Hereditary Hemorrhagic Telangiectasia: A Primer for Critical Care Nurses

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Hereditary hemorrhagic telangiectasia is a rare, autosomal dominant genetic disease that causes abnormal growth of blood vessels and, subsequently, life-threatening arteriovenous malformations in vital organs. Epistaxis may be one of the initial clues that a patient has more serious, generalized arteriovenous malformations. Recommended treatment involves careful evaluation to determine the severity and risk of spontaneous rupture of the malformations and the management of various signs and symptoms. The disease remains undiagnosed in many patients, and health care providers may miss the diagnosis until catastrophic events happen in multiple family members. Prompt recognition of hereditary hemorrhagic telangiectasia and early intervention can halt the dangerous course of the disease. Critical care nurses can assist with early diagnosis within families with this genetic disease, thus preventing early death and disability. (Critical Care Nurse. 2016;36[3]:36-49)

Mr J, a 19-year-old man, was admitted to the critical care unit of a community hospital with an intracerebral hemorrhage. His mother, father, siblings, and extended family visited often and were attentive and concerned. After initial stabilization of his condition, a ruptured cerebral arteriovenous malformation (AVM) was diagnosed. Mr J was subsequently intubated and sedated for 12 days before he had a tracheostomy and placement of a feeding tube. During this time, the critical care nurses had a chance to become acquainted with his family. As the family was grieving about this tragic event, the nurses became aware that several other members of the family had experienced the same tragedy at similarly young ages.

This article has been designated for CE contact hour(s). The evaluation tests your knowledge of the following objectives:
1. Describe the pathophysiology and known causes of hereditary hemorrhagic telangiectasia (HHT)
2. Identify the main physiological complications and treatment strategies of HHT
3. Discuss the nursing interventions to support HHT patients across the lifespan

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Mr J continued to slowly improve. He regained consciousness and was able to have placement of a T-piece and, eventually, a speaking valve. He had residual left-sided hemiparesis, but he readily partnered with his physical and occupational therapists to decrease his deficits. A few days before his transfer to the telemetry unit, a nurse happened to mention to one of Mr J’s physicians, a pulmonologist, that the family had knowledge of 6 other family members on the father’s side who had had the same fate, and all when they were less than 29 years old. The physician agreed that the situation was unusual and proceeded to investigate. Later that day, the physician spoke with the family and asked them if anyone in the family had experienced epistaxis that seemed unusually frequent or severe. To everyone’s amazement, the patient’s father stated that he had had severe epistaxis since he was an adolescent and that his son also had frequent epistaxis. The father proceeded to explain that 2 of the father’s siblings, several cousins, and his mother and grandmother also had epistaxis. The family members had assumed it was a family trait, much like their propensity for hypertension; however, no one attributed any significance to the nosebleeds. After hearing this information, the pulmonologist asked Mr J’s father if the father or any other family members had noticed any red or pink spots on their mucous membranes or fingers. Again, the father affirmed that he had them, as did the same members who had nosebleeds. The physician examined the father and confirmed the presence of several telangiectasias on the father’s lips and tongue. At that point, the physician spoke with the family and told them that they had sufficient diagnostic criteria consistent with a somewhat rare genetic disorder called hereditary hemorrhagic telangiectasia (HHT).

Mr J was eventually transferred to the telemetry unit and subsequently entered an acute rehabilitation unit. The family was referred to a local tertiary center that specialized in HHT. The family members had genetic tests, and the diagnosis was confirmed. Most important, Mr J’s 13-year-old sister also tested positive for HHT. Because she had intermittent headaches, she had follow-up imaging, which revealed a small cerebral AVM. The tertiary HHT team, the patient, and the patient’s family agreed that watchful waiting was the best strategy for treatment. The patient was relieved that she did not need an embolization procedure and that the diagnosis of HHT possibly saved her from future disability or premature death. Approximately 6 months later, Mr J, his parents, and his sister visited the critical care unit to thank the nurses. The patient’s mother was tearful as she hugged the nurses and told them that because of their persistence and the physician’s astute diagnostic skills, the family had received the necessary diagnosis and counseling.

This case study underscores the important contribution of nurses in actively listening, recognizing a potentially dire circumstance, and acting as patient advocates. HHT, also known as Osler-Weber-Rendu syndrome, is an uncommon disease, yet it has serious and sometimes deadly complications. HHT is easily underdiagnosed, a situation that places patients at increased risk for serious sequelae such as hemorrhage, brain abscesses, and stroke. Even though the diagnosis is infrequent, patients with HHT complications often require care in critical care units, postanesthesia care units, and other general acute care units. Many family physicians may not be aware of the disease, so nurses may be the first health care providers to fit the diagnostic pieces together to help in the diagnosis. Early recognition of the presence of the disease can have major positive effects on an entire family’s well-being. The purpose of this article is to inform critical care nurses about HHT, diagnosis, treatment, and nursing considerations in caring for patients with HHT and the patients’ families.

