**Tricuspid Regurgitation**

*Setting Standards for Diagnosis, Repair & Replacement*

The Valve Team at Washington University School of Medicine is among the first in the world to use a transfemoral transcatheter device for the treatment of severe tricuspid regurgitation (TR).

“In the middle of the COVID pandemic, we submitted a request to the Food & Drug Administration (FDA) for “expanded access” — or compassionate use — of the Intrepid™ mitral valve system to treat an elderly gentleman who had had three previous bypass surgeries and was experiencing severe TR,” said interventional cardiologist Alan Zajarias, MD, co-director of the Washington University/Barnes-Jewish Hospital Center for Valvular Heart Disease. “We used a transfemoral approach and it worked beautifully! We’re now working to make this an option for other patients.”

The procedure was the fifth in the country of using the manufactured mitral valve for transcatheter tricuspid valve replacement. Six months ago, Dr. Zajarias, along with cardiovascular surgeon Puja Kachroo, MD, and other colleagues, performed the same procedure on a second patient, a female diagnosed with severe pulmonary hypertension. She also was granted FDA-expanded access approval and is doing well.

“We have made great strides in aortic and mitral valve repair and replacement,” said Dr. Zajarias. “Now there’s raised awareness that tricuspid valve problems are not as benign as we thought, and we need to better understand who will benefit from these procedures. We have several new patients a week that have severe TR, and while surgery is considered the standard of care, we see good options on the horizon for transcatheter repair and replacement that are currently being evaluated in clinical trials.”

In the United States, there are no FDA-approved devices for catheter-based tricuspid valve replacement or repair. While some devices exist that can repair the valves, none are FDA-approved for use in the United States. Dr. Zajarias believes that could change within the next two to three years. The Washington University Valve team has joined the CLASP-2TR study, a large, multi-center clinical trial evaluating the Pascal Transcatheter Tricuspid Valve Repair (TTVR) System. The device was approved for use in Europe last year.

As the field rapidly evolves, Washington University cardiologists are leading efforts to establish standardization of image acquisition for valvular heart disease. Nishath Quader, MD, chair of the Interventional Echo Council for the American Society of Echocardiography, said, “When it comes to assessing patients for percutaneous valve therapies, there appears to be a lot of discrepancies in the screening TEE. The Council just published guidelines that will standardize the images needed for tricuspid regurgitation."

Continued on page 2
Tricuspid Regurgitation
Continued from page 1

valve analysis prior to considering patients for tricuspid valve therapies.”

Majesh Makan, MD, associate director of the Cardiac Diagnostic Laboratory, already is working to implement new protocols for TR analysis here at Washington University/Barnes-Jewish Hospital. “Transesophageal echocardiography (TEE) is very challenging in obese and elderly patients,” he noted. “It takes an experienced sonographer to get all of the images necessary to understand the etiology and severity of TR and TV pathologies. With Dr. Quader’s efforts to develop national guidelines, we have a jumpstart in implementing those here.”

“I’m very optimistic that with new imaging guidelines, we can accurately diagnose TR earlier and determine who is a good candidate for surgery or transcatheter therapies,” said Dr. Zajarias. “We envision that better diagnosis, early detection and new devices coming soon will help lower the risk of heart failure, hospitalizations, or death as a result of severe tricuspid valve regurgitation.”

Treatment of aortic stenosis continues to evolve. In addition to Drs. Zajarias, Quader and Makan, other members of the valve team include cardiologists Marc Sintek, MD, and John Lasala, MD, PhD, as well as cardiovascular surgeons Puja Kachroo, MD; Spencer Melby, MD; and Harold Roberts, Jr., MD.
At Washington University School of Medicine, we once again are raising the profile of education as a vibrant component within the Cardiovascular Division. I recently assumed a new role as Associate Chief for Education. In addition to fellowship program educational activities, this role brings together division-wide educational series, Grand Rounds, symposiums, educational outreach to community physicians, faculty development and mentoring activities, and core curriculum for medical residency training under one umbrella.

Advancing educational opportunities within the field of cardiovascular medicine has been a long-standing passion of mine. Through such programs, we can share, advance, and transform cardiovascular care to enhance patient outcomes. By melding various educational opportunities together, we can readily share resources and best educational practices.

