

References

1. Facchinetti F, Marozio L, Grandone E, Pizzi C, Volpe A, Benedetto C. Thrombophilic mutations are a main risk factor for placental abruption. *Haematologica* 2003;88:785-8.
2. Roberts JM, Taylor RN, Musci TJ, Rodgers GM, Hubel CA, McLaughlin MK. Pre-eclampsia: an endothelial cell disorder. *Am J Obstet Gynecol* 1989;161:1200-4.
3. Salafia CM, Pezzulo JC, Lopez-Zeno JA, Minior VK, Vintzileos AM. Placental pathologic features of preterm preeclampsia. *Am J Obstet Gynecol* 1995;173:1079-105.
4. Shanklin DR, Sibai BM. Ultrastructural aspects of preeclampsia. *Am J Obstet Gynecol* 1989;161:735-41.
5. Khong TY, Pearce JM, Robertson WB. Acute atherosclerosis in preeclampsia: maternal determination and fetal outcome in the presence of the lesion. *Am J Obstet Gynecol* 1987;157:360-3.
6. Salafia CM, Minior VK, Pezzulo JC, Popek EJ, Rosenkrantz TS, Vintzileos AM. Intrauterine growth restriction in infants of less than thirty-two weeks' gestation: associated placental pathologic features. *Am J Obstet Gynecol* 1995;173:1049-57.
7. Green JR. Placenta previa and abruptio placentae. In: Creasy RK, Resnik R. editors. *Maternal Fetal Medicine: principles and Practice*. Philadelphia: W. B. Saunders; 1994. p. 609-10.
8. Infante-Rievard C, David M, Gauthier R, Ribard GE. Lupus anticoagulants, anticardiolipin antibodies and fetal loss. *N Engl J Med* 1991;325:1063-6.
9. Dekker GA, Sibai BM. Etiology and pathophysiology of preeclampsia: current concepts. *AJOG Review*. *Am J Obstet Gynecol*. 1998;179:1359-75.
10. Many A, Schreiber L, Rosner S, Lessing JB, Eldor A, Kupferminc MJ. Pathologic features of the placenta in women with severe pregnancy complications and thrombophilia. *Obstet Gynecol* 2001;98:1041-4.
11. Mousa HA, Alfirevic Z. Do placental lesions reflect thrombophilia state in women with adverse pregnancy outcome? *Hum Reprod* 2000;15:1830-3.
12. Sikkema JM, Franx A, Bruinse HW, van der Wijk NG, de Valk HW, Nikkels PG. Placental pathology in early onset preeclampsia and intra-uterine growth restriction in women with and without thrombophilia. *Placenta* 2002;23:337-42.
13. Arias F, Romero R, Joist H, Kraus FT. Thrombophilia: a mechanism of disease in women with adverse pregnancy outcome and thrombotic lesions in the placenta. *J Matern Fetal Med* 1998;7:277-86.
14. Dekker GA, de Vries JIP, Doelitzsch PM, Huijgens PC, Blomberg von BME, Jakobs C, et al. Underlying disorders associated with severe early-onset preeclampsia. *Am J Obstet Gynecol* 1995;173:1042-8.
15. Kupferminc MJ, Eldor A, Steinman N, Many A, Bar-Am A, Jaffa A, et al. Increased frequency of the genetic thrombophilia in women with complications of pregnancy. *N Engl J Med* 1999;340:9-13.
16. Lima F, Khamashta MA, Buchanan NM, Kerslake S, Hunt BI, Hughes GRV. A study of sixty pregnancies in patients with the antiphospholipid syndrome. *Clin Exp Rheumatol* 1996;14:131-6.
17. Polzin WJ, Kopelman JN, Robinson RD, Read JA, Brady K. The association of antiphospholipid antibodies with pregnancy complicated by fetal growth restriction. *Obstet Gynecol* 1991;78:1108-11.
18. Murphy RP, Donoghue C, Nallen RJ, D'Mello M, Regan C, Whitehead AS, et al. Prospective evaluation of the risk conferred by factor V Leiden and the thermolabile methylenetetrahydrofolate reductase polymorphisms in pregnancy. *Arterioscler Thromb Vasc Biol* 2000;20:266-70.
19. Martinelli I, Taioli E, Cetin I, Marinoni A, Gerosa S, Villa MV, Bozzo M, Mannucci PM. Mutations in coagulation factors in women with unexplained late fetal loss. *N Engl J Med* 2000;343:1015-8.
20. Many A, Elad R, Yaron Y, Eldor A, Lessing JB, Kupferminc MJ. Third-trimester unexplained intrauterine fetal death is associated with inherited thrombophilia. *Obstet Gynecol* 2002;99:684-7.
21. Grandone E, Margaglione M, Colaizzo D, d'Addetta M, Capucci G, Vecchione G, et al. Factor V Leiden is associated with repeated and recurrent unexplained fetal losses. *Thromb Haemost* 1997;77:822-4.
22. Deitcher SR, Park VM, Kutteh WH. Methylene tetrahydrofolate reductase 677C T mutation analysis in Caucasian women with early first trimester recurrent pregnancy loss. *Blood* 1998;92 Suppl 1:117b[abstract].
23. Martinelli I, Legnani C, Bucciarelli P, Grandone E, De Stefano V, Mannucci PM. Risk of pregnancy-related venous thrombosis in carriers of severe inherited thrombophilia. *Thromb Haemost* 2001;86:800-3.
24. Duley L, Henderson-Smart D, Knight M, King J. Antiplatelet drugs for prevention of pre-eclampsia and its consequences: systematic review. *Br Med J* 2001;322:329-33.
25. North RA, Ferrier C, Gamble G, Fairley KF, Kincaid-Smith P. Prevention of preeclampsia with heparin and antiplatelet drugs in women with renal disease. *Aus NZ J Obstet Gynaecol* 1995;35:357-62.
26. Kupferminc MJ, Fait G, Many A, Lessing JB, Yair D, Bar-Am A, et al. A. Low-molecular-weight heparin for the prevention of obstetric complications in women with thrombophilias. *Hypertens Pregnancy* 2001;20:35-44.

