 2002 to issue advance prescriptions for EC. ***(CTU* reported on the group's advocate stance in the May 2002 issue; see "Emergency contraception is gaining momentum from local to national levels"; p. 49.)**

What does your clinic dispense when it comes to EC? The majority of respondents to the 2003 *CTU* survey say they use Plan B, the levonorgestrel regimen marketed by the Washington, DC-based Women's Capital Corp. About 58% of responses indicated use of the drug, with 12% listing the other dedicated ECP, Preven (Gynétics of Belle Mead, NJ), and 18% listing one of the 18 other contraceptive pills recognized as safe and effective for EC use by the Food and Drug Administration. These pills are:

- Ovral, Lo/Ovral, Ovrette, Triphasil and Alesse (Wyeth-Ayerst, Philadelphia);
- Ogestrel, Low-Ogestrel, Levora, and Trivora (Watson Pharmaceuticals, Corona, CA);
- Levlen, Levlite and Tri-Levlen (Berlex Laboratories, Montville, NJ);
- Aviane, Lessina, Portia, Enpresse, and Cryselle (Barr Laboratories, Pomona, NY);
- Nordette (King Pharmaceuticals, Bristol, TN).

Clinicians at the Charlottesville-based University of Virginia Student Health Center use Plan B, reports **Christine Peterson**, MD, the center's director of gynecology. Research indicates that the levonorgestrel-only EC approach offers better effectiveness, a lower rate of nausea, and less vomiting than that experienced with the Yuzpe regimen,[3] she notes.

Clinicians at the health center saw a 50% increase in the use of EC in 2003, reports Peterson. The center has offered the method since 1988 and has advertised its availability through a variety of avenues, including trained peer health educators, brochures, fliers, and its web site (www.virginia.edu/studenthealth/contraception.html). (Take a look at the school's EC information, as well as its EC triage protocol, at *CTU's* web site, www.contraceptiveupdate.com. Your user name is your subscriber number from your mailing label. Your password is ctu (lowercase) plus your subscriber number, with no spaces. Click on "toolkit.")

It received heightened awareness in 2003 when another Virginia school, Harrisonburg-based James Madison University, ended sale of ECPs at its student health center following opposition raised by Virginia state legislator Robert Marshall of Prince William County. While clinicians at James Madison's student health center still can write prescriptions for EC, they no longer can dispense ECP through the student health center.[4]

"Fortunately, we have always had a well-defined evaluation protocol and an informed consent procedure that includes information on possible mechanisms of action, as well as side effects, etc.," states Peterson. "Those have stood up to scrutiny by medical and administrative reviewers; nonetheless, we expect continued political efforts to deprive our patients of this vital service."

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CTU UPDATES
News ■ Resources ■ Events

ACNM web site offers breast-feeding resources

Help women overcome barriers to breast-feeding with information from a new on-line resource, www.GotMom.org, developed by the Washington, DC-based American College of Nurse-Midwives (ACNM).

The web site features information on why "breast is best," as well as outlines the ABCs of breast-feeding. It also addresses concerns often posed to clinicians during discussions of breast-feeding. Resource listings and recommended reading materials are included, as well as the latest news and research on breast-feeding. Information also is included for employers to help support breast-feeding mothers.

ACNM has partnered with several government and nongovernmental agencies to ensure that the information is relevant for women who choose breast-feeding. Future plans include a Spanish-language version of the web site. ▼

New condom now available from Trojan

Trojan brand condoms, distributed by Church & Dwight Co. in Princeton, NJ, have added another option: Twisted Pleasure condoms.

The latex condom features a patented double twist bulbous contour at the closed end of the condom.. The condoms, which arrived on retail shelves in June, are available in boxes of 12 for a suggested retail price of $8.99. ■

New Arabic web site offers EC information

Reproductive health advocates have now launched the first Arabic language web site dedicated to emergency contraception (EC).

The Arabic EC web site can be accessed directly through the address ec.princeton.edu/arabic or through the Emergency Contraception web site at www.not-2-late.com. It provides EC information, a directory of clinicians willing to provide EC in the United States and Canada, and a searchable database of contraceptives available worldwide that can be used for EC. Advocates affiliated with the Washington, DC-based Association of Reproductive Health Professionals, the Cambridge, MA-based Ibis Reproductive Health, and the Office of Population Research at Princeton (NJ) University united to develop the site. ■

Seasonale

(continued from cover)

