In 1965, hematologist Olav Egeberg examined a Norwegian family, members of which had been severely symptomatic of excessive blood clotting within the veins, a condition known as venous thrombosis. The results of his examination would change the hematology landscape forever. Egeberg concluded that the antithrombin levels for all of the family members with venous thrombosis were approximately 50 percent less than non-affected family members. This was the first case that provided solid evidence of a hereditary link between blood coagulation and thrombotic disease. Thus, hereditary antithrombin deficiency (HD) was born into the hematology community.

Overview
Produced in the liver, antithrombin is a crucial serine protease inhibitor of coagulation. People with HD produce low levels of, or nonfunctioning, antithrombin.

Literature and case studies on HD indicate it is a fairly rare condition. Dr. W. Keith Hoots concurs. He is a professor of pediatrics and the division head of pediatric hematology at the University of Texas Medical School at Houston and the section head of pediatric hematology at the University of Texas M.D. Anderson Cancer Center. Dr. Hoots says that about one in 3,000 people is diagnosed with HD and “most of those one in 3,000 are pretty mild.”

There are two major types of HD. Type I pertains to low levels of antithrombin (40 percent to 60 percent reduction), while type II HD patients produce defective antithrombin. The common thread between the two types is the risk of a thrombosis, which is a formation of a thrombus, or blood clot, within a blood vessel. “Most of the time the presenting symptom is venous thrombosis,” Dr. Hoots says, adding that this typically involves painful swelling in part of the leg.

Management
The main concern when managing HD is to decrease the risk of a thrombotic event. More than 85 percent of patients with HD will have at least one thrombotic episode by age 50. The incidence of thrombosis for women with HD has been reported to be 70 percent during pregnancy. Patients with hereditary antithrombin deficiency are also at increased risk of thrombosis during surgery.

The literature on HD has split patient management into two broad categories: short-term treatment for patients in a high-risk situation and long-term treatment for those patients who have experienced thrombosis in the past. The American Society of Hematology reports that “[w]hen considering the use of long-term prophylactic anticoagulation, in particular vitamin K antagonists, the benefits of the use of these agents must be carefully weighed against the risk of bleeding complications associated with their use.”

Situations that present a high risk of thrombosis require treatment with a therapy such as Thrombate III, manufactured by Talecris. Thrombate III is a concentrated human antithrombin, fractionated from human plasma. According to Dr. Hoots, high-risk situations include “when [patients] undergo surgery or when a woman delivers a baby.”

Treatment
As the only FDA-approved product for treating HD, Thrombate III provides crucial therapy to prevent thrombosis when patients with HD undergo obstetrical or surgical procedures. Thrombate III does not increase the risk of bleeding, possesses no known contraindications, has never been linked to the transmission of a virus and has been on the market for more than 15 years. It is the only treatment indicated to restore hemostasis in these patients. Dr. Hoots affirms that if a patient has very low levels of antithrombin, the most effective way to increase the levels is with Thrombate III.

“FFP [fresh frozen plasma] is the only other alternative source,” Dr. Hoots says. However, there are dangers involved when using FFP. “There is a risk of pulmonary edema when there are volume constraints with the patient, and when it’s used in pregnancy,” he says, adding that “in older patients, there is a problem with using FFP.”

As always, the patient’s personal physician is the best source of guidance for what treatments are most appropriate.

For more general information, visit the National Alliance for Thrombosis and Thrombophilia at www.nattinfo.org and www.thrombate.com.