Contraception in Wisconsin: A Review

Sarina Schrager, MD, MS; Elizabeth Paddock, MD; Jessica Dalby, MD; Lara Knudsen, MD, MPH

ABSTRACT
The Contraceptive Equality Mandate took effect in Wisconsin on January 1, 2010. This mandate from the Wisconsin Office of the Commissioner of Insurance requires all insurance companies in the state of Wisconsin to cover all types of contraception, making Wisconsin the 28th state to do so. This article reviews the literature related to several types of contraception including Implanon (a newly available implantable contraception), drospirenone-containing oral contraceptive pills, and intrauterine devices. We also review evidence regarding depot medroxyprogesterone acetate and bone mineral density, and new cycling regimens for oral contraceptive pills.

BACKGROUND
In 2004, the Equal Rights Division of the Wisconsin Department of Workforce Development ruled that the failure of an employer to cover prescription contraceptives represents sexual discrimination under the Fair Labor Employment Act. Wisconsin Attorney General Peg Lautenschlager also wrote a letter expressing the opinion that current Wisconsin law prohibits employers and state colleges or universities from excluding contraception from their coverage if they provided coverage for other prescription medications.

The Contraceptive Equality Mandate took effect January 1, 2010, making Wisconsin the 28th state to require contraceptive coverage. This mandate specifically requires health insurance plans and employers to cover contraception if the plan provides other prescription coverage. Insurers are required to cover consultations, exams, procedures, and medical services related to contraception. There is no refusal clause written into the mandate, meaning that no insurance company or employer can refuse to provide contraception. However, exceptions include health care plans offered by limited service health organizations, preferred provider plans that are not a defined network plan, and some Medicare supplemental plans. This article provides an update for Wisconsin clinicians on new methods of contraception and reviews several currently available contraceptive methods.

IMPLANON
Implanon is an implantable long-acting reversible contraceptive that was approved by the US Food and Drug Administration (FDA) in July 2006. It consists of a single, 4-cm long rod that is 2 mm in diameter. Implanon contains etonogestrel (ENG), a metabolite of desogestrel, which is the same progestin present in NuvaRing. Approximate total cost for Implanon is $600-$1000, which is equal to $20-$25 per month if used for 3 years, the recommended limit for duration of use. The progestin-only contraceptive is inserted subdermally into the groove between the biceps and triceps of the non-dominant arm. This simple office procedure takes an average of 30 seconds; removal requires about 3.5 minutes. The continuous release of ENG effectively inhibits the luteinizing hormone (LH) surge, thereby preventing ovulation. Additional contraceptive mechanisms of Implanon include thickening of cervical mucus and thinning of the endometrial lining. Implanon differs from other progestin-only methods in that serum estradiol levels initially decrease, but then gradually return to normal levels.

Decreased serum estradiol levels may cause reductions in bone density. A small study of women using Implanon over 2 years showed no decrease in bone mineral density compared to women using the non-hormonal intrauterine device (IUD).

Additional non-contraceptive benefits of Implanon...
include decreased symptoms of dysmenorrhea. The main side effect of Implanon is irregular bleeding, which becomes less frequent with increased duration of use. Bleeding patterns are unpredictable and may vary. In a review of 11 clinical trials (which included over 900 women), after 6 months of use, 19% of women experienced amenorrhea, 34% reported infrequent bleeding, and 39% had normal bleeding episodes, while only 8% had frequent bleeding. However, 21% of women in the trials experienced prolonged bleeding episodes (>14 days uninterrupted). Eleven percent of women in these trials discontinued Implanon use specifically because of bleeding irregularities.

Implanon is very effective, with a failure rate estimated at 0.05%-0.1%. In clinical trials, no pregnancies were reported out of 942 women using this contraceptive method for 2 or 3 years. However, 6 women became pregnant within the first 14 days after removal, and these pregnancies were included in the calculations for failure rate. This highlights the rapid return to normal cycles following device removal. ENG levels are undetectable within a week, and ovulation resumes thereafter. There have been no reports of infertility. In post-marketing analysis of Implanon in Australia, the failure rate was 1 in 1000. The most common reason for these unintended pregnancies was unrecognized failed insertions. Clinical trials excluded women over 130% of their ideal body weight, therefore efficacy in this population is unknown. Because ENG is lipophilic, there is a theoretical risk for decreased contraceptive efficacy in obese women as excess adipose tissue may result in lower serum ENG levels. Clinicians should counsel overweight and obese women about the possible decreased efficacy. Implanon does not affect breast milk composition, quantity, or infant growth rate and is a good postpartum contraceptive choice. Implanon is contraindicated in women on medications upregulating the liver Cyp3A system, such as anti-epileptic or antiretroviral medications, due to the potential for decreased ENG levels that could result in unintended pregnancy.