Inherited thrombophilia is unlikely to affect the outcome of assisted reproductive techniques

In recent years, *Haematologica* has published several papers on the subject of genetic thrombophilia.¹⁻¹⁰ More recently, Grandone *et al.*¹¹ reported data suggesting that maternal thrombophilia is significantly associated with fetal death, and that a family history of obstetric complications is significantly associated with the occurrence of fetal death. In this issue, Facchinetti and co-workers¹² report studies indicating that patients suffering from abruptio placentae need to be screened for thrombophilic disorders. The related editorial¹³ discusses the relationship between obstetric complications and inherited thrombophilia.

The paper by Martinelli and co-workers¹⁴ adds an important contribution to the role of inherited thrombophilia in women who fail to become pregnant after assisted reproductive techniques. In particular, the prevalence of thrombophilia due to factor V Leiden or prothrombin 20210GA in women with implantation failure after assisted reproductive procedures is similar to that found in the general population. Therefore, anticoagulant treatment is not warranted in women undergoing assisted reproductive procedures.

References

1. Zoller B, Garcia de Frutos P, Hillarp A, Dahlback B. Thrombophilia as a multigenic disease. *Haematologica* 1999;84:59-70.
2. Aznar J, Vaya A, Estelles A, Mira Y, Segui R, Villa P, et al. Risk of venous thrombosis in carriers of the prothrombin G20210A variant and factor V Leiden and their interaction with oral contraceptives. *Haematologica* 2000;85:1271-6.
3. Franco RF, Fagundes MG, Meijers JC, Reitsma PH, Lourenco D, Morelli V, et al. Identification of polymorphisms in the 5'-untranslated region of the TAFI gene: relationship with plas-

- ma TAFI levels and risk of venous thrombosis. *Haematologica* 2001;86:510-7.
4. Margaglione M, Brancaccio V, Ciampa A, Papa ML, Grandone E, Di Minno G. Inherited thrombophilic risk factors in a large cohort of individuals referred to Italian thrombophilia centers: distinct roles in different clinical settings. *Haematologica* 2001;86:634-9.
 5. Soria JM, Baiget M, Castano L, Tejada MI, Perez-Nanclares G, Fontcuberta J. Genetic risk factors for thrombosis in a Basque population and its possible contribution to the analysis of a complex disease such as thrombophilia. *Haematologica* 2001;86:889-90.
 6. Santamaria A, Mateo J, Oliver A, Menendez B, Souto JC, Borrell M, et al. Risk of thrombosis associated with oral contraceptives of women from 97 families with inherited thrombophilia: high risk of thrombosis in carriers of the G20210A mutation of the prothrombin gene. *Haematologica* 2001;86:965-71.
 7. Tirado I, Mateo J, Soria JM, Oliver A, Borrell M, Coll I, et al. Contribution of prothrombin 20210A allele and factor V Leiden mutation to thrombosis risk in thrombophilic families with other hemostatic deficiencies. *Haematologica* 2001;86:1200-8.
 8. Zalavras CG, Malizos KN, Dokou E, Vartholomatos G. The 677C→T mutation of the methylene-tetrahydrofolate reductase gene in the pathogenesis of osteonecrosis of the femoral head. *Haematologica* 2002;87:111-2.
 9. Grandone E, Margaglione M, Colaizzo D, Pavone G, Paladini D, Martinelli P, et al. Lower birth-weight in neonates of mothers carrying factor V G1691A and factor II A(20210) mutations. *Haematologica*. 2002;87:177-81.
 10. De Stefano V, Rossi E, Paciaroni K, Leone G. Screening for inherited thrombophilia: indications and therapeutic implications. *Haematologica* 2002;87:1095-108.
 11. Grandone E, Colaizzo D, Brancaccio V, Ciampa A, Di Minno G, Margaglione M. Impact of prothrombotic mutations and family history on the occurrence of intra-uterine fetal deaths. *Haematologica* 2002;87:1118-9.
 12. Facchinetti F, Marozio L, Grandone E, Pizzi C, Volpe A, Benedetto C. Thrombophilic mutations are a main risk factor for placental abruption. *Haematologica* 2003;88:785-8.
 13. Many A, Kupferminc MJ. Thrombophilias and adverse pregnancy outcome. *Haematologica* 2003;88:729-31.
 14. Martinelli I, Taioli E, Ragni G, Levi-Setti P, Passamonti SM, Battaglioli T, et al. Embryo implantation after assisted reproductive procedures and maternal thrombophilia. *Haematologica* 2003;88:789-93.