### Background and Pathophysiology

Sir John Legg first described HHT in 1876 as a form of hemophilia with nevi and frequent epistaxis. Doctors Osler, Weber, and Rendu were physicians in the 1890s who continued Legg’s work and realized that HHT was not a clotting disorder but a blood vessel abnormality. Osler, Weber, and Rendu later identified a familial
association and continued the research. HHT is an autosomal dominant condition that causes formation of dysfunctional blood vessels and multiple AVMs in various organs of the body. According to estimates, the incidence of HHT is 1 in 5000 to 1 in 8000. The syndrome occurs globally and in all races and ethnic groups. Males and females are equally affected. The common characteristics of the disease are telangiectasias (small, red lines or dots) on the skin, especially the face, nasopharynx, and fingers; visceral AVMs; and epistaxis.

HHT can be divided into several genetic types. Each type has dominant features, but many features overlap between types. The pathophysiology of HHT includes gene mutations on the endoglin (ENG) gene (type 1), activin A receptorlike kinase (ALK1/ACVRL1) gene (type 2), and sometimes the SMAD4 (similar to mothers against decapentaplegic) family member genes. The SMAD4 family of genes has been identified as tumor-suppressing genes. Alterations in these genes not only contribute to HHT and neoplasms of the pancreas, head, and neck but also are associated with a syndrome called juvenile polypsis. Families with juvenile polypsis have a high risk for early colon cancer and HHT. The defective HHT genes code for proteins that mediate signaling pathways in vascular endothelial cells. The alteration in the signaling pathways causes abnormal development of blood vessels, such as dilated venules (eg, telangiectasias) and open arteriovenous channels. The current understanding is that some unknown vessel injury causes angiogenic stimulation, which results in the vessels’ inability to mature correctly.

Complications

Telangiectasias, epistaxis, and visceral AVMs are the hallmark signs of HHT. The disease is severe in some patients and extremely mild in others, even among family members who share the same mutation. Some families endure decades of sudden, tragic deaths of young children due to ruptured cerebral aneurysms before the families realize a medical condition is present. Health care providers must recognize the telltale indications of HHT and refer patients for diagnosis before a catastrophic event occurs. Historically, all HHT patients were thought to have similar life expectancies. However, recent studies have indicated that HHT patients have a significantly higher risk for dying of neurological and hemorrhagic complications than do patients without the syndrome. This difference is especially true for patients less than 60 years old.

Epistaxis and Telangiectasias

Epistaxis or nosebleed, the most common sign of HHT, usually does not begin until early adolescence, often making HHT a silent disease in children. According to estimates, 95% of patients will have some degree of epistaxis by age 20 years. Some patients deal with an occasional, annoying nosebleed, whereas others have frequent, debilitating epistaxis that requires hospitalization. The severity and degree of epistaxis correlate neither with disease severity nor with the presence of visceral AVMs.

Most HHT patients also experience characteristic telangiectasias on the mouth, nose, oropharynx, face, lips, and fingers (Figures 1-3). Usually these signs manifest later in life, often developing when patients are in their 30s and 40s. The size of telangiectasias ranges from...
pinpoint to approximately 4 mm, and the abnormalities often increase in number and size over time.\textsuperscript{13}


\section*{Systemic Effects}

\subsection*{Cerebral and Spinal AVMs}

Cerebral AVMs can cause intracerebral hemorrhage and death (Figure 4). Patients with signs and symptoms of cerebral AVMs need investigation and magnetic resonance imaging to determine a treatment plan. Although approximately 10\% of HHT patients have cerebral AVMs, most cerebral malformations will never bleed and medical management is advised.\textsuperscript{14} Recent findings\textsuperscript{14} suggest that most of the neurological consequences of HHT are related to embolic events caused by pulmonary AVMs, rather than rupture of a cerebral AVM. Furthermore, although spinal AVMs occur more rarely than do cerebral malformations, HHT patients can have spinal AVMs, which are usually diagnosed during childhood.\textsuperscript{11}

\subsection*{Pulmonary AVMs}

Approximately 40\% to 60\% of HHT patients are affected with pulmonary AVMs\textsuperscript{14} (Figures 5 and 6). When these AVMs are symptomatic, the most common manifestations are related to hypoxemia and dyspnea. However, pulmonary AVMs also are associated with pulmonary hypertension, heart failure, stroke, and cerebral abscesses. Other sequelae include massive hemoptysis and spontaneous hemothorax.

In the general population, 70\% of pulmonary AVMs are related to HHT.\textsuperscript{7} The diagnosis of HHT should be assumed until it is ruled out. Patients may have dyspnea, hemoptysis, or orthodeoxia (ie, decreased oxygen saturation in the upright position and improvement while lying down). Patients may also have migraines and polycythemia due to chronic hypoxemia. Additionally, migraines may be associated with the presence of pulmonary AVMs because of the passage of microthrombi and vasoactive substances from the venous system to the cerebral circulation.\textsuperscript{14} Clubbing and cyanosis are possible in severe cases of pulmonary AVMs.\textsuperscript{11}

In the normal lung circulation, the microscopic capillary vascular bed acts as a filter to trap minute particles of embolic material, clots, bacteria, and air. When a major pulmonary AVM is present (ie, $\geq 3$ mm), the particulate matter does not get trapped in the pulmonary vasculature; rather, it flows unimpeded to the systemic circulation in a right-to-left shunt.\textsuperscript{7} This process can cause an embolic stroke or a brain abscess, depending on the shunted material. Pulmonary AVMs can also rupture, causing hemorrhage, hemoptysis, or hemothorax. The increased blood volume during pregnancy can exacerbate pulmonary AVMs, making prepregnancy assessment beneficial for HHT patients.
Recently, Clark et al. found evidence that pulmonary AVMs are also implicated in angina pectoris and myocardial infarctions. The researchers found that the embolus flows to the coronary arteries, rather than to the brain, a situation that results in coronary artery occlusion. Clark et al. postulated that this type of ischemic process might also affect other organs, including the gut and kidneys.