Implanon has been available for more than 10 years on the worldwide market. It is currently the only contraceptive implant available in the United States. Its predecessor, Norplant, consisted of 6 rods that released levonorgestrel, which provided contraceptive efficacy for 5 years. Norplant, available in the United States from 1991 until distribution was stopped officially in 2002, incurred multiple lawsuits based on side effects and technical difficulty removing the device. Given the history with Norplant, FDA approval of Implanon was granted with the requirement that eligible providers complete a specific training program only offered through the company. This limited access to training is a barrier to widespread use of Implanon. Clinicians may contact the pharmaceutical representative for Merck (the new owners of Implanon) to find training sessions in their area.

**UPDATE ON IUDS**

The IUD is among the safest and most effective forms of birth control, and has the advantage of being a long-acting reversible contraceptive method (LARC). Its effectiveness is comparable to that of female and male sterilization and contraceptive implants—fewer than 1 pregnancy per 100 women in 1 year. Use of IUDs and other LARCs is significantly higher in many countries with lower rates of unintended pregnancy than the United States. IUDs have few contraindications, and almost all women are appropriate candidates for an IUD. In US-based surveys, women state that the ideal contraceptive is effective, reversible, and does not require frequent thought, yet the majority of young women have never heard of the IUD. Two IUDs are currently available in the United States: the Copper T380A (Paraguard), for use up to 10 years, and the levonorgestrel intrauterine system (Mirena), for use up to 5 years.

IUDs may be safely used by nulliparous women and by adolescents. In the past, concern that the presence of an IUD increased the risk of pelvic inflammatory disease (PID) and infertility led many health professionals to discourage IUD use in women who were not in strictly monogamous relationships. More recent evidence, however, has indicated there is no increased risk of PID or infertility in IUD users. There is a slight increase in risk of infection in the 20 days following IUD insertion. A Cochrane review found that using doxycycline 200mg or azithromycin 500mg by mouth prior to IUD insertion confers little benefit in preventing infection and did not change the discontinuation rate at 3 months.

IUD insertion in nulliparous women can be technically challenging. A recent randomized controlled study found that cervical priming with sublingual misoprostol prior to IUD insertion in nulliparous women significantly increased the ease with which the IUD was inserted (as judged by the provider). In this study, women were randomized to receive misoprostol
400 mcg sublingually 1 hour prior to IUD insertion versus placebo. Although using misoprostol did not change the women’s pain ratings on an analogue scale, using misoprostol did reduce the number of difficult and failed attempts at IUD insertion. Side effects for the 2 groups did not differ in this particular study, though common side effects of misoprostol include diarrhea and cramping.

IUD insertion immediately postpartum and post-abortion is safe and effective. The expulsion rate for placing an IUD immediately post-abortion was found to be 7% in 1 study, compared to 3% during interval insertion. The expulsion rate for IUD insertion immediately after delivery of the placenta is 10%-15% when the IUD is placed with a ring forceps or sterile gloved hand, a rather uncomfortable experience for many women. Although the expulsion rate is higher when placed postpartum or post-abortion, the advantage to timely placement is significant, particularly for women with poor access to care or inconsistent follow-up.

The IUD requires higher costs up front, but over time is a cost-efficient birth control method. A 2009 American Congress of Obstetricians and Gynecologists Committee Opinion recommends that health care providers “encourage implants and IUDs for all appropriate candidates, including nulliparous women and adolescents.” The Committee further recommends adopting same-day insertion protocols, avoiding unnecessary delays such as waiting to time insertion with menses or waiting after delivery, miscarriage, or abortion. Screening for gonorrhea, chlamydia, and cervical cancer should not delay insertion. Increasing the use of IUDs in women could significantly lower unintended pregnancy rates.

**DROSPIRENONE-CONTAINING OCPS**

There are 2 combined oral contraceptive pills (OCPs) available in the United States that contain the new progestin drospirenone: Yasmin (approved in 2001) contains 3 mg of drospirenone combined with 30 mcg of ethinyl estradiol and is dosed in a standard 21/7 day regimen; Yaz (approved in 2006) contains 3 mg of drospirenone combined with 20 mcg of ethinyl estradiol and is dosed in a 24/4 day regimen. Drospirenone is different than the other progestins used in OCPs because it is derived from 17 alpha spironolactone as opposed to 19-nortestosterone. Drospirenone has both antimineralcorticoid and antiandrogenic actions. Pills with drospirenone have comparable efficacy and safety profiles to other OCPs.

