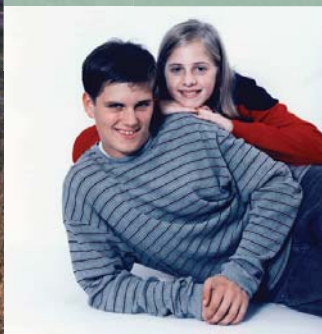
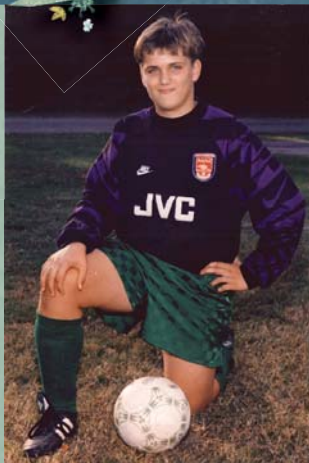


A LOOK INSIDE Thrombotic Storm



REMEMBERING AN EXTRAORDINARY PERSON

This research project has developed due to the legacy of a kind, compassionate and intelligent 14-year-old boy, JJ Vance, who was stricken with Thrombotic Storm in 1998. His death profoundly affected his friends, school and his family, including his parents Margaret A. Pericak-Vance and Jeffery M. Vance. The Vances are the investigators of this study.

We anticipate the impact of the results obtained from this study will extend substantially beyond the relatively small number who develop thrombotic storm each year. It has the potential to impact our approach to the diagnosis and management of the thousands of patients with venous thromboembolism.

For more information about this research or Thrombotic Storm, please go to www.HIHG.org or call 305-243-2365 during business hours, or toll free 24 hours a day at 1-877-740-7744. Our email address is HIHGTS@med.miami.edu. Medical questions and clinical criteria pertaining to Thrombotic Storm may be directed to:

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by the generous support of the
John P. Hussman Foundation.*



This University of Miami IRB-approved (20080730) research study is conducted in accordance with Federal guidelines and current US laws.

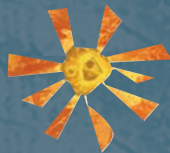


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RESEARCHERS AND FAMILIES WORKING TOGETHER TO LEARN ABOUT THROMBOTIC STORM

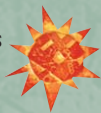


WHAT IS THE PURPOSE OF THIS RESEARCH?

We are investigating a rare hypercoagulable state (thrombotic storm) characterized by multiple, severe, life-threatening thromboembolic events. The purpose is to refine the extreme clinical phenotype definition of thrombotic storm and identify potential gene mutations that place these individuals at risk, so prevention and treatment strategies can be developed and applied. In addition, identifying new genes involved in the thrombotic process will provide new insights into thrombotic disease in general.

WHAT IS THROMBOTIC STORM?

Thrombotic storm was first described in 1998 by Craig Kitchens as a self-perpetuating process in which an initial thrombotic event could lead to multiple thromboses and even death. This pattern of rapidly-progressive life-threatening vascular occlusions has been described as a rare complication in association with several types of hypercoagulable states, inherited as well as acquired. The initial report included three patients who most likely had catastrophic antiphospholipid syndrome (APS), one with apparent protein S deficiency, but two had no clear underlying hypercoagulable state. For most patients, an acquired risk factor (pregnancy, immobilization, surgical procedure) initiated the process, which was characteristically followed by multiple additional events. Patients presented with venous as well as arterial thromboembolic events, and affected vascular beds were not those typical for most patients with venous thrombosis.



Unlike other well characterized clotting disorders, TS is nebulous in the medical community mostly due to the fact that it is rare, complex, and largely unpublished. However, collaborators representing eight sub-specialties met in March 2009 to initiate this study and develop inclusion and exclusion criteria for Thrombotic Storm.

THROMBOTIC STORM INCLUSION AND EXCLUSION CRITERIA



Inclusion criteria:

INDIVIDUALS WHO WERE AGE 55 YEARS OR YOUNGER AT THE TIME THEY MANIFESTED 2 OR MORE OF THE FOLLOWING:

- acute, >2 arterial and/or venous thromboemboli, and/or thrombotic microangiopathy
- unusual location (e.g., cerebral sinus thrombosis)
- progressive/recent unexplained recurrence
- refractory to acute therapy and/or an atypical response to therapy

Exclusion criteria:

THIS MUST BE IN THE ABSENCE OF:



- active cancer
- advanced coronary artery disease
- cocaine use associated with symptom onset
- intravascular devices
- paroxysmal nocturnal hemoglobinuria or myeloproliferative syndromes
- subtherapeutic treatment
- multiple/severe trauma
- pre-morbid clinical status



PATIENTS WITH CATASTROPHIC APS WILL BE INCLUDED IN THIS STUDY.

WHAT DOES PARTICIPATION INVOLVE?

- a blood sample
- detailed family and medical history
- permission to review medical records
- updated information on a yearly basis

Travel is not required. Study personnel will visit participants in their home or other desired location. There is no cost to participate, and there is no compensation for participating.

RESEARCH TEAM

Margaret Pericak-Vance, PhD, is the Director of the John P. Hussman Institute for Human Genomics (HIHG) and the principal investigator of this study. Thomas Ortel, MD, PhD, a hematologist from Duke University, is the lead clinical investigator.

HIHG faculty have led the field in identifying the genetic variants that underlie common human disease. They have identified genes for more than 60 human illnesses, including neurological disorders, cardiovascular diseases, and eye diseases.

HOW CAN YOU HELP?

Given the rarity and complexity of this disorder, lay individuals are unlikely to be able to appropriately self refer. As such, the role of the physician in recruitment is paramount. We need all eligible and willing individuals to participate. If you have or encounter a patient who has had a catastrophic thrombotic event, please inform them about the study. Patients who are interested to participate can contact us directly, or can be referred by you with the patient's permission. We are happy to answer your questions or provide you with patient brochures. You and/or your patients may also visit www.thromboticstorm.com. All contact information is located on the back page of this brochure.