

Cardiovascular REPORT



NEWS FOR PHYSICIANS FROM JOHNS HOPKINS MEDICINE

Winter 2009



Trunk Music

Better news for
aortic dissections.

Vascular surgeon James Black is on the hunt for better ways to identify and treat aortic dissections.

It's possibly one of the most sinister medical conditions in the books—killing one-quarter of patients within 24 hours of diagnosis. That's the obvious downside of an acute aortic dissection.

But, depending on what type of aortic dissection you're looking at—an A or B—vascular surgeon **James Black** says the news is better today for patients than it's been in the past.

Identifying aortic dissections

It's still true that patients who have type A dissections, those that literally slash their way through the ascending aorta, may face fatal ruptures. Acute type A dissections are what killed actors Lucille Ball and John Ritter.

"For these dissections, the challenge is getting a quick and accurate diagnosis," says Black. Type A dissections are so difficult to recognize, he adds, that patients are frequently misdiagnosed—especially in emergency rooms—and their pain is wrongly categorized as musculoskeletal or a heart condition.

"These patients go on to die when they might otherwise have been saved by the tremendous advances in cardiac surgical care," says Black. Recognizing that which has been unrecognized is at

least a step in the right direction.

But, that's not good enough for Black, so he's taking it a step even further. This year, he began a study that simulates aortic dissections in mice to determine whether a biomarker exists for the condition. His goal is to locate a group of enzymes or chemical signals that could be identified through a blood test, which would then indicate an imminent or occurring aortic dissection.

"If we can do this, we would be able to diagnose aortic dissections and intervene more rapidly," says Black.

Less offers more for type Bs

Though just as difficult to correctly identify as their type A sisters, type B dissections are less ominous. They don't rupture and aren't as frequently fatal, but their affect on the descending aorta can lead to hypertension, ischemia and obstructions to the kidneys and legs.

Traditionally, type B dissections, which originate in the aorta as it turns down the chest, have been managed with medication, but up to 40 percent of those patients fail medication therapy and require surgery to treat visceral ischemia, impending rupture, intractable pain or a sudden reduction in aortic size.

That's where the outlook is good. Past surgeries for type B dissections have been open procedures in which complications like paraplegia occurred between 20 to 40 percent of the time. Newer, less invasive therapies that included aortic fenestration with bare metal stents have sent that complication rate plummeting to about 2 to 4 percent.

New use, familiar technology

Now, Johns Hopkins is one of a handful of centers in the country preparing clinical trials on endovascular stent grafts for acute type B dissections. The procedure has been applied successfully to abdominal aortic aneurysms, and now that same technology is showing promise for type B dissections. Black describes the device as even smaller and more flexible than ones made in the past for aneurysms. Not only will that further decrease the chance for complications, he says, but it also offers an additional choice, not a replacement, to fenestration.

"One technique over the other may be the better option, depending on how large an aortic territory as well as which specific branches of the descending aorta are being affected," says Black. "That's what we want, more choices for better outcomes." ■

Consultation: **Steven Jones**

*Director of Inpatient Cardiology,
John Hopkins Heart and Vascular Institute*

In about one-third of all coronary artery disease cases, patients are asymptomatic until a sudden heart attack occurs. If they're lucky, they survive and are treated. If they're not, as in the recent case of journalist Tim Russert, the heart attack is fatal. Cardiologist **Steven Jones** says avoiding that scenario means identifying people whose risk for CAD lies somewhere in the middle—neither very high nor very low.

Why is it most important to identify people whose risk for CAD is in the middle?

It's the folks in the middle who slip through the cracks. Those who are at the highest risk for coronary artery disease have usually already been identified. Probably, they've experienced some angina episodes and they're being treated medically or through lifestyle changes. We also know that men are at greater risk for CAD than women, as are people with diabetes. People with very low risk are those with no family history, with blood pressure and cholesterol levels that are healthy, and who don't have other lifestyle-related risk factors.

What's the biggest challenge when trying to identify asymptomatic CAD?

Obviously, the most significant challenge is the absence of symptoms, so where do you begin? The problem is that coronary artery disease begins in childhood, progresses over time and by the time most adults are over age 50, is present to some extent. It's a question of severity—or potential severity. That's why we believe it's important to look at those people in the

middle of the spectrum and to identify them in a presymptomatic stage before their first event is a heart attack.

