Mayo Clinic Announces
New Center for Cardiovascular Sciences

Mayo Clinic has announced the formation of the Center for Cardiovascular Sciences, created by the merger of the departments of cardiovascular diseases and cardiovascular surgery along with the division of pediatric cardiology. This system-wide merger encompasses the practices at Mayo Clinic in Rochester, Minnesota, Mayo Clinic in Florida, Mayo Clinic in Arizona, and the Mayo Clinic Health System, and will be jointly led by Charanjit S. Rihal, MD, MBA, chair of cardiovascular disease, and Joseph A. Dearani, MD, chair of cardiovascular surgery.

The goal of this reorganization is to integrate the practice to better reflect cardiovascular services as they are actually provided. “The delivery of our services is increasingly collaborative. For example, the assessment and treatment of structural heart disease is currently a cooperative effort by cardiologists and cardiovascular surgeons, and many of the treatment modalities we have to offer are combined operative and percutaneous procedures,” says Dr Rihal. Additionally, this reorganization will be better able to provide seamless care to patients among all the Mayo campuses, important in today’s mobile society.

The center will also provide for better integration of scientific research across all Mayo Clinic sites, with shared protocols, databases, and study coordinators. “This reorganization will allow us to rapidly develop and deliver innovations and new technologies to patients at all Mayo sites,” according to Dr Dearani. Additionally, the merger will provide more opportunities for fellows in cardiology and cardiovascular surgery training programs to expand their training experience across the Mayo Clinic enterprise. “We look forward to system-wide collaboration and planning,” says Dr Dearani.

For more information, to schedule an appointment, or to contact a provider, visit mayoclinic.org/medicalprofs or phone Mayo Clinic in Phoenix/Scottsdale, Arizona, at 866-629-6362; Mayo Clinic in Jacksonville, Florida, at 800-634-1417; or Mayo Clinic in Rochester, Minnesota, at 800-533-1564.
The Heart-Brain Clinic: Optimal Team-Based Coordinated Care

Heart-Brain Clinic
Mayo Clinic in Rochester, Minnesota
Naser M. Ammash, MD, Codirector
Robert D. Brown Jr, MD, MPH, Codirector
Cardiology
Samuel J. Asirvatham, MD
Paul A. Friedman, MD
David R. Holmes Jr, MD
Thomas M. Munger, MD
Guy S. Reeder, MD
Neurology
Kelly D. Flemming, MD
Jimmy R. Fulgham, MD
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Jonathan Graff-Radford, MD
Irene Meissner, MD
George W. Petty, MD
Lindsay N. Williams, MD
Alejandro A. Rabinstein, MD

Ischemic cerebrovascular events such as stroke and transient ischemic attack (TIA) are the most feared complications of cardiovascular disease. They are a focus of concern for all patients and for physicians and health care providers often represent a conundrum in both diagnosis and treatment. Is the TIA a result of paradoxical embolus across a patent foramen ovale (PFO)? Is the embolic stroke caused by a thrombus in the left atrial appendage (LAA) in an individual with atrial fibrillation (AF)? Establishment of a cause-and-effect relationship frequently is difficult but affects diagnostic and treatment strategies made even more problematic because some patients have multiple coexistent substrates. To address these issues and as a logical development of team-based care, Mayo Clinic in Rochester, Minnesota, has created the Heart-Brain Clinic (HBC), which provides multidisciplinary evaluations to individuals who have had neurologic symptoms that may be attributable to a cardiac etiology such as PFO or AF. Specialists from the Department of Cardiovascular Diseases and the Division of Stroke and Cerebrovascular Disease in the Department of Neurology collaboratively evaluate patients, directing the further evaluation, educating patients and families, and making a joint recommendation for management.

Atrial Fibrillation
Atrial fibrillation is associated with up to 20% of strokes, particularly in older patients. This incidence may be even higher in patients who have silent short episodes of AF. Although anticoagulation has been found to be effective for stroke prevention, it may not be prescribed or used in up to 50% of patients at risk. Indeed, in patients at highest risk of stroke, the use of routine anticoagulation may be even less because of various clinical and patient issues and concerns. The role of LAA thrombus in the pathophysiology of stroke in patients with nonvalvular AF has long been recognized. Based on autopsy and echocardiographic studies, the vast majority of strokes in these individuals are believed to be embolic in nature. LAA thrombus formation in AF may be related to the anatomy of the left atrium and pectinate muscles, inflammation, and fibrosis, hence the interest in developing site-specific therapy such as LAA occlusion, with either percutaneous devices or ligation. The appeal of these approaches is greatest in those patients for whom chronic anticoagulation poses special risks. Standard anticoagulation regimens may be problematic in individuals prone to falls, those who have had prior brain or systemic hemorrhage, or those with extensive renal or hepatic disease, although these patients may be at high risk for stroke and have the most to gain by stroke prevention.

