

## **Contraception in Medically Complex Patients**

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*Learning Objectives:* After participating in this continuing professional development activity, the provider should be better able to:

1. Recommend contraceptives for patients with common medical conditions.

2. Explain why various contraceptives are contraindicated in some situations.

3. Describe effective prescription of emergency contraception in patients with specific medical conditions.

Key Words: Contraception, Heart disease, Hypertension, Shared decision-making

Pregnancy-related deaths within the United States have been increasing in recent years.<sup>1</sup> Recent studies indicate that an increasing number of women have chronic health conditions such as hypertension, diabetes, and chronic heart disease.<sup>2</sup> Pregnancy and related changes in physiology confer greater risk to patients with these underlying diseases, and important attention must be given to those who are seeking to prevent pregnancy.

One aspect of prevention includes providing sound contraceptive advice to those at risk for medically complex pregnancies, as approximately half (45%) of all pregnancies within the United States are unintended.<sup>1</sup> Contraception counseling encompassing all available options is essential for all patients, especially those living with medical comorbidities. Of reproductive-aged females in the United States, 64.9% are currently using contraception.<sup>3</sup> Contraceptive options in the United States include permanent surgical sterilization (tubal sterilization and vasectomy), intrauterine device (IUD) [copper and levonorgestrel (LNG)], contraceptive implant, injection, oral contraceptive pills (combined and progestin-only), patch, ring, diaphragm, sponge, cervical cap, condom (internal and external), spermicide, and emergency contraception.<sup>4</sup> These contraceptive options may be limited based on patients' comorbid medical conditions.<sup>4</sup>

This article aims to offer guidance for contraceptive management for patients with common medical conditions. For further guidance on contraception and medical conditions, practitioners can reference the US Medical Eligibility Criteria (US MEC) for Contraceptive Use. US MEC is available online, as a printable summary chart, and as a free phone app.<sup>5</sup>

## Hypertension

The rate of hypertension has continued to increase in reproductive-aged females in the United States, currently at an estimated 9.3%. Hypertension has been noted to complicate about 5% of pregnancies in the United States. While many women are aware of their hypertensive status, approximately 17% are unaware. This has many health implications in pregnancy, including an increased risk of stroke, heart disease, and worsening maternal/fetal

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William D. Petok, PhD Baltimore, Maryland outcomes.<sup>6</sup> Therefore, the choice of contraception is an important consideration for practicing obstetrician-gynecologists and their patients.

The increased risks associated with estrogen-containing combined oral contraceptives (COCs) have been well documented for women with hypertension. COCs have been shown to increase blood pressure and the risk of myocardial infarction. Although inconsistent and sometimes contradictory, studies also suggest an increased risk of ischemic stroke. Data for other forms of estrogen-containing contraceptives, including the patch and the ring, are limited in hypertensive patients, but these options are not recommended based on the cautionary data from COCs.<sup>4</sup>

Progestin-only pills (POPs) have not been shown to increase the risk of hypertension. Similarly, depot medroxyprogesterone acetate (DMPA) has been proven safe for women with hypertension. Copper or LNG IUDs and contraceptive implants have not been studied as extensively. However, based on the data abstracted from progestin-only pills, there appears to be no increased risk associated with these methods.<sup>4</sup>

Based on the currently available evidence, the recommendations for patients with hypertension include LNG IUDs, copper IUDs, DMPA, POPs, etonogestrel (ENG) implants, and barrier contraceptive methods. If a patient with hypertension wishes to continue combined hormonal contraceptives instead of other forms, it is crucial to consider the risks of the contraceptive versus the risks of pregnancy. It is recommended that these patients use the lowest dose of estrogen possible, as dose-dependent relationships corresponding to estrogen have been demonstrated.<sup>4</sup> Throughout the COVID-19 pandemic, the Society for Family Planning recommended that access to contraception should not be denied even in times of global crisis. During such times, blood pressure risk can be assessed using history, at-home blood pressure monitoring, or a blood pressure cuff at a pharmacy for patients who desire estrogen-containing contraception and have had no documented blood pressure in the last year.<sup>7</sup>

