

valves, pregnant patients (including those with maternal or fetal hemorrhage or potential teratogenicity), and patients with epidural bleeding was posted on January 9, 2002.²

I also refer readers to Figure 4 and Table 6 of the meta-analysis by Dolovich et al.,³ which shows that the relative risk of major hemorrhage with the use of dalteparin, as compared with unfractionated heparin, is 0.31, and with enoxaparin, the relative risk is 1.60.

Rodger L. Bick, M.D., Ph.D.

University of Texas Southwestern Medical School
Dallas, TX 75231
rbick@thrombosis.com

1. FDA MedWatch. LOVENOX (enoxaparin sodium) injection [May 30, 2000: Aventis Pharmaceuticals]: precautions: geriatric use: new subsection. (Accessed September 11, 2003, at <http://www.fda.gov/medwatch/safety/2000/may00.htm#lovenox>.)
2. FDA MedWatch. LOVENOX (enoxaparin sodium) injection [January 9, 2002: Aventis]: warnings. (Accessed September 11, 2003, at <http://www.fda.gov/medwatch/SAFETY/2002/jan02.htm#lovenox>.)
3. Dolovich LR, Ginsberg JS, Douketis JD, Holbrook AM, Cheah G. A meta-analysis comparing low-molecular-weight heparins with unfractionated heparin in the treatment of venous thromboembolism: examining some unanswered questions regarding location of treatment, product type, and dosing frequency. *Arch Intern Med* 2000;160:181-8.

Valvular Heart Disease in Pregnancy

TO THE EDITOR: In their review of valvular heart disease in pregnancy, Reimold and Rutherford (July 3 issue)¹ do not address the early puerperium. In our opinion, this period may be crucial. Many clinicians tend to believe that pregnancy in a patient at risk has been successfully completed after an uncomplicated delivery. Although the authors briefly discuss issues related to cardiovascular physiology immediately after delivery, the literature emphasizes the importance of the puerperium.^{2,3} Confidential inquiries into maternal deaths have revealed that care may be suboptimal during the postnatal period, since the intensity of monitoring is often decreased at this time, despite the fact that the majority of deaths occur after delivery.^{4,5}

The early puerperium may be a period associated with a risk of heart failure because of the physiologic return of extravascular fluid from the limbs and lower body to the systemic circulation. This mobi-

lization phase may take nearly a week. Clinicians should be aware of this risk and be advised to conduct continuous, close monitoring for a minimum of 72 hours after delivery, preferably in a multidisciplinary setting.

Barbara J.M. Mulder, M.D., Ph.D.

Otto P. Bleker, M.D., Ph.D.

Academic Medical Center
1105 AZ Amsterdam, the Netherlands
b.j.mulder@amc.uva.nl

1. Reimold SC, Rutherford JD. Valvular heart disease in pregnancy. *N Engl J Med* 2003;349:52-9.
2. Kaemmerer H, Bauer U, Stein J-I, et al. Pregnancy in congenital cardiac disease: an increasing challenge for cardiologists and obstetricians — a prospective multicenter study. *Z Kardiol* 2003;92:16-23.
3. Silversides CK, Colman JM, Sermer M, Farine D, Siu SC. Early and intermediate-term outcomes of pregnancy with congenital aortic stenosis. *Am J Cardiol* 2003;91:1386-9.
4. Lupton M, Oteng-Ntim E, Ayida G, Steer PJ. Cardiac disease in pregnancy. *Curr Opin Obstet Gynecol* 2002;14:137-43.
5. Cooper GM, Lewis G, Neilson J. Confidential enquiries into maternal deaths, 1997-1999. *Br J Anaesth* 2002;89:369-72.

Cardiovascular Genomics

TO THE EDITOR: I believe that Table 2 of the article by Nabel (July 3 issue)¹ gives misleading information concerning apparent mineralocorticoid excess: this disease is said to be due to mutations in the gene encoding 11 β -hydroxylase, but in fact, mutations in this gene cause one form of congenital adrenal hyperplasia.² Apparent mineralocorticoid excess is caused by inactivating mutations in the gene encoding 11 β -hydroxysteroid dehydrogenase type 2,³ the microsomal enzyme that metabolizes cortisol into its receptor-inactive keto form, cortisone, in sodi-

um-transporting epithelia, such as the kidney, and thus protects the nonselective mineralocorticoid receptor from occupation by cortisol itself. In the same table, apparent mineralocorticoid excess is said to be associated with an absence of circulating aldosterone and decreased plasma volume, but in fact, plasma volume is expanded, as in states involving true mineralocorticoid excess, because of sodium retention induced by the unopposed activation of the aldosterone receptor by cortisol.