Also problematic is establishing causality in the individual with ischemic stroke and sinus rhythm, but with suspected or documented paroxysmal atrial fibrillation. The prevalence of AF increases with age, as does the risk of comorbid conditions that also increase the risk of ischemic stroke such as atheromatous carotid or vertebral disease, small artery occlusive disease in the brain, or other cardiac conditions. Therefore, individuals with ischemic stroke and AF benefit from comprehensive evaluation to consider other causes before recommending a specific treatment course.

Patent Foramen Ovale
The prevalence of PFO in the adult general population may be as high as 25%; usually these interatrial shunts are asymptomatic and of no hemodynamic importance. Until the advent of echocardiography, it was difficult to diagnose PFO antemortem. Transthoracic imaging, especially with agitated saline contrast injection, transesophageal echocardiography, and transcranial Doppler, is widely used to identify and characterize PFO (Figure). Case reports from the echocardiographic literature illustrate venous
or actual failure of the selected treatment strategy is unknown. The effectiveness of the new oral anticoagulants in preventing stroke in patients with PFO has not been evaluated.

Bringing together expertise in cardiology and neurology in the same clinical setting allows these complex clinical issues to be seamlessly addressed for patients and their families. After the initial consultations, the multidisciplinary group of caregivers recommends and implements any additional testing and provides a recommendation regarding the optimal management approach.

For more information about the Heart-Brain Clinic at Mayo Clinic in Rochester, please call 507-284-1588 (neurology) or 507-255-4244 (cardiology).

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**Figure.** A 63-year-old woman who had a remote history of migraine headache awakened with a headache with visual aura, as well as nausea, vomiting, and incoordination. She was a former smoker but had no history of hypertension, estrogen replacement, or family history of stroke. A and B, MRI demonstrated a left cerebellar infarct. C and D, Transesophageal echocardiography demonstrated a large PFO (arrow) with an atrial septal aneurysm. E, Contrast injection demonstrated generous flow across the PFO (arrow) with Valsalva. Percutaneous closure was performed. LA, left atrium; RA, right atrium.

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**RECOGNITION**

**Mayo Clinic in Arizona Receives Get With the Guidelines—Heart Failure Gold Plus Quality Achievement Award**

Mayo Clinic Arizona has received the American Heart Association/American Stroke Association’s Get With the Guidelines—Heart Failure Gold Plus Quality Achievement Award. The award recognizes Mayo Clinic’s commitment and success in implementing the highest quality care for heart failure patients according to evidence-based guidelines. “This designation was achieved through the collaborative effort of every member of Mayo’s heart failure team,” says Robert Scott, MD, a cardiologist at Mayo Clinic in Arizona, who is the medical director for pulmonary hypertension and consultant in advanced heart failure/transplant cardiology. “This is an award we achieved together and will celebrate together.” Certification standards help organize the disease management program to maintain a consistently high level of quality, using effective data-driven performance improvement.
The past 30 years have seen much progress in the diagnosis and treatment of the Marfan syndrome and related disorders. When Victor McKusick first described Marfan syndrome in 1955, he predicted that these patients with serious ocular, musculoskeletal, and cardiovascular problems would eventually be found to have a mutation in a structural connective tissue protein. In 1991, his prediction was fulfilled when mutations in a component of elastic microfibrils, fibrillin 1 (FBN1), were found to be the cause of Marfan syndrome. Further research showed that apart from its structural role, fibrillin also has a regulatory function through its interaction with transforming growth factor β (TGF-β), a signaling protein involved in many connective tissue functions. Working with the Marfan mouse model, investigators found that FBN1 mutations result in excessive TGF-β signaling. The Marfan phenotype (long limbs, scoliosis, pectus deformity, severe myopia, aortic aneurysm, valvular regurgitation) is the result of disordered TGF-β signaling mediated by the angiotensin II type 1 (AT1) receptor (Figures 1 and 2).

Even before the causative mutation was identified, clinical care for Marfan syndrome patients had advanced. Preventive aortic repair became effective when composite graft repair of the ascending aorta began to be widely used in the 1970s (Figure 3). β-Blockers were shown to slow the rate of aortic enlargement in the 1990s, and clinical care that incorporated medical aortic protection and timely preventive surgery led to a major increase in life expectancy.

