# Clinical Pathology Selected Abstracts, 7/13

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## Risk factors for first venous thromboembolism around pregnancy

Venous thromboembolism is a serious maternal complication occurring at a rate of one to two per 1,000 maternities during pregnancy and the puerperium. Venous thromboembolism (VTE) is a leading cause of maternal mortality in developed countries and an important source of morbidity in the form of post-thrombotic syndrome. Women who are at higher risk for VTE require thromboprophylaxis, but it may be challenging to identify these women due to the lack of data about absolute risk factors for VTE. The authors conducted a study in the United Kingdom to identify the level of absolute and relative risks of VTE in accordance with a woman's pre-existing and pregnancy-related factors in the antepartum and postpartum periods. The primary objective of the study was to identify women requiring obstetric thromboprophylaxis. The study also aimed to estimate the specific absolute risks of VTE in women with low, intermediate, and high-risk pregnancies according to guidelines on who should receive prophylaxis. The authors used a large primary care database of 376,154 pregnancies that ended in live birth or stillbirth from women aged 15 to 44 years between 1995 and 2009. The investigators assessed the impact of risk factors for antepartum and postpartum VTE in terms of absolute risk and incidence rate ratios. Results showed that during the antepartum period, varicose veins, inflammatory bowel disease, urinary tract infection, and pre-existing diabetes were associated with an increased risk of VTE (absolute risk, 139 per 100,000 person-years or greater; incidence rate ratio, 1.8 or greater). In the postpartum period, the greatest risk factor was stillbirth (absolute risk, 2,444 per 100,000 person-years; incidence rate ratio, 6.2) followed by co-morbidities, body mass index of 30 kg/m2 or greater, obstetric hemorrhage, preterm delivery, and Caesarean section (absolute risk, 637 per 100,000 person-years or greater; incidence rate ratio, 1.9 or greater). The authors concluded that VTE risk varies modestly with different risk factors and, except for pre-existing diabetes, risk factors have a greater impact in the postpartum period in terms of affecting the absolute risk of VTE, than in the antepartum period. Study results also showed a low relative increase in the risk of VTE among women over the age of 35, current smokers, and women with a high body mass index during the antepartum period, which are findings consistent with previous studies.

Sultan AA, Tata LJ, West J, et al. Risk factors for first venous thromboembolism around pregnancy: a population based cohort study from the United Kingdom [published online ahead of print April 2, 2013]. *Blood.* doi:10.1182/blood-2012-11-469551.
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## H-Y antigen-binding B cells in male recipients of female hematopoietic cells

A significant cause of morbidity and mortality from hematopoietic cell transplantation is chronic graft versus host disease. Several studies have indicated that donor-derived alloreactive B and T cells are involved in the etiology of the disease. Predominant B-cell subsets and B-cell–related markers have been demonstrated in patients with chronic graft versus host disease (cGVHD). These B-cell biomarkers may be used in characterizing and scoring cGVHD. In addition, Rituximab, a therapy that depletes B cells, has been used successfully to treat cGVHD. Investigators in this study were interested in detecting one of these subsets, anti-DBY-2 B cells, to predict cGVHD. The authors have shown previously that male hematopoietic cell transplant patients receiving a graft from a female donor (F→M) develop alloantibody responses. These alloantibodies include donor-derived alloreactive IgG that recognizes one or more Y chromosome-encoded proteins (H-Y antigens). One of these proteins, donor-derived anti-DBY antibodies, appears in serum in association with cGVHD in female donors and male recipients. For this study, the authors developed a FACS stain for isolating and characterizing H-Y–specific B cells contributing to

cGVHD. They characterized a series of 28 consecutive F→M hematopoietic cell transplants at six and 12 months after transplant. Their results showed that after six months, more than half of the 28 male patients with female donors developed circulating B cells that bind DBY-2. Furthermore, 15 of 16 patients with DBY-2 B cells developed cGVHD. However, cGVHD occurred in only five of the 12 for whom DBY-2 B cells were not detected. The authors concluded that detecting anti-DBY-2 cells may predict cGVHD, and there may be a role for prospective monitoring of anti-DBY-2 B cells to help direct cGVHD therapy in F→M hematopoietic cell transplant. These findings also may provide a mechanistic explanation for the moderate efficacy of in vivo B-cell depletion in treating cGVHD. Larger prospective studies are needed to validate these findings.

Sahaf B, Yang Y, Aria S, et al. H-Y antigen-binding B cells develop in male recipients of female hematopoietic cells and associate with chronic graft vs. host disease. *PNAS*. doi:10.1073/pnas.1222900110.
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## Laboratory-based surveillance for hepatitis E virus infection

Hepatitis E virus is primarily spread via water, and the jaundice from a hepatitis E infection usually resolves spontaneously. However, fulminant hepatic failure can occur. Hepatitis E is endogenous in Africa, southern and central Asia, and Central America. In Asia and Europe, sporadic cases of hepatitis E may be acquired through international travel or foodborne illness. In the United States, hepatitis E virus (HEV) infection is well described after travel to regions to which waterborne HEV transmission is endemic. However, cases of HEV unassociated with travel abroad have been observed in the United States, implying infection by indigenous HEV strains. There are four known HEV genotypes found in humans. This study reports demographic, clinical, travel-related, and virologic characteristics of people with HEV infection from a diverse patient cohort. The authors identified U.S. patients with incident HEV using completed questionnaires and specimens that were submitted to the Centers for Disease Control and Prevention for HEV testing between 2005 and 2012. They analyzed testing for IgM anti-HEV and real-time polymerase chain reaction to identify cases of HEV infection from people seronegative for acute hepatitis A and B. The results showed that 26 case-patients, or 17 percent of the 154 people tested, had hepatitis E. The authors did not distinguish between acute and chronic HEV infection. Although this study was not prospective, the researchers did identify three case-patients with fulminant hepatic failure. Interestingly, hepatitis E cases were found among people who had not recently traveled abroad, and these people were infected exclusively by HEV genotype 3 strains. Although not conclusive, the similarity between HEV genotype 3 strains and those in swines suggests a link in HEV transmission between humans and pigs. The authors noted that data from this study were not derived from a program of epidemiologic surveillance. Therefore, the cases identified herein may not fully reflect the extent of HEV in the United States. However, clinicians should consider hepatitis E virus infection in the differential diagnosis of hepatitis, regardless of a patient’s travel history.

Drobeniuc J, Greene-Montfort T, Le N-T, et al. Laboratory-based surveillance for hepatitis E virus infection, United States, 2005–2012. *Emerg Infect Dis*. 2013;9:218–222.

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