



EDUCATIONAL OBJECTIVE: Readers will engage their female patients in a dialogue about their contraceptive and fertility decisions

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Update on contraceptive options: A case-based discussion

ABSTRACT

As health care providers, we must engage our female patients in a dialogue about their contraceptive and fertility decisions. Empowering and educating our patients about their bodies' hormones, the menstrual cycle, and the risk of unintended pregnancy are central to effective contraceptive counseling. Selecting an appropriate method for a patient and her medical profile is rewarding and challenging in view of new medications, novel delivery systems, and evolving research.

KEY POINTS

Hormonal contraceptives have a number of noncontraceptive benefits, such as regulating the menstrual cycle.

The Pearl index is the number of unintended pregnancies per 100 women per year. Rates are 15% using male condoms, 8% with oral contraceptives, 3% with depot medroxyprogesterone acetate (Depo-Provera) injections, and less than 1% with intrauterine devices or female or male sterilization.

Estrogen-containing products should be avoided in patients with hypertension or who are at risk of venous thromboembolism.

CONTRACEPTIVE COUNSELING is both an art and a science. The role of the health care provider is to determine the patient's medical eligibility and match her preferences and lifestyle to an appropriate method for both contraceptive and potentially noncontraceptive benefits, while minimizing the risk of unintended pregnancy.

Women throughout the range of reproductive years need appropriate counseling and education on hormones, the menstrual cycle, and the efficacy of contraception as part of their routine gynecologic evaluation. Issues of access to birth control, cost, possible side effects, and actual effectiveness of methods are important to discuss.

In this paper we will discuss common clinical practice case scenarios to illustrate contraceptive counseling and management, including:

- Perimenopausal women
- Women with thrombophilia
- Women who contemplate becoming pregnant in the future
- Women with psychiatric illness
- Women with hypertension.

HALF OF ALL PREGNANCIES ARE UNPLANNED

Although many contraceptive options are available, 48% of all pregnancies in the United States are unintended.¹ In 2009, the national teen birth rate was 39.1 births per 1,000 girls and women age 15 to 19 years, which was 37% lower than in 1991.² Still, African American and Hispanic teenagers living in southern states have disproportionately higher rates.

The rate of unintended pregnancy is a little

lower at the older end of the reproductive age range, but still high: 35% of all pregnancies in women over 40 years old are also unintended.²

To find out why these numbers are so high, in 2007 the US Centers for Disease Control and Prevention (CDC) conducted a survey³ that included 8,000 women reporting unintended pregnancy who had not used contraception. Of these, 39% were married. Surprisingly, more than one-third of women said they did not know they could get pregnant when they did.³

■ WHAT'S NEW IN CONTRACEPTION?

The “pill” was approved by the US Food and Drug Administration (FDA) more than 50 years ago, and it is still the most commonly used contraceptive method (followed by surgical sterilization). Enovid, the pill formulated by Dr. John Rock and Dr. Gregory Pincus in the 1950s, contained 150 µg of mestranol (equivalent to 90 µg of ethinyl estradiol) and 9.85 mg of norethynodrel, a very potent progestin. Our current oral contraceptive pills contain much lower hormone doses and have fewer androgenic side effects.⁴

In May 2010, the CDC and the World Health Organization (WHO) updated their safety guidelines for all hormonal contraceptives and the use of these agents in patients with various medical and family histories. They ranked contraceptive methods from those with no restriction to those with unacceptable risk to their use. This document can be accessed at www.cdc.gov/mmwr/preview/mmwrhtml/rr5904a13.htm.⁵

New developments in oral contraceptives are notably in the 19-nortestosterone derivatives, the family that includes the second-generation progestogens already available such as norgestimate (contained in Ortho-Cyclen) and norethindrone (contained in Loestrin). A newer progestin, dienogest, is available in a preparation that also contains estradiol valerate (Natazia). Drospirenone, which is similar to spironolactone, is contained in Yaz, Yasmin, and newer products that also contain levomefolate calcium (Beyaz, Safyral).

LoLoestrin Fe, which contains active pills containing 10 µg of ethinyl estradiol and 1 mg of norethindrone and placebo pills with 75 mg

of ferrous fumarate, was recently approved by the FDA and offers an ultra-low dose of estrogen.

Depot medroxyprogesterone acetate now comes in a 104-mg suspension for subcutaneous injection every 3 months; it is called depo-subQ provera 104. Standard medroxyprogesterone acetate 150 mg for intramuscular injection every 3 months (Depo-Provera) is still available and has gone generic. The newer product offers the advantages of lower dose and less weight-gain. Also, it allows capable and willing patients to self-administer their contraceptives. However, it is more expensive—\$104 per injection for a patient without insurance at Cleveland Clinic, compared with \$46 for Depo-Provera and \$10 for the generic intramuscular preparation for a patient with insurance.