## **Heart Disease**

The incidence of cardiac disease in reproductive-aged women has been increasing, along with associated maternal morbidity.<sup>8</sup> Cardiac disease is an encompassing term and covers a broad range of conditions including congenital heart disease, arrhythmias, and structural and valvular disease. The risks associated with pregnancy are dependent upon the condition, with pulmonary hypertension most notably associated with a 50% risk of maternal death in pregnancy.9 Many of the risks associated with contraception are due to thromboembolic complications associated with estrogen use. This risk is not entirely mitigated by anticoagulation in women with these conditions.<sup>4</sup> A schematic device was created by the World Health Organization to help stratify risk of contraceptive use and pregnancy in patients with cardiovascular disease.9 Although the scope of all cardiac diseases and contraceptives is beyond the scope of this article, some common conditions practitioners may encounter are addressed later.

Low-risk cardiac conditions include small shunts, mitral valve prolapse without significant insufficiency, isolated premature ventricular contractions, premature atrial contractions, and incidental patent foramen ovale. For these conditions, no contraindications exist for contraceptive methods. Patients with mild

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pulmonic stenosis can safely use progestin-only contraceptives and both forms of IUDs. Combined hormonal contraceptives are not recommended for patients with unrepaired atrial septal defects because of the risk of paradoxical embolism. Still, these patients are candidates for progestin-only contraceptives and IUDs.

Moderate-risk conditions include repaired tetralogy of Fallot, arrhythmias, and hypertrophic cardiomyopathy. In patients with repaired tetralogy of Fallot, all forms of contraception are acceptable but with more careful follow-up recommended for those using the copper IUD, given the theoretical risk of endocarditis. In patients who have isolated hypertrophic cardiomyopathy, all forms of progestin contraceptives and copper IUDs are considered to be appropriate. Estrogen-containing contraception is contraindicated in patients with atrial fibrillation and atrial flutter because of their prothrombotic effects. If a patient is anticoagulated, caution should be exercised with DMPA due to risk of hematoma formation.<sup>4</sup> Antibiotic prophylaxis for endocarditis is not routinely indicated for IUD placement in patients with cardiac conditions.<sup>10</sup>

High-risk conditions include ischemic cardiovascular disease, myocardial infarction, and mechanical prosthetic valves. In patients with a history of ischemic cardiovascular disease or myocardial infarction, COCs are absolutely contraindicated. In this scenario, the safest higher-efficacy contraceptive is a copper IUD or other nonhormonal options. DMPA should be avoided secondary to concern for reduced high-density lipoprotein. Other progestin-containing contraceptive recommendations are dependent on whether the US MEC or Working Group definitions are used, but clinicians must consider the increased risk of pregnancy with these conditions. Patients with mechanical prosthetic valves often receive anticoagulation, which can impact the metabolism of contraceptive drugs. Those who take warfarin concurrently with hormonal contraceptives should have close monitoring of their international normalized ratio (INR). In these patients, progestin-only methods are safe, with the implant and LNG IUD preferred secondary to the risk of DMPA injection site hematoma. In these patients, the LNG IUD can have the additional benefit of decreasing menstrual blood loss.<sup>4</sup>

Pregnancy is not recommended in patients who are considered New York Heart Association functional class III or IV, or who have severe pulmonary hypertension.<sup>4</sup> For patients with these conditions, shared decision-making discussions regarding use of high-risk contraceptives (as classified by the US MEC) along with the risks and benefits of both contraceptives and pregnancy are essential.