Another challenge is risk stratification. In the past, we've looked to Framingham risk scores to try to determine the more likely suspects for CAD. The challenge with this method is that it's based on population statistics rather than individual assessments. It often falls short of complete and accurate diagnoses.

Then how do you identify those potential patients in the middle?

The first things to look at are the behavioral and familial influences. If heart disease hasn't been diagnosed and there are no symptoms, but those risk factors are there, you may want to test for the presence of arteriosclerosis. Coronary calcium scoring

Unfortunately, too many people make the mistake of looking at the ultimate outcome of CAD—a heart attack—as the disease.



Steven Jones is getting to the heart of asymptomatic CAD.

and high-resolution ultrasound to measure the thickness of the carotid artery layer, and blood tests such as hs-CRP are some of the newer technologies that we use to diagnose or predict CAD, especially in patients who are asymptomatic.

Based on those results, many patients are reclassified to a higher or lower risk group. Such advanced testing is likely to become more cost-effective as well for these potential patients.

If arteriosclerosis is detected in asymptomatic patients, what do you do?

Those who've been identified at an increased risk for CAD are managed aggressively through diet, exercise and intensive medical therapy with risk-lowering drugs. Also, commitment on the part of patients to modify their behavioral risks is critical. Without it, even the best diagnosis and medical

treatment will fail.

It's so important for patients who are asymptomatic—and probably feeling just fine—to recognize that the presence of arteriosclerosis often has nothing to do with how they feel. If they have arteriosclerosis, and therefore CAD, they have the disease and it needs to be treated. Unfortunately, too many people make the mistake of looking at the ultimate outcome of CAD—a heart attack—as the disease.

What else should I know about asymptomatic CAD?

Sudden death events are most common in people who've been previously asymptomatic for CAD. Though AEDs are common in malls, airports and other public places, the greatest reduction in risk for sudden death are aggressive measures to diagnose and prevent arteriosclerosis in the first place. ■



Newer LVADs are on the road to becoming destination therapies, says John Conte.

Newer LVADs Are Going With the Flow

If analogies are your thing, think large, obnoxious SUV versus smaller, sleeker and more energy-efficient automobile. That's roughly the comparison that cardiac surgeon John Conte makes between the new left-ventricular assist devices coming to market and their clunkier predecessors.

"Or you could say it's like looking at a watermelon versus an apple," he says.

But, it's not just the size of the newer left-ventricular assist devices—or LVADs—that has Conte making such comparisons, though they are about 60 percent smaller than previous models. What's especially breathtaking about the newest wave of LVADs is their simplicity and precision.

For end-stage heart failure patients, that's literally breath-giving.

"These are small, quiet devices," says Conte, "with engineering that makes it possible for them to last up to 10 years." That's compared to just two years with the older LVADs. Plus, unlike the conventional pusher-plate apparatus that produce pulsatile flow, the new LVAD technology has a continuous flow action that pumps up to 10 liters of blood per minute. That's about the full output of a healthy heart. Past LVADs also have been limited to larger patients who could tolerate their bulk, but the newer devices have broadened that patient eligibility.

"We can implant into smaller patients, yet still provide good blood flow for all-size patients," says Conte.

With one of the most sophisticated ventricular assist device programs in the country, Johns Hopkins was among a handful of centers participating in trials of the latest LVADs before they were FDA approved last year as bridge-to-transplant solutions for end-stage heart failure patients. Those same devices are being looked at as destination therapies as well. And, a new trial is upcoming for yet another version of magnet-driven LVADs that are even smaller with greater durability.

More experience, says Conte, combined with the lack of growth in organ availability continues to propel design and development of ventricular assist devices forward. That's making it even more likely for them to become permanent alternatives to heart transplantation, rather than just bridge options.

"We're not there, yet," says Conte. "But the idea behind the newer LVADs is that they never wear out." ■

Bypassing Brain Injury

Despite the advances made in all areas of cardiac surgery, among the snarls that remain most troublesome for cardiac surgeon **William Baumgartner** is the risk of neurologic injury.

But, he and surgical colleague **Duke Cameron**, as well as neurologists **Guy McKhann** and **Michael Johnston** believe they may be on to something.

This year, the group began a pilot study on heart surgery patients to look at the neuroprotective effects of valproate—an anti-convulsive drug typically given to epilepsy patients.

