

Under-diagnosed Genetic Disorder Causes Life-threatening Malformations in Blood Vessels Throughout Body ***Interventional Radiologists Offer Nonsurgical Treatment for Hereditary Hemorrhagic Telangiectasia***

Hereditary hemorrhagic telangiectasia (HHT) is a genetic disorder that affects about one in 5,000 people and causes arterial blood to flow directly into the veins, creating weakened ballooned vessels that can rupture.¹ Interventional radiologists are one of the few specialists who can permanently treat this disease that affects approximately half a million people worldwide.¹ As vascular experts, interventional radiologists perform embolization—blocking the blood flow to the affected area—to prevent a life-threatening rupture.

Most patients with HHT function normally. Forty percent have brain or lung involvement that may lead to unexpected severe complications. Physicians treating complications often don't realize that the underlying disorder is HHT. As a result, most patients are undiagnosed.

In the normal circulatory system, arteries take oxygenated blood from the heart and push it out to all parts of the body under high pressure, while the veins return the blood to the heart. Small capillaries typically connect the arteries to the veins. A person with HHT lacks capillaries in a few blood vessels in critical locations. Arteries connect directly into veins, creating a fragile site that can rupture and bleed. These abnormal blood vessels are called telangiectasia (tel-AN-jee-eck-TAZE-ee-ya) if they involve small blood vessels (nose, stomach and small bowel) and arteriovenous malformations (AVM) if they involve a larger blood vessel (lung, brain and liver). Telangiectases often occur near the surface of the skin like the mucous membrane in the nose while AVMs appear in the internal organs of the body.

The location of the telangiectases or AVM affects what problems a person with HHT might face. A person with abnormal GI tract blood vessels should watch for black stools and anemia, which can cause fatigue, shortness of breath, chest pain or light-headedness. Those with AVMs in the lung face the possibility of a life threatening rupture, stroke or brain abscess—especially during pregnancy. HHT patients with brain AVMs do not generally have warning symptoms prior to a life-threatening brain hemorrhage. Heart failure is another risk HHT patients face, due to high flow liver AVMs.

Regardless of location or size, abnormal blood vessels have a greater tendency to rupture and bleed compared to normal blood vessels and should be closely monitored.

Those with HHT may have blood vessel abnormalities in the:¹

- Nose
- Skin of the face, hands and mouth

- Lungs
- Brain
- Lining of the stomach and intestines (GI tract)

Prevalence

- About 9 percent of those with HHT have recurring nosebleeds.
- 95 percent of HHT patients have telangiectases in the skin of the hands, face and mouth that generally become apparent in their 30s or 40s.
- GI bleeding will develop in about 25% of HHT patients (after age 50), which can result in black stools or anemia.
- 30 percent will have one or more AVMs in the lung. These are life threatening should they rupture. Pregnant women with HHT are at increased risk of AVM rupture in the lung due to an increase in blood volume and cardiac output in the last trimester. Patients with lung AVMs are also at risk for stroke or a brain abscess from the lack of capillaries to filter impurities like clots, bacteria and air bubbles.
- Brain AVMs are found in 15 percent of HHT patients and can be life threatening.
- Spinal AVMs are fairly rare. They cause back pain or loss of feeling/function in arms and legs.

Symptoms

Approximately 95 percent of HHT patients eventually have recurrent nosebleeds, with one-third having onset by the age of 10 and 90 percent by age 21. Other characteristics of HHT include small red to purple spots and lacy red vessels.

Diagnosing HHT

In the mid-1990's scientists discovered that an abnormal gene on either chromosome 9 or 12 causes HHT. Chromosome 9 (endoglin) and chromosome 12 (activin-like kinase) tell the body to produce a substance that is involved in the formation of blood vessels. HHT is a "dominant" disorder since one abnormal copy of the gene from one parent can cause the disorder. Although there is a 50 percent chance of inheriting this abnormal gene, children who do not have it cannot pass on the disease.

In 2003, genetic testing for HHT became available at only a few genetics laboratories in the United States. The complicated family-based testing should be run, ordered and managed by an HHT center or genetics professional. According to recently published clinical diagnostic criteria, a person has HHT if they have three or more of the following criteria and are suspect if they have two or more of the criteria:

1. Nosebleeds are spontaneous and recurrent.
2. Telangiectases are prevalent at characteristic sites such as lips, oral cavity, fingers and nose.
3. AVMs are present in lung, brain, GI, liver or spine.
4. Family history indicates a parent, sibling or child has HHT.