**Gastrointestinal, Hepatic, and Pancreatic AVMs**

Approximately 80% of HHT patients have gastric or small-bowel telangiectasias, but these AVMs can also form in the esophagus and colon. Gastrointestinal telangiectasias are generally asymptomatic until a patient is 50 to 60 years old, when approximately one-quarter of patients have overt gastrointestinal bleeding. The bleeding may be slow and intermittent and also may cause various degrees of anemia. Women have an incidence 2 to 3 times greater than that of men.

Hepatic AVMs are fairly common (Figure 7). Most patients are asymptomatic, but portal hypertension and high-output cardiac failure occur in some. Most commonly, signs and symptoms of hepatic AVMs occur late in life after the heart has been strained by years of circulating blood through the passive, low-resistance tract of a hepatic AVM while simultaneously supplying blood to the entire body. A state of continuously high cardiac output eventually causes heart failure. Other hepatic complications include biliary duct abnormalities and enlarged hepatic arteries, with or without aneurysms. AVMs within the hepatic parenchyma contribute to portal hypertension, cirrhosis, bile duct dilatation, and fibrosis that can lead to complete hepatic failure. Increased capabilities of computed tomography (CT) have increased the ability of clinicians to diagnose intrahepatic abnormalities sooner. Of interest in hepatic AVMs is the decreased first-pass effect that occurs in some HHT patients. The first-pass effect is defined as the initial hepatic metabolism of drugs or substances before the drugs or substances reach the systemic circulation. Candelli et al. found that oral medications primarily metabolized by the liver have increased bioavailability in patients with marked HHT-related hepatic shunting. Altered drug metabolism has implications for the administration of these types of medications to HHT patients who have hepatic AVMs.

Additional rare complications can occur in HHT patients. For example, involvement of the pancreas has been detected in up to 31% of patients with HHT.
With the use of 64-slice CT scanners, more information than before can be obtained on the pancreas. A few patients with HHT have median arcuate ligament syndrome, another rare condition. This syndrome causes abdominal pain and a possible pulsatile abdominal mass due to compression of the celiac artery and nerves by the median arcuate ligament. Median arcuate ligament syndrome also usually involves multiple changes in abdominal and hepatic vasculature.

Hematologic Dysfunction

Bleeding telangiectasias and chronic nasal and gastrointestinal hemorrhages can contribute to blood loss and chronic anemia. In a recent study, Shovlin et al\(^\text{20}\) elucidated the association between elevated coagulation factor VIII in HHT patients and the possible increased risk for venous thromboembolism. The patients had an independently elevated factor VIII, despite the lack of recent medical intervention. In another study,\(^\text{21}\) as iron stores were depleted, patients had an associated increase in the levels of factor VIII. Elevation of coagulation proteins is an important risk factor for pulmonary embolus and deep vein thrombosis.\(^\text{21}\) This association must be considered in any determination of the best strategy for risk mitigation.

Altered Immune Function

A lesser-known complication of HHT involves an alteration in immune function and a propensity for severe bacterial infections. Critical care nurses must consider HHT patients at increased risk for sepsis. Guilhem et al\(^\text{22}\) found that HHT patients have an altered adaptive immunity with decreased T-cell counts, specifically CD4 and natural killer cells. Serum concentrations of immunoglobulins A and G are increased, whereas the concentration of immunoglobulin M is decreased. Patients have a greater incidence of cerebral abscesses and staphylococcal osteoarthritis than do patients without HHT; however, this difference could be attributed to either the embolic shunting related to pulmonary AVMs or to the prolonged presence of nasal packing associated with severe epistaxis.\(^\text{22}\) Of note, many HHT patients routinely take iron supplements, and researchers have hypothesized that iron is toxic to lymphocytes. The added iron increases oxidative stress, and an overarching lymphopenia results.\(^\text{22}\)

In another recent study, Hosman et al\(^\text{23}\) proposed that patients with HHT might have different prevalence patterns for several solid tumor cancers than do non-HHT patients. An often cited concern is the effect of repeated exposure to radiation from frequent imaging studies. Surprisingly, compared with prevalences in the general population, prevalence in HHT patients was lower for lung cancers, higher for breast cancer, and about the same for prostate and colorectal cancers.

Last, Massarenti and Yilmaz\(^\text{24}\) described altered endothelialization in patients with HHT. In an HHT patient treated with a left atrial appendage closure device, no endothelialization had occurred after 10 months. The researchers\(^\text{24}\) postulated that HHT was involved because the lack of endothelialization of the
device was the first case noted in the literature. Much remains to be learned about the far-reaching, systemic effects of HHT.