I’ve been a member of the American College of Cardiology’s Program Director and Graduate Medical Educator Council for several years. In 2019 and 2020, I was privileged to serve as chair of the ACC’s Annual Scientific Session. This year, I am chair-elect of the ACC’s Lifelong Learning Oversight Committee, which guides the College’s educational portfolio. Other faculty also are involved in education at the national level. Prashanth Thakker, MD, our Associate Fellowship Program Director for Program Development, leads the ACC’s Fellows in Training Section Leadership Council. Abhinav Diwan, MD, our Director of the T32-supported Principles in Cardiovascular Research Training Program, chairs the ACC’s Research Fellowship Awards Committee. Other faculty are actively involved in state and national organizations.

Through research, education, and clinical care, we advance knowledge and therapeutics. I’m excited that many here share my passion to identify and advocate for novel ways that enhance lifelong educational activities.

Alumni Update

Paul R. Eisenberg, MD, MPH, FACP, FACC
Fellow, Pulmonology and Cardiovascular divisions, 1983–1985
Faculty, 1985–1998; Director, Cardiac Care Unit (1990–1998)
Current: Venture Partner and Chief Medical Officer, Apple Tree Partners, a life sciences venture capital firm that focuses on early biotech investments and creation of new biotech companies with primarily academic scientists.

Favorite Fellowship & Faculty Memories:

My time at WU shaped my entire career. I had the opportunity to focus on critical care medicine training during my fellowship and served as an attending physician in the CCU and medical ICUs before becoming Director of the Cardiac Care Unit. I also ran a research lab focused on the mechanisms of thrombosis in cardiovascular disease. My research led to the identification of factor Xa as a target for antithrombotic therapy. That led to my moving to industry to develop anti-Xa therapeutics. Moving to industry gave me the opportunity to lead development of new therapeutics from basic research to the clinic. The science and clinical experiences at WU were the foundation for my subsequent professional development.

One of the most impactful experiences I had at WU was the administration of the first dose of TPA in a patient in the U.S. In the middle of the night, Dr. Burton Sobel and most of the senior faculty in the Division were in the cardiac cath suite. The human TPA was flown to WU from Belgium where it was isolated, and given via intracoronary infusion to a patient with an occluded coronary artery. I participated as part of the research team by collecting blood samples and measuring molecular biomarkers of the breakdown of the clot after TPA was administered.

One of my favorite fun memories was going to St. Louis Cardinals baseball games with my lab team and some visiting fellows from Italy who had never been to a baseball game before. We sat in “Big Mac Land” where we also wore yellow plastic hardhats for fun because Mark McGwire hit so many home runs to that area of the stadium!

Favorite Leisure Activities:

My wife Patti and I travel extensively on photography tours. In addition to exploring national parks in the U.S., we’ve interacted with wolves in Norway, orangutans in Indonesia, and polar bears in Canada! I swim with a masters team, which I started doing when I was at WU. I also enjoy sports car driving on racetracks with coaches to improve my skills and performance!
specific splenic immune cell mediators such as macrophages and dendritic cells.

“Heart failure is characterized by the expansion of malfunctional dendritic cells,” he explained. “Restoration of normal dendritic cell function could potentially be investigated as a therapeutic avenue in heart failure.”

In addition to Hamid and Ismahil, other lab members on faculty include D. Gregg Rokosh, PhD, whose focus is the role of neutrophils in heart failure, and Qiongxin Wang, PhD, who is characterizing macrophages in the failing heart. Yujie Zhu, PhD, serves as a staff scientist.

Sumanth Prabhu, MD, to: 

Best Poster by a Predoctoral Trainee
Mandy Chan: Transcription Factor EB (TFEB) Preserves Kupffer Cells during Non-alcoholic Steatohepatitis

Best Poster by a Postdoctoral Fellow
Carla Valenzuela Ripoll: Dapagliflozin Improves Endothelial Integrity and Cardiac Loading through an ApoM/Sphingosine-1-Phosphate

Best Translational Poster
Pan Ma: Immune Checkpoint Inhibition Reshapes Cardiac Immune Landscape

Molecular biologist Tariq Hamid, PhD, is one of the researchers. “I am interested in understanding the molecular mechanisms underlying cardiac fibrosis,” he said. “Specifically, I am evaluating inflammation-induced responses in the pathophysiology of heart failure progression and how inflammation influences cardiac stem cell biology.” Already, Hamid and his fellow researchers have discovered that inflammation promotes a maladaptive pro-fibrotic and pro-inflammatory stem cell phenotype in failing hearts.