The discovery of a signaling pathway malfunction indicated that there was more to the Marfan syndrome than structurally weak connective tissue. Investigations using the mouse model demonstrated that when the AT1 receptor was blocked with losartan, young Marfan mice did not develop the expected phenotypic changes, including aortic aneurysm. An early human trial in infants with severe FBN1 mutations confirmed that losartan also reduced the rate of aortic enlargement in humans. Several trials of losartan in young people have confirmed the effectiveness of losartan, although important questions remain and will be addressed in future trials.

Additional mutations causing thoracic aortic aneurysm continue to be identified. Some encode for proteins in the extracellular matrix, others for proteins involved in cellular signaling, and others for aortic smooth muscle contractile proteins. Patients often have a marfanoid phenotype, but many have a completely normal appearance with no syndromic features. Genetic testing is often required for an accurate diagnosis.
Diagnosis

The Marfan and Thoracic Aorta Clinic at Mayo Clinic in Rochester, Minnesota, has provided care for patients with Marfan syndrome and related disorders since 2002. Patients are seen at a joint cardiology and medical genetics appointment, where the medical history, family history, clinical examination, and imaging results are reviewed.

The diagnostic criteria for Marfan syndrome are summarized in Tables 1 and 2 on page 6. Genetic testing is commonly needed because of overlap in the clinical features between Marfan syndrome and other genetic aorticopathies.

Treatment

When a specific genetic diagnosis is made, the clinical management is guided by that diagnosis. Examples of conditions that appear similar but have specific management are Loeys-Dietz syndrome and vascular Ehlers-Danlos syndrome (Table 3 on page 6). Cases without a definite diagnosis often require multidisciplinary discussion. The care of an individual patient may involve experts in adult and pediatric cardiology, clinical and laboratory genetics, cardiac and vascular imaging, cardiovascular surgery, and cardiovascular pathology.

Patients with Marfan syndrome and related disorders require multidisciplinary care. Physical activity modifications and either a β-blocker or losartan help to protect the aorta. Preventive aortic repair with either a composite graft or a valve-sparing operation is done when the aorta reaches a diameter.
between 40 and 50 mm. Earlier preventive surgery is recommended when there is a family history of aortic dissection or when there has been rapid growth of the aorta. Ocular and musculoskeletal problems often need specialty care.

Effective treatment for previously fatal cardiovascular disease has resulted in longer lives for patients with Marfan syndrome. Their care involves lifelong monitoring of cardiovascular health as well as management of noncardiovascular problems. A number of dedicated clinics throughout the United States now help with this care. The Mayo Marfan and Thoracic Aorta Clinic has been selected by the Marfan Foundation to host the Marfan Foundation 32nd Annual Family Conference. For additional information visit www.marfan.org.

### Table 1. Marfan Syndrome Diagnostic Criteria

**Negative family history**
1. The presence of an aortic root aneurysm (with a z score ≥2 when standardized to age and body size) or aortic dissection and ectopia lentis
2. The presence of an aortic root aneurysm (with a z score ≥2 when standardized to age and body size) or aortic dissection and the identification of the FBN1 gene mutation
3. The presence of an aortic root aneurysm (with a z score ≥2 when standardized to age and body size) or aortic dissection and the presence of systemic features with a score of 7 or more points (Table 2)
4. The presence of ecopia lentis and identification of the FBN1 gene mutation previously associated with aortic disease

**Positive family history**
1. Ectopia lentis
2. Systemic features with a score of 7 or more points
3. Aortic root dilation (with a z score ≥2 for adults aged 20 years or older or a z score ≥3 for patients younger than 20 years)

### Table 2. Systemic Feature Scoring Table

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist AND thumb sign</td>
<td>3</td>
</tr>
<tr>
<td>Wrist OR thumb sign</td>
<td>1</td>
</tr>
<tr>
<td>Pectus carinatum deformity</td>
<td>2</td>
</tr>
<tr>
<td>Pectus excavatum or chest asymmetry</td>
<td>1</td>
</tr>
<tr>
<td>Hindfoot deformity</td>
<td>2</td>
</tr>
<tr>
<td>Plain flat foot (pes planus)</td>
<td>1</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>2</td>
</tr>
<tr>
<td>Dural ectasia</td>
<td>1</td>
</tr>
<tr>
<td>Protrusio acetabulae</td>
<td>2</td>
</tr>
<tr>
<td>Reduced upper segment/lower segment and increased armspan/height without severe scoliosis</td>
<td>1</td>
</tr>
<tr>
<td>Scoliosis ≥20°or thoracolumbar kyphosis</td>
<td>1</td>
</tr>
<tr>
<td>Reduced elbow extension</td>
<td>1</td>
</tr>
<tr>
<td>3 of 5 facial features:</td>
<td>1</td>
</tr>
<tr>
<td>• Dolichocephaly</td>
<td>1</td>
</tr>
<tr>
<td>• Malar hypoplasia</td>
<td>1</td>
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<tr>
<td>• Enophthalmos</td>
<td>1</td>
</tr>
<tr>
<td>• Retrogнатhia</td>
<td>1</td>
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<tr>
<td>• Down-slanting palpebral fissures</td>
<td>1</td>
</tr>
<tr>
<td>Skin striae</td>
<td>1</td>
</tr>
<tr>
<td>Myopia (−0.3 diopter)</td>
<td>1</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total score:</strong></td>
<td></td>
</tr>
<tr>
<td>Systemic score ≥7 = criteria required for diagnosis</td>
<td>___</td>
</tr>
</tbody>
</table>