## Obesity

Obesity is an epidemic in the United States. The prevalence continues to increase in all groups, including reproductive-aged women.<sup>11</sup> Patients with obesity who become pregnant have increased risks of stillbirth, gestational hypertension, diabetes, preeclampsia, cesarean delivery, and venous thromboembolism (VTE).<sup>12</sup> Women with obesity have been shown to have several obesity-related comorbidities, which should be considered, including polycystic ovarian syndrome, with associated oligomenorrhea. Fertility awareness methods may be more difficult in the setting of oligomenorrhea.<sup>13</sup>

Patients with obesity have been excluded from many contraceptive studies, making the data more difficult to apply to these patients. All IUDs have been proven to be effective in patients with obesity.<sup>14</sup> Considerations for IUD placement include visualization, additional retractors, and difficulty with assessing the uterine position. The LNG-IUD offers the additional benefits of reducing uterine bleeding and can help to protect the endometrium in women at risk of developing endometrial hyperplasia.<sup>4</sup> Contraceptive implants have been proven to have consistent serum ENG levels regardless of body mass index (BMI) across 3 years, and are an effective form of contraceptive for patients with obesity.<sup>4,15</sup> Permanent surgical contraception also remains a safe option for patients with obesity.<sup>4</sup> The data remain unclear on whether COC failure rates differ in patients with obesity, with different studies showing conflicting data but an overall low failure rate.<sup>4,14</sup> There was an increased risk of VTE in obese COC users; however, this rate remained lower than in pregnant women with obesity. The contraceptive ring appears to have equal efficacy in obese and nonobese women. Studies of the contraceptive patch showed an increased risk of failure in women weighing more than 90 kg (198 lb). DMPA is effective regardless of BMI, although it is associated with increased weight gain in some patient populations, particularly adolescents.<sup>4</sup>

Emergency contraception efficacy varies in patients with obesity. LNG is less effective for emergency contraception in overweight and obese women, patients who weigh greater than 70 kg/154 lb or BMI greater than 26 kg/m<sup>2</sup>. Ulipristal acetate is ineffective for patients who weigh more than 88 kg/194 lb or BMI greater than 35 kg/m<sup>2</sup>. Both the copper IUD and the LNG IUD have proven to be effective forms of emergency contraceptive, regardless of BMI.<sup>4,16</sup>

Bariatric surgery can be classified as either malabsorptive or restrictive, with recommendations to have a delay of 12 to 24 months between surgery and conception. Patients may have increasing fertility as they lose weight in the postoperative period. Highly effective forms of contraception are recommended during this period including IUDs and ENG implants. DMPA can be administered in this population. COCs have uncertain pharmacokinetics and efficacy in the postoperative period; therefore, nonoral contraceptives are preferred.<sup>4</sup>

## Venous Thromboembolism

Venous thromboembolism (VTE) is a term encompassing both deep vein thrombosis (DVT) and pulmonary embolism. Women are at a 4- to 5-fold increased risk of thromboembolism during pregnancy and the postpartum period. This risk is the greatest in the immediate postpartum period. Increased risk factors include a personal history of thrombosis, presence of thrombophilia, cesarean delivery, obesity, hypertension, autoimmune disease, heart disease, sickle cell disease, preeclampsia, and multiple gestations.<sup>17</sup>

Thrombophilias that may increase the risk of VTE in both pregnant and nonpregnant patients include antiphospholipid syndrome, factor V Leiden mutation, prothrombin gene mutation, antithrombin deficiency, protein C deficiency, and protein S deficiency.<sup>4</sup> Combined hormonal contraceptives (COCs, patch, and ring) are not recommended for patients with prior VTE even in the absence of thrombophilia, as these could be associated with unacceptable levels of risk.<sup>18</sup> Few studies have examined VTE association in the setting of hormonal contraception during the period of active anticoagulation. The benefits of progestin-only contraceptives (including POPs, DMPA, and ENG implants) have been proven to outweigh the risks except for patients with systemic lupus erythematosus or antiphospholipid antibodies. For patients interested in pursuing permanent surgical contraception, preoperative counseling should include a discussion of the efficacy of long-acting reversible contraception and increased risk of VTE with surgery. These include anticoagulation in the preoperative period and postoperative states. All forms of emergency contraceptives are safe for patients with a history of VTE.<sup>4</sup>

### **Diabetes**

Diabetes mellitus in women of reproductive age has a prevalence of 3.1% to 6.8%. Rates of pregestational diabetes,

both type 2 and type 2, have increased in recent years, with type 2 diabetes associated with the increasing rates of obesity in the United States.<sup>19</sup> Prediabetes and the associated comorbidities continue to increase as well.<sup>4</sup> Complications associated with diabetes include nephropathy, neuropathy, and retinopathy. Preexisting diabetes in patients who become pregnant contributes to maternal and fetal morbidity, including spontaneous miscarriage, congenital malformation, stillbirth, and worsening maternal end-organ damage.<sup>19</sup> Effective contraception in patients with diabetes is essential, as glycemic optimization before pregnancy is critical.