Another researcher, Mohamed Ameen Ismahil, PhD, is focused on identifying through Crosstalk between Macrophage and T-cell

Best Poster by Clinical Fellow
Jonathan Schweber: Assessing the Financial Viability and Patient Satisfaction of a Pediatric Electrophysiology Telehealth Program

E. Dale Abel, MD, PhD, served as the keynote speaker for the Burton E. Sobel Lecture. Dr. Abel is the Francois M. Abboud Chair in Internal Medicine, the John B. Stokes III Chair in Diabetes Research, and Chair of the Department of Internal Medicine at the University of Iowa. He spoke on “Novel Mitochondrial Mechanisms for Cardiometabolic Disease.”

An important draw that attracted Sumanth Prabhu, MD, to the Cardiovascular Division at Washington University School of Medicine is a robust and collaborative research environment, and scientists who are leaders in the rapidly developing field of cardio-immunology. Dr. Prabhu, the new chief of the Division, is a leading researcher investigating how immune cells contribute to the pathogenesis of heart failure, and how the immune system may be modulated to develop new therapies.

“Immune system activation plays a central role in the progression of disease,” he noted. “We’re looking at the underlying mechanisms that cause the immune system to become dysregulated.”

Among the research efforts in the lab are investigations into how immune cell activation affects cardiac remodeling and dysfunction. Dr. Prabhu’s laboratory here includes five researchers from his former lab at the University of Alabama at Birmingham, including four now appointed as research faculty in the Division, and a career staff scientist.

The Prabhu Lab: The Role the Immune System Plays in Heart Failure

Sumanth Prabhu, MD (center), with the research team in his new lab in the WU Cardiovascular Division.
New Faculty

Mark Huffman, MD, MPH, joins the Cardiovascular Division this year as professor of medicine and co-director of the Global Health Center in the Department of Medicine. Dr. Huffman earned his medical and Master of Public Health degrees from Tulane University in 2003, trained in internal medicine at University of Michigan, and completed a fellowship in cardiovascular medicine at Northwestern University. After his Fogarty post-doctoral research fellowship in Argentina, he joined the faculty at Northwestern in 2011. While there, he served in multiple roles focused on global health including as chair of the Department of Preventive Medicine’s Global Health Training Task Force. He also was the inaugural director of the Center for Global Cardiovascular Health and was the university’s first Quentin D. Young Professor of Health Policy. In 2019, he was named an Emerging Leader in Health and Medicine Scholar by the National Academy of Medicine.

Frank Seghatol-Eslami, MD, joins the Division as associate professor. He comes to Washington University from the Division of Cardiology at the University of Alabama (UAB), where he has been since 2006. Dr. Seghatol earned his medical degree from the Université Libre de Bruxelles in Belgium and completed postdoctoral studies in cardiovascular pathology in France. He also completed cardiology fellowships in Michigan as well as advanced echocardiography and research fellowships at Northwestern University in Chicago. He is board-certified in Level III echocardiography. At UAB, he served as Director of Clinical Echocardiography Research. His interests relate to how echocardiography can be used as a research tool in the fields of valve disease and heart failure.

Eisenberg Research Scholar Award Established

Former faculty member and cardiovascular fellowship alumnus Paul Eisenberg, MD, MPH, FACP, FACC, and his wife, Patti, have made a generous contribution to the Cardiovascular Division in support of junior faculty research. As a result, the Division will establish the Eisenberg Research Scholar Award for a junior investigator to advance novel early career research in the cardiovascular field.

“Patti and I feel very strongly that it is important to afford the opportunity for physicians, scientists and nurses who are interested in research to have the support to start their careers,” says Dr. Eisenberg. “We know from personal experience how difficult it is to get funding for the first grant and how discouraging it often is to not be able to have the opportunity to advance research interests because of funding.”