Drospirenone has similar properties to progesterone and works as an aldosterone antagonist (by binding to the mineralcorticoid receptor) to prevent sodium and fluid retention. This effect is equivalent to a 25 mg dose of spironolactone. Because of this aldosterone effect, there is potential for drospirenone containing OCPs to cause hyperkalemia. However, a large matched cohort study of over 20,000 women starting Yasmin and over 40,000 starting another OCP found no difference between groups in rates of hyperkalemia. Product labeling suggests that clinicians monitor potassium levels after the first month of taking Yaz or Yasmin, but evidence is lacking in support of this recommendation. Clinicians should be cautious in initiating Yaz or Yasmin in women with other risks for hyperkalemia (ie renal insufficiency or use of medications such as angiotensin converting enzyme inhibitors, diuretics, or angiotensin II agonists).

Yaz has FDA indications for contraception, treatment of acne, and premenstrual dysphoric disorder (PMDD). Several randomized controlled studies demonstrate the efficacy of Yaz in treatment of acne. However, no studies demonstrate that it works better than other OCPs in treatment of acne. Yaz has an FDA indication for PMDD, but its effectiveness in treating less severe symptoms of premenstrual syndrome (PMS) is unclear. A Cochrane review of Yaz as a treatment of PMS evaluated 5 trials that included over 1600 women. The group that took Yaz had improved PMS symptoms in the first 3 cycles. It was concluded that larger and longer trials are needed to determine whether Yaz is better than placebo in treating women with PMS for longer periods of time. As with all estrogen-containing contraceptives, both Yaz and Yasmin increase a woman’s risk of thromboembolism.

**DMPA AND BONE DENSITY**

Depot medroxyprogesterone acetate (Depo-Provera, DMPA) is an easy to use injectable progestin-only contraception that requires only 4 intramuscular injections per year. It also is used medically for endometriosis and dysmenorrhea. It is a popular form of contraception especially in adolescent females because of ease of use, privacy (no pills or patches), and because it does not require partner involvement.

DMPA works by delivering a high dose of progestin that inhibits ovulation in most women. This anovulation can cause decreased serum estradiol levels. The resultant hypoestrogenic state has been linked to decreased bone mineral density (BMD). In November 2004, the FDA issued a black box warning that reads:
Use of Depo-Provera may cause you to lose calcium stored in your bones. The longer you use Depo-Provera, the more calcium you are likely to lose. The calcium may not return completely once you stop using Depo-Provera. Loss of calcium may cause weak bones that could increase the risk that your bones might break, especially after menopause. It is not known whether your risk of developing osteoporosis may be greater if you are a teenager when you start to use Depo-Provera. You should only use Depo-Provera long term (more than 2 years) if other methods of birth control are not right for you. The concern about bone mineral density loss is highlighted in adolescent females. Normally bone density increases in this population, so any loss in bone mass is of clinical concern in terms of future risk of osteoporosis. A 2006 position paper by the Society of Adolescent Medicine (SAM) reviewed 4 prospective observational studies of adolescents who received DMPA every 12 weeks for 2 years and found that in these patients bone density at the lumbar spine decreased -3.1% compared to a gain of +7.2% in untreated females. Other factors in adolescence that can affect BMD are genetics, pregnancy, anorexia, and the female athlete triad. There are no studies to date looking at adolescent DMPA use and risk of postmenopausal fracture.

There are a number of studies that evaluate BMD after discontinuation of DMPA. A 2006 study showed that in women aged 25-36 there was almost full recovery of BMD. Another study more specific to adolescents done by Cundy et al showed that in women aged 18-39 there was rebound recovery of BMD at 36 months after discontinuation, though not to the point of matching non-users. Finally, a 2008 Brazilian study showed that, in postmenopausal women who had previously used DMPA, there was no significant difference in BMD to controls.

There has been some suggestion that supplementing estrogen in DMPA users would counteract the loss in BMD. This is substantiated by evidence of the bone protective effects of estrogen in post-menopausal women as well as adolescents with the female athlete triad. A few studies have evaluated this and have shown some improvement in BMD but were limited by small sample size and high attrition rates.

Important to the review of DMPA usage in adolescents is the fact that most young women use DMPA for short periods and frequently change types of contraception, alternating between OCPs, DMPA, and no contraceptive use. Over 50% of users discontinue DMPA by 1 year. The most common reason for discontinuation is menstrual irregularity.

The World Health Organization has recommended that no restrictions should be placed on the use of DMPA due to BMD, including no restriction on duration of use. SAM suggests that practitioners should continue prescribing DMPA to adolescent girls who desire contraception while adequately describing the risks and benefits. Clinicians can evaluate a patient’s risk of developing low bone density as well as encouraging adequate calcium and vitamin D intake and daily weight bearing exercise. They do not recommend restricting use to less than 2 years. Adolescents with known osteopenia or other risk factors may benefit from estrogen supplementation. A 2009 Cochrane review of hormonal contraceptives and bone health in women determined there was not enough evidence to evaluate whether hormonal contraceptives affected fracture risk.