A new option for emergency contraception, ulipristal (ella) is a progesterone antagonist-agonist available only by prescription. Taken in a single oral dose of 30 µg, it is effective for up to 120 hours after unprotected intercourse. It joins Plan B (levonorgestrel 1.5 mg in a single dose) and Next Choice (two doses of levonorgestrel 0.75 mg each), which are available over-the-counter for women age 17 years or older, and by prescription for those 16 years and younger, for use up to 72 hours after unprotected intercourse.

■ CASE 1: CONTRACEPTION IN PERIMENOPAUSE

A 48-year-old attorney who has had two children complains of irregular menstrual cycles and of occasional hot flashes at night that wake her from sleep. She keeps a menstrual calendar; it shows her last menstrual period was 3 months ago. She took oral contraceptives for 15 years before she had her first child. She is using condoms intermittently for contraception. Her body mass index is normal at 24 kg/m², and she does not smoke. How do you counsel her?

A variety of hormonal options

This healthy perimenopausal woman has a variety of hormonal contraception options that would have the added benefit of regulating her menstrual cycle or suppressing it altogether.

Current oral contraceptives contain much lower hormone doses and have fewer androgenic side effects

These include the levonorgestrel intrauterine system (Mirena IUS), various injectable products (such as Depo-Provera or the newer depo-subQ provera 104), contraceptive pills, the Ortho Evra contraceptive patch, and the vaginal contraceptive ring (NuvaRing). Of these, low-dose birth control pills may be the best option, as they would help with cycle control, offer contraception, and better regulate hormonal fluctuations to reduce her hot flashes.

Hormonal contraception can safely be used in women in their 30s and 40s, and often until menopause if the benefit outweighs the risk.

An estradiol valerate-dienogest oral contraceptive with a quadriphasic dosing schedule (Natazia) has been studied in women up to age 50. Although it was approved in 2010 in the United States, this pill has been used in Europe since the 1990s. The 26 active pills contain tapering doses of the active drugs, with the aim of mimicking the natural menstrual cycle, similar to triphasic pills. Estradiol valerate is a bioidentical estrogen, as it is rapidly metabolized to estradiol (E2), which is identical to 17-beta estradiol and estrone (E3) produced by the ovary. A dose of 2 mg of estradiol valerate is equivalent to 10 µg of ethinyl estradiol, which is the estrogen component in most other oral contraceptives. Low-dose pills by definition contain less than 50 µg of ethinyl estradiol. Dienogest, the progesterone component, has a 17-cyanomethyl group that accounts for its strongly progestogenic and weakly antiandrogenic properties.

All oral hormonal contraceptives can increase triglycerides by inducing the CYP450 system in the liver. However, in clinical trials, estradiol valerate-dienogest also caused other changes in lipid metabolism, such as a nonsignificant increase in high-density lipoprotein cholesterol and a slight reduction in low-density lipoprotein cholesterol and lipoprotein(a) compared with ethinyl estradiol-levonorgestrel preparations.⁶

It is important to advise patients that, compared with users of other oral contraceptives, estradiol valerate-dienogest users may experience fewer days of menstrual bleeding and more cycles without withdrawal bleeding. This product can therefore be an effective alternative for women with menorrhagia.

All classes of hormonal contraception carry a similar risk of side effects, such as headache, breast tenderness, nausea, irregular bleeding, and mood changes. Some women have no side effects.

CASE 2: THROMBOPHILIA

A 39-year-old woman with a body mass index of 31 kg/m² (obese) has a history of protein S deficiency with active lower-extremity deep vein thrombosis, for which she is taking warfarin (Coumadin). She experiences menorrhagia and dysmenorrhea due to intramural fibroids and possible adenomyosis seen on transvaginal ultrasonography and confirmed by magnetic resonance imaging. Hysteroscopy reveals no polyps or submucosal fibroids. An endometrial biopsy is negative for malignancy.

She desires contraception. How do you counsel her?

Estrogens are contraindicated—except, perhaps, in select cases

This patient has many reasons for heavy bleeding. She is on warfarin, which effectively inhibits synthesis of vitamin K-dependent coagulation factor. She also has fibroids and adenomyosis. The latter is a difficult condition to control, as the location of the intramural glands makes treatments such as ablation, dilation and curettage, and oral agents ineffective.