While the concept of using pills for more than 21 days at a time is not a new one, the introduction of Seasonale will have the same impact on extended regimen contraception as was seen in the increase in prescription of emergency contraception (EC) following the arrival of dedicated EC pills, reports **Robert Hatcher**, MD, MPH, professor of gynecology and obstetrics at Emory University School of Medicine in Atlanta. "The availability of two emergency contraceptive pills with instructions for their use lends credibility to the use of hormones used sparingly as emergency contraceptives since the early 1970s," he remarks. "The formal approval of Seasonale may have an even more dramatic effect, because not only does Seasonale contain the same hormones as five currently available pills: Lo-Ovral (Wyeth-Ayerst, Philadelphia); Levlen (Berlex Laboratories, Montville, NJ); Levora and Lo-Ogestrel (Watson Pharmaceuticals, Corona, CA); and Nordette (King Pharmaceuticals, Bristol, TN), but Seasonale provides these hormones in a completely new regimen."

EXECUTIVE SUMMARY

Shipment of the first dedicated extended regimen oral contraceptive, Seasonale, marketed by Barr Laboratories, is on its way to retail pharmacy shelves following its September 2003 approval from the Food and Drug Administration.

- Look for other companies to develop other forms of extended regimen contraception. Researchers are evaluating extended use of the Ortho Evra transdermal contraceptive and the NuvaRing contraceptive vaginal ring.
- As with other forms of hormonal contraception, clinicians should be prepared to counsel on expected side effects of Seasonale. Unscheduled spotting/bleeding is common during the initial months of use.

Look for other companies to develop other forms of extended regimen contraception; researchers are evaluating extended use of the Ortho Evra transdermal contraceptive and the NuvaRing contraceptive vaginal ring. Barr Laboratories plans to explore other forms of extended contraception as well; another of its oral contraceptive products, known as DP3, now is in clinical trials. This extended regimen OC includes levonorgestrel and ethinyl estradiol taken for up to 84 days, followed by seven days of ethinyl estradiol.

Scientists are looking at different uses for extended regimen contraception. Researchers at the Penn State Milton S. Hershey Medical Center in Hershey, PA, are conducting a six-month study designed to examine the effects of a continuous oral contraceptive pill on ovarian and endometrial function.

New research indicates that long-term continuous OC use can be proposed to women with symptomatic endometriosis and menstruation-related pain symptoms.[1] The study followed 50 women who had undergone surgery for endometriosis in the previous year and experienced recurrent dysmenorrhea despite cyclic OC use. Participants underwent continuous use of an OC containing ethinyl estradiol (0.02 mg) and desogestrel (0.15 mg) for two years. At final evaluation, 80% said they

Audio conference looks at revolutionary contraceptive

Free presentation to target Seasonale

Extended hormonal contraception is drawing dramatic attention due to the desire of many women to reduce or eliminate the number of withdrawal bleeds associated with current birth control methods. The first extended-use oral contraceptive, Seasonale, was just approved by the Food and Drug Administration and is expected to have an enormous impact on family planners and OB/GYNs. This new therapy will reduce the number of periods a woman has to four a year. Researchers also are looking at extended use of the NuvaRing contraceptive vaginal ring and the Evra transdermal contraceptive patch.

To bring you up to speed with the exciting changes in this field, Thomson American Health Consultants offers a free audio conference program. **Extended-use Contraception: What You Should Know About Seasonale and Other Options** will be held Oct. 9, from 2-3 p.m., ET, and is open to the first 500 facilities to register. The conference will be replayed continuously for 48 hours following the original airdate to make it as convenient as possible for busy professionals to attend.

"I consider this [Seasonale] to be the most important change in hormonal contraception since birth control pills initially became available," says **Robert Hatcher**, MD, MPH, chairman of the editorial advisory board of *Contraceptive Technology Update* and professor of gynecology and obstetrics at Emory University.

Presenters will be Hatcher, who will act as moderator; **Lee Shulman**, MD, professor of OB/GYN at Northwestern University in Chicago; and **Sharon Schnare**, RN, FNP, CNM, MSN, a family planning clinician and consultant in Seattle.

After listening to this program, participants will be able to:

- discuss current and future options for extended-use hormonal contraception;
- list advantages of extended-use hormonal contraception;
- recognize potential problems with extended-use hormonal contraception;
- identify best candidates for extended use hormonal contraception.

Space is limited. This audio conference is open to the first 500 facilities to register. Each participant in the conference can earn FREE CE or CME — 1 nursing contact hour or 1 AMA Category 1 CME credit. The conference package includes handouts, additional reading, and a free 48-hour replay of the live conference. For more information, or to register, call Thomson American Health Consultants' customer service department at (800) 688-2421 or (404) 262-5476, or e-mail customerservice@ahcpub.com. This program is sponsored by an educational grant from Duramed, a division of Barr Laboratories. When calling, reference effort code: **84271**. ■

were satisfied with the treatment.[1]

As clinicians begin to offer extended regimen contraception to patients, the task at hand will be to explain that for women using hormonal contraceptives, there is no health advantage or necessity for monthly bleeding, says **Andrew Kaunitz**, MD, professor and assistant chair in the obstetrics and gynecology department at the University of Florida Health Science Center/Jacksonville.

