

Program: Deficiency of Plasminogen Activator Inhibitor Type 1 (PAI-1) Problems and Promises of a Genetic Mutation

Speaker: Sweta Gupta, MD, IU Health, St. Vincent, and Indiana Hemophilia & Thrombosis Center

Introduced by: Alison Brown

Attendance: 101

Guests: Glenn Bingle, Ted Danielson, Patricia Jacob, Charles Poland

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The speaker graduated from medical school and a pediatric residency in India in 2002. She completed a second pediatric residency with a Pediatric Hematology and Oncology Fellowship at Medical College of Wisconsin in 2010. She is presently affiliated with the Indiana Hemophilia and Thrombosis Center and Riley Hospital for Children.

The lecture started with the definition of Plasminogen Activator Inhibitor-1 or PAI-1: It is a protein in blood secreted by endothelial cells, megakaryocytes and hepatocytes. It plays a role in hemostasis, wound healing, angiogenesis, ovulation, and tumor metastasis. It is located on chromosome 7q. This protein is active in prevention of bleeding by “preventing the breakdown of clots.”

Deficiency of this PAI- protein is high in the Amish population and severe deficiency may result in clinical bleeding episodes. Clinically, minor bruising and hematomas may develop in PAI-1 deficiency. But major bleeding such as post-operative hemorrhage or intracranial hemorrhage may also occur. The first such case was reported in 1992 in a 26-year-old Amish woman.

Research conducted in Amish areas in Berne, Indiana, among 177 individuals resulted in finding 96 carriers and 11 homozygotes with PAI-1 deficiency. The carriers have not had any bleeding episode but the 11 homozygotes had experienced excessive bleeding episodes.

Additional evidence is found that deficient PAI-1 appears to offer protection against aging in animal models. Of a study's 43 carriers, 50% had lower PAI-1 values but seemed to have lower fasting insulin levels and lower risk for the development of type 2 diabetes. The few that had completely deficient PAI-1 levels appear to be at risk for homeostatic abnormalities and development of age-dependent cardiac fibrosis. The bioprotective nature of low PAI-1 was also seen in the Amish.

Further research is ongoing to obtain a larger sample and data for statistical significance.



Dr. Sweta Gupta