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## Venous Thromboembolic Disease: Diagnosis and Treatment

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# Venous Thromboembolic Disease: Diagnosis and Treatment

Elliott S. Cohen, MD

## I. INTRODUCTION

Venous thromboembolic disease remains one of the most important preventable causes of morbidity and mortality among hospitalized patients. Although deep venous thrombosis (DVT) and pulmonary embolism (PE) are often considered in the differential diagnosis of sudden or worsening dyspnea, the unequivocal diagnosis of these conditions is difficult to make. The true incidence of venous thromboembolism (VTE) is unclear because there are many cases of DVT and PE that are never diagnosed, either because of sudden death or failure to consider the possibility of these conditions. Failure to consider the diagnosis among patients with widely varying presenting symptoms leads to delays in therapy and ultimately increased morbidity and mortality from the disease. This manual reviews the predisposing conditions, diagnostic modalities, and treatment options for venous thromboembolic disease and uses case presentations to illustrate key points.

## II. ACQUIRED AND HEREDITARY RISK FACTORS

Virchow's original nineteenth century description of the risk factors for VTE encompassing the triad of hypercoagulability, stasis, and injury to the vessel wall remains clinically relevant, as nearly all of the known risk factors fall into one or more of these categories (**Table 1**).<sup>1</sup> Although the role of stasis and injury in increasing risk for VTE may be intuitively obvious, there have been important recent developments in our understanding of inherited hypercoagulable states (**Table 2**). Prior to 1994, an inherited cause of hypercoagulability was detectable in a relatively small percentage of patients presenting with VTE, and the known hereditary causes were restricted to deficiencies in antithrombin III, protein C, and protein S. In 1994, resistance to activated protein C was reported as a new risk factor for VTE and was later found to be caused by a single point mutation in the factor V gene at the major cleavage site for activated protein C

(Arg506Gln).<sup>2,3</sup> In 1996, the prothrombin G20210A mutation was discovered to be a significant cause of inherited hypercoagulability, leading to an approximately 30% increase in prothrombin activity in heterozygotes compared to normal persons.<sup>4</sup> In addition, hyperhomocystinemia, which occurs in several inborn errors of metabolism, has been shown to be a significant risk factor for VTE and to increase the risk of arterial thrombosis.<sup>5</sup> For some time, the antiphospholipid antibody syndrome has been recognized as a predictor of acquired or inherited risk for VTE, but only recently has it become clear that patients with a single episode of VTE and this syndrome are at significant risk of recurrent VTE and death if anticoagulation is stopped.<sup>6</sup>

Deficiencies of antithrombin III, protein C, and protein S are rare and if present are associated with recurrent episodes of VTE. Therefore, it may not be cost-effective to test for these conditions in patients who are "weakly thrombophilic" (first episode of VTE after 50 years of age, no history of recurrent thrombosis, and no family history of VTE).<sup>7</sup> Testing may be appropriate in patients having one or more of the following: first episode before 50 years of age, history of recurrent thrombosis, or positive family history (**Table 3**). If one is going to test for these conditions, however, it should be remembered that anticoagulation by whatever means might complicate the interpretation of the tests. Testing 2 weeks after discontinuation of anticoagulation therapy is recommended.<sup>7</sup> Since there is no evidence of a higher risk of hereditary causes in patients with an episode of VTE in the setting of a clearly identifiable acquired cause of hypercoagulability, testing for hereditary causes of thrombophilia in this clinical scenario may not be warranted. However, patients who have a VTE episode associated with pregnancy, the puerperium, or oral contraceptive use should be tested.<sup>7</sup>

### CASE PATIENT 1: PRESENTATION

A 35-year-old woman presents to the emergency department with the complaint of sudden onset of dyspnea and chest tightness. The symptoms began 1 hour after the patient arrived at her office, where she works