Complex Contraception

Jennifer Kerns, MD, MS, MPH, Assistant Professor of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco, School of Medicine, San Francisco

Overview: increasing prevalence of use of contraception associated with lower maternal mortality; US Medical Eligibility Criteria for Contraception and US Selected Practice Recommendations for Contraception good sources of information; Medical Eligibility Criteria (MEC) from Centers for Disease Control and Prevention offer evidence-based ranks for each combination of contraceptive method and medical comorbidity; 1 — patient with medical condition described may use method without restrictions, and good data available on safety and effectiveness; 2 — may use method; studies less robust but advantages outweigh risks; 4 — good data indicate risk unacceptable; 5 — some data show risks may outweigh benefits, but physician and patient should discuss in context of other available methods of contraception; in some cases, recommendations for initiating method differ from those for continuing it; eg, recommendations for initiation in patient with hypertension may differ from those for continuing method in patient who develops hypertension while using method

Case 1: 19-yr-old gravida 0 (G0), newly sexually active; patient interested in ethinyl estradiol (EE)/etonogestrel vaginal ring (NuvaRing) but concerned about blood clots

Risk for clots: risk for blood clot 1 to 5 per 10,000 woman-years (TWY) in women not using combination hormonal contraceptives, 3 to 12/10TWY in those on combined hormonal contraception, and 5 to 20/10TWY during pregnancy; risk also elevated postpartum; pregnancy associated with higher risk for venous thromboembolism (VTE) than any method of contraception; well-conducted studies define risk associated with vaginal ring; retrospective cohort study — evaluated >9 million woman-years using Danish registry; risk for VTE ≈2/10TWY in nonusers of hormonal contraception; risk similar in users of combination oral contraceptives (COCs), transdermal patch, and vaginal ring; however, relative risk for VTE 6.5 with vaginal ring and 3.2 with COCs, suggesting that ring doubles risk; these findings correspond to 1.6 additional cases/TWY; however, inclusion of new (vs continuing) users affects observed rates; VTEs observed more frequently in new users who may have unidentified mutation predisposing them to VTE; study may have been biased because more new users used ring than COCs; multicenter prospective cohort study — evaluating 66,000 woman-years found no difference in relative risk for VTE in women using ring vs COCs; study divided users of COCs into those using pills containing levonorgestrel ( LNG) vs all COCs; LNG may be associated with lower risk than third-generation progestins such as drospirenone and desogestrel; however, ring not associated with increased risk compared with any COC; retrospective cohort study — compared ring with COCs in 500,000 new users; after adjustment, no increased risk for VTE observed in users of ring; conclusions — these studies suggest that risk for VTE from ring low, and no more than twice that associated with COCs

Management of case 1: conflicting level 2 evidence exists; based on level 1 evidence, women more likely to use ring correctly than COCs, so ring may prevent more unintended pregnancies; therefore, use of ring might result in fewer VTEs if it prevents more pregnancies; among oral progestins, LNG carries lowest risk for VTE; however, absolute risk low with any progestin, so no need to switch users of third-generation progestins to another progestin

Choosing COCs: level 1 evidence shows that low-dose pills containing 20 μg EE associated with more breakthrough bleeding and lower rate of continuance than pills containing 30 μg EE; pills containing 30 μg EE may cause more nausea and breast tenderness, but discontinuance for these reasons less likely; other COCs not superior to monophasic pills; drospirenone confers no clear benefit over other progestins; recommended regimen — monophasic COC containing 30 μg or 35 μg EE plus LNG, with shortened or erased placebo week to provide maximum ovarian suppression

Progestin-only methods: safe in patients with current VTE who are not on anticoagulation, and in patients with provoked or unprovoked VTE

Case 2: 38-yr-old G2 para 1 presents for contraception; patient has history of preeclampsia but otherwise healthy; body mass index (BMI) 37.6 and blood pressure (BP) 138/89 mm Hg; for obese women, all contraceptive methods ranked 1 or 2

Efficacy: obesity not associated with reduced efficacy in women using injectable depot medroxyprogesterone acetate (DMPA), ring, implant, intrauterine device (IUD), or COCs; subanalysis of one small study showed that patch less effective in women weighing >90 kg; however, other studies found no association between BMI and effectiveness; reasonable to counsel women weighing >90 kg that patch may be less effective

