

PREGNANCY

Nancy L. Shapiro

INTRODUCTION

Pregnancy is considered an acquired hypercoagulable state due to increased concentrations of several clotting factors, increased fibrinogen, and reductions in the natural anticoagulants free protein S and antithrombin.^{1,2} The increase in hypercoagulability during pregnancy predisposes the mother to deep vein thrombosis (DVT) and pulmonary embolism (PE), and the fetus to gestational complications of recurrent pregnancy loss, intrauterine growth restriction, preeclampsia, and placental abruption. These complications affect up to 15% of pregnancies, and they are a major cause of fetal morbidity and mortality.³ The risk of venous thromboembolism (VTE), composed of DVT and PE, is 2- to 5-fold higher in pregnancy compared to nonpregnant women of child-bearing age.^{1,2,4-6} The incidence of VTE ranges between 0.5 to 2 women per 1,000 pregnancies. Most symptomatic cases are DVT, with two-thirds of cases occurring antepartum, and half of these events occurring before the third trimester.^{7,8} PE is the leading cause of mortality in pregnant women but occurs more often in the postpartum period than during pregnancy. In the postpartum period, the risk of VTE has been estimated to be increased 20-fold. VTE accounts for 1.1 deaths per 100,000 deliveries or 10% of all maternal deaths.⁹ Areas of controversy include management of anticoagulation in pregnant patients with mechanical heart valves, selection of a safe anticoagulant, management of a patient on a direct-acting oral anticoagulant (DOAC) who becomes pregnant, and peripartum anticoagulation management.

USE OF ANTICOAGULANTS DURING PREGNANCY AND LACTATION

Anticoagulation is used in pregnancy for the prevention and treatment of thrombosis, as well as for the prevention of pregnancy loss. A summary of indications for anticoagulation use in pregnancy can be found in **Table 19-1**. The definitions used by the American College of Chest Physicians (ACCP), the American College of Obstetrics and Gynecology (ACOG), and the American Heart Association (AHA) for their grades of recommendations are provided in **Table 19-2** and will be referred to throughout the chapter.

TABLE 19-1: Indications for Anticoagulation During Pregnancy

- Prevention of thrombosis during pregnancy
 - Prophylaxis against VTE
 - Prophylaxis against arterial thrombosis
 - Stroke prevention in patients with mechanical heart valves
 - Stroke prevention in atrial fibrillation
- Treatment of thrombosis during pregnancy
 - Treatment of VTE during pregnancy
 - Treatment of arterial events during pregnancy
- Prevention of pregnancy loss

VTE: venous thromboembolism

TABLE 19-2: Definitions for Grading Recommendations¹⁰⁻¹²

ACCP	<i>Grade 1A:</i> Strong recommendation, high-quality evidence <i>Grade 1B:</i> Strong recommendation, moderate-quality evidence <i>Grade 1C:</i> Strong recommendation, low or very low-quality evidence <i>Grade 2A:</i> Weak recommendation, high-quality evidence <i>Grade 2B:</i> Weak recommendation, moderate-quality evidence <i>Grade 2C:</i> Weak recommendation, low or very low-quality evidence
ACOG	<i>Level A:</i> Based on good and consistent scientific evidence <i>Level B:</i> Based on limited or inconsistent scientific evidence <i>Level C:</i> Based primarily on consensus and expert opinion
AHA	<i>Size of treatment effect:</i> <i>Class 1:</i> Procedure/treatment should be performed/administered <i>Class IIa:</i> It is reasonable to perform procedure/administer treatment <i>Class IIb:</i> Procedure/treatment may be considered <i>Class III:</i> No benefit or harmful <i>Estimate of certainty:</i> <i>Level A:</i> Multiple populations evaluated, multiple RCT or meta-analyses <i>Level B:</i> Limited populations evaluated, single RCT or nonrandomized studies <i>Level C:</i> Very limited populations evaluated, only consensus opinion of experts, case studies, or standard of care

ACCP: American College of Chest Physicians, ACOG: American College of Obstetrics and Gynecology, AHA: American Heart Association, RCT: randomized controlled trial

Safety of Anticoagulants During Pregnancy

Use of anticoagulants in pregnancy must consider the safety to the fetus (**Table 19-3**) and the mother (**Table 19-4**). Use of anticoagulants for breast-feeding mothers must consider drug and metabolite transmission into breast milk and safety to the infant (**Table 19-5**).