Mayo Surgeon Brings Cardiovascular Team to Haiti

Current events have again focused the spotlight on the difficulties faced by the people of Haiti. Much of the country does without much that is considered necessary infrastructure such as water, sewer systems, roads, and medical care.

Theodore J. Dubuque, Jr, MD, a retired St Louis, Missouri, general surgeon, helped develop the Center for the Rural Development of Milot (CRUDEM) Foundation, dedicated to providing medical care to the Haitian people. What began in 1986 as a modest gathering of health care professionals trying to provide basic medical assistance has grown into a community of medical teams who visit between September and June (July and August are too hot and humid for elective operations).

Mayo Clinic cardiovascular surgeon Thomas A. Orszulak, MD, a medical school student and general surgical resident of Dr Dubuque, joined the group in 1999. Each year, the mission and the people staffing it have increased the time, effort, and intensity of commitment to the people of Haiti.

The route from the airport to the mission goes through the residential and business areas surrounding Cap Haitien, gradually changing to a flatland of sugarcane. The road is pockmarked and crowded with people, animals, bicycles, and vehicles. The Hôpital Sacre Coeur is in the village of Milot in the northern horn of the country, which was also the site of a recent political uprising. Despite its poverty, the town has an exciting atmosphere, with people, music, and local artisans peddling their wares.

Arriving at the hospital, the visit begins with a rapid division of labor, simultaneously setting up the OR and ICU and seeing patients. Dr Orszulak outlines some of the difficulties: “Equipment rapidly deteriorates in the hot, humid Haitian climate. Transportation and communication are limited, so anticipated patients do not always arrive when expected.” Languages include French and Creole, so translators are frequently required.

Patients are prescreened by local physicians with echocardiography capability; the team cardiologist has a portable echo device that helps confirm the diagnosis and formulate a treatment plan. “With the facilities...
FDA Approves Nonprescription AEDs

Automatic external defibrillator (AED) use has improved survival after cardiac arrest. The success of the AED is attributable to the device’s availability to first responders who arrive at the scene of a cardiac arrest and deliver life-saving therapy within a few minutes after the arrest. In Rochester, use of the AED by first responders is associated with 40% of patients surviving an arrest and leaving the hospital neurologically intact,” says Stephen C. Hammill, MD, director of Heart Rhythm Services at Mayo Clinic in Rochester and 2004 president of NASPE/Heart Rhythm Society. “This is compared with less than 5% survival in large metropolitan areas.” Now that the AED has been approved by the US Food and Drug Administration for over-the-counter purchase without a prescription, the question is whether the excellent survival data associated with the AED in the hands of first responders can be translated to home use by untrained and inexperienced users. A recent article demonstrated that laypersons can be trained to use an AED safely and effectively, and training and equipping the public to attempt early defibrillation using the AED within a structured response system can increase the number of survivals to hospital discharge after cardiac arrest in public locations. Use of AEDs sold over-the-counter raises concerns, however. Ideally, the AED is placed in a convenient location within the home, used by a trained person, and applied within the first few minutes of a witnessed cardiac arrest. But an AED may provide a false sense of security and prevent use of 911.

Mayo Clinic is participating in the Home Automatic Defibrillator Trial, funded by the National Institutes of Health to test using AEDs versus calling 911 in high-risk patients after myocardial infarction. The results of the trial will be available in 2 years and determine if AEDs are equivalent to or better than the 911 system. “At this time, I believe the most important approach is to identify high-risk patients and make certain they see a cardiologist or an electrophysiologist to decide whether a home AED or an implantable cardioverter-defibrillator (ICD) is the better approach for preventing sudden death,” says Dr Hammill. Patients who would clearly benefit from use of the ICD are those with a prior myocardial infarction or a history of congestive heart failure associated with an ejection fraction of 30% or less. These patients need the ICD and not the AED.