**Diagnosis**

**Clinical Diagnostic Criteria**

According to estimates,11 90% of HHT-affected persons may not know they have the disease. The diagnosis can be made on the basis of several clinical signs and symptoms but can also usually be confirmed by genetic testing. Clinical diagnosis is based on the Curacao criteria,6 which were published as an expert consensus model in 2000. The Curacao criteria have 4 aspects: spontaneous and recurrent epistaxis, presence of telangiectasias, family history of the disease, and the presence of visceral AVMs.6 Of the 4 criteria, 3 must be present for a definitive diagnosis; however, patients with fewer than 3 may still have HHT. Suspected cases require genetic testing to confirm a diagnosis. The results of a more recent validation study by van Gent et al25 supported the Curacao criteria as having good diagnostic ability with high sensitivity and specificity.

**Genetic Testing**

Genetic testing benefits HHT patients in several ways. Signs and symptoms vary between family members, and genetic penetrance is a function of age, a factor that makes diagnosis more complicated among young patients compared with older patients. Genetic testing is valuable because the results confirm possible cases of HHT and can pinpoint the specific gene mutation causing the disease. In most persons with HHT, the causal mutation is in 1 of the 3 genes previously mentioned. Occasionally, a patient has a new mutation, and, thus, all the patient’s family members would test negative for HHT. When a patient is recognized as having HHT, both the patient and the patient’s family members are highly encouraged to seek genetic testing. The index patient receives a comprehensive DNA sequencing and deletion-duplication analysis of his or her genes. Once the mutation is discovered on the specific gene (eg, ENG, ACVR1, or SMAD4), the successive family members need only specific testing for that gene.6 In a small minority of families, approximately 2%, HHT is caused by an unknown gene.11 The diagnosis can be difficult because not all genes that cause HHT have been identified. The abnormalities do not follow universal patterns, although the gene abnormalities are specific to families. Although the occurrence is extremely rare, an individual patient may have a random genetic mutation and be the only person in the patient’s family who has HHT.

Genetic testing has other beneficial results. Because many children do not manifest signs or symptoms of HHT until adolescence, genetic testing can rule out HHT early in life. Early detection not only prevents catastrophic complications but also obviates unnecessary worry, scans, testing, and the anesthetic-related risks associated with imaging in children. Current DNA tests are performed on a small sample of blood or saliva; collection of such specimens is fairly nontraumatic for younger children. The cost11 of initial DNA sequencing is approximately $2000. Specific analysis for the presence of a known gene ranges from $200 to $400. Many insurance plans cover the testing and hold the patient responsible for only a small sum.

Although differentiating between the genetic types of HHT is not a reason for genetic testing (the recommended treatments and screening are the same except as mentioned in the following material), differentiation can yield additional research and clinical information. Patients with type 1 HHT have a propensity for the formation of pulmonary AVMs, and patients with type 2 HHT have increased rates of hepatic AVMs. Despite these generalizations, all varieties of AVMs are associated with both clinical types. Most patients (about 87%) have HHT type 1 or type 2, and approximately 2% have the SMAD4 juvenile polyposis form.11 The juvenile polyposis form of HHT is the only type in which knowledge of the genotype changes the screening recommendations. Patients with the juvenile polyposis form need frequent colorectal screening because of their increased risk for colon cancer. The remaining 11% of patients with HHT have the more rare mutations on chromosomes 3 and 7, which cause HHT 3 and HHT 4, respectively. The mutations causing HHT 3 and HHT 4 have not been as extensively studied as the other mutations, but study of them may increase the breadth of knowledge about HHT and serve to expand the treatment modalities. HHT is almost always a heterozygous disease, and Govani and Shovlin26 report studies that have indicated that infants of 2 HHT parents (ie, homozygous) often die in utero.
The homozygous form is thought to be almost always lethal. Genetic testing and counseling can help stratify the risk in these rare cases.

**Secondary Evaluation**

**Pulmonary AVM Screening**

Once HHT is diagnosed, patients must be referred for further evaluation. Of note, the severity of signs and symptoms does not always correlate with the severity of the disease and rate of serious complications. Contrast echocardiography is the preferred initial screening examination. If a shunt is detected, then chest CT should be done to confirm the presence of an AVM. Patients must understand that initial screening can be accomplished by using a noninvasive, convenient test with no exposure to radiation. Additionally, if CT is required, low-dose CT scanning, with approximately 50% of the standard radiation dose, is diagnostically acceptable.

National HHT treatment centers also offer transcranial Doppler imaging bubble studies, which are performed much as a cardiac bubble study is. In a transcranial Doppler imaging bubble study, an ultrasound probe is placed over the temporal window to “listen” for bubbles that have been injected peripherally. The presence of bubbles in the temporal window indicates that a pulmonary AVM exists and that material was shunted to the cerebral circulation. Thoracic CT and echocardiograms also allow assessment of pulmonary artery hypertension, which can be a relative contraindication for AVM treatment by embolization. Current international consensus guidelines suggest subsequent CT scanning at 5- to 10-year intervals because pulmonary AVMs are capable of growing. Pregnancy is a known factor in the evolution of pulmonary AVMs; therefore, pregnant women with HHT need careful observation.