Adverse events: VTE — COCs and obesity independent risk factors for VTE; obesity doubles risk for VTE; however, no data show that obese women using COCs have synergistic increase in risk; in obese women, use of COCs carries lower risk for VTE

Educational Objectives

The goals of this program are to improve management of contraception and induction of labor (IOL). After hearing and assimilating this program, the clinician will be better able to:

1. Use the Medical Eligibility Criteria to inform discussions with patients requesting contraception.
2. Offer appropriate forms of emergency contraception to a patient presenting with recent unprotected intercourse who desires to prevent pregnancy.
3. Manage a patient with risk factors for sexually transmitted infection who requests an intrauterine device.
4. Advise a hospital committee charged with reducing the institutional rate of elective IOL at <39 wk gestation.
5. Counsel a patient asking about the relationship between autism and IOL.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, members of the faculty and planning committee reported nothing to disclose.
than pregnancy does; however, few data on risks in women with highest BMIs; weight gain — COCs, patch, ring, LNG IUD, and etonogestrel implant not expected to cause weight gain; however, DMPA associated with gain of 5 to 6 kg over 3 to 5 yr; weight gain observed in normal and overweight women; although one study showed that weight gain more pronounced in adolescents, data not consistent; women who gain >5% of body weight within 6 mo of beginning treatment with DMPA have higher risk for additional weight gain; metabolic syndrome — constellation of findings that increase risk for coronary heart disease, stroke, and type 2 diabetes (DM); lipids — COCs, patch, and ring associated with increases in triglycerides and high-density lipoprotein (HDL) and decrease in low-density lipoprotein (LDL); improvement in ratio of LDL to HDL observed in women with polycystic ovarian syndrome (PCOS); DMPA produces transient worsening of lipids after injection; etonogestrel implant decreases cholesterol, LDL, and HDL; BP — 5% of women develop reversible hypertension on COCs (increase of ≈7 mm Hg); insulin resistance — COCs, LNG IUD, and implant do not change insulin resistance in women who do not have DM; ring may improve insulin resistance in women with PCOS; some studies suggest that DMPA associated with small increase in fasting blood sugar (FBS) of ≈3 mg/dL over 2 yr; DMPA increases insulin resistance in obese women; no randomized controlled trials (RCTs) have studied DMPA in women with DM, but reports suggest increase in FBS; women with DM who use COCs do not have greater insulin requirement or end-organ damage; high-risk categories — in MEC, risk grades of 3 or 4 associated with use of some contraceptives in women with metabolic syndrome; COCs, patch, ring, and DMPA should be avoided in presence of multiple risk factors for arterial cardiovascular disease such as older age, smoking, DM, and hypertension; risk grade 2 or 3 for women with hyperlipidemia, but acceptable to use these methods in women with hyperlipidemia, but women who develop hyperlipidemia on these methods should be switched to another method; risk grade 3 or 4 for women with end-organ damage from DM such as nephropathy, retinopathy, or neuropathy, but in absence of end-organ damage, women may use combined hormonal methods

**Bariatric surgery:** women should wait 1 to 2 yr after surgery before planning pregnancy; fecundity and pregnancy rates often increase after surgery, especially in adolescents

**Management of case 2:** if patient not in high-risk category, all methods safe for pregnancy; if patient smokes or has other risk factors, other methods may be safer than combined hormonal contraceptives; patient may develop insulin resistance and weight gain from DMPA; if she needs emergency contraception (EC), ulipristal or copper IUD better choices than LNG

**Case 3:** 18-yr-old with BMI of 34 requests EC after having unprotected sex; patient has difficulty remembering to take COCs; options include ulipristal (Ella), copper IUD (most effective method of EC), and LNG (Plan B)

**Emergency contraception:** ulipristal and LNG may be used for ≤5 days after intercourse; ulipristal selective estrogen receptor modulator that delays rupture of follicles; ulipristal does not harm existing pregnancy; dose 30 mg; women with BMI ≥26 who require EC should be offered ulipristal because obese women have higher failure rates with LNG than ulipristal; copper IUD should be offered to all patients requesting EC; bedside.org good resource for patients

**Case 3:** 23-yr-old interested in IUD; patient has history of chlamydia and 3 male partners in past year; provider considering whether to screen patient for gonorrhea and chlamydia; LNG IUD (Skyla) good choice for this patient

