



Cardiovascular REPORT

NEWS FOR PHYSICIANS FROM JOHNS HOPKINS MEDICINE

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Totally Wireless

For end-stage heart disease, the total artificial heart offers hope.

Cardiac surgeon John Conte well understands the benefits—and limits—of the breakthrough.

When the world's first total artificial heart was implanted into a human in 1969, it broke more than one barrier. As it stepped from the realm of science fiction into the land of the living, it carried with it a fatal flaw—external wires and tubes that broke the skin barrier.

It was a critical blemish, since breaking the skin increased the risk of infection and blood clots.

Nearly 40 years and much refining later, Johns Hopkins is one of only four hospitals in the world with FDA approval to implant the first self-contained total artificial heart.

“All past devices have had external lines that cross the skin,” says cardiac surgeon and director of heart transplantation **John Conte**. But, the newest total artificial heart—or TAH—solves the problem of breaking the skin barrier by operating on both internal and external bat-

teries. Connected to four locations in the heart—the atria, aorta and pulmonary artery—the TAH works via a hydraulic pump that shuttles fluid from side to side.

“Power is transmitted back and forth through the skin, but without the tubes and wires breaking the skin,” Conte explains.

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Conte is all too keenly aware of the 3,000 or so patients who are on waitlists for heart transplants. But, even with its promise of more positive outcomes than with devices of the past, the TAH isn't for everyone on a transplant waitlist.

The best candidates, says Conte, are patients with biventricular heart failure, who also may be too sick for human heart transplantation—people who may have no other alternatives.

“That's a small percentage of end-stage heart disease patients,” says Conte. Another challenge that trims the candidate list is the

mere size of the device. By human heart standards, it's big—about 4 pounds and the size of a grapefruit. So, while “fit” is in part determined by CT scans of potential patients, the bottom line is that size matters.

“This is going to be mostly for larger patients,” says Conte.

Despite its limitations, Conte is encouraged by the technology. Though it's difficult to pinpoint numbers precisely, the TAH can prolong life—even double its expectancy—and improve its quality, lower the risk of infection, and offer autonomy and mobility for this small group of patients.

“It's really a niche device right now,” says Conte.

In fact, the TAH is just one tool in an overall arsenal of ventricular assist devices that are making their mark on heart disease. Hopkins has the largest and most active center in the country for implanting the life-saving apparatus, as either bridges to heart transplantation or as destination therapies.

“So, we're really not trying to create the bionic man, yet,” says Conte. “But, with the total artificial heart and other ventricular assist devices, we are offering hope.” ■

Consultation: Hunter Champion

Cardiologist, Johns Hopkins Heart and Vascular Institute and Johns Hopkins Pulmonary Hypertension Program



Pulmonary hypertension is a common cause of shortness of breath in patients. While traditionally thought to be relatively rare, the disease is frequently unrecognized or misdiagnosed. Cardiologist Hunter Champion says physicians should be taking a closer look at this major contributor to heart failure.

Why is pulmonary hypertension misdiagnosed, or not diagnosed at all?

Not all pulmonary hypertension is the same. There's wide variability in severity, so evaluating and accurately diagnosing it can be complex. On one end, people with the condition may not actually have any identifiable symptoms. At the other end, once symptoms do appear, the disease may already have progressed quite far. Shortness of breath is one of the classic symptoms of pulmonary hypertension, but unfortunately it's often misdiagnosed as asthma or as simply being out of shape.

If that's the case, then what should physicians be on the lookout for?

Unlike with coronary artery disease, we don't have a good way of identifying people early, though we are making progress. But, since undiagnosed and untreated pulmonary hypertension can be fatal in the form of right heart failure, physicians should be paying close attention.

Right now, knowing who the candidate patients are is a good start. People with valvular disease, obstructive lung disease, sleep apnea and connective tissue diseases like scleroderma are more at risk. Those who've had blood clots or HIV infection or

who have liver disease also are more likely to develop pulmonary hypertension. And, there's a strong correlation to developing the condition if you're over age 70.

In addition to shortness of breath, physicians should also be looking for other tell-tale symptoms like unusual fatigue, chest pain, ankle swelling, and fainting or near-fainting episodes.

If I suspect pulmonary hypertension in one of my patients, what's the best way to confirm a diagnosis?