**Neurological AVM Screening**

Cerebral hemorrhage from an undiagnosed AVM can have devastating effects. Patients with HHT who are symptomatic (eg, headaches, visual change, or other neurological symptoms) should have magnetic resonance imaging. Older recommendations by Faughnan et al stated that cerebral angiography was the gold standard for detecting cerebral AVMs, but the method also was associated with a 0.5% risk for causing a permanent stroke. Recently, investigators have proposed that the screening strategy is best determined by an individualized approach that includes discussions between the patient and the provider of the risks and benefits related to the particular patient. Providers should remember that most neurological complications of HHT are related to embolism of clots and bacteria via shunting by pulmonary AVMs and are not caused by cerebral hemorrhage. International guidelines also mention the use of transcranial Doppler imaging as an additional option in assessment of cerebral AVMs. For adults in whom the presence of a cerebral AVM is excluded, no evidence indicates that new cerebral AVMs will develop as the adults grow older. Spinal AVMs are rare, and the current consensus does not recommend routine spinal screening.

**Gastrointestinal Tract Screening**

Although most patients with HHT have involvement of the gastrointestinal system, only one-quarter experience symptomatic bleeding, which usually occurs after middle age. An expert international panel has made no specific recommendations except for an annual evaluation of hemoglobin and hematocrit levels beginning at age 35 years. Any HHT patient with gastrointestinal bleeding should be referred for endoscopic visualization, just as any non-HHT patient would. HHT patients with elevated liver enzyme levels should be assessed for signs and symptoms of heart failure (eg, dyspnea, orthopnea, edema), portal hypertension (eg, variceal bleeding, ascites), biliary abnormalities (eg, jaundice, fever, abdominal pain), and hepatic encephalopathy. For these patients, simple ultrasound and abdominal CT are recommended and are highly successful for diagnosis of hepatic AVMs. Liver biopsies are strongly discouraged because of the risk for hemorrhage. In the small percentage of patients with the SMAD4 genetic type of HHT (ie, juvenile polyposis), early and frequent colonoscopies are recommended to detect malignant neoplasms. The first colonoscopy should be performed when the patient is 15 to 18 years old; thereafter, repeat colonoscopies should be done every 1 to 2 years.

**Epistaxis Assessment**

Epistaxis, although rarely life-threatening, is a serious threat to an HHT patient’s quality of life. The
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epistaxis screening scale was developed for objective assessment of the severity of epistaxis and the efficacy of treatment rendered within the preceding 3 months. The scale consists of 6 questions about the frequency, duration, and intensity of epistaxis; the presence of anemia; and the need for medical attention or transfusion because of epistaxis. Practitioners can use this tool to assess epistaxis severity and determine the level of treatment needed. The tool has been validated and can be accessed for free at the HHT Foundation International website.11

Specialty Center Screening

In addition to the interventions previously mentioned, one of the most important recommendations for evaluation of HHT patients is follow-up at an HHT Center of Excellence. These centers are associated with tertiary medical centers and are located throughout the United States, Canada, Europe, and Asia. These facilities provide comprehensive, multidisciplinary care that includes pulmonology, neurology, interventional radiology, gastroenterology, social services, insurance coordination, and genetic counseling.6 Providers at HHT Centers of Excellence also assist local practitioners in routine HHT patient management after initial evaluation at a center. Many insurance companies will cover the cost of referral but not the cost of travel. Charities, such as the National Patient Travel Center,27 can assist patients who cannot afford long-distance travel. HHT Centers of Excellence also have administrative personnel who can help arrange travel, insurance authorization, and the logistics of a 1-day evaluation.11 After the initial evaluation, most follow-up care is then accomplished locally.

Treatment Embolization

Once a diagnosis has been made and subsequent evaluation is completed, patients can be stratified into risk categories. For those with pulmonary AVMs, transcatheter embolization is the treatment of choice; the embolization ameliorates the risk of hemorrhage and an embolic event and yet is only minimally invasive. The patient often experiences a marked improvement in oxygen saturation immediately after the procedure. Embolization has also been used successfully in pregnancy in women with HHT, although recommendations are that any necessary embolization should take place before pregnancy. Embolization is not performed on the liver because marked morbidity and mortality may result. In the past, cerebral AVMs might have been treated with embolization; microsurgery; or stereotactic radiation, such as the gamma knife.6 However, recent evidence14 supports medical management of cerebral AVMs rather than interventional management because the risk for stroke or death is higher in the intervention group.