### Table 3. Marfan Syndrome Differential Diagnosis

**Homocystinuria**
MASS phenotype (myopia, mitral valve prolapse, mild aortic enlargement, nonspecific skin and skeletal features)

**Vascular Ehlers-Danlos syndrome**

**Stickler syndrome**

**Congenital contractual arachnodactyly (Beals syndrome)**

**Familial thoracic aortic aneurysm**

**Congenital bicuspid aortic valve disease with associated aortopathy**

**Loeys-Dietz syndrome**
Named Professorships
Margaret M. Redfield, MD (right), has been named the Walter and Leonore Annenberg Professor of Cardiology and Critical Care in Honor of Dr. Raymond Gibbons. Jae K. Oh, MD (left), has been named the Samsung Professor of Cardiovascular Diseases. Consultants are appointed to named professorships through nomination and endorsement of their peers and then confirmed by Mayo Clinic senior leadership. Appointed individuals are recognized for distinguished achievement in their specialty areas and service to the institution. The professorships are named in honor of Mayo Clinic benefactors who recognize Mayo’s role in pursuing answers in health and medicine.

RECOGNITION
John P. Bois, MD, fellow in cardiovascular disease at Mayo Clinic in Rochester, Minnesota, has received the Mayo Brothers Distinguished Fellowship Award for 2016. This is the most prestigious award given by the Mayo School of Graduate Medical Education and is based on the qualities associated with the founders, Drs. William and Charles Mayo, including outstanding clinical performance, humanitarianism, and scholarly activity. Dr. Bois graduated from Dartmouth College and Mayo Clinic College of Medicine and is joining the Mayo Clinic staff in July after completing his training.

Karol E. Watson, MD, PhD (left), professor of medicine/cardiology and codirector of the Program in Preventive Cardiology at the Geffen School of Medicine at University of California, Los Angeles delivered the 10th annual Gerald T. Gau Lecture at Mayo Clinic in Rochester, Minnesota. Her presentation was titled “Disparities in Cardiovascular Care: Causes, Consequences and Potential Cures.” This lectureship is in honor of Gerald T. Gau MD (right), emeritus staff, who dedicated his career to the field of preventive cardiology.

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CME Program Announcement
Mayo Clinic’s Center for Cardiovascular Sciences announces a new and unique CME program—The Genetics of Heart & Vascular Diseases—to be held October 28-29, 2016, at the Ritz-Carlton on Amelia Island, Florida. Experts in the field of cardiovascular genetics will discuss the current role of genetics in the diagnosis, risk stratification, and treatment of diseases that affect the heart and vasculature. Course directors Michael J. Ackerman, MD, PhD, Naveen Pereira, MD, and Iftikhar J. Kullo, MD, are all experts in their areas of cardiovascular disease in general and genetic cardiology in particular. Lecture topics include

- Genetics and Genetic Testing 101
- Cardiomyopathies: Diagnostic, Prognostic, and Therapeutic
- Genetic Counseling Implications of Genetic Testing
- “Genetic Purgatory”
- Pharmacogenetics of Coronary Artery Disease
- Genetics of Lipidemias and the Aortopathies

At the end of the course, attendees will be able to summarize the probabilistic nature of genetic testing and develop a strategy to manage the variant of uncertain significance test result; identify the role of genetic testing in the diagnosis and pathophysiology of the heritable cardiomyopathies, channelopathies, and aortopathies; define genetic markers of atherosclerosis and their role in risk stratification of coronary artery disease; identify the genetic basis of heritable causes of the hyperlipidemias and implications for prevention and familial screening; and define the role of inheritance in cardiovascular drug response and to utilize genetics to minimize adverse events and maximize drug efficacy.

