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## Q / Should you test or treat pregnant women with a history of pregnancy-related VTE?

### EVIDENCE-BASED ANSWER

**A / YOU PROBABLY SHOULDN'T TEST,** although you may want to treat your patient with low-molecular-weight heparin (LMWH).

No high-quality evidence supports testing for thrombophilia in pregnant patients who have experienced venous thromboembolism (VTE) in a previous pregnancy (strength of recommendation [SOR]: C, expert opinion and extrapolation from studies of nonpregnant patients).

Antepartum and postpartum anticoagulation with LMWH produces low-

er rates of VTE in patients with a prior history of VTE in pregnancy (SOR: B, based on a prospective cohort study and extrapolation from a meta-analysis of treatment in nonpregnant patients). Pregnant women with a prior history of VTE who are not treated with anticoagulation have about a 5% risk of antepartum or postpartum VTE (SOR: B, based on a prospective cohort study).

Expert opinion recommends graduated compression stockings (SOR: C, expert/consensus clinical opinion).

### Evidence summary

A population-based cohort study centered in Olmsted County, Minn (N=50,080 births between 1966 and 1995) established a baseline rate of VTE among pregnant patients (105 total events; 0.2% incidence), and found an increased relative risk of VTE among pregnant and postpartum patients (RR=4.29; 95% confidence interval [CI], 3.49-5.22;  $P<.001$ ) compared with nonpregnant patients. The incidence of VTE was 199.7 per 100,000 woman-years. The postpartum annual incidence of VTE was 5 times higher than antepartum (511.2 vs 95.8 per 100,000).<sup>1</sup>

### Thrombophilia testing typically isn't useful

There is no evidence of improved outcomes from screening pregnant women with prior VTEs for some of the more common hypercoagulable conditions, including factor V Leiden, prothrombin G20210A mutation,

protein C and S deficiency, and antiphospholipid syndrome. A recent Clinical Inquiry addressed this question for general medical patients with idiopathic deep venous thrombosis and found no quality evidence to support a thrombophilia work-up in most patients.<sup>2</sup> A subsequent review, which addressed pregnant patients specifically, made the same recommendation, that is, no quality evidence supports a thrombophilia work-up in patients at risk for VTE.<sup>3</sup>

### How effective is prophylactic anticoagulation?

A meta-analysis in the American College of Chest Physicians (ACCP) Evidence-Based Clinical Practice Guidelines reviewing data from 1953 orthopedic and medical patients who were mostly postoperative (and not including pregnant women) found that prophylactic anticoagulation with LMWH for patients at risk for VTE produced a relative risk for recurrent VTE of 0.36 (95% CI, 0.20-0.67).<sup>4</sup>

In a more recent prospective cohort study, prophylactic LMWH was given to 177 of 286 (62% treated) patients according to risk-based scoring for recurrent VTE.<sup>5</sup> The treatment protocol called for anticoagulation antepartum, postpartum, or both, depending on risk score (the higher the risk, the longer the period of thromboprophylaxis). Patients with previous pregnancy-associated VTE received both antepartum and postpartum anticoagulation. The study found recurrent VTE rates of 0.35% (95% CI, 0-1.03) antepartum and 0.7% (95% CI, 0-1.67) postpartum among treated patients.<sup>5</sup>

Data from an earlier report summarized the expected VTE rate in patients not exposed to anticoagulation prophylaxis. This prospective cohort study evaluated 125 pregnant women with a history of prior VTE who had anticoagulation withheld and determined the rate of recurrent antepartum and postpartum VTE. Three women had an antepartum VTE (2.4%; 95% CI, 0.2-6.9). Three additional women developed postpartum VTE, for a total of 6 VTEs (4.8%, no CI reported).<sup>6</sup>

### LMWH is beneficial, but dosing can be tricky

Patients with a history of pregnancy-associated VTE—whether or not they have known thrombophilia—do benefit from routine ante- and postpartum thromboprophylaxis, per expert opinion in practice guidelines.<sup>4,7,8</sup> LMWH is the preferred agent because of its safety during pregnancy and ease of dosing.

Precise dosing is nonetheless difficult to determine because clinical studies in pregnant patients are lacking and renal clearance of LMWH increases during pregnancy. Most authors recommend doses between the prophylactic and therapeutic ranges.<sup>4</sup> Subcutaneous enoxaparin, for example, can be given at 40 mg every 24 hours (more aggressive, thus higher-risk, dosing is as much as 1 mg/kg every 12 hours); dalteparin can be administered at 5000 units every 24 hours up to as much as 100 units/kg every 12 hours.<sup>9</sup>

### Recommendations

The American College of Obstetricians and Gynecologists (ACOG) 2011 updated Practice Bulletin recommends thrombophilia testing for pregnant patients previously diagnosed with a pregnancy-associated VTE, although they acknowledge the lack of quality evidence to support this recommendation. ACOG also recommends ante- and postpartum thromboprophylaxis for such patients.<sup>9</sup>

The ACCP expert review recommends that all pregnant women diagnosed with VTE during a previous pregnancy wear graduated elastic compression stockings throughout pregnancy and for at least 6 weeks postpartum.<sup>7</sup>

The ACCP also recommends LMWH for all pregnant patients with a prior VTE. Additionally, the ACCP says that a thrombophilia work-up, while not routinely recommended, might be appropriate—contingent on additional risk assessment.<sup>7</sup>

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**Women with a history of pregnancy-associated VTE—whether or not they have known thrombophilia—benefit from routine ante- and postpartum thromboprophylaxis with LMWH.**

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