Medical Management

Several complications of HHT, such as liver and heart failure, can be managed medically. A small risk exists that some patients with severe hepatic AVMs will eventually need a liver transplant. Treatment methods that involve manipulation of the liver, such as embolization for the lungs and cerebrum, have been largely ineffective and even harmful for HHT patients. Systemic treatment with bevacizumab, a monoclonal antibody that binds to vascular endothelial growth factor, can lead to improvement in both signs and symptoms associated with hepatic AVMs and epistaxis.14

Medical management is also offered to reduce chronic gastrointestinal bleeding. Hormonal therapy (ie, estrogen-progesterone preparations), antifibrinolytics (tranexamic acid and aminocaproic acid), antihormonal therapy (tamoxifen and raloxifene), angiogenesis inhibitors (thalidomide), and sirolimus have all been used to decrease gastrointestinal bleeding, although only weak evidence supports the use of most of them.6 Combined estrogen-progesterone oral contraceptives may be an option for women of childbearing age and may have a beneficial effect by decreasing bleeding.14

Anemia is also managed medically by administration of blood transfusions and oral iron supplements. Long-term and sufficient repetition of iron stores may obviate transfusions and the associated risks.14 The international guidelines6 do not require the avoidance of anticoagulant or antiplatelet therapy, but a careful risk-benefit assessment is encouraged.

Epistaxis Management

Management of epistaxis involves many therapies with various levels of efficacy. Traditional treatments such as nasal packing, argon laser treatments, or
electrochemical cautery have been the mainstays. Some patients have such severe bleeding that they have resorted to the Young nasal closure procedure, in which the nasal passages are sewn shut. However, this procedure is a last resort because it affects taste and smell. Most authorities recommend humidification of the air and lubrication of nasal passages, steps that are moderately effective in reducing the severity of bleeding. Reh et al found that a topical application of sesame-rose-geranium oil significantly decreased the frequency and severity of epistaxis.

In another study with promising results, a new use was found for thalidomide. Known for its antiangiogenic effects, thalidomide was effective in ameliorating bleeding and in increasing the hematocrit and hemoglobin levels of patients with severe, recurrent HHT-related epistaxis. Cantone et al had success in using Surgiflo (a gelatin-thrombin matrix made of sterile, absorbable porcine gelatin paste) instead of traditional packing, because Surgiflo is not known to cause the rebleeding that can occur after removal of traditional nasal packing. Treatment with estrogen and bevacizumab has been successful in small trials. Recently, study results have suggested that HHT patients have higher levels of vascular endothelial growth factor, a characteristic that could explain the patients’ increased tendencies for nasal bleeding. Riss et al recently published the findings of a small, double-blind, placebo-controlled trial in which intranasal injection of bevacizumab led to a significant decrease in epistaxis. In the ELLIPSE study, investigators examined the efficacy of topical bevacizumab (nasal spray) as an easier and less invasive treatment than systemic administration of the drug but found a lack of efficacy with the topical route. Some initial research has been done with the antioxidant N-acetylcysteine to ascertain its effect on epistaxis. In a study of 43 patients with HHT, the results suggested that the antioxidant might decrease the severity and frequency of diurnal epistaxis, but it was most effective in men.

Silva et al found that most treatments were temporary measures and that most therapies needed repetition. They also found that avoidance of fish oils and high-salicylate foods (eg, alcohol, red wine, cayenne pepper, capsicum, chocolate, coffee) was associated with a decrease in epistaxis. Lifestyle modifications may have some benefit and are without risk. Health care providers must be cognizant in assessing the airway and mucous membranes of HHT patients before anesthesia or other procedures that disturb the airway are implemented. Such measures may prevent aggravation of bleeding telangiectasias.

**Nursing Interventions**

Critical care nurses may be involved in several stages of an HHT patient’s care, whether care after a serious vascular event or after a procedure to correct one of the various vascular defects these patients experience. Nurses should know about the pathophysiology and treatment of HHT, as well as the physical and psychological ramifications for the patient and the patient’s family. Nurses should develop a care plan with interventions that support, educate, and empower the patient and the patient’s family.

**Prevention of Air Embolism**

Nurses need to aggressively protect patients from air embolism. Expert opinion suggests the use of in-line air filters on all intravenous equipment, although no empirical evidence indicates that such use is effective in preventing embolism. Nurses are cautioned to be extra diligent in preparing catheters and in teaching HHT patients to educate future caregivers on the importance of reducing the risk of air embolism. Nurses should teach patients to avoid scuba diving because of the theoretical increased risk of decompression sickness if pulmonary AVMs are present or undiagnosed.

**Antibiotic Prophylaxis and Pharmacological Considerations**

Nurses need to know that experts recommend antibiotic prophylaxis for dental and other bacteremic procedures in any HHT patients with current or previous pulmonary AVMs. Patients need education on increased risk for infection. Cerebral abscesses present a significant risk in HHT patients and the consequences are tragic. Current international guidelines recommend the American Heart Association guidelines for choice of antibiotic prophylaxis.

Nurses need to teach patients to avoid aspirin and nonsteroidal anti-inflammatory agents, if possible. If needed, anticoagulants and drugs that alter platelet function may be given, but the risk and benefits associated with these agents
should be discussed thoroughly by the health care team. Some HHT patients may have altered drug metabolism because of a decreased first-pass effect from hepatic AVMs, a situation that may decrease their need for some drugs. Nurses need to be aware of possible altered drug metabolism and to assess patients’ reactions to medications.

Flight-Related Complications

Patients with HHT and pulmonary AVMs often have low oxygen saturation and decreased hemoglobin and hematocrit levels. Traditionally, these parameters have been used to assess readiness for air travel. Mason and Shovlin, recognized experts in HHT and pulmonary medicine, found that flying is safe for most HHT patients. The researchers determined that most patients could fly without adverse events, even if the patients had abnormal oxygen saturation and anemia. The most reported adverse event was epistaxis, but even then the nosebleeding was self-limited. Because HHT patients may be at increased risk for thromboembolism, nurses should teach them the signs and symptoms of this entity. Patients should follow measures to prevent thrombus formation while on long flights.