Applications will be accepted from the Division’s instructors and assistant professors in the coming months, with a committee selecting the first Scholar. Dr. Eisenberg completed his residency and fellowships in cardiovascular and pulmonary medicine at Washington University, joining the faculty in 1985. He served as Director of the Cardiac Care Unit for eight years and remained on faculty until 1998. He then moved to Indianapolis to begin a career in biopharmaceuticals for Lilly Research Laboratories, serving as director of the Cardiovascular Therapeutic Area and then Vice President of Global Drug Safety before joining Amgen in California in 2005. At Amgen, he was vice president and senior vice president for Global Regulatory Affairs and Safety as well as Chief Medical Officer. In 2019, he joined Apple Tree Partners in New York as a venture partner.

His passion for scientific research and the development of novel therapeutics is widely recognized. He has maintained long-standing ties to WU and donated to the Smith Oliver Alumni Society in support of the Division’s medical education fellowship track as well as participated in the annual Cardiovascular Research Day. “When I was there, I was impressed with the quality of work that was presented,” he says. “I continue to maintain an interest in research at WU and would be delighted to see junior faculty supported by this fund advance their research interests, change cardiology practice, and, perhaps, see their work lead to the start-up of a biotech company.”

Quader Chairs New ASE Interventional ECHO Council

Nishath Quader, MD, is chair of American Society of Echocardiography (ASE)’s new Interventional ECHO Council. The Council is one of six within the ASE and builds upon an initial Interventional ECHO Special Interest Group that was formed in 2020 and was co-chaired by Dr. Quader. With the increasing number of structural heart disease (SHD) procedures and the importance of ECHO guidance for these procedures, the Council will play an instrumental role in education, advancement, and advocacy in the field of interventional echocardiography. Under Dr. Quader’s leadership in the IE SIG, physician training and guidelines for the standardization of TEE for SHD procedures (see page 1) were developed late last year.
In Memoriam: Robert Kleiger, MD

It is with great sadness that we note the passing of Robert Kleiger, MD. Dr. Kleiger, who had been on the faculty for more than 53 years, passed away at age 87 in late January.

Kleiger, who completed his residency training at Barnes Hospital from 1961-1963 before completing two cardiology fellowships at Harvard School of Public Health and Stanford University, returned to join our Division faculty in 1969. He was the first to establish an electrocardiography service at The Jewish Hospital of St. Louis. He also served as director of the hospital’s Cardiac Care Unit and was interim chief of the cardiology division for three years. “I trained at Harvard’s Peter Brigham Hospital, which had one of the first three CCUs in the country,” Dr. Kleiger recalled recently.

Nationally recognized for his expertise in electrocardiography, Dr. Kleiger not only taught cardiology fellows, but he also initiated a two-week electrocardiography rotation for fourth year medical students at Washington University beginning in 1972. Starting with one student, the course remained a much-requested rotation. Kleiger noted in December 2021 that training medical students was a career highlight. “You really can train students to a high level in a short period of time if the teaching is one-on-one, intensive, and if you correlate the ECG with the clinical data,” he said. “It was very satisfying to see that most students could read ECGs well by their third day of training.”

He recently established the Robert E. Kleiger Endowment in Cardiology to provide unrestricted funds to the Division to support junior faculty cardiovascular research as well as lectures and general educational programs for house staff and medical students. He has a long-standing legacy in philanthropy and made other donations in support of cardiovascular research and medical education. Examples include contributions to the Mentors in Medicine program within the Department of Internal Medicine’s residency program as well as the Washington University School’s Medical Teaching Fund, Peck Scholars, and the Division’s John Boineau, MD Lectureship.

“Dr. Kleiger’s legacy and his passion for education and research will be highlighted through his gifts to our Division and WU and through the memories recalled by many of our faculty, fellows, physician scientists, and medical students,” said Sumanth Prabhu, MD, Chief of the Cardiovascular Division. “His love of teaching was visibly transparent and through his time, expertise and teaching, he has influenced the course of patient care and outcomes in cardiovascular medicine.”