Establishing a Diagnosis and Developing a Treatment Plan

Currently, there are nine multi-disciplinary centers for management of these patients and their families. It is recommended that an initial diagnosis and treatment plan should be developed for each patient by one of these centers. Centers are located at:

- Yale University
- University of Toronto
- University of Utah
- Washington University, St. Louis
- Oregon Health and Science University
- University of California, San Diego
- University of Pennsylvania
- Mayo Clinic
- Medical College of Georgia

Treatment

The location of the telangiectases determines the course of treatment for HHT patients. Interventional radiologists treat malformations in the lung and brain using embolization.

Lung – These malformations should be treated, even prior to symptoms appearing, due to their life-threatening/disabling nature. Interventional radiologists, vascular experts who treat patients internally using imaging to guide them, can permanently treat lung AVMs using a minimally invasive procedure known as embolization. During this procedure, an interventional radiologist makes a small nick in the skin, inserts a catheter into the femoral vein in the groin and then directs it to the abnormal blood vessels in the lung. Next, dacron platinum coils are placed in the artery feeding the AVM to permanently block the blood flow to the AVM. Patients should be seen one year after treatment by the interventional radiologist to be sure the AVM has been resolved.

Patients are treated either as outpatients (single AVM) or as inpatients (multiple AVMs). Local anesthesia is given and the procedure may take one to three hours.

Brain – Size, structure and location in the brain affect how these AVMs are treated. Surgery, embolization and stereotactic radiosurgery are treatment options that can be used separately or in combination. Decisions about whether to treat and types of treatment should be made by a team including neurovascular neurologists, neurosurgeons, and interventional neuroradiologists.

HHT, Women and Pregnancy

Female hormones are known to affect bleeding of abnormal HHT blood vessels. For some women, nosebleeds vary through the menstrual cycle and become worse after menopause.

Most pregnant women with HHT can expect no serious HHT-related complications. For some, new skin telangiectases are detected, while others report improvements. There is great concern for a pregnant women with an AVM in their lung. During pregnancy, there is a 60 percent increase in blood circulation that is essential to the development of the baby.¹ This increase in pressure on weak abnormal blood vessels increases the risk of a life-threatening rupture in the lung. Research shows that it is safe and efficacious to perform embolization on pulmonary AVMs during the second trimester of pregnancy.⁷

Both HHT mothers and their babies can generally expect a safe pregnancy.

About Interventional Radiologists

Interventional radiologists are doctors who specialize in minimally invasive, targeted treatments that have less risk, less pain and less recovery time compared to open surgery. They use their expertise in interpreting X-rays, ultrasound, MRI and other diagnostic imaging studies to understand, visualize and diagnose the full scope of the disease's pathology and to map out the procedure tailored to the individual patient. Then during the procedure, they image as they go to guide tiny instruments, such as catheters, through blood vessels or skin, to treat diseases at the site of the illness nonsurgically.

Interventional radiology is a recognized medical specialty by the American Board of Medical Specialties. Interventional radiologists complete preliminary training in Diagnostic Radiology and advanced training in Vascular and Interventional Radiology. The American Board of Radiology certifies their specialized training.

For Further Information

For more information on HHT or interventional radiology, visit the SIR Web site at www.SIRweb.org.

References

1. HHT Foundation. Available at www.HHT.org.
2. Shovlin CL, Winstock AR, Peters AM, Jackson JE, Hughes JMB. Medical complications of pregnancy in HHT. *Quart J Med* 1995; 88:879-887.
3. Ference BA, Shannon TM, White RI, Zawin M, Burdge CM. Life threatening pulmonary hemorrhage with PAVMs and HHT. *Chest* 1994; 106:138:1392.
4. Shovlin CL, Letarte M. Hereditary haemorrhagic telangiectasia and pulmonary arteriovenous malformations: issues in clinical management and review of pathogenic mechanisms. *Thorax* 1999; 54:714-729.
5. Gershon AS, Faughnan ME, Chon KS. Transcatheter embolotherapy of maternal pulmonary arteriovenous malformations during pregnancy. *Chest* 2001; 119:470-477.
6. Guttmacher AE, Marchuk DA, White RI, Hereditary hemorrhagic telangiectasis. *New Engl J Med* 1995; 333:918-24.
7. White RI. *Chest*, vol. 119, 470-477, Feb. 2001.