Pregnancy-Related Concerns

In most women with HHT, pregnancies will be successful. However, data indicate that during pregnancy, women with HHT have a significantly increased mortality rate due to pulmonary AVM hemorrhage, strokes, and myocardial infarction as compared with those without HHT. Diagnosis and awareness of HHT and pulmonary AVMs before pregnancy are associated with increased survival for both mother and infant. When complications do occur, they usually arise in the second or third trimester because of the effects of the hemodynamic changes of pregnancy; namely, increased volume and cardiac output and reduced peripheral vascular resistance. Patients should be considered at high risk for complications and should be educated to immediately seek care if they have any new signs or symptoms, including hemoptysis or sudden dyspnea. If possible, screenings for pulmonary AVMs should be done before an HHT patient becomes pregnant. The only pregnant patients who need to be screened for cerebral AVMs are those with a family history of cerebral hemorrhage or cerebral symptoms. Shovlin et al also recommend that pregnant HHT patients should have magnetic resonance imaging to detect spinal AVMs, because the presence of spinal AVMs could preclude provision of epidural pain management. Last, during delivery, antibiotic prophylaxis is recommended as well as limiting a prolonged second stage of labor in women who have not had imaging to detect cerebral AVMs.

 Radiation Concerns

Patients with HHT can be exposed to a high amount of radiation during their lifetimes, and this risk can be mitigated by evaluation at an experienced center where imaging techniques can be optimized. Interventional procedures, such as embolizations and diagnostic CT scans, contribute the largest amount of cumulative exposure to radiation. Measures to decrease the cumulative lifetime dose are important to protect patients’ future health. Strategies to reduce exposure include using low-dose thoracic CTs and ultrasound and magnetic resonance imaging, when appropriate, instead of abdominal CT scans. Patients can be instructed to inform health care providers that the patients have a history of multiple exposures to radiation, thus allowing patients and providers to choose imaging techniques that are the least risky.

 Education and Support

Nurses need to know the available resources for HHT families. Nurses have an important role in encouraging HHT patients and the patients’ families to participate in research. Nurses can help accomplish such participation by educating patients and explaining the importance of the research, including evaluations at tertiary centers and participation in clinical trials and other studies. Patients need education and introduction to the HHT International website for resources to share with their future health care providers. Nurses can be instrumental in empowering patients to understand and advocate for the patients’ care, because many providers are not familiar with HHT. Some patients have even received erroneous, frightening diagnoses, such as pulmonary metastasis, after providers had misdiagnosed an AVM.

The severity of epistaxis can have a detrimental effect on quality of life and is associated with depression and anxiety. Nurses need to help patients cope with and lessen the psychological distress of the disease.
patients how to use the epistaxis screening scale to talk to health care providers will help the patients address threats to the quality of life.

Patients and their families may need resources to understand how to get other family members tested. Reinforcing the need to be evaluated at least once in the patient’s lifetime at an HHT Center of Excellence is imperative. Additionally, patients need support to gain control over their disease process and to realize that adherence to a treatment plan can result in a normal lifespan. Balancing information with encouragement and support is essential, especially when dealing with families who are considering diagnosis and treatment for children. The HHT Foundation can provide lists of local support groups and HHT-friendly health care providers in a patient’s area. See the Table for additional nursing interventions aimed at providing support and education to HHT families.

Summary

Providing care to patients and families who may have experienced a life-threatening event can be challenging, yet rewarding. HHT patients and their families require expert physical care, emotional support, and teaching to promote their future health. Critical care nurses must establish rapport and be compassionate and supportive, while simultaneously reinforcing the patient’s and the family’s coping and self-care skills. Because HHT can affect multiple family members, nurses have an excellent opportunity to facilitate a beneficial change for not only the patient, but also for the extended family. Many resources exist for the continuity of care after discharge. However, nursing skill is required to help patients and patients’ family members make the transition to the community setting and restoration of functional capacity. CCN