All estrogen-containing formulations (pills, ring, patch) are contraindicated in women with acute venous thromboembolism (VTE) and known thrombophilia. A newer agent approved for treating menorrhagia (not for contraception), tranexamic acid (Lysteda), also carries a contraindication for patients with thrombophilia or history of VTE; however, the evidence for the latter is controversial.⁷

The updated CDC guidelines for the use of hormonal contraceptives state that patients who receive anticoagulation for at least 3 months and who have no history of VTE or a low risk of recurrent VTE (no evidence of active cancer, no known thrombophilia) may use estrogen-containing contraceptives in select cases (category 3—*theoretical risk outweighs benefits, but not an absolute contraindication*).⁵ Although this is not common clinical practice, select patients may benefit

Hormonal contraception can safely be used in women in their 30s and 40s, and often until menopause

The risk of VTE is exponentially higher during pregnancy than while using hormonal contraceptives

from menstrual cycle control while receiving anticoagulation. However, other contraceptive alternatives are preferred if possible.

Progestin-only treatments such as the Mirena IUS (if the fibroids do not distort the uterine cavity) and the etonogestrel implant (Implanon) are nonsurgical options that may reduce menorrhagia and are safer alternatives for patients with thrombophilia.

The Paragard (copper) intrauterine device would provide nonhormonal contraception without diminishing menorrhagia. Obviously, barrier methods (which are less effective than hormonal contraception) can be suggested for contraception alone. A viable option for women finished with childbearing is hysterectomy, which provides contraceptive benefit and definitive treatment of menorrhagia due to adenomyosis.

Laboratory screening for VTE is not required before starting estrogen-containing contraceptives. However, one should take a detailed history and inquire about VTE events or a family history of recurrent VTE.

VTE rates among reproductive-age women are 4 to 5 per 10,000 women per year.⁸ The rate of VTE in oral contraceptive users is estimated as 9 to 10 per 10,000 women per year.⁹ However, rates of VTE associated with pregnancy and postpartum states are exponentially greater. Although recent studies have shown some discrepancy in rates of VTE across different classes of progestins,^{10,11} the absolute risk of VTE with hormonal contraceptives is very low.

In December 2011, an FDA panel voted 15 to 11 that the benefits of drospirenone-containing contraceptives (eg, Yaz, Yasmin, Beyaz, Safyral), such as preventing pregnancy, outweigh the potential risk. However, product labeling may change in the future to more accurately reflect the risk-benefit ratio. Stay tuned for better-designed trials to further assess VTE risk across progestins.

Health care providers should engage patients in an informed discussion about all risks and benefits of hormonal contraceptives and note this risk of VTE is higher in gravid women.

■ CASE 3: FUTURE FERTILITY

A 30-year-old surgical resident who has never been pregnant comes for her annual examina-

tion. She currently desires birth control but would like to be pregnant 1 to 2 years from now. She has no history of significant medical illness. Her body mass index is 23 kg/m², and she takes no medications. How do you counsel her?

Many options; also consider folic acid

Effective counseling leads to patient-centered decision-making for all treatments and procedures. Contraceptive counseling should elicit the patient's perspective about hormonal methods and educate her on efficacy, proper use, and common adverse effects.

Contraception should fit the patient's lifestyle. Questions as simple as "Are you a good pill-taker?" or "Are you comfortable with injections?" will help you and the patient assess what will work effectively and will maintain good adherence.

Deciding on a contraceptive option that is cost-effective is crucial, particularly for many young women or adolescents. Many oral contraceptives are widely available as generic formulations for less than \$10 per month. Although generic drugs are not required to be 100% bioequivalent to their brand-name counterparts, they can provide a more economical option. For a complete guide to different hormonal contraceptive formulations, we suggest *Choosing a birth control method*, available on the Web site of the Association of Reproductive Health Professionals at www.arhp.org/upload-Docs/choosingqrg.pdf.¹²

As discussed earlier, half of all pregnancies are unplanned, and so women of childbearing age should be ingesting 400 µg of folic acid daily. Debate exists as to whether Americans who eat a balanced diet need a multivitamin.¹³ However, there is no debate about folic acid, which is proven to prevent neural tube defects. Newer formulations of ethinyl estradiol-drospirenone (Beyaz, Safyral) now contain an active form of folic acid (levomefolate calcium 451 mg in each pill). For the above patient who needs contraception and is willing to take birth control, the addition of folic acid provides an essential element in preconception counseling.

Regardless of the current contraceptive choice, patients who actively desire pregnancy should take a prenatal vitamin that contains folic acid and iron.