"In addition, we need to help women considering Seasonale, as with women starting any hormonal contraceptive, understand that unscheduled spotting/bleeding is common during the initial months of use," he states. "Over time, unscheduled bleeding declines to levels comparable to conventional 21/7 oral contraceptive use."

Women who use Seasonale should be counseled to expect to have more bleeding or spotting between their menstrual periods than if they were taking an oral contraceptive with a 28-day treatment cycle, states the product literature.[2]

Explain to women that during the first Seasonale treatment cycle, about one in three women may have 20 or more days of unplanned bleeding or spotting, but this bleeding or spotting tends to decrease during later cycles. Women should not stop taking Seasonale because of the bleeding; if the spotting continues for more than seven consecutive days or if the bleeding is heavy, they should be instructed to call your office.

COMING IN FUTURE MONTHS

- Check chlamydia screening and treatment updates
- HPV and cervical dysplasia: When and how to screen and treat
- Dealing with premenstrual symptoms — new options are out
- Review new information on vasectomy
- Microbicide update: What's in the development pipeline?

Because Seasonale users can expect to have fewer periods, its labeling also advises women to consider the possibility that they may be pregnant if they miss any scheduled periods. Be sure to review this point with your patients, advises **David Archer**, MD, professor of obstetrics and gynecology and director of the Clinical Research Center at the Eastern Virginia Medical Center in Norfolk.

Counsel women to consider the possibility of pregnancy if they experience no bleeding on the days that they are taking the white tablets in the Seasonale pill package, state package instructions.[1] Tell them to notify your office if they have missed their period or if they have symptoms of pregnancy such as morning sickness or unusual breast tenderness.[2]

(Editor's note: If you are a subscriber to Contraceptive Technology Update *and have shared your e-mail address with us, you should have received an e-mail on Sept. 8 that gave you the news on Seasonale's regulatory approval. If you would like to receive future e-mails regarding news events about contraceptives, please contact customer service with your e-mail address. Customer service can be reached at (800) 688-2421 or customer service@ahcpub.com. To obtain more information on Seasonale, see information on audio conference, p. 130.)*

References

1. Vercellini P, Frontino G, De Giorgi O, et al. Continuous use of an oral contraceptive for endometriosis-associated recurrent dysmenorrhea that does not respond to a cyclic pill regimen. *Fertil Steril* 2003; 80:560-563.

2. Barr Laboratories Inc. *Patient Product Information. Seasonale.* Accessed at www.seasonale.com. ■

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Physicians and nurses participate in this continuing medical education/continuing education program by reading the articles, using the provided references for further research, and studying the questions at the end of the issue. Participants should select what they believe to be the correct answers and refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity with the December issue, you must complete the evaluation form provided and return it in the reply envelope provided in that issue to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you. ■

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CE/CME Questions

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

- Identify clinical, legal, or scientific issues related to development and provisions of contraceptive technology or other reproductive services. **(See "Interest in extended-regimen contraception to grow" and "Readers rank top oral contraceptives" in this issue.)**
- Describe how those issues affect service delivery and note the benefits or problems created in patient care in the participant's practice area. **(See "Emergency contraception provision catches on.")**
- Cite practical solutions to problems and integrate information into daily practices, according to advice from nationally recognized family planning experts. **(See "Move over, Pill: New contraceptives expand acceptance among women.")**

17. Where can women wear an Ortho Evra transdermal contraceptive?

A. On the buttock, abdomen, upper torso (excluding the breasts), or on the outside of the upper arm
B. On the buttock, abdomen, upper torso (including the breasts), or on the outside of the upper arm
C. Only on the buttock or abdomen
D. Only on the upper torso (excluding the breasts)

18. About how many women may have 20 or more days of unplanned bleeding or spotting during the first treatment cycle of the extended-regimen oral contraceptive Seasonale?

A. 1 in 3
B. 1 in 4
C. 1 in 5
D. 1 in 10

19. Which of the following choices represents the 18 contraceptive pills recognized as safe and effective for emergency contraceptive use by the Food and Drug Administration?