**IUDs:** compared with Mirena, Skyla smaller and contains lower dose of LNG; Skyla lasts for 3 yr; preinsertion pain medication or paracervical block may be used; previous sexually transmitted infection (STI) or pelvic inflammatory disease (PID) not contraindication to any method of contraception; however, patient with current gonorrhea, chlamydia, purulent cervicitis, or active PID should not receive IUD; transient risk for PID at time of insertion of IUD; after insertion, risk for PID lower in patients receiving LNG IUD and not increased in patients receiving copper IUD; in retrospective study of >5000 insertions, screening for STI before insertion did not alter risk for PID; among screened women, risk for PID same whether screening performed before insertion or on same day, but results probably more accurate when screening performed on day of insertion; patient with positive screen should be treated without removing IUD; criteria for screening specified by CDC and US Preventive Services Task Force include sexually active women <26 yr of age and those with risk factors including new partner, symptoms, or other STI; prophylactic antibiotics at time of insertion confer no benefit

**Induction of Labor: Update on the Evidence**

**Sarah B. Wilson, MD, MEd,** Assistant Professor of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco, School of Medicine, San Francisco

**Incidence:** 22% of gravids in United States undergo induction of labor (IOL); rate of IOL doubled between 1995 and 2006; discussion today focuses on elective IOL; rate of elective IOL now decreasing in response to national campaigns

**Timing of induction:** American Congress of Obstetricians and Gynecologists (ACOG) strongly cautions against elective IOL at <39 wk and lists acceptable methods for confirming gestational age (GA) before performing elective IOL; documentation of maturity of fetal lungs at <39 wk not sufficient because feeding problems, increased admissions to neonatal intensive care unit (NICU), and other undesirable outcomes still possible; in retrospective study of 17,000 deliveries, 44% of early deliveries occurring at <37 wk planned, 71% of planned deliveries elective, and 10% of deliveries elective IOLs or planned cesareans performed at 37 to 39 wk and not medically indicated

**Decreasing elective IOL:** study evaluated 3 strategies to decrease elective IOL at <39 wk; these included hard stop (hospital policy), soft stop (providers agree not to perform IOL at <39 wk), and educational program; hard stop associated with greatest reduction in early elective IOL; study of 24,000 deliveries found that institutional hard-stop policy significantly reduced elective IOL at <39 wk and admission to NICU; but also documented significant increase in stillbirths at 37 to 38 wk

**Discussions with patients:** <39 wk toolkit from California Maternal Quality Care Collaborative useful; Choosing Wisely campaign from American Board of Internal Medicine emphasizes risk from unindicated IOL at <39 wk

**IOL after 39 wk:** some pregnancies may benefit from IOL; may be beneficial to induce all women; problems with widespread IOL include expense and possibility of increasing risk for cesarean delivery; observational studies comparing IOL with spontaneous labor at same GA found that IOL associated with cesarean delivery; however, more relevant clinical question whether IOL superior to expectant management; with expectant management, fetus enlarges and cervix may ripen but risk for stillbirth increases

**Large meta-analysis:** compared IOL with expectant management; included studies used different methods of induction; IOL resulted in moderate but significant reduction in rate of cesarean delivery; although no differences in other maternal or neonatal outcomes, nonsignificant increase in stillbirth observed in expectancy-managed pregnancies; finding suggests that IOL may be advisable if pregnancies likely to benefit can be identified; limitations of study — higher GA may increase anxiety of clinicians, leading to more cesareans in expectantly managed group; fewer methods for IOL available to expectantly managed patients who develop oligohydramnios or fetal distress; in study showing higher rate of cesarean in patients undergoing IOL, women with unfavorable cervixes had higher risk for cesarean delivery; based on this meta-analysis, expectant management might not lower risk for cesarean when cervix unripe; policies for elective induction also must consider costs
IOL after 41 wk: 41 to 42 wk gestation considered late term; ≥42 wk considered postterm; postterm pregnancies have higher rates of stillbirth, postmaturity syndrome, meconium aspiration, macrosomia, severe perineal laceration, cesarean delivery, and postpartum hemorrhage

Other studies: RCT randomized 3700 women at 41 wk to expectant management vs IOL; IOL group had decreased risk for cesarean delivery; expectant management group had more cesareans for fetal distress; patients in RCT included in afore-mentioned meta-analysis; another meta-analysis that included this RCT and other studies concluded that policy of IOL at 41 wk associated with fewer perinatal deaths

