

NORTHWEST PERINATAL  
CENTER

# PERINATAL PROGRESS

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## THROMBOEMBOLISM and INHERITED THROMBOPHILIA

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**I**n recent years there has been a great deal of attention focused on the prevention of venous thromboembolism (VTE) in the general population. In fact, taking appropriate action to prevent VTE is now a major quality measure for the Center for Medicare and Medicaid Services (CMS) on which hospitals are graded and reimbursed. Not surprisingly, attention has subsequently focused on the pregnant population, although there is significantly less information to guide prevention efforts. As a result, many of the interventions used in the nonpregnant population have been empirically applied in pregnancy because of the known thrombogenic physiologic changes that occur during gestation. A number of inherited and acquired thrombophilias are also known to increase the risk of VTE. These conditions, in combination with pregnancy, further increase the risk of thrombosis and present an often confusing and challenging clinical situation.

The job of the obstetrician is made even more difficult by the frequently reported association of various thrombophilias with other adverse obstetric outcomes, such as early onset preeclampsia, intrauterine growth restriction (IUGR), placental abruption, stillbirth and recurrent miscarriage. This has led to an explosion of thrombophilia testing resulting in the perplexing questions: what does it all mean and what should be done? The answers to these questions have been somewhat elusive due to a lack of quality data complicated by the obvious emotion that surrounds adverse pregnancy outcomes.

In recent years a great deal has been learned, and although unanswered questions remain, there is now some better guidance available from both the American College of Chest Physicians (ACCP)<sup>1,2</sup> and the American Congress of Obstetrics and Gynecology (ACOG).<sup>3</sup> This review is meant to be a brief look at risk assessment and perioperative cesarean section prophylaxis recommendations for VTE, as well as screening recommendations for thrombophilias related to pregnancy-related complications. For more detailed discussion of more complex clinical scenarios, please refer to the cited references.

VTE associated with pregnancy is a significant concern and occurs in approximately one per 1,000 live births, with roughly half occurring during pregnancy and the other half during the postpartum period.<sup>4,5</sup> It was the leading cause of maternal

mortality during the 1990s, accounting for 20% of pregnancy-related deaths in the United States.<sup>6</sup> Fortunately, despite the significant contribution to maternal mortality, actual death due to VTE is quite rare with a rate of 1.1 per 100,000 deliveries in 2000 and 2001.<sup>7</sup> Although the risk of VTE associated with pregnancy is approximately three to five times higher than in an age-matched nonpregnant woman, the incidence of objectively determined VTE associated with pregnancy is still very low. This is because advancing age is a major risk factor for VTE, and, since reproductive-age women are relatively young, they inherently are at an extremely low baseline risk. Even with the addition of a known risk factor, such as cesarean section, the absolute risk remains relatively low at two to three per 1,000 deliveries.<sup>8</sup>

### DEFINING RISK

With these background rates in mind, it is important to put the term “high risk,” as it relates to pregnancy-associated VTE, in perspective. The term is typically used subjectively to denote the difference in incidence between pregnant and nonpregnant women. The ACCP has quantitatively stratified risk and provided prophylaxis recommendations based on these quantitative risk rates. The terms “low,” “moderate” and “high” are defined based on incidence of deep venous thrombosis (DVT), as illustrated in Table 1:

**TABLE 1: RISK STRATIFICATION FOR VTE IN NONPREGNANT PATIENTS<sup>2</sup>**

Risk Level	DVT Risk Without Thromboprophylaxis
Low	<10%
Moderate	10% - 40%
High	40% - 80%

Using the ACCP-defined risk categories based on expected incidence of VTE, pregnancy and the postpartum period overall are classified as low risk. The confusion with the terminology—“high risk” versus “low risk”—again relates an extremely low risk comparison group (young, nonpregnant women) rather than an absolute scale. For example, one event per 1,000 deliveries, even multiplied by three to five, is still uncommon.

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Once a basic objective criteria of risk stratification has been defined, other factors need to be taken into account, such as advancing age, obesity, thrombophilia and previous VTE. Although the absolute increase in VTE risk attributable to individual factors is not well defined, consideration of these additional factors becomes important when making decisions about therapy. Since the postpartum period accounts for a large portion of the VTE events and cesarean section is also known to be associated with an increased risk, this would seem a logical intervention point in efforts to prevent VTE.

## APPROACH to the PERIOPERATIVE PATIENT

There certainly has been a substantial effort to increase perioperative prophylactic interventions in the nonpregnant population. The mainstay of any effort to mitigate postoperative VTE is early and aggressive ambulation. In fact, this is all that is recommended by the ACCP in low risk patients (see table), which includes a large proportion of obstetric patients.<sup>12</sup> As the risk status increases, mechanical (pneumatic compression devices) or pharmacologic (heparin) methods are added, with both being advocated in the highest risk categories. Some have advocated universal use of pneumatic compression devices perioperatively in cesarean section patients, while others have questioned the utility of this approach.<sup>9,10</sup> This recommendation is certainly counter to the guidelines for pregnancy from the ACCP.<sup>1</sup> Utilizing mechanical prophylaxis universally has little known risk; however, the cost of such a plan is significant and the benefits in terms of DVT prevention are unknown. In practice, it seems the devices are often removed shortly after surgery due to discomfort or with the first trip to the bathroom and are typically found dangling from the end of the bed, thus limiting efficacy.