A. Ovral, Lo/Ovral, Ovrette, Triphasil, Alesse, Ogestrel, Low-Ogestrel, Levora, Trivora, Levlen, Levlite, Tri-Levlen, Aviane, Lessina, Portia, Enpresse, Cryselle, Ortho-Cept
B. Ovral, Lo/Ovral, Ovrette, Triphasil, Alesse, Ogestrel, Low-Ogestrel, Levora, Trivora, Levlen, Levlite, Tri-Levlen, Aviane, Lessina, Portia, Enpresse, Cryselle, Desogen
C. Ovral, Lo/Ovral, Ovrette, Triphasil, Alesse, Ogestrel, Low-Ogestrel, Levora, Trivora, Levlen, Levlite, Tri-Levlen, Aviane, Lessina, Portia, Enpresse, Cryselle, Nordette
D. Ovral, Lo/Ovral, Ovrette, Triphasil, Alesse, Ogestrel, Low-Ogestrel, Levora, Trivora, Levlen, Levlite, Tri-Levlen, Aviane, Lessina, Portia, Enpresse, Cryselle, Ortho-Cyclen

20. What is the progestin component used in Ortho Tri-Cyclen Lo?

A. Desogestrel
B. Norgestimate
C. Gestodene
D. Levonorgestrel

Answers: 17. A; 18. A; 19. C; 20. B.

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Contraceptive Technology Reports

A supplement to *Contraceptive Technology Update* **November 2003, BB #03176**

Overview: Rationale for Extended-Cycle Oral Contraception

Seasonale (Barr Laboratories, Pomona, NY), the first extended-cycle oral contraceptive (12 weeks continuous daily active pill followed by a one-week inactive pill) approved by the Food and Drug Administration (FDA) is expected to become clinically available by the end of this month. This approval represents a bold but precedented step away from the traditional model of 28-day oral contraceptive pill (OC)-induced cycles. The idea of giving the pill for 21 days with a seven-day hiatus (21/7 OC) to allow a withdrawal bleed was based primarily on the historical desire to mimic the natural menstrual cycle. A monthly bleed at that time point was reassuring to patient and physician alike that pregnancy was unlikely, and at that point, the potential teratogenicity of the pill and long-term effects on fertility were unknown. From a political and religious standpoint, a "natural" cycle would be more acceptable to secular and religious authorities who were opposed to contraception that eliminated the monthly withdrawal bleed entirely.[1] Although the pill underwent the most extensive scrutiny and clinical trials of any compound up to that date, no dose ranging or dose extension (beyond 21 days) studies were carried out. It was only with time and experience that it was discovered that the higher estrogen doses [the original combinations contained 100-150 mcg ethinyl estradiol (EE)] were associated with a higher risk of thrombotic events, and the dose then was lowered with minimal effects on breakthrough bleeding.[2]

The clinical use of the OC now has extended beyond contraception to the treatment of several benign gynecologic conditions such as hyperandrogenism (acne and hirsutism), chronic pelvic pain, dysfunctional uterine bleeding, dysmenorrhea, and endometriosis;[3] prevention of multiple disorders such as anemia, endometrial cancer, ovarian cancer, benign breast disease, and pelvic inflammatory disease;[3] and finally personal and professional preference to avoid vaginal bleeding. A strong voice has emerged advocating elimination of the withdrawal-bleeding component completely.[4,5]

Hormone replacement therapy (HRT) in postmenopausal women has undergone a similar evolution. Bleeding not only is undesirable from a personal preference, but also as a side effect, as unexpected bleeding (frequently termed "breakthrough bleeding") is the single most common reason for discontinuing the 21/7-day OC regimen.[6] Other common reasons for discontinuing use include nausea, weight gain, mood changes, breast tenderness, and headaches.[6] Thirty-two percent of women starting 21/7-day OC therapy will discontinue their use within six months, largely due to these symptoms.[7]

A 1996 Dutch survey found that the majority of women in all age groups prefer either a decreased frequency of bleeding to less than once a month or complete elimination of bleeding through the use of oral contraceptives.[8] Additionally, the majority of the women surveyed preferred to have less painful, shorter, and less heavy periods, or most desired: complete amenorrhea. In the United States, the Washington, DC-based Association of Reproductive Health Professionals commissioned the Rochester, NY-based Harris Interactive to conduct a telephone survey of U.S. women regarding their preferences on frequency and characteristics of menstrual bleeding.[9] Of the 491 women ages 18-49 included in the survey conducted in 2002, 44% stated that they would prefer never to menstruate, and this preference increased

A Review of Extended-Cycle Oral Contraception

Author: **Richard S. Legro, MD,** Professor of Obstetrics and Gynecology, Pennsylvania State University College of Medicine, Hershey.