American Congress of Obstetricians and Gynecologists: does not mandate induction at 41 wk but states that IOL may be considered at 41 to 42 wk and should be recommended at 42 wk

Cost-effectiveness: in study examining quality-adjusted life years, IOL at 41 wk cost-effective compared with expectant management until 42 wk

Autism: oxytocin pathway or receptors may be affected in children with autism spectrum disorder; although no causal relationship demonstrated, manipulation of oxytocin during IOL might disrupt oxytocin pathways; one study showed weak and nonsignificant association between IOL and autism; subsequent study of 600,000 births showed that IOL, augmentation, and IOL with augmentation all associated with increased risk for autism (odds ratio 1.1 to 1.2); however, study did not demonstrate causal relationship; effect persisted in multivariate analysis that controlled for confounders; database did not include method used for IOL

Acknowledgments

Drs. Kerns and Wilson were recorded at the 2014 Obstetrics and Gynecology Update: What Does the Evidence Tell Us?, presented by University of California, San Francisco, Department of Obstetrics, Gynecology, and Reproductive Sciences, and held October 22-24, 2014, in San Francisco, CA. For information on upcoming meetings sponsored by UCSF School of Medicine, go to cme.ucsf.edu. The Audio Digest Foundation thanks the speakers and the UCSF School of Medicine for their cooperation in the production of this program.

Suggested Reading

1. When using the Medical Eligibility Criteria from the Centers for Disease Control and Prevention to assess a contraceptive method in a patient with a specific comorbidity, category 4 means:
   (A) The method may be used without restriction
   (B) The method poses an unacceptable health risk
   (C) No good data are available on safety or effectiveness
   (D) The risk associated with initiating the method differs from the risk for continuing it

2. A multicenter prospective cohort study evaluating risk for venous thromboembolism (VTE) found that compared with combination oral contraceptives (COCs), the risk for VTE in users of the vaginal ring was:
   (A) The same
   (B) Lower
   (C) Higher
   (D) Higher, but only in women with mutations associated with thrombophilia

3. Which progestin is associated with the lowest risk for VTE?
   (A) Drospirenone
   (B) Desogestrel
   (C) Levonorgestrel (LNG)
   (D) None of the above; all carry approximately equal risk

4. Compared with nonobese women, obese women may experience reduced efficacy when using which method of birth control?
   (A) Contraceptive patch
   (B) Combination oral contraceptives
   (C) Injectable depot medroxyprogesterone acetate
   (D) Intrauterine device

5. A decrease in high-density lipoprotein is associated with use of:
   (A) COCs
   (B) Contraceptive patch
   (C) Vaginal contraceptive ring
   (D) Etonogestrel implant

6. Which method of emergency contraception is not recommended in a patient with a body mass index of 30?
   (A) Ulipristal
   (B) LNG
   (C) Copper IUD

7. A 25-yr-old patient with a history of pelvic inflammatory disease but no current signs or symptoms of sexually transmitted infection (STI) requests an IUD. Which of the following is the best course of action?
   (A) Insert the IUD and screen for STIs at the same time
   (B) Screen for STIs and insert the IUD later if the screen is negative
   (C) Give a prophylactic antibiotic, insert the IUD, and screen for STIs at the same time
   (D) Counsel the patient that she is not an appropriate candidate for an IUD

8. In a study aimed at decreasing the rate of elective induction of labor (IOL) at <39 wk gestation, which of the following strategies was found most effective?
   (A) Patient education
   (B) Provider education
   (C) Agreement by providers not to perform elective IOL at <39 wk
   (D) Hospital policy forbidding such inductions

9. In a large meta-analysis comparing IOL with expectant management, patients with IOL were ______ likely to be born by cesarean delivery.
   (A) More
   (B) Less
   (C) Equally

10. A study of approximately 600,000 births showed that autism is:
    (A) Associated with IOL
    (B) Associated with augmentation of labor, but only when labor is induced
    (C) Caused by IOL
    (D) Caused by augmentation of labor with oxytocin

Answers to Audio Digest Obstetrics/Gynecology Volume 62, Issue 01: 1-A, 2-D, 3-B, 4-C, 5-B, 6-D, 7-C, 8-C, 9-C, 10-B

Remarks represent viewpoints of the speakers, not necessarily those of the Audio Digest Foundation.