**Table** Nursing interventions and considerations for patients with HHT across the lifespan

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Teach patients that the worst complications of HHT can usually be prevented;</td>
<td>Patients have control over their disease process, and positive outcomes</td>
</tr>
<tr>
<td></td>
<td>most patients can live a normal lifespan after diagnosis and treatment</td>
<td>are related to follow-up</td>
</tr>
<tr>
<td></td>
<td>Teach patients the signs and symptoms of HHT and encourage family members</td>
<td>Reinforces positive coping skills and gives hope</td>
</tr>
<tr>
<td></td>
<td>to get tested</td>
<td>Fosters follow-up and mitigates family tragedies, thus increasing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>quality of life</td>
</tr>
<tr>
<td>Children</td>
<td>Provide age-appropriate explanations; encourage involvement of adults</td>
<td>Helps normalize the child’s experience and promotes positive coping</td>
</tr>
<tr>
<td></td>
<td>important in the child’s life (teachers, coaches, friends)</td>
<td>Decreases the child’s stress when the child has been emotionally</td>
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<td></td>
<td>Help the child anticipate needs, such as having</td>
<td>prepared and has the resources available</td>
</tr>
<tr>
<td></td>
<td>tissues ready for dealing with sudden epistaxis</td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>Encourage a visit to an HHT Center of Excellence every 5 years for follow-up</td>
<td>Ensures complete evaluation for the formation of new AVMs and</td>
</tr>
<tr>
<td></td>
<td>Instruct adults to watch for and report signs and symptoms of iron deficiency</td>
<td>complications that could otherwise be missed</td>
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<tr>
<td></td>
<td>Encourage adults to join a local support group and become involved in</td>
<td>Reminds patients that iron deficiency can cause them to feel generally</td>
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<td></td>
<td>patient support groups, if desired</td>
<td>ill, possibly affecting their quality of life</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Can help empower an HHT patient, possibly increasing subjective quality</td>
</tr>
<tr>
<td></td>
<td></td>
<td>of life</td>
</tr>
<tr>
<td>Adolescents</td>
<td>Teach this group how to handle epistaxis and strategies for explaining</td>
<td>Allows the adolescent a sense of control over his or her symptoms, can</td>
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<tr>
<td></td>
<td>their condition to peers</td>
<td>decrease feelings of powerlessness and encourages socialization</td>
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<tr>
<td></td>
<td>Involve teachers, coaches, and other leaders, if student agrees</td>
<td>Helps prevent shock in others at the frequency or severity of</td>
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<td></td>
<td>Teach teens to carry a small bottle of hydrogen</td>
<td>epistaxis, thus not calling attention to the teen’s situation, which can</td>
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<tr>
<td></td>
<td>peroxide for use in removing blood stains from clothing during epistaxis</td>
<td>be uncomfortable for adolescents</td>
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<tr>
<td></td>
<td></td>
<td>Can help decrease a teen’s stress because teens frequently can be self-</td>
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<td></td>
<td></td>
<td>conscious about personal appearance</td>
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<tr>
<td>Elderly</td>
<td>Teach geriatric HHT patients that they may have an increased risk of</td>
<td>Gives aging patients with HHT support and helps them adapt to their</td>
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<tr>
<td></td>
<td>gastrointestinal bleeding, telangiectasias, and liver AVMs that can increase</td>
<td>developmental level</td>
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<tr>
<td></td>
<td>the risk of heart failure</td>
<td>Increased symptoms, anemia, decreased oxygen saturation levels, and</td>
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<tr>
<td></td>
<td>Screen for depression; elderly HHT patients are at risk for depression</td>
<td>migraines can contribute to elderly HHT patients not feeling well, which</td>
</tr>
<tr>
<td></td>
<td></td>
<td>can contribute to their risk for depression</td>
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</tbody>
</table>

Abbreviations: AVM, arteriovenous malformation; HHT, hereditary hemorrhagic telangiectasia.

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Hereditary hemorrhagic telangiectasia (HHT) is a rare, autosomal dominant genetic disease that causes abnormal growth of blood vessels and, subsequently, life-threatening arteriovenous malformations (AVMs) in vital organs. Critical care nurses may be involved in several stages of an HHT patient’s care, whether care after a serious vascular event or after a procedure to correct one of the various vascular defects these patients experience. Nurses should develop a care plan with interventions that support, educate, and empower the patient and the patient’s family.

**Prevention of Air Embolism**

Nurses need to aggressively protect patients from air embolism. Nurses are cautioned to be extra diligent in preparing catheters and in teaching HHT patients to educate future caregivers on the importance of reducing the risk of air embolism. Nurses should teach patients to avoid scuba diving because of the theoretical increased risk of decompression sickness if pulmonary AVMs are present or undiagnosed.

**Antibiotic Prophylaxis and Pharmacological Considerations**

Nurses need to know that experts recommend antibiotic prophylaxis for dental and other bacteremic procedures in any HHT patients with current or previous pulmonary AVMs. Patients need education on increased risk for infection.

Nurses need to teach patients to avoid aspirin and nonsteroidal anti-inflammatory agents, if possible. If needed, anticoagulants and drugs that alter platelet function may be given, but the risk and benefits should be discussed thoroughly by the health care team. Some HHT patients may have altered drug metabolism because of a decreased first-pass effect from hepatic AVMs, a situation that may decrease their need for some drugs.

**Flight-Related Complications**

Patients with HHT and pulmonary AVMs often have low oxygen saturation and decreased hemoglobin and hematocrit levels. Traditionally, these parameters have been used to assess readiness for air travel. Because HHT patients may be at increased risk for thromboembolism, nurses should teach them the signs and symptoms of this entity. Patients should follow measures to prevent thrombus formation while on long flights.

**Pregnancy-Related Concerns**

In most women with HHT, pregnancies will be successful. Diagnosis and awareness of HHT and pulmonary AVMs before pregnancy are associated with increased survival for both mother and infant. When complications do occur, they usually arise in the second or third trimester because of the effects of the hemodynamic changes of pregnancy; namely, increased volume and cardiac output and reduced peripheral vascular resistance.

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