Peer Reviewer: **Leslie Miller, MD,** Associate Professor, Obstetrics and Gynecology, University of Washington, Seattle.

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to 59% when only those ages 40-49 were analyzed. (Fewer than 30% preferred monthly menses. More than one in four women had missed professional, social, athletic, or family-oriented events because of their period, menstrual cramps, or other menstrual effects. Of the 70% of women who currently or previously used OCs, 15% stated that they had used their OC regimen to delay or stop their period.[9]

The first large study on the acceptability of an extended 84-day regimen was performed by Loudon and colleagues in 1977.[10] There was a certain institutional reluctance to this change as noted in the article: "The doctors and nurses on the clinic staff were less enthusiastic about this regimen than the volunteers themselves."[10] However, the women in the study welcomed the reduced number of periods and associated relief from menstrual symptoms. This study of 196 women looked at reducing menstruation to a three-month cycle event (84 active days/seven placebo) which is very similar to the Seasonale schedule, although this study used an 50-mcg ethinyl estradiol/lynestrenol monophasic OC. Breakthrough bleeding decreased with each three-month cycle of use, and no breakthrough bleeding was cited after nine months of use. At the conclusion of the study, many of the patients refused to return to a monthly cycle and preferred the trimonthly regimen. There have subsequently been a number of other studies or extended contraception.[11-13]

Overview of Seasonale

Seasonale is the first FDA-approved extended-cycle oral contraceptive for the prevention of pregnancy. Seasonale is a 91-day regimen taken daily as 84 active monophasic tablets of 30-mcg EE and 150 mcg levonorgestrel, followed by seven inactive tablets. According to the package insert, in a one-year controlled trial with Seasonale, four pregnancies occurred in women 18-35 years of age during 809 completed 91-day cycles of Seasonale during which no backup contraception was utilized. This represents an overall use-efficacy (typical user efficacy) pregnancy rate of 1.98 per 100 women-years of use. In the published study, sponsored by Barr Laboratories, Seasonale was compared to monthly cycles of Nordette (30 mcg EE/150 mcg levonorgestrel) in a parallel, randomized, multicenter, open label study.[14] Pregnancy rates were comparable between the extended-cycle and traditional cycle regimens.

Results on Seasonale were better when compliance was included in the calculation of pregnancy rates. "Compliant use" patients were defined by eliminating all cycles in which a patient skipped two or more consecutive pills, had a pattern of overall noncompliance (< 80% pill-taking), or used or alternate forms of contraception-prohibited medications (that interacted with OC metabolism). Using a life table analysis of treatment failures (i.e. pregnancy) among compliant use patients, the life table point estimate was 0.55 pregnancies per 100 women for Seasonale and 1.45 per 100 women for Nordette. In this study, no formal statistical tests were conducted between treatment groups, and only descriptive statistics were reported.[14] Thus, while there may be a theoretical benefit to extended-cycle use in lowering pregnancy rates for women on oral contraception, further and larger studies are necessary to document this benefit.

Bleeding Patterns on Seasonale

The reported bleeding patterns on Seasonale were obtained in a select group of women, and care should be taken in extrapolating to the larger population until more data emerges. The majority in the study had used OCs in the past; less than 10% were new users.[14] A large percentage in both groups had used OCs in an extended fashion in the past. Additionally those prior users who had experienced prolonged breakthrough bleeding (≥ 10 days) while previously on OCs were excluded from participation. More women on Seasonale discontinued the study prematurely for unacceptable bleeding than did women in the 21/7-day regimen (7.7% vs. 1.8%). The authors noted that there was no correlation between "bleeding" reported as an adverse event, "bleeding" reported in an electronic diary the patients kept, and "bleeding" given as a patient-specified reason for study discontinuation. However the percentage of subjects experiencing breakthrough bleeding declined with each successive 91-day extended-cycle, from a median of 12 days per cycle during cycle one to a median

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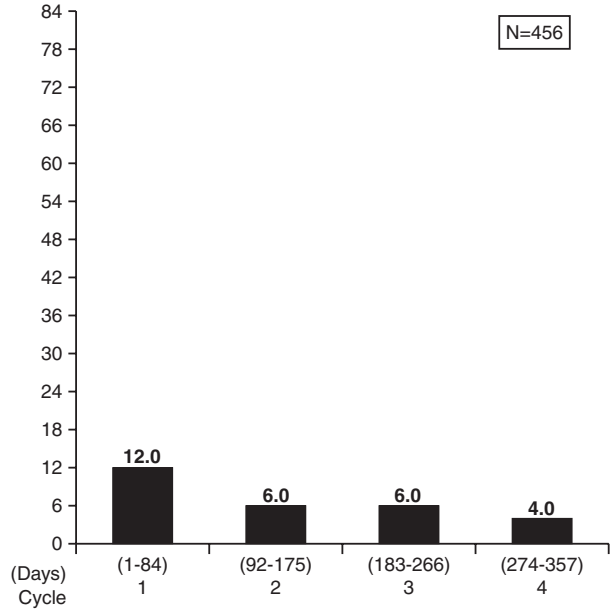
Figure 1: Median Number of Days of Breakthrough Bleeding/Spotting by Cycle in Patients