For more, see the CV Update Web site.
Systemic amyloidosis is an uncommon syndrome caused by extracellular deposition of amyloid proteins in solid organs. Organs involved may include peripheral nerves, the gastrointestinal tract, kidneys, liver, skin, and lungs, as well as the heart. The presentation of systemic amyloidosis is varied and may include heart failure, nephrosis, hepatomegaly, peripheral or autonomic neuropathy, diarrhea or constipation, and soft tissue involvement with arthropathy and enlargement of the tongue and submandibular glands. “Patients often present with multisystem disease; hence, a multidisciplinary approach is often required for the evaluation and management of these complex patients,” according to Lyle J. Olson, MD, a cardiologist at Mayo Clinic in Rochester.

Recent advances in the management of systemic amyloidosis have greatly improved the outlook for affected individuals. To achieve optimal outcomes for patients with amyloidosis, the Dysproteinemia Clinic in the Division of Hematology collaborates with the Division of Cardiovascular Diseases. “In the past 3 decades, the Dysproteinemia Clinic has evaluated more than 3,800 patients with amyloidosis and evaluates approximately 200 new amyloidosis patients per year,” says Morie A. Gertz, MD, a hematologist at Mayo Clinic in Rochester and member of the Dysproteinemia Clinic consulting staff. “In this setting, state-of-the-art care is available, and patients have the opportunity to participate in clinical trials that evaluate new therapeutic interventions for the disorders that constitute the amyloid syndrome.”

The syndrome of amyloidosis has multiple different specific causes. However, all forms of amyloidosis are characterized by positive histologic staining with Congo red, which is a requirement for diagnosis. By light microscopy, amyloid deposits are amorphous extracellular deposits (Figure 1), and with polarized light, amyloid fibrils demonstrate a characteristic green birefringence. On electron microscopy, all forms of amyloid demonstrate a fibrillar appearance.

The finding of tissue amyloid deposits does not distinguish among the various forms of amyloidosis, including immunoglobulin light-chain disease (primary amyloidosis or AL), secondary amyloidosis (AA), familial amyloidosis (AF), or one of the many localized forms of amyloidosis (Table). Moreover, correct classification of the type of amyloidosis is central to the development of appropriate management, which in some cases may require chemotherapy and bone marrow transplantation, while in others observation alone may be optimal.

AL is derived from immunoglobulin light chains, and most individuals with this disorder have a detectable plasma cell dyscrasia, with a clonal population of plasma cells in the bone marrow. Other individuals with amyloidosis classified as AF, AA, and others do not have an associated plasma cell dyscrasia (unless an incidental monoclonal gammopathy of undetermined significance coexists in the same patient).

AA is exceedingly rare in the Western world and represents only 3% of cases with amyloidosis evaluated at Mayo Clinic. In North America, inherited forms of amyloidosis are more common than AA. In clinical practice, these disorders may be difficult to distinguish from AL. AF patients most often present with progressive axonal peripheral and autonomic neuropathy, but patients may present with cardiac, hepatic, or renal involvement with nephrosis.

The most common forms of AF are caused by mutations of the transthyretin molecule (TTR), of which more than 60 different mutations have been described. Importantly, in the Mayo Clinic series, half these patients do not have a family history of amyloid. Hence, the absence of a family history is not useful in the discrimination of AF from AL. Routine evaluation of patients with familial disease also includes screening for specific mutations. A specific type of AF has been
Figure 2. Cross-section of heart. Cardiac amyloidosis with massive wall thickening and biventricular cavity obliteration. The cardiac weight was 675g. LV, left ventricle; RV, right ventricle.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Treatment</th>
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<tr>
<td>Primary systemic amyloidosis (AL)</td>
<td>Stem cell therapy/Chemotherapy</td>
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<tr>
<td>Multiple myeloma associated amyloidosis (AL)</td>
<td>Stem cell therapy/Chemotherapy</td>
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<tr>
<td>Familial amyloidosis (AF)</td>
<td>Liver transplant</td>
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<tr>
<td>Senile amyloidosis (ASC)</td>
<td>Symptomatic</td>
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<td>Secondary amyloidosis (AA)</td>
<td>Directed at underlying disorder</td>
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Cardiac amyloidosis can also be caused by deposition of the wild-type TTR instead of a mutant TTR and has been referred to as “senile cardiac amyloidosis.” It has been described in autopsy studies in 8% to 25% of individuals older than 80 years. The clinical picture may be indistinguishable from cardiac involvement due to AL.