Mayo Clinic College of Medicine designates this live activity for a maximum of 13.75 AMA PRA Category 1 credits. More information is available at ce.mayo.edu/cardiovascular-diseases/content/genetics-heart-vascular-disease-2016.

Michael J. Ackerman, MD, PhD, a pediatric cardiologist at Mayo Clinic in Rochester and the Windland Smith Rice Cardiovascular Genomics Research Professor received the 2015 Distinguished Mayo Clinician Award. This award recognizes individuals who make outstanding contributions in patient care and embody Mayo’s primary value: The needs of the patient come first.
Continuing Medical Education, Mayo Clinic
For additional information:
Web: https://ce.mayo.edu/cardiovascular-diseases
Email: cvcme@mayo.edu
Phone: 800-283-6296, 507-266-0677, or 507-266-6703

Cardiac Rhythm Device Summit: Implantation, Management, and Follow-up
Jun 17-19, 2016, Chicago, IL

Success With Failure: Strategies for the Evaluation and Treatment of Heart Failure in Clinical Practice
Jun 18-20, 2016, Bolton Landing, NY

Jul 18-21, 2016, Vail, CO

Cardiology Update 2016: The Heart of the Matter
Aug 4-7, 2016, Sedona, AZ

Marfan Foundation 32nd Annual Family Conference
Aug 4-7, 2016, Rochester, MN

13th Annual Mayo Clinic Electrophysiology Board Review Course
Aug 13-15, 2016, Rochester, MN

5th Annual Mayo Clinic Pediatric Cardiology 2016 Review Course
Aug 21-26, 2016, Dana Point, CA

21st Annual Mayo Clinic Cardiovascular Board Review and Recertification Course Optional Echo Focus Pre-Course Session
Aug 26-31, 2016, Rochester, MN

Challenges in Clinical Cardiology: A Case-Based Update
Sep 9-11, 2016, Chicago, IL

Advanced Catheter Ablation: New Tips, Techniques and Technologies for Complex Arrhythmias
Sep 10-13, 2016, Chicago, IL

13th Annual Mayo Clinic Interventional Cardiology Board Review Course
Sep 16-18, 2016, Rochester, MN

Echo for the Sonographer in the City of Rivers: Practical Review of Valvular Heart Disease
Sep 24-25, 2016, Pittsburgh, PA

Innovations in Atrial Fibrillation: Detection and Management
Sep 24-25, 2016, Seattle, WA

Internal Medicine Review for Nurse Practitioners, Physician Assistants, and Primary Care Providers
Sep 28-30, 2016, Rochester, MN

Heart Disease in Women: A New Era of Understanding, Recognition, Prevention, Diagnosis, and Treatment
Oct 8-9, 2016, Rochester, MN

26th Annual Cases in Echocardiography, Cardio CT and MRI
Oct 19-22, 2016, Napa, CA

Cardiovascular Medicine 2016: Updates for Practitioners From Brigham and Women's Hospital and Mayo Clinic
Oct 21-22, 2016, Boston, MA

7th Annual Cardiology Conference for Health Care Professionals
Oct 22-23, 2016, Wisconsin Dells, WI

The Genetics of Heart and Vascular Disease
Oct 28-29, 2016, Amelia Island, FL

Mayo Clinic Update in Echocardiography: Role of Echo From Prevention to Intervention
Nov 3-6, 2016, Phoenix, AZ

32nd Annual Echocardiography in Pediatric and Adult Congenital Heart Disease
Nov 3-6, 2016, Phoenix, AZ

AHA—The Heart Brain Clinic Symposium
Nov 12-16, 2016, New Orleans, LA

Coronary Artery Disease: Prevention, Detection, and Treatment
Nov 18-20, 2016, Las Vegas, NV

5th Annual ECG and Heart Rhythm: A Case-Based Approach
Dec 1-4, 2016, Scottsdale, AZ

Echo on Marco Island: Case-Based Approach
Dec 1-4, 2016, Marco Island, FL

9th Annual The Heart Beat of Cardiology: Practical Application of Echocardiography
Dec 8-10, 2016, Chicago, IL

CARDIOVASCULAR SELF-STUDY
https://cardiovascular.education-registration.com/selfstudy
www.celinks.mayo.edu/cme/cvselfstudy

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800-533-1564

Resources
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Clinical trials, CME, Grand Rounds, scientific videos, and online referrals

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Bookmark our Medical Professional Video Center Watch Grand Rounds lectures and other presentations and videos describing advances in disease and condition treatment, procedures, and surgeries: http://www.mayoclinic.org/medical-professionals/video-center

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