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of four days during cycle four. **(See Figure 1, above.)**

Further an increasing number of women became completely amenorrheic during the expected withdrawal period as the study progressed. The total days of bleeding and/or spotting (withdrawal plus intermenstrual) were similar over one year for Seasonale subjects and subjects on the 21/7-day cycle regimen. However, the extent of bleeding also appears to be less on the extended-cycle regimen. Among patients treated with the extended-cycle regimen, more than half of the overall days were due to spotting and not bleeding. This contributed to a greater percentage of bleeding-only days with the conventional regimen (median 12.2%) compared to the extended-cycle regimen (5.7%). But 58.5% of the extended-cycle users still had breakthrough bleeding during cycle four.

Other Adverse Effects of Seasonale

Reports of headache were lower for extended-cycle regimen patients than for the conventional patients (21% vs. 28%) in the reported trial of Seasonale, though this difference was not reported as statistically significant.[14] Other adverse events were comparable across the treatment groups. Specifically, there were no differences in lipid changes between treatment groups, with expected changes in low-density lipoprotein cholesterol and triglycerides reported in both groups. Further, there were "no clinically meaningful changes" in other important parameters between groups including body weight, heart rate, blood pressure, or other physical exam results. (These data were not specifically reported in the paper, and this comment was noted in the discussion section of the paper.) Finally, it is premature to speculate about increased risk for serious adverse events. Although no woman developed endometrial hyperplasia or cancer on Seasonale, one woman in the extended-cycle developed a pulmonary embolus. Contributing factors may have included age (the subject was 39), obesity, and recent air travel.[14] Theoretically, a more prolonged exposure (an additional 14 days every 91 days) to synthetic estrogen/progestin in the extended-cycle regimen may increase the risk for deep venous thrombosis and embolus. Further study and use of the medication is needed to address this important safety concern.

Clinical Use of Seasonale

During the study, Seasonale was started in the same fashion as conventional OCs. That is, the first active pill was taken on the first Sunday following the onset of menses. The Seasonale tablet dispenser includes three trays of cards holding 12 weeks of active medication (pink) and on the third tray, one week of inactive pills without hormone (white) for week 13. The package insert recommends using a backup form of contraception (such as condom or spermicide) for the first seven days on the pill. Otherwise the use recommendation is similar to that of conventional low-dose OCs. It is recommended to take the Seasonale pill the same time every day and to double up the pill the next day if an active pill is missed. Further recommendations include to double up on two consecutive days if two days are missed and to use alternate forms of contraception for the next seven days.

As noted above, unexpected bleeding is common with Seasonale. During the first extended cycle, about one in three women will have 20 or more days of unplanned bleeding or spotting. Thus, it is recommended to continue the pill during unscheduled breakthrough bleeding episodes during this first extended cycle, especially since this breakthrough bleeding is likely to decrease in subsequent extended-cycles. Inactive pills should be taken at their scheduled times, especially during the initial cycles. Stopping the active pill, intentionally skipping active pills, or combining active pills during bleeding episodes are empiric treatments that have little data to support their use to treat breakthrough bleeding in extended regimens. Women on Seasonale who have prolonged, unscheduled bleeding should contact their physicians. Such bleeding may be a result of pregnancy, intrauterine abnormalities, or endometritis. These possibilities should be considered and evaluated in such patients, although there is no evidence that these causes are more likely in extended regimen patients.

For those subjects who have no definable cause of bleeding, and it is presumed to be due to the extended-cycle regimen, there is little evidence at present that administering an alternative formulation in an extended-cycle fashion may achieve a better result as there have been no head-to-head comparisons of varying extended-cycle regimens. While other studies using conventional monophasic pills have shown lower bleeding rates on extended therapy, the comparatively small size and single center focus of these studies limit the universality of their conclusions.

One recent randomized study of a 168-day extended regimen vs. a 21/7-day cycle used OCs containing 20 mcg EE/

100 mcg levonorgestrel but only contained 32 subjects.[13] In this study, there were fewer total bleeding days in the extended regimen compared to the conventional (25.9 vs. 34.9 days), but no statistical difference was noted, most likely due to the small sample size.

