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Quantitation of Seminal Factor IX and Factor IXa in Fertile, Nonfertile, and Vasectomy Subjects: A Step Closer Toward Identifying a Functional Clotting System in Human Semen

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Coagulation factor (F) IX is a zymogen of the plasma serine proteases, one that plays an essential role in the regulation of normal blood coagulation. Congenital defects of FIX synthesis or function cause hemophilia B (originally called hemophilia C). Factor IX is activated by Tissue Factor (TF):FVII/FVIIa complex and FXIa. Subsequent to its activation, FIXa combines with FVIIIa on the platelet surface and activates FX to FXa. Human semen forms a semi-solid gelatinous coagulum, which then liquefies within 5-20 minutes in vitro. In spite of evidence demonstrating the importance of the seminal coagulation and liquefaction process in terms of global fertility and despite the fact that the seminal coagulum is composed of fibrin-like material, it has always been addressed from the perspective of High Molecular Weight Seminal Vesicle (HMW-SV) proteins (Semenogelin I and II) and their cleavage by prostate-specific antigen rather than the conventional hemostatic factors. In this study and as part of our continuing investigation of human seminal clotting factors, we report here on seminal FIX and FIXa in normal, subfertile, and vasectomized subjects. Factors IX and FIXa were studied in a total of 119 semen specimens obtained from subfertile (n = 18), normally fertile (n = 34), and fertile sperm donors (n = 27) and vasectomy subjects (n = 40). Seminal FIX and FIXa levels were also measured in a group defined by normality in several parameters derived from the World Health Organization fertility criteria and termed "pooled normal semen parameters." Both FIX and FIXa were quantifiable in human semen. There was a wide individual variation in FIX and FIXa levels within groups. Despite the group size, statistically significant associations with fertility-related parameters were infrequent. There is a positive correlation between FIX and its activation product, FIXa (n = 36; r = 0.51; $P < .05$). Factor IXa elevation in the high sperm-clump group was significant ($P < .05$), and days of abstention correlated with FIXa levels (n = 63; r = 0.3; $P < .05$). The key finding of the present study is that both FIX and FIXa are present in concentrations that are not dissimilar to plasma levels and that are apparently functional, as the activated form is also present. This fact, taken with other reports of coagulation factors in semen, raises the likelihood that a functional set of hemostatic

coagulation proteins exists in semen, potentially to interact with the HMW-SV proteins and the prostate-specific antigen system.

Key words: Fertility, novel finding.