You want to look for elevated lung pressure. Normal average pulmonary artery pressure is about 14mm Hg. In people with pulmonary hypertension, that average is greater than 25mm Hg. An echocardiogram is a good screening study for elevated lung pressures, and that's something that primary care or internal medicine physicians can do themselves. The presence or absence of pulmonary hypertension, however, can only be confirmed by right-heart catheterization.

Specialized programs like the one at Johns Hopkins that integrate cardiology and pulmonology can take some of that diagnostic pressure off and help you to determine the treatment that may be most effective for your patient.

What about treatments and interventions—is there anything new?

We've come a long way from just a decade ago, but medical treatment is still complex and very individual. Some patients can be successfully treated with oral calcium channel-blocking drugs, while others respond better to intravenous prostacyclins. Newer oral medicines like endothelin receptor antagonists such as bosentan

(Tracleer) and drugs that have been traditionally used to treat erectile dysfunction (such as sildenafil; Revatio) are helping patients with pulmonary hypertension. Johns Hopkins is also studying a number of new investigational drugs that would be given orally or with inhaler devices.

Surgical interventions include pulmonary thromboendarterectomy, which removes blood clots from the lungs. In the

very worst cases, of course, lung transplantation may be recommended.

What's the outlook like?

Despite the fact that we can't actually cure pulmonary hypertension, overall the outlook is certainly better today than it was even just 10 years ago. Accurate, early diagnosis and initiation of treatment have not only improved quality of life, but have saved lives. ■

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A Boot Camp for CPR

Ask **Betsy Hunt** about her favorite scenarios, and she'll tell you it's those "aha!" moments that hit medical students and residents right between the eyes.

A critical care specialist and director of the new Johns Hopkins Medicine Simulation Center, Hunt sees more of those moments than most, but the ones that really get her are during mock CPR codes.

This past year, Hunt published results of a study that found alarming delays and lapses in emergency care among hospital-based first-responders during the critical five minutes after a heart or breathing stops. Though that study staged pediatric cardiac and respiratory arrests, Hunt is now also turning her attention to adult studies.

"In children, we saw that the fundamentals were being done wrong," says Hunt. "The same thing is happening in adult cardiac emergencies."

And, what exactly is—or isn't—happening?



Simulation Center Director Betsy Hunt makes things go wrong on purpose.

Hunt says it's in part about the loss of basic CPR instincts and remembering that every second counts. In particular, delays and long pauses in chest compressions and the idea behind "no flow-fraction."

"For so long, rapid defibrillation has been the emphasis," she explains. "Meanwhile, while you're preparing the defibrillator, no one is doing compressions. You've lost precious time—and possibly, your patient."

Simulation exercises have been crucial to identifying those and other tumbles, and the new center is making quantifying and measuring what goes wrong in resuscitation emergencies even easier. It's a different and more realistic way of teaching medicine, says Hunt. Seeing yourself played back on video, for example, makes it hard to dispute where and how something went awry.

Hunt doesn't miss much, nor is she above throwing a curve. Her goal during a mock code is to throw it out of kilter as much as possible, then deconstruct it and put it back together the way it should be.

"We need to know how to get people to comply with the guidelines and basic CPR maneuvers," says Hunt. "So, first we quantify the errors, then we intervene to improve the process," she says.

Part of that process revolves around communication and teamwork, she adds. That includes looking at how code teams are formed, what each person's

role should be, whether they're adhering to that role—or not—and where the communication breakdowns occur. Then, each person looks at himself and everyone else. Finally, they get to practice again and again, as a team, until they get it right.

"Deep down, people are aware that something didn't go right," says Hunt. But those between-the-eyeball thumps are what bring it home. ■

Triple-Header for Heart Failure

Cardiologists **David Kass** and **Susan Zieman** are going for a one-two-three punch that they hope will knock out heart failure. Three human trials are taking strategic aim at the chronic condition's disease process and attacking it from three different angles. Two of those angles include treating precursors of heart failure: systolic hypertension and hypertensive hypertrophy.