There are significant concerns regarding diabetes and contraception, particularly with estrogen-containing contraceptives and their effect on microvascular disease. This is based on theoretical risk, as no robust data have been found to demonstrate an effect.<sup>20</sup> Combined hormonal contraceptives and injectable DMPA are not recommended for women with microvascular and macrovascular diabetic disease or patients with diabetes for more than 20 years. POPs, the ENG implant, copper IUD, and LNG IUD are acceptable options for this population. For diabetic patients without microvascular or macrovascular disease, and those without other comorbidities, all forms of contraception can be considered.<sup>4</sup> It has been shown that COCs have no significant difference in glycemic metabolism and are safe option for these patients.<sup>4,20</sup>

Table	1.	Can This	Contracer	otion Be	Recomme	ended for	This	Patient	With	This	Medical	Condition?
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	Contraception Types										
Medical Condition	Barrier	POPs	COCs	<b>DMPA</b> Injection	Patch	Ring	ENG Implant	LNG IUD	Copper IUD		
Hypertension	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes		
Mitral valve prolapse without insufficiency	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes		
Incidental patent foramen ovale	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes		
Isolated premature ventricu- lar/atrial contractions	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes		
Mild pulmonic stenosis	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes		
Unrepaired atrial septal defect	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes		
Repaired tetralogy of Fallot	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes <sup>†</sup>		
Isolated hypertrophic cardi- omyopathy	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes		
Atrial fibrillation/flutter	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes		
Ischemic cardiac disease, myocardial infarction	Yes	No‡	No	No	No	No	No <sup>‡</sup>	Yes	Yes		
Obesity	Yes	Yes	Yes	Yes	Yes <sup>§</sup>	Yes	Yes	Yes	Yes		
Known thrombophilia	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes		
Seizure disorder											
Not on medications	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes		
On medications	Yes	No∥	No∥	Yes	No	No∥	Yes	Yes	Yes		

\*This is a limited table; further information can be obtained from the medically eligible criteria.

† With caution, given theoretical risk of endocarditis.

§Dependent on weight, increased risk of failure in women weighing more than 90 kg (198 lb).

Based on metabolism of various medications, including phenytoin, carbamazepine, primidone, topiramate, oxcarbazepine, and lamotrigine. Consideration of these methods should be based on the metabolism of the specific medication.

COC, combined oral contraceptive; DMPA, depot medroxyprogesterone acetate; ENG, etonogestrel; IUD, intrauterine device; LNG, levonorgestrel.

<sup>\*</sup>Progestin-containing medications can be considered, based on counseling with the patient and clinician with consideration of the risks of pregnancy associated with these conditions.

### **Seizure Disorder**

Seizure disorder encompasses various clinical conditions associated with seizures, including epilepsy, brain infections, and traumatic brain injury. Of these conditions, epilepsy impacts about 6.4 per 1000 individuals. Fetal antiepileptic drug (AED) exposure is associated with a 2- to -3-fold increased risk of major congenital malformations. It is crucial that women who are attempting to conceive take a folic acid supplement and are started on the safest medication for pregnancy.<sup>4,21</sup>