In addition to combined oral contraceptives, other options for this patient include medroxyprogesterone acetate (intramuscular or subcutaneous), NuvaRing, or intrauterine devices. The Ortho Evra patch is also an option for this patient. However, since 2008 the patch has carried an FDA warning that the risk of VTE is twice as high with this product than with oral contraceptives that contain 30 µg of ethinyl estradiol plus levonorgestrel.¹⁴ Postmarketing data did not show any higher risk of VTE in patch users compared with oral contraceptive users less than 40 years of age, however.¹⁵

■ CASE 4: PSYCHIATRIC ILLNESS

A 21-year-old woman who has bipolar II disorder comes to your office for her annual gynecologic evaluation. She has one sexual partner and desires oral contraceptive pills. Lithium treatment has failed for her, but her condition is stable on carbamazepine (Tegretol). She asks if it is true that women can still get pregnant while on the birth control pill. How do you counsel her?

Possible interactions with psychiatric drugs

Like the woman in case 3, this patient has many options, including estrogen-containing pills, the vaginal ring, the patch, injectable contraceptives, and intrauterine devices.

Certain antiepileptic, antipsychotic, or headache medications such as carbamazepine, phenytoin (Dilantin), oxcarbazepine (Trileptal), and topiramate (Topamax) decrease levels of hormonal contraceptives by induction of the CYP450 enzymes. Conversely, it is suggested that lamotrigine (Lamictal) levels decrease by up to 49% while patients concomitantly take oral contraceptive pills, which can induce seizure activity.¹⁶ Also, antibiotics such as rifampin (Rifadin) and even herbs such as St. John's Wort can decrease the effectiveness of hormonal contraceptives by increasing their metabolism.

On the positive side, depot medroxyprogesterone acetate raises the seizure threshold by a mechanism attributed to high levels of progestins and is a better option for epileptic patients. A bulletin of the American College of Gynecologists addresses the paucity of data

on hormonal treatments in depressed patients. However, some evidence points to slight improvement of depressive symptoms after 1 year in patients who took Depo-Provera compared with those who discontinued the drug.¹⁷

The Pearl index, a measure of contraceptive efficacy

We refer to the Pearl index when answering our patients' questions about contraceptive efficacy. The Pearl index is defined as the number of unintended pregnancies per 100 women per year. The typical (or actual) effectiveness for each contraceptive method is quoted rather than the theoretical (perfect-use) efficacy.

We suggest simplifying this discussion with patients. For example, for every 100 women using male condoms for contraception, 15 women have unintended pregnancies per year. With hormonal contraceptives (pill, patch, or ring), for every 100 women there are 8 per year with unintended pregnancy, 3 of 100 with Depo-Provera, and less than 1 in 100 using intrauterine devices or female or male sterilization.¹⁸

Efficacy decreases (and the failure rate increases) with frequency of intercourse, irregular menstrual cycles, missed pills, improper dosing, and drug-drug interactions as described above.

■ CASE 5: HYPERTENSION

A 33-year-old woman who has been pregnant twice experienced preeclampsia in her last pregnancy, and now her blood pressure is consistently approximately 140/90 mm Hg on multiple office visits and ambulatory monitoring. She desires contraception. How do you counsel her?

Avoid estrogen-containing products

According to the WHO and CDC guidelines,⁵ women with controlled or uncontrolled hypertension should not be offered combined oral contraceptives, the patch, or the ring (category 3—theoretical or proven risks outweigh the benefits, and category 4 for systolic blood pressure greater than 160 mm Hg or diastolic blood pressure greater than 100 mm Hg).

All women who may become pregnant should be taking folic acid before conceiving

The progesterone-only pill ("mini pill"), medroxyprogesterone acetate (intramuscular or subcutaneous), Mirena IUS, the copper intrauterine device, and the etonogestrel implant are all safer options.

A small subset of patients develop elevated blood pressure after starting hormonal contraceptives. Estrogen-containing hormones can increase the liver's output of angiotensinogen, which is a renin substrate that activates the renin-angiotensin-aldosterone system. If this becomes clinically apparent, these patients

should refrain from estrogen-containing products and use progestin-only formulations as a safer alternative.

Patients with isolated elevated hypertriglyceridemia should avoid oral contraceptives. However, the patch, the ring, and progestin-only methods may be acceptable.

Diabetic patients with microvascular complications of retinopathy or nephropathy and any patient with macrovascular disease (stroke, cardiovascular disease) should not be offered estrogen-containing contraception. ■

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