ADDENDUM | Genetics inMedicine

Addendum: American College of Medical Genetics consensus statement on factor V Leiden mutation testing

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Addendum to: "American College of Medical Genetics Consensus Statement on Factor V Leiden Mutation Testing". Wayne W. Grody, MD, PhD, John H. Griffin, PhD, Annette K. Taylor, MS, PhD, Bruce R. Korf, MD, PhD and John A. Heit, MD (ACMG Factor V Leiden Working Group) *Genetics in Medicine* **3**:139–148 (2001); https://doi.org/10.1097/00125817-200103000-00009; published online March 2001.

This document was retired by the ACMG Board of Directors as of 14 December 2020 with the following addendum:

The Addendum Workgroup of the ACMG Professional Practice and Guidelines Committee (PP&G) conducted a critical review of this consensus statement. After seeking technical input from the ACMG Laboratory Quality Assurance Committee's Molecular Genetics Subcommittee, on 5 August 2020, the PP&G Committee voted to retire this document. We provide the following focused revision to the original document.

- Factor V Leiden, along with factor II genetic testing, remains an important testing option in venous thromboembolism (VTE).
- The ACMG Technical Standard "Venous thromboembolism laboratory testing (factor V Leiden and factor II c.*97G>A), 2018 update"[1] represents a more up-to-date overview of the field and covers appropriate recommendations on factor V Leiden and factor II c.*97G>A (formerly designated as 20210G>A) testing including indications, methodologies, and follow-up, along with the following comments and additions.
  - The possibility of homozygosity and double heterozygosity for factor V Leiden and factor II c.*97G>A (as well as more complex genotype combinations) should be considered in testing scenarios, as knowing the presence of these genotypes may influence management and other clinical decisions. Factor V Leiden homozygosity is not rare in initial isolated cases of VTE (~1% of cases), and 6–12% of individuals who are heterozygous for factor V Leiden also have factor II c.*97G>A.[1] In addition, complex genotype combinations including (1) double homozygosity for factor V Leiden and factor II c.*97G>A, (2) homozygosity for factor V Leiden plus heterozygosity for factor II c.*97G>A, and (3) homozygosity for factor II c.*97G>A plus heterozygosity for factor V Leiden are very rare but have previously been reported.[2] The relative risk for VTE in homozygotes and double heterozygotes is very high, as are estimates for lifetime risk, and the risks are likely to be even higher in cases with more complex genotypes.[1,3,4]
  - Individuals identified with inherited thrombophilia variants through direct-to-consumer (DTC) testing who then come to medical attention should receive appropriate counseling.[5]

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