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A reasonable approach to perioperative cesarean section VTE prophylaxis is early ambulation, as advocated by the ACCP, with some notable exceptions. In the obese patient, the preeclamptic patient, or those with multiple risk factors, pneumatic compression devices should be applied. Management of patients with a thrombophilia or previous VTE will often require pharmacologic prophylaxis or perioperative anticoagulation. Several factors need to be considered when determining the management of patients with thrombophilia. A few commonly encountered scenarios will be described. A recent

ACOG Practice Bulletin addresses these situations, as well as more complex clinical presentations.<sup>3</sup> Consultation with a practitioner experienced in the management of these patients may also be helpful.

## PATIENTS with LOW-RISK THROMBOPHILIA

Patients often present with a known low-risk thrombophilia, such as a heterozygote Factor V Leiden mutation or prothrombin G20210A gene mutation without a previous history of thrombosis. The risk of thrombosis during pregnancy is low (<1%) in these women and no anticoagulation is required. Prophylactic heparin may be preferred by some patients, however, and is acceptable. Although the postpartum risk of thrombosis is higher, no anticoagulation continues to be an acceptable approach in the absence of other risk factors. If there is a strong family history, obesity, or postoperative ambulation is going to be delayed, as in the case of severe preeclampsia, then prophylactic heparin should be initiated. Women with a low-risk thrombophilia and a prior VTE should receive prophylactic heparin during pregnancy and the postpartum period.<sup>3</sup>

The association of hereditary thrombophilias with VTE is well established. Screening is indicated in patients with a personal history of VTE in the presence of a nonrecurring risk factor, such as trauma, surgery or immobilization, or a first-degree relative with a VTE in the absence of risk factors. Early reports of associations between hereditary thrombophilias and adverse pregnancy outcomes have also led to frequent screening when an adverse outcome occurs. Testing was followed by empiric treatment despite a lack of demonstrated benefit. More recently, mounting evidence has questioned the utility of thrombophilia screening following adverse pregnancy outcomes, as well as subsequent pharmacologic anticoagulant therapy in efforts to prevent future events.

Most clinical studies investigating an association between inherited thrombophilias and preeclampsia or IUGR have not found a link. An association between recurrent abortion and inherited thrombophilias has not been identified either. Although some evidence suggests that there may be an association between placental abruption and thrombophilia, it is not sufficient to clearly establish such a relationship. On the other hand, an association between pregnancy loss after the first trimester and inherited thrombophilias has been identified. However anticoagulant therapy with heparin has not been shown to prevent recurrence. Thus, thrombophilia screening and anticoagulant therapy are not recommended for any of

## Thromboembolism and Inherited Thrombophilia continued...

**Thrombophilia screening and anticoagulant therapy are not recommended for any of these adverse pregnancy outcomes.**

these adverse pregnancy outcomes, either because of a lack of association or a lack of effective therapy. The only exception is antiphospholipid antibody testing in patients with recurrent abortion or IUFD.<sup>3</sup>

In conclusion, pregnancy does increase the risk of VTE compared to the nonpregnant state. The absolute risk is still low,

however. Low-risk patients should ambulate early after surgery and prophylaxis is not necessary. In patients undergoing cesarean section with risk factors, such as obesity or advanced maternal age, mechanical prophylaxis should be considered. Those with inherited thrombophilias should receive individual risk assessment and be managed accordingly. The majority of adverse pregnancy events are not associated with inherited thrombophilias and screening is not indicated. In the few situations where there appears to be an association, anticoagulant therapy has not been shown to decrease recurrence. Thus, in the absence of effective therapy, screening is not indicated.

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A Michigan native, Dr. Tomlinson received his medical degree from Wayne State University in Detroit. He completed his residency in obstetrics and gynecology at Harbor/UCLA Medical Center in Torrance, California. After residency, his first assignment was from the U.S. Air Force in Anchorage, Alaska. He attained his board certification in obstetrics and gynecology before returning to Wayne State University for his subspecialty training in maternal-fetal medicine. He then joined the medical school faculty teaching obstetrics and maternal-fetal medicine. In 1997 he was board certified in maternal-fetal medicine.

Dr. Tomlinson joined Northwest Perinatal Center in 2000. He has served as the Portland Regional Director of Obstetric Services for Providence Medical System since 2007. He has authored and co-authored topics in *High Risk Pregnancy Management Options* and *Critical Care Obstetrics*. Dr. Tomlinson has also been published in *Gynecology and Obstetrics*, *Obstetrics and Gynecology*, and *Contemporary OB/GYN*. Recently he presented several topics at the Best Practices in Prevention and Management of Preterm Birth conference at Hermann Memorial Medical Center in Houston, Texas.

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The clinicians of **NORTHWEST PERINATAL CENTER** specialize in complete medical services for the highest risk pregnancies. We are located in Portland, Oregon in the Peterkort medical offices near Providence St. Vincent Medical Center. We provide comprehensive high-risk obstetrical care that includes:

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- Amniocentesis
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- Rh disease
- fetal complications

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