

ommended to provide a definitive diagnosis. The intriguing possibilities mentioned by Kent et al. are certainly in play, as is the more prosaic α -thalassemia trait.

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Postpartum Venous Thromboembolism

TO THE EDITOR: In their Image in Clinical Medicine, Zalts and Hayek (Dec. 18 issue)¹ describe a woman with postpartum venous thromboembolism. The patient was found to be heterozygous for a mutation in the gene encoding for 5,10-methylenetetrahydrofolate reductase (MTHFR). The authors suggest that the mutation was most likely the source of her susceptibility to hypercoagulation. However, a recent, large-scale, prospective study involving 66,140 participants did not show an association between a homozygous or heterozygous MTHFR genotype and the risk of venous thromboembolism.² The odds ratio for the development of venous thromboembolism was 1.01 for the heterozygous (C677CT) or homozygous (C677TT) genotype, as compared with the normal MTHFR genotype. Moreover, a heterozygous genotype was found in 41% of the population, in both the case and control groups, suggesting a much higher prevalence of the aberrant

genotype than of venous thromboembolism.² Therefore, in the patient described by Zalts and Hayek, the acquired risk factors (pregnancy and postpartum period, surgery, and reduced mobility), which were recently reviewed in the *Journal*,³ appear to be a more likely cause of venous thromboembolism than the observed mutation in the gene encoding MTHFR.

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Ending Propylthiouracil-Induced Liver Failure in Children

TO THE EDITOR: Graves' disease is treated with antithyroid drugs, radioactive iodine, or surgery.^{1,2} Propylthiouracil and methimazole are widely used in children as first-line therapy.^{1,2} Over the past 60 years of propylthiouracil and methimazole use, reports of propylthiouracil-related liver failure and death have accumulated.³⁻⁵ In contrast, this problem has not been reported with methimazole use in children.^{3,5}

Several observations can be made on the basis of the medical literature, adverse event reports from the Food and Drug Administration (FDA), and extensive data presented at a workshop at the Eunice Kennedy Shriver National Institute of

Child Health and Human Development on October 28, 2008, to discuss the safety of propylthiouracil use in children.⁵ Each year in the United States, 4000 pediatric patients with Graves' disease are treated with antithyroid drugs, with up to 40% receiving propylthiouracil over the past several years.⁵ Propylthiouracil-induced liver failure may occur in 1 in 2000 to 1 in 4000 treated children, but the number in whom reversible propylthiouracil-induced liver injury develops may be 10 times that range.⁵ However, the true extent of propylthiouracil-induced liver injury is unknown.⁵ Routine biochemical surveillance of liver function and hepatocellular integrity is not