The heart is frequently involved in patients with AL or AF, and cardiac involvement is a common cause of morbidity and the most frequent cause of mortality (Figure 2). Cardiovascular morbidity associated with cardiac amyloidosis includes congestive heart failure, arrhythmias, conduction block, and orthostatic hypotension due to autonomic involvement. When heart failure is present, it is often associated with preserved systolic function and is caused by restrictive cardiomyopathy. Echocardiography has proven to be invaluable in the detection and characterization of cardiac involvement and for follow-up of disease progression. Confirmation of cardiac involvement and assessment of morphologic and hemodynamic features of mild, moderate, or severe disease are important for risk stratification, which contributes to clinical decision-making regarding the most appropriate therapeutic interventions. "Endomyocardial biopsy is performed in selected patients to confirm suspected cardiac involvement when echocardiographic findings are not characteristic or to establish the diagnosis when the biopsy findings from other organs are not definitive," says Dr Olson.

For amyloid cardiomyopathy, treatment considerations include pharmacotherapy and cardiac pacing in selected individuals. Congestive heart failure is often advanced and rapidly progressive. Diuretics are the mainstay of therapy, and patients may require dosing 3 times a day for adequate management of edema. Other medications routinely used in the management of patients with congestive heart failure due to other causes have limited efficacy in patients with cardiac amyloidosis because of systemic hypotension associated with autonomic nervous system disease, as well as reduced plasma oncotic pressure caused by hypoalbuminemia and hypoproteinemias associated with nephrosis. Orthostatic hypotension associated with amyloidosis is a difficult management problem. Elastic garments fitted to the lower extremities reduce edema, increase intravascular volume, and decrease the need for use of α-agonists to promote peripheral vasoconstriction and raise systemic blood pressure. Orthostatic hypotension may also require the use of fluorohydrocortisone to facilitate plasma volume expansion, but this strategy can exacerbate heart failure and supine hypertension. β-Blockers and angiotensin-converting enzyme inhibitors are of unproven efficacy in this syndrome and may not be well tolerated. Digitalis is not generally useful because systolic function of the heart is often preserved, and this agent has no known benefit for diastolic heart failure. The risk for digitalis toxicity may be increased. Similarly, calcium channel blockers can promote increased congestion and may have enhanced binding to amyloid fibrils that may promote cardiotoxicity.

Conduction system disease associated with amyloidosis is not uncommon and may present with presyncope, syncope, or orthostatism. Selected patients with symptomatic bradycardia due to sinus node...
A 58-year-old teacher who had coronary artery bypass graft surgery 2 years ago is now having increasing shortness of breath and leg swelling. After extensive evaluation, the cause for his debilitating symptoms is uncertain. A 24-year-old graduate student has a diagnosis of liver cirrhosis with swelling of the abdomen and abnormal liver function test results. Evaluation found constrictive pericarditis in both of these patients, and their symptoms were eliminated with pericardiectomy.

Constrictive pericarditis is a chronic syndrome consisting of obliteration of the pericardial cavity by fibrosis or granulation tissue, leading to the formation of tough scar tissue encasing the heart. Fifty years ago, most cases of constrictive pericarditis in the United States were infectious (especially tuberculosis) or idiopathic in etiology. The aging population and changing medical practice have altered the natural history of constrictive pericarditis in this country, and previous cardiac surgery is now the most common cause (29%) of this potentially curable disease.

Because of the varying potential etiologies, protean manifestations (edema, fatigue, dyspnea, ascites, pleural effusion), and additional comorbid conditions, pericarditis is often difficult to diagnose. “It is gratifying to make this diagnosis because constrictive pericarditis is an entirely curable disease,” according to Jae K. Oh, MD, a cardiologist at Mayo Clinic in Rochester. “Quality of life and longevity improve remarkably after pericardiectomy.”

Another difficulty in making the diagnosis is that constrictive pericarditis and restrictive cardiomyopathy have similar clinical presentations, and distinguishing between them can be challenging even for experienced clinicians. A classic scenario is a clinical picture of...
hepatic cirrhosis or liver function abnormalities but with distended neck veins and a pericardial knock. More than half the patients with an ultimate diagnosis of constrictive pericarditis are subjected to numerous cardiac and noncardiac procedures such as liver biopsy, bronchoscopy, exploration of the abdomen, and thoracocentesis before the diagnosis is made.