Another larger randomized study of 79 subjects using the same formulation (20 mcg EE/100 mcg levonorgestrel) in traditional vs. a 336-day continuous OC dosing without any period week found a highly significant decrease in total bleeding days at any time point in the study.[15]

However, there were no differences in total spotting days between treatment groups, and when the analysis was restricted to cycle days 1 to 21 when the cyclic user is not supposed to have bleeding or spotting, there was an initial increase in spotting in the extended group (at least in the first 84 days of the continuous regimen) compared to the 21/7-day regimen.[15]

A larger clinical problem may become the substantial number of women who develop amenorrhea on the extended cycle. While the package insert recommends considering the possibility of pregnancy should amenorrhea continue through the inactive pill period, the need for clinical follow-up and/or pregnancy testing should be individualized. Amenorhea could be a desired condition but more reassuring in the setting of continuous use, with an active pill every day.

Patients for Extended-Cycle Regimens

This issue of selecting patients still is being addressed. We can begin with the demographics of women who have participated in extended-regimen studies. They tend to be in their 20s, with a body mass index (BMI) of about 25 (i.e., just at the threshold of being overweight), and most have had prior experience with OCs.[13-15] This latter characteristic suggests that there may be a stepwise progression from traditional OC to a desire to try extended regimen OC. In one study reporting educational background, 90% had a college and/or graduate school background, which implies an educated cohort.[15]

Other studies have suggested that there may be a varying incidence of adverse effects on extended regimen depending on initial BMI, with obese women (BMI > 30) more likely to experience menorrhagia but less likely to experience dysmenorrhea. But this study was a retrospective study and reflected potential selection bias in treatment regimen.[16] Thus, body habitus would seem a poor selection criterion at this point.

Another patient group that may benefit are the periodically noncompliant patients at risk for pregnancy, especially those that forget the first pill(s) of a new pack. This transition to the new pack is associated with higher noncompliance rates.[17] With fewer transitions on the extended-cycle (four vs. 13 on the 21/7-day cycle), there will be fewer opportunities to forget, and there will be a lower premium on forgetting one to two days of other pills in the middle of the extended cycle (with the exception of probably increased breakthrough bleeding).

The Future of Seasonale

FDA approval of this drug legitimizes the extended-cycle regimen concept, though the same formulation may be available by discarding the inactive pills from a number of available 21/7-day products that are identical with Seasonale. These include Nordette (Monarch Pharmaceuticals; Bristol, TN), Levlen (Berlex Laboratories; Richmond CA), and Levora (Watson Laboratories; Corona, CA). Comparable, if not bioequivalent, products contain the same dose of ethinyl estradiol (EE) as is present in Seasonale (30 mcg) but contain 300 mcg norgestrel, of which 50% is metabolized to levonorgestrel: Lo-Ovral, (Wyeth Pharmaceuticals; Philadelphia) and Low-Ogestrel (Watson Laboratories; Corona, CA).

However, one immediate advantage of Seasonale over the extended use of these other formulations is that an FDA-approved product is more likely to be covered by insurance companies, many of which will not pay for more than 13 21/7-day packs in a calendar year. Thus there may be less out-of-pocket expense for patients if Seasonale is selected. Some, however, have questioned the cost-effectiveness of a trimonthly regimen compared to a 21/7-day regimen for the average patient only seeking contraception when one compares hygiene product cost to OC pill cost.[18]

The majority of patients in the Seasonale trial rated their overall satisfaction with the extended-cycle OC as good to excellent and stated they would choose to continue with fewer menstrual periods even after the study.[14] Patient acceptance will more likely depend on a patient's desire to reduce the overall number of bleeding days on oral contraception rather than a desire to mimic a natural cycle. OCs by definition are "unnatural" as the ovaries do not secrete supraphysiological amounts of estrogen and progestin 21 days out of 28 and a withdrawal bleed is not necessary for contraception. As with traditional OCs, patients will need to be counseled about the unique benefits and side effects of extended-cycle contraception. There is certainly a misconception that there is endometrial buildup on hormonal contraception that requires a withdrawal bleed to shed on a regular basis. Patients and perhaps a few practitioners will need to be dispelled of this myth. Even after one year of continuous OC use, monitoring of the endometrium with ultrasound and biopsy in a subset of patients showed endometrial atrophy and not proliferation as was noted in cyclic users.[15]

It appears from the preliminary study that the discontinuation rate may be higher for extended-cycle oral contraception than for the traditional 21/7-day cycle and that this may be due to the initial higher breakthrough bleeding/spotting rates on extended-cycle treatment.[15]