As a very rare condition, apparent mineralocor-

ticoid excess may not be an attractive object of study for most physicians. However, as a natural model of the more common condition of hypertension due to licorice abuse,³ it can help us to understand some basic mechanisms of disease.

Giacomo Colussi, M.D.

A.O. Ospedale di Circolo e Fondazione Macchi
21100 Varese, Italy
giacomo.colussi@ospedale.varese.it

1. Nabel EG. Cardiovascular disease. *N Engl J Med* 2003;349:60-72. [Erratum, *N Engl J Med* 2003;349:620.]
2. Burren CP, Montalto J, Yong AB, Batch JA. CYP11 beta 1 (11-beta-hydroxylase) deficiency in congenital adrenal hyperplasia. *J Paediatr Child Health* 1996;32:433-8.
3. Quinkler M, Stewart PM. Hypertension and the cortisol-cortisone shuttle. *J Clin Endocrinol Metab* 2003;88:2384-92.

TO THE EDITOR: I believe that Nabel makes a misstatement with regard to factor V Leiden. Although this polymorphism is definitely associated with venous thrombotic disease, it is uncertain whether it is associated with arterial vascular disease. In the study she cites,¹ there was no observed increase in the rate of myocardial infarction or stroke among healthy male subjects harboring the mutation. Additional large studies have confirmed this finding,² although smaller studies in selected groups of patients have suggested some interaction of the polymorphism with additional risk factors.³

Because of the ease and accessibility of testing for many of these polymorphisms, I have seen more widespread, indiscriminate genetic screening, performed without regard to the underlying disease process itself or to the modification of risk factors. A classic example is a young woman who was referred to me with premature atherosclerotic vascular disease because she was found to have factor V Leiden but who continues to smoke two packs of cigarettes a day.

Scott W. Hall, M.D., Ph.D.

Christiana Care Hospital
Newark, DE 19713
shall@dclp.com

1. Ridker PM, Hennekens CH, Lindpaintner K, Stampfer MJ, Eisenberg PR, Miletich JP. Mutation in the gene coding for coagulation factor V and the risk of myocardial infarction, stroke, and venous thrombosis in apparently healthy men. *N Engl J Med* 1995;332:912-7.
2. Cushman M, Rosendaal FR, Psaty BM, et al. Factor V Leiden is not a risk factor for arterial vascular disease in the elderly: results from the Cardiovascular Health Study. *Thromb Haemostasis* 1998;79:912-5.
3. Doggen CJM, Cats VM, Bertina RM, Rosendaal FR. Interaction of coagulation defects and cardiovascular risk factors: increased risk of myocardial infarction associated with factor V Leiden or prothrombin 20210A. *Circulation* 1998;97:1037-41.

DR. NABEL REPLIES: I agree with Dr. Hall's comment that the factor V Leiden polymorphism has been associated with venous, not arterial, thrombotic disease and, furthermore, that common medical practices, such as the reduction of risk factors, should be pursued, especially in patients with known genetic mutations. The last sentence of the left-hand column on page 65 of my article should have read, "Factor V Leiden increases the risk of venous thrombosis in men but not the risk of myocardial infarction or stroke."

Dr. Colussi is correct in stating that apparent mineralocorticoid excess results from a mutation in the gene encoding 11 β -hydroxysteroid dehydrogenase. In Table 2 of my article, the description of the mutation associated with apparent mineralocorticoid excess should have read, "Mutation in the gene encoding 11 β -hydroxysteroid dehydrogenase," and the description of the molecular mechanism should have read, "Cortisol-mediated activation of the mineralocorticoid receptor; sodium retention; plasma volume."

Elizabeth G. Nabel, M.D.

National Institutes of Health
Bethesda, MD 20892

Cardiac Transplantation in an HIV-1–Infected Patient

TO THE EDITOR: Calabrese et al. (June 5 issue)¹ describe cardiac transplantation in a patient with a 15-year history of human immunodeficiency virus type 1 (HIV-1) infection and multiple opportunistic infections who had dilated cardiomyopathy due to daunorubicin therapy. Two years ago, we performed a cardiac transplantation in a 42-year-old man with a two-year history of HIV infection, an undetectable

viral load, a CD4 cell count of 637 per cubic millimeter, and no history of opportunistic infections; the patient had dilated cardiomyopathy and an ejection fraction of 10 percent. The patient's hospital course was unremarkable, and he was discharged on the ninth day after surgery. No opportunistic infections have developed, and the patient has returned to work. He is receiving maintenance therapy consist-