How can constriction be diagnosed reliably? Pericardial calcification on chest radiography is seen in 25% of patients with constrictive pericarditis (Figure 1). Constriction is likely if a patient with predominantly right heart failure has pericardial calcification, which requires further hemodynamic study by echocardiography or cardiac catheterization.

Cardiac catheterization has been the diagnostic gold standard for many years and is still performed in those patients whose diagnosis is in doubt after comprehensive noninvasive evaluation. However, a diagnosis can be made in many patients by comprehensive Doppler echocardiographic examination, usually the first step when constriction is suspected. “Characteristic hemodynamic findings during catheterization and Doppler echocardiographic assessment are caused by the dissociation of intrathoracic and intracardiac pressures and ventricular interdependence created by a rigid, noncompliant pericardium,” says Dr Oh. Normally, the change in intrathoracic pressure with respiration is fully transmitted to the intracardiac space. However, patients with a thick and noncompliant pericardium have less than full transmission of those pressure changes, resulting in respiratory variation in ventricular filling (Figure 2). The variation in filling of the left and right ventricles is reversed in constriction (not in myocardial disease) (Figure 3). Traditional hemodynamic criteria such as equalization of diastolic pressures are not specific enough to distinguish constriction from other myocardial diseases. Therefore, discordant systolic pressure changes of the left and right ventricles should be demonstrated to diagnose constrictive pericarditis if cardiac catheterization is used for hemodynamic evaluation.

These characteristic hemodynamic changes are also reliably demonstrated by 2-dimensional and Doppler echocardiography. The variation in ventricular filling is detected by changes in mitral velocities by Doppler echocardiography (usually more than 25% variation).

Respiratory variations in Doppler echocardiographic mitral flow velocities in patients with constriction typically not found in those with restrictive cardiomyopathies include 1) 25% or more expiratory increase in mitral E velocity and 2) expiratory decrease in hepatic vein diastolic flow velocity in conjunction with 3) 25% or more increase in diastolic flow reversals compared with inspiratory velocities.

Some patients with constriction may not exhibit typical respiratory variations. “Volume loading accentuates typical hemodynamic findings in most; however, a subset of patients with markedly elevated left atrial pressures demonstrates hemodynamic abnormalities only after preload reduction,” says Dr Oh. Scarring of the epicardial surface may create a component of myocardial restriction in addition to pericardial constriction (further confusing the
adhesion of the pericardium to the myocardium, Risk of pericardiectomy is related to the degree of evidence of constrictive pericarditis. In patients with clinical and/or hemodynamic should not exclude the consideration of consideration thickness; therefore, normal pericardial thickness with confirmed constriction have normal pericardial and hepatic congestion. Approximately 15% of patients tubular-shaped ventricles, ascites, pleural effusions, CT or MRI imaging in constriction include distorted, patient is in an irregular rhythm such as atrial cannot demonstrate calcification. Furthermore, MRI resonance imaging (MRI) may be performed. MRI is superior at delineating pericardial fluid from tissue but contrast material is contraindicated, magnetic Rochester. In those patients for whom iodinated diagnosis (Figure 6). “The demonstration of thickened pericardial effusion, and infiltrative myopathies can all be detected by CT imaging and may contribute to obliterati of the pericardial space by scar tissue or tumor, Pericardial thickening, subtle calcification, obliteration of the pericardium, including relapsing pericarditis. A more recent advance in tissue Doppler imaging may detect pericardial thickening (Figure 5), computed tomography (CT) is used routinely for imaging of the pericardium when constriction is suspected. Pericardial thickening, subtle calcification, obliteration of the pericardial space by scar tissue or tumor, pericardial effusion, and infiltrative myopathies can all be detected by CT imaging and may contribute to diagnosis (Figure 6). “The demonstration of thickened pericardium with or without calcification is diagnostic of constriction in the right clinical setting,” according to Jerome F. Breen, MD, a radiologist at Mayo Clinic in Rochester. In those patients for whom iodinated contrast material is contraindicated, magnetic resonance imaging (MRI) may be performed. MRI is superior at delineating pericardial fluid from tissue but cannot demonstrate calcification. Furthermore, MRI requires gated images that are difficult to obtain if the patient is in an irregular rhythm such as atrial fibrillation. Additional findings that may be seen with CT or MRI imaging in constriction include distorted, tubular-shaped ventricles, ascites, pleural effusions, and hepatic congestion. Approximately 15% of patients with confirmed constriction have normal pericardial thickness; therefore, normal pericardial thickness should not exclude the consideration of consideration in patients with clinical and/or hemodynamic evidence of constrictive pericarditis.