The statistics behind neurologic injury during or following cardiac surgery are unnerving: stroke—the most serious complication—in up to 6 percent of certain high-risk cases; some form of cognitive impairment 25 percent to 65 percent of the time; and other types of problems related to regaining and maintaining consciousness in about 10 percent of patients. Although most cognitive changes are gone in a few months following surgery, they can be a problem during the early postoperative period. Not only might that increase the time patients are on ventilators, but it has an impact on recovery time, too.

"Most people don't think about the effect that cardiac surgery has on the brain," says Baumgartner. "But, it's top of mind for heart surgeons."

Baumgartner's lab has long focused its efforts in part on the mechanisms of neurologic injury in cardiac surgery patients. That work—part of a 15-year collaboration with Johnston's Kennedy Krieger Institute lab—has revealed information on what happens at both the cellular and subcellular levels, including the role of glutamate excitotoxicity and nitric oxide and their effects on gene expression.

Using that information, subsequent animal studies tested promising drugs for avoiding neurologic injury, but none showed more promise than valproate, says McKhann.

"For patients at the highest risk for injury—those who undergo induced hypothermic circulatory arrest—we believe valproate may have significant neuroprotective effects," he says.

Why valproate may be so successful is measured by its ability to calm and enhance at the same time. The power it has to reduce brain excitability in epilepsy patients is the very same mechanism at work on heart surgery patients. As Johnston explains, where valproate is calming the neurons that have become excited by a toxic insult, it's also regulating—or enhancing—gene expression in cells that are protective. And, another bonus is that it may diminish the number of inflammatory cells, offering even more protection.

"It's such a simple compound," says Johnston. "It has so much potential for this application." ■



William Baumgartner and Guy McKhann are working together to prevent neurologic injury during heart surgery.

Pulmonary Valve Replacement: Getting It Right

Ask cardiologist **Jane Crosson** what's one of the biggest challenges facing adult congenital heart disease patients—and their physicians—and she doesn't skip a beat.

"Timing tops the list," she says.

It's the sort of irony that persistently greets science and medicine: leaps in understanding and technology save lives, but also leave behind a new set of challenges.

In the case of adult patients with congenital heart conditions like tetralogy of Fallot and pulmonary stenosis, the conundrum centers on the optimal timing of pulmonary valve replacement.

Surgical valve repair of such congenital conditions at birth or shortly afterwards has translated to rising numbers of long-term survivors. Today, there are as many adults as children with congenital heart disease. Patients can go several decades—or a lifetime—without problems or symptoms.

But, often by their 20s or 30s, those patients begin experiencing the symptoms of right ventricular dilatation and dysfunction

that include excess fatigue, shortness of breath and reduced exercise tolerance.

"When that happens," says Crosson, "then they're looking at pulmonary valve replacement." There's some controversy surrounding the timing, though. Crosson says it's a balance between the fact that replacements don't last forever—stenosis and regurgitation are likely to occur within 10 years of replacement—and that waiting too long may make it too late.

"Patients obviously don't like the prospect of multiple surgeries—and these are open-heart procedures," she says. But, delaying replacement may be akin to Russian roulette.

The key for adult congenital heart disease patients is multidisciplinary coordination that includes cardiology, imaging and cardiac surgery. Along with the leaps that have allowed these patients to survive into adulthood, other advances have been growing up



Timing is key for pulmonary valve replacement, says Jane Crosson.

as well, making it easier for physicians to advocate the right time for replacement.

"MRI is a good example of technology that is giving us a clearer view of the size and function of the pulmonary valve," says Crosson. "That has a great impact on decision making." And, Crosson says that though it's early and still in a study phase, percutaneous pulmonary valve replacement may soon be an alternative to open-heart surgery.

"Either way, patients will need lifelong cardiology follow-up," she says. "But, right now, traditional replacement outcomes remain very good and improve function." ■

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Cardiovascular REPORT

The Johns Hopkins Heart and Vascular Institute *Cardiovascular Report* is one of the many ways we seek to enhance our partnership with our thousands of referring physicians. Comments, questions and thoughts on topics you would like to see covered in upcoming issues are always welcome.

This newsletter is published for the Johns Hopkins Heart and Vascular Institute by Johns Hopkins Medicine Marketing and Communications.

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