The reported range of discontinuation for extended-cycle treatment ranges widely in the literature. In 1994, a trimonthly extended-cycle regimen using levonorgestrel and a low-dose estrogen was investigated. Two hundred and three women were enrolled, but only 30% completed the 52-week study. Women cited breakthrough bleeding, breast tenderness, and headaches as the primary reasons for discontinuing.[19] However, much lower discontinuation rates have been reported in individual case series,

Table 1: Potential Off-Label Uses for Extended-Cycle Contraception

1. **Reduction in Menstrual-Related Symptoms**
   - Migraine headache
   - Dysmenorrhea
   - Menorrhagia
   - Mood changes
   - Other premenstrual/cyclic symptoms
2. **Suppression of Ovarian Hyperandrogenism**
   - Hirsutism
   - Acne
   - Androgenic alopecial
3. **Treatment of Chronic Pelvic Pain**
   - Endometriosis-related
   - Other
4. **Prevention of Gynecological Malignancies**
   - Ovarian cancer
   - Uterine cancer
5. **Patient convenience**
   - Avoid bleeding at specific dates

when more intensive counseling may improve compliance.[16]

Off-Label Uses of Seasonale

As with the traditional OCs, off-label uses eventually may become one of the larger markets for this product. However, here is a word of caution: There are few data about its utility in off-label indications. Table 1, **above,** summarizes potential areas where an extended-cycle regimen may be theoretically beneficial. They include personal choice, whether it be out of professional obligations, such as the desire to avoid menstruation while on active combat duty, during athletic competitions (female swimmers, etc.), or for unique events (vacation, honeymoon, etc.). However for other indications, proper studies, and preferably FDA-regulated trials, need to be conducted before these can be utilized routinely. Some of these indications, such as a theoretical decreased risk for endometrial and/or ovarian cancer through the more prolonged suppression, probably will not be answered in our academic lifetimes, given the number of women and extended duration that such a study would require.

Studies of menstrual-related symptoms may be more manageable to conduct. These menstrual-related symptoms flare up during the pill-free interval and persist even after extended use of the 21/7-day OC.[20] Hyperandrogenism is another fertile area for further study. Several OCs currently have FDA indications for the treatment of acne, and it is reasonable to suppose that an extended-cycle regimen will seek the same indication. What is potentially more intriguing is to compare in a double blind, randomized, placebo control trial the effects of a 21/7-day regimen compared to an extended-cycle regimen on acne. A benefit of extended-cycle regimen would further legitimize the use of an extended-cycle regimen for prolonged ovarian suppression.

Summary

Seasonale is the first FDA-approved extended-cycle oral contraceptive for the prevention of pregnancy. Seasonale is a 91-day regimen taken daily as 84 active tablets of 150 mcg of levonorgestrel and 30 mcg of ethinyl estradiol followed by seven inactive tablets. Seasonale is effective in preventing pregnancy.

Breakthrough bleeding is more common in the initial extended-cycle compared to 21/7-day OC regimens, but bleeding tends to decrease with time. The side effect profile of Seasonale is comparable with a 21/7-day regimen, but further study is needed to comment on rare serious adverse events. The discontinuation rate of Seasonale may be slightly higher than that of the 21/7-day regimen, but this may be overcome with proper counseling and patience. Overall satisfaction with this form of contraception appears high. Further off-label uses of extended-cycle regimens need further investigations before they can be recommended routinely.

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CE/CME Instructions

Physicians and nurses participate in this continuing education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity, you must complete the evaluation form provided and return it in the reply envelope provided in order to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you.

CE/CME Objectives/Questions

After reading this article, the reader will be able to:

- Compare the pregnancy rates of extended-cycle contraception with Seasonale to conventional oral contraceptives.
- Review the bleeding profile on extended-cycle contraception with Seasonale with conventional oral contraceptives.
- Discuss the side effect profile of Seasonale.

1. Seasonale is composed of 84 continuous days of what monophasic combination?

A. Ethinyl estradiol (EE) 20 mcg/levonorgestrel 150 mcg
B. EE 20 mcg/levonorgestrel 200 mcg
C. EE 30 mcg/levonorgestrel 150 mcg
D. EE 30 mcg/levonorgestrel 200 mcg

2. Seasonale has been approved by the Food and Drug Administration as:

A. a contraceptive.
B. treatment for acne.
C. treatment for chronic pelvic pain.
D. All of the above

3. Which serious adverse event was noted in the Seasonale user group in the published clinical trial of Seasonale?

A. A case of endometrial cancer
B. A myocardial infarction
C. A pulmonary embolus
D. None of the above

Answers: 1. C 2. A 3. C