Treatment is usually (but not invariably) surgical. Risk of pericardiectomy is related to the degree of adhesion of the pericardium to the myocardium, calcification of adjacent myocardium, and the degree of atrophy of the underlying myocardium; patients with the most severe disease are at highest surgical risk (Figure 7). “Previous radiotherapy is the most powerful predictor of surgical outcome at Mayo,” says Hartzell V. Schaff, MD, chair of the Division of Cardiovascular Surgery. “Mediastinal fibrosis limits resectability, and chest wall fibrosis delays healing.” Long-term survival in these patients is additionally compromised by recurrent malignancy, impaired immunologic status, additional myocardial involvement, and pulmonary fibrosis. Previously placed bypass grafts are jeopardized, especially in patients with densely adherent pericardium. Ultrasonic débridement of calcified pericardium may be necessary. Radical pericardiectomy should be attempted; incomplete pericardiectomy may result in regional constriction, which may have progressive hemodynamic consequences requiring additional surgery.

In a subset of patients with a recent onset of symptoms (within 6 months), constrictive pericarditis can be managed medically. The pericardium is thickened due to inflammation, but permanent scar has not yet developed. Normalization of thickened pericardium occurs after 1 to 2 months of treatment with nonsteroidal or steroidal anti-inflammatory agents. Most patients with effusive-constrictive pericarditis probably belong to this category of having transient treatable constriction.

A group of cardiologists, radiologists, pathologists, and cardiac surgeons with a special interest in pericardial diseases form the Pericardiology Interest Group at Mayo Clinic in Rochester. The group has the multidisciplinary expertise to manage these patients with the most intriguing and often difficult problems of the pericardium, including relapsing pericarditis, cardiac tamponade, effusive-constrictive pericarditis, and chronic constrictive pericarditis. With better understanding of the pathophysiology and hemodynamics of constrictive pericarditis, this condition is diagnosed more reliably, resulting in a marked increase in the number of patients who benefit from pericardiectomy.
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Mayo Clinic cardiology fellows who completed their training this year: Seated, Sabrina D. Phillips, MD, Heart Place, Baylor University Medical Center, Dallas; Andre Terzic, MD, PhD, co-program director; Guy S. Reeder, MD, program director; Chari Y. T. Hart, MD, Queen’s Medical Center, Honolulu; and Deepak R. Talreja, MD, Eastern Virginia Medical School, Cardiovascular Associates, Norfolk. Standing, Sean C. Halligan, MD, Mayo Regional Practice, LaCrosse; Emmanuel S. Brilakis, MD, University of Texas Southwestern Medical School and Dallas VA Medical Center; Gurpreet S. Sandhu, MD, PhD, Mayo Clinic, Rochester; and Mark A. Milton, MD, Heart Center/St John Medical Center, Tulsa. Not pictured: Ashwani K. Bedi, MD, Houston Arrhythmia Associates, Houston; Shang-Chiun Lee, MD, St. John’s Health Center, Springfield, Mo; David H. Fitzemenmaier II, MD, Vascular Care of Maine, Bangor; and Lambert A. Wu, MD, Stormont-Vail Health Center, Topeka.

The 2004 Department of Medicine Recognition Awards were presented September 21, 2004, by Nicholas F. LaRusso, MD, chair of the Department of Medicine at Mayo Clinic in Rochester. Honored from the Division of Cardiology were Mark J. Callahan, MD, who received the department’s Laureate Award; Carole A. Warnes, MD, who received the Henry S. Plummer Distinguished Physician Award; and David R. Holmes, MD, who received the Research Career Achievement Award.