TEST: Endothelial Nitric Oxide Synthase (eNOS) G894T (Glu298Asp) Mutation

PRINCIPLE: Nitric oxide (NO) plays an important role in maintaining basal vascular tone. It is a smooth muscle relaxant and inhibits the adhesion, activation, and aggregation of platelets. A deficiency in NO synthesis may predispose individuals to coronary spasm, angina pectoris and myocardial infarction. Endothelium derived NO is synthesized from L-arginine by endothelial nitric oxide synthase (eNOS) which is encoded by the NOS3 gene on chromosome 7. A G/T base-pair change at position 894 in exon 7 of NOS3 gene predicts a Glu298Asp substitution which influences enzyme stability. The 298Asp isoform is degraded more rapidly than its 298Glu counterpart. Numerous studies have identified the role for this polymorphism in atherothrombotic disease and risk of myocardial infarction. The eNOS G894T mutation increases risk for premature myocardial infarction.

Presence of a T-786C mutation in the 5’ flanking region of the eNOS gene causes a significant reduction in the NOS3 gene promoter activity. This results in decreased synthesis of nitric oxide and confers a greater risk for coronary spasm. Single nucleotide polymorphisms in the promoter region (T-786C) and in exon 7 (G894T), and a variable number of tandem repeats in intron-4 have been evaluated in preeclampsia. The eNOS Glu298Asp polymorphism and the Asp298-789C-4b haplotype were found to be risk factors for preeclampsia. Recently, a meta-analysis which was performed to determine the association between eNOS gene mutations and preeclampsia concluded that eNOS gene-786 T>C and 4b/a polymorphisms contributed significantly to PE risk, especially in Europeans.

SPECIMEN COLLECTION AND PREPARATION:

Collect 10ml blood by standard venipuncture technique in lavender top EDTA tubes (two to three tubes). Heparinized blood cannot be used. Specimen should be delivered to the laboratory within 72 hours at ambient temperature. Peripheral blood specimens that are clotted, frozen or have not been collected in EDTA are not acceptable.

METHOD: Polymerase chain reaction (PCR) and reverse hybridization.

REPORTING RESULTS: The results are reported as “Normal”, “Heterozygous”, or “Homozygous”

- eNOS polymorphism at position 894
  - Normal GG
  - Heterozygous GT
  - Homozygous TT

Turnaround Time: One Month

REFERENCES:
3) Serrano, N.C. et al., Hypertension 2004, 44:702-707
4) Yoshimura, M et al., Am J Cardiol 2000, Mar 15;85(6):710-4