Immunological abnormalities in patients with chronic myeloid leukemia

The approach to treatment of the individual patient with chronic myeloid leukemia (CML) has changed considerably in the last few years, as also documented in this journal.¹⁻¹² Two studies in this issue address the question of immunologic abnormalities in CML patients. Observations by Kiani and coworkers¹³ point to T cell dysfunction as a potential pathogenetic mechanism: reversal of T-cell dysfunction might be the basis for future immune therapeutic approaches. Steegman and coworkers¹⁴ report data indicating that hypogammaglobulinemia can develop in as many as 25% of CML

patients previously exposed to interferon-alpha and who are then treated with imatinib. This may reflect a dysregulation of B-lymphocyte function, and requires close immunologic evaluation.

References

1. Carreras E, Tomas JF, Sanz G, Iriondo A, Boque C, Lopez J, et al. Unrelated donor bone marrow transplantation as treatment for chronic myeloid leukemia: the Spanish experience. The Chronic Myeloid Leukemia Subcommittee of the GETH. Grupo Espanol de Trasplante Hemopoyetico. *Haematologica* 2000;85:530-8.
2. Martinelli G, Montefusco V, Testoni N, Amabile M, Saglio G, Ottaviani E, et al. Clinical value of quantitative long-term assessment of bcr-abl chimeric transcript in chronic myelogenous leukemia patients after allogeneic bone marrow transplantation. *Haematologica* 2000;85:653-8.
3. Roman J, Alvarez MA, Torres A. Molecular basis for therapeutic decisions in chronic myeloid leukemia patients after allogeneic bone marrow transplantation. *Haematologica* 2000;85:1072-82.
4. Amabile M, Giannini B, Testoni N, Montefusco V, Rosti G, Zardini C, et al. Real-time quantification of different types of bcr-abl transcript in chronic myeloid leukemia. *Haematologica* 2001;86:252-9.
5. Meloni G, Capria S, Vignetti M, Alimena G, de Fabritiis P, Montefusco E, et al. Ten-year follow-up of a single center prospective trial of unmanipulated peripheral blood stem cell autograft and interferon-alpha in early phase chronic myeloid leukemia. *Haematologica* 2001;86:596-6.
6. Luzzatto L, Frassoni F, Melo JV. Imatinib: can one outwit chronic myeloid leukemia? *Haematologica* 2002;87:898-901.
7. de la Camara R, Alonso A, Steegmann JL, Arranz R, Granados E, Rodriguez-Macias G, et al. Allogeneic hematopoietic stem cell transplantation in patients 50 years of age and older. *Haematologica* 2002;87:965-72.
8. Marin D, Markt S, Bua M, Armstrong L, Goldman JM, Apperley JF, et al. The use of imatinib (STI571) in chronic myeloid leukemia: some practical considerations. *Haematologica* 2002;87:979-88.
9. Gomez M, Urbano-Ispizua A, Cervantes F, Fernandez-Aviles F, Rovira M, Carreras E. Late response to donor lymphocyte infusions in patients with chronic myeloid leukemia relapsing after allogeneic stem cell transplantation. *Haematologica* 2002;87:1003-5.
10. Baron F, Frere P, Herens C, Fillet G, Beguin Y. Combination of nonmyeloablative stem cell transplantation and Imatinib in accelerated phase CML. *Haematologica* 2002; 87(12): ECR43.
11. O'Dwyer M. Current use of Imatinib in the treatment of chronic myeloid leukemia. *Haematologica* 2003M;88:241-4.
12. Markt S, Marin D, Foot N, Szydlo R, Bua M, Karadimitris A, et al. Chronic myeloid leukemia in chronic phase responding to imatinib: the occurrence of additional cytogenetic abnormalities predicts disease progression. *Haematologica* 2003;88:260-7.
13. Kiani A, Habermann I, Schäke K, Neubauer A, Rogge L, Ehninger G. Normal intrinsic Th1/Th2 balance in patients with chronic phase chronic myeloid leukemia not treated with interferon- α or imatinib. *Haematologica* 2003; 88:754-61.
14. Steegmann JL, Moreno G, Aláez C, Osorio S, Granda A, de la Cámara R, et al. Chronic myeloid leukemia patients resistant to or intolerant of interferon α and subsequently treated with Imatinib show reduced immunoglobulin levels and hypogammaglobulinemia. *Haematologica* 2003; 88:762-8.