Combined hormonal contraceptives have no restriction for use in patients with epilepsy; however, practitioners must pay attention to the anticonvulsant therapy or AEDs when starting contraceptive medication. Many anticonvulsant drugs induce cytochrome P450 or uridine 5'-diphosphoglucuronosyltransferase enzymes, which increase the metabolism of sex corticosteroids and may increase the risk of both contraceptive and AED failure. COCs are not recommended for these patients. Liver enzyme inducers include carbamazepine, felbamate, oxcarbazepine, phenobarbital, phenytoin, primidone, and rufinamide. Noninducers of liver enzymes include clobazam, clonazepam, ethosuximide, lamotrigine, levetiracetam, topiramate, and valproate. One pertinent example is the interaction between COCs and lamotrigine; COCs have been shown to decrease the lamotrigine concentration by 50%. On one hand, this effect could increase the risk of seizures during active treatment, and on the other, it could result in a drastic rise in lamotrigine concentration during the pillfree interval. If unable to avoid COCs while on AEDs, particularly lamotrigine, the AED may need to be doseadjusted and an extended cycle formulation of contraceptives may be necessary.<sup>21</sup>

Other contraceptive methods, such as injectable DMPA, LNG IUD, and copper IUD, can be used while on AEDs without concern.<sup>4,21</sup> The ENG implant can be given to those not on AEDs without concern, and for those on anticonvulsants, the benefits generally outweigh the risks. The hesitation surrounding the device stems from a theoretical risk due to decreased serum levels. POPs should not be used for patients on AEDs.<sup>4,21</sup> All forms of emergency contraception can be used (Table 1).<sup>21</sup>

## Conclusion

Contraceptive counseling should always be a discussion of shared decision-making between the patient and the clinician. This is a practice associated with increased patient satisfaction.<sup>22,23</sup> For each patient, the differing risks, benefits, and alternatives of each contraceptive option compared with pregnancy should be discussed. It should be noted that the risks of pregnancy (planned or unplanned) in the setting of medical complexity are always greater when compared with the risks of contraception. Finally, although we often emphasize highly effective forms of contraception, the contraception that is the best for the patient is the one that they choose and continue to use.

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- 1. In the United States, unintended pregnancy accounts for
  - A. 25% of pregnancies.
  - B. 35% of pregnancies.
  - C. 45% of pregnancies.
  - D. 55% of pregnancies.
- 2. For patients with a history of type 1 diabetes, COCs are *not* recommended in patients who have
  - A. evidence of microvascular disease.
  - B. been diabetic for 20 years or more.
  - C. both of the above.
  - **D.** neither of the above, as COCs are appropriate in all patients with type 1 diabetes.
- 3. Women with hypertension should *not* use contraception containing
  - A. progesterone
  - B. estrogen.
  - C. LNG.
  - D. drospirenone.
- 4. For patients with an incidental foramen ovale,
  - A. the copper IUD is contraindicated.
  - B. COCs are contraindicated.
  - C. the ENG implant is contraindicated.
  - **D.** there are no contraindications.
- 5. In patients with cardiac disease, use of antibiotic endocarditis prophylaxis for IUD placement
  - **A.** is indicated all of the time.
  - B. depends on the cardiac condition.
  - **C.** depends on type of IUD.
  - **D.** is not indicated.
- 6. In patients weighing greater than 90 kg (198 lb), increased risk of failure has been demonstrated with
  - A. Depo-Provera injection.
  - B. copper IUDs.
  - **C.** the contraceptive patch.
  - **D.** ENG implantation.

- 7. Emergency contraceptives that are equally effective in obese and nonobese patients include
  - A. the copper IUD.
  - B. LNG.
  - C. ulipristal acetate.
  - D. none of the above.
- 8. In the setting of bariatric surgery, nonoral contraceptives are recommended due to
  - A. concern for changes in pharmacokinetics and efficacy.
  - **B.** less effectiveness by oral contraceptive pills compared with nonoral forms of contraception.
  - C. both of the above.
  - **D.** neither of the above, as OCPs can be administered without concern in this setting.
- 9. Which one of the following forms of contraception should be recommended to a patient with a history of VTE?
  - A. LNG IUD
  - B. COCs
  - C. contraceptive patch
  - **D.** contraceptive ring
- **10.** Which of the following statements is/are *true*?
  - **A.** Patients with a history of epilepsy, not on medication, can take COCs.
  - **B.** Patients on AEDs metabolized by cytochrome P450 should not take COCs.
  - **C.** Both forms of IUDs can be used in patients on antiepileptic medications.
  - **D.** All of the above.