

Arizona Society of Pathologists
2013 Fall Conference - October 26, 2013

Laboratory Investigation of Hypercoagulability

Mark Cunningham, MD
Department of Pathology and Laboratory Medicine
University of Kansas Medical Center, Kansas City, KS

Outline

A. Mechanisms that down-regulate thrombin generation

1. Heparin - Antithrombin system
2. Thrombomodulin - Protein C - Protein S system

B. Venous thromboembolism

1. Definition
2. Anatomic locations
3. Epidemiology
4. Pathogenesis

5. Risk factors

6. Prognosis

C. Case studies

1. Case 1: Heterozygous Factor V Leiden mutation

a. History

b. Lab studies

c. Discussion

2. Case 2: Antiphospholipid antibody syndrome

a. History

b. Lab studies

c. Discussion

D. References

1. Ballard RB, Marques MB. Pathology consultation on the laboratory evaluation of thrombophilia. When, how, and why. *Am J Clin Pathol* 2012; 137(4): 553-560.
2. Bezemer ID, Doggen CJ, Vos HL, Rosendaal FR. No association between the common MTHFR 677C->T polymorphism and venous thrombosis: Results from the MEGA study. *Arch Intern Med* 2007; 167(5): 497-501.
3. Brouwer JL, Lijfering WM, Ten Kate MK, Kluin-Nelemans HC, Veeger NJ, van der Meer J. High long-term absolute risk of recurrent venous thrombosis in patients with hereditary deficiencies of protein S, protein C or antithrombin. *Thromb Haemost* 2009; 101(1): 93-99.
4. Cunningham MT, Olson JD, Chandler WL, Van Cott EM, Eby CS, Teruya J, Hollensead SC, Adcock DM, Allison PM, Kottke-Marchant KK, Smith MD. External quality assurance of antithrombin, protein C, and protein S assays. Results of the College of American Pathologists proficiency testing program in thrombophilia. *Arch Pathol Lab Med* 2011; 135(2): 227-232.
5. Eichinger S, Stumflen A, Hirschl M, Bialonczyk C, Herkner K, Stain M, Schneider B, Pabinger I, Lechner K, Kyrle PA. Hyperhomocysteinemia is a risk factor of recurrent venous thromboembolism. *Thromb Haemost* 1998; 80(4): 566-569.
6. Heit JA. Predicting the risk of thromboembolism recurrence. *Am J Hematol* 2012; 87(Suppl. 1): S63-S67.
7. Ho WK, Hankey GJ, Quinlan DJ, Eikelboom JW. Risk of recurrent venous thromboembolism in patients with common thrombophilia: A systematic review. *Arch Intern Med* 2006; 166(7):729-736.
8. Hron G, Eichinger S, Weltermann A, Quehenberger P, Halbmayer WM, Kyrle PA. Prediction of recurrent venous thromboembolism by the activated partial thromboplastin time. *J. Thromb Haemost* 2006; 4(4): 752-756.
9. Johnson NV, Khor B, Van Cott EM. Advances in laboratory testing for thrombophilia. *Am J Hematol* 2012; 87(Suppl. 1): S108-S112.
10. Kearon C, Julian JA, Kovacs MJ, Anderson DR, Wells P, Mackinnon B, Weitz JI, Crowther MA, Dolan S, Turpie AG, Geerts W, Solymoss S, van Nguyen P, Demers C, Kahn SR, Kassis J, Rodger M, Hambleton J, Gent M, Ginsberg JS; ELATE Investigators. Influence of thrombophilia on risk of recurrent venous

- thromboembolism while on warfarin: Results from a randomized trial. *Blood* 2008; 112(12): 4432-4436.
11. Kottke-Marchant K (Ed). *An Algorithmic Approach to Hemostasis Testing*. Northfield, IL: College of American Pathologists, 2008.
 12. Kyrle PA, Minar E, Hirschl M, Bialonczyk C, Stain M, Schneider B, Weltermann A, Speiser W, Lechner K, Eichinger S. High plasma levels of factor VIII and the risk of recurrent venous thromboembolism. *N Engl J Med* 2000; 343(7): 457-462.
 13. Legnani C, Mattarozzi S, Cini M, Cosmi B, Favaretto E, Palareti G. Abnormally short activated partial thromboplastin time values are associated with increased risk of recurrence of venous thromboembolism after oral anticoagulation withdrawal. *Br J Haematol* 2006; 134(2): 227-232.
 14. Mina A, Favaloro EJ, Koutts J. Relationship between short activated partial thromboplastin times, thrombin generation, procoagulant factors and procoagulant phospholipid activity. *Blood Coagul Fibrinolysis* 2012; 23(3): 203-207.
 15. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, Derksen RH, de Groot PG, Koike T, Meroni PL, Reber G, Shoenfeld Y, Tincani A, Vlachoyiannopoulos PG, Krilis SA. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost* 2006; 4(2): 295-306.
 16. Ortel TL. Antiphospholipid syndrome: Laboratory testing and diagnostic strategies. *Am J Hematol* 2012; 87(Suppl. 1): S75-S81.
 17. Pengo V, Tripodi A, Reber G, Rand JH, Ortel TL, Galli M, de Groot PG. Update of the guidelines for lupus anticoagulant detection. *J Thromb Haemost* 2009; 7(10): 1737-1740.
 18. Schulman S, Svenungsson E, Granqvist S. Anticardiolipin antibodies predict early recurrence of thromboembolism and death among patients with venous thromboembolism following anticoagulant therapy. Duration of Anticoagulation Study Group. *Am J Med* 1998; 104(4): 332-338.
 19. Weltermann A, Eichinger S, Bialonczyk C, Minar E, Hirschl M, Quehenberger P, Schonauer V, Kyrle PA. The risk of recurrent venous thromboembolism among patients with high factor IX levels. *J Thromb Haemost* 2003; 1(1): 28-32.