Like all medications, the risks and benefits of DMPA should be discussed with each patient. In many adolescent women, DMPA is a good choice for contraception. Based on the limited data available at this time regarding DMPA and BMD, there is no compelling evidence to limit DMPA usage in adolescents. The potential risk of future fracture is unknown.

EXTENDED CYCLING OF OCPS

Traditionally, oral contraceptive pills have been dosed based on a typical menstrual cycle with 21 days of active hormone pills and then 7 days of placebo pills. During the 7-day hormone free interval, women experience a withdrawal bleed from the absence of hormones. There is no medical reason for a woman to have a menstrual period every month. An extended prescribing regimen of OCPs involves more than 3 weeks of active hormone pills. Often, women take 2-3 packs of active pills before having 1 hormone-free week.

A Cochrane review compared 28-day cycles and extended regimens and found no difference in contraceptive efficacy and safety profiles. However, these results are limited due to the multiple different regimens evaluated and the lack of long-term data. Because there is no difference in daily estrogen dose, it is unlikely that overall clotting risk is increased with an extended cycle. A 2-year study of a 91-day extended cycle regimen with ethinyl estradiol and levonorgestrel (.03/.15 mg) that included 84 days of active hormone (the equivalent of 4 pill packs) and 7 days of placebo pill found continued efficacy and safety over a 2-year period.

Extended cycle contraception can be useful to treat medical conditions related to menses or ovulation such as menstrual irregularity, alternating between OCPs, DMPA, and no contraceptive use. Over 50% of users discontinue DMPA by 1 year. The most common reason for discontinuation is menstrual irregularity.
as dysmenorrhea, endometriosis, menstrual migraines, and some premenstrual symptoms. A clinical trial of 114 women with menstrual migraines had decreased headaches on an extended pill regimen as compared to a 21/7 day regimen.45

The main side effect of extended cycle contraception is irregular bleeding patterns. Most women have more unscheduled bleeding on extended cycle contraception than on the traditional 28-day regimens.46 However, these symptoms decrease significantly after the first few months on the extended regimen. Women may experience amenorrhea after long use of extended cycle contraception. One small trial of 32 women found that 88% experienced amenorrhea during months 10-12 of continuous ingestion of monophasic oral contraceptive pills (ethinyl estradiol/levonorgestrel 0.2/0.1mg).47

A randomized controlled trial of 62 women compared the bleeding patterns between a 28-day pill regimen to a continuous 168-day regimen (pills with 0.2 mg ethinyl estradiol and 1 mg norethindrone) over a 6-month time period. There was no difference in total number of bleeding days between groups, but the incidence of heavy bleeding was significantly lower in the extended cycle group.48 The presumed mechanism of irregular bleeding comes from endometrial atrophy, which is why many regimens either add low-dose estrogen during the placebo week or shorten the duration of inactive pills. Addition of low-dose estrogen (10 mcg of ethinyl estradiol) to the placebo pills can significantly decrease the unscheduled bleeding.49 Shortening the pill-free interval from 7 to 4 days may also help decrease abnormal bleeding by preventing activation of the hypothalamic pituitary axis, thereby preventing development of a dominant follicle.49

Extended cycling regimens also may be effective with the contraceptive ring. A study of 289 women compared the traditional 28-day regimen of the vaginal ring with a 49-day cycle, a 91-day cycle and continuous use. As the cycles increased in length, days of unscheduled bleeding increased.50 Women on extended cycles had less heavy bleeding but more days of unpredictable spotting.

Physiologic changes induced with extended cycle regimens include smaller ovarian volume, lower estradiol levels, and smaller lead follicle size, all indicative of greater ovarian suppression.48 Endometrial biopsies of 63 women on a 91-day extended cycle regimen found no evidence of endometrial hyperplasia.51

CONCLUSION
This article provides a review for primary care clinicians and should serve as a reminder to review contraception with all reproductive-aged women, especially now that Wisconsin law mandates contraceptive coverage.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES
The mission of the *Wisconsin Medical Journal* is to provide a vehicle for professional communication and continuing education of Wisconsin physicians.

The *Wisconsin Medical Journal* (ISSN 1098-1861) is the official publication of the Wisconsin Medical Society and is devoted to the interests of the medical profession and health care in Wisconsin. The managing editor is responsible for overseeing the production, business operation and contents of *Wisconsin Medical Journal*. The editorial board, chaired by the medical editor, solicits and peer reviews all scientific articles; it does not screen public health, socioeconomic or organizational articles. Although letters to the editor are reviewed by the medical editor, all signed expressions of opinion belong to the author(s) for which neither the *Wisconsin Medical Journal* nor the Society take responsibility. The *Wisconsin Medical Journal* is indexed in Index Medicus, Hospital Literature Index and Cambridge Scientific Abstracts.

For reprints of this article, contact the *Wisconsin Medical Journal* at 866.442.3800 or e-mail wmj@wismed.org.

© 2010 Wisconsin Medical Society