David Kass and Susan Zieman

"We know that systolic hypertension results in hypertrophy," says Kass, "and that increases the risk of heart disease and in particular heart failure with a preserved ejection fraction"

Wiping out one, the other or both, says Kass, means the risk for developing heart failure withers and wanes. To that end, Kass and Zieman are looking at new uses for old remedies. The pharmaceutical formulation of tetrahydrobiopterin—or BH4—a vitamin-like enzyme cofactor, has been used to treat genetic diseases like phenylketonuria (PKU). It's also essential for the formation of nitric oxide in blood vessels and so has an important role in forms of hypertension.

"A single-center study at Hopkins showed favorable results for oral BH4 to enhance vascular function in patients with isolated systolic hypertension," says Zieman. "So now we want to take the next step."

In another back-to-the-future twist, the drug that was originally supposed to treat hypertension but instead launched a revolution for men with erectile dysfunction is making a comeback. Lost in the afterglow of its bask in the sunshine were the potential cardiac and vascular benefits of sildenafil citrate—Viagra. Today, the drug is FDA approved to treat pulmonary hypertension. But, in animal studies, Kass has also shown that it reverses and blocks the development of ventricular hypertrophy. Now, Zieman and Kass are looking at human trials to treat hypertrophy with the longer-acting tadalafil (Cialis).

"Unlike our current treatments that largely inhibit neurohormones, drugs like sildenafil or tadalafil act as an internal cellular brake," says Kass. "And, that can block the adverse effects of sustained-pressure stress."

If assailing the brass tacks of heart failure isn't enough, then another trial is meeting its end game head-on. Nearly half of patients with heart failure have a preserved ejection fraction. Diastolic dysfunction plays a role, but so too may impairment of the heart rate response. The RESET trial will use implanted atrial rate-responsive pacemakers to determine possible benefits on the exertional capacity of heart failure patients.

"If we can get to any one of the phases of this disease process in patients, then we're going to make a difference," says Kass. "Hopefully, we will strike at all three." ■

Heart Trials

Johns Hopkins is seeking eligible volunteers for these three studies:

- **Tadalafil Study:** Tadalafil (Cialis) for the treatment of hypertensive heart disease and ventricular hypertrophy.
- **BH4 for Hypertension:** Therapeutic potential of tetrahydrobiopterin (BH4) for treating systolic hypertension in patients with vascular disease.

- **RESET Trial:** This study aims to learn more about a pacemaker treatment to improve exercise capacity in heart failure patients.

For information, contact Barbara Peterson at bpeter21@jhmi.edu or 410-955-9864.

Stents Without Stats

Pediatric cardiologist **Richard Ringel** doesn't have a problem jumping through some hoops—however many it takes, in fact, to find the best solution for both child and adult heart patients.

For interventional treatment of coarctation of the aorta, he's on a mission to get covered stents on the table.

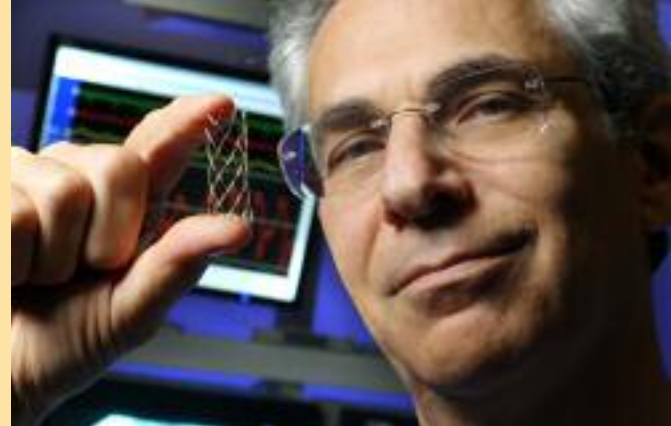
Though the congenital heart condition is usually caught and treated surgically at birth or shortly after, it can go undiagnosed well into late adolescence or adulthood. At that point, says Ringel, stent therapy rather than surgery is likely going to be the best option.

The challenge for interventional cardiologists like Ringel is that while stent therapy for coarctation has become the standard of care around the world, no one's been able to truly measure its statistical success. Add to that, the bare metal stents used in the United States for coarctation of the aorta since about 1992 are off-label biliary stents.

"There aren't any balloon expandable bare metal stents approved by the FDA for aortic use in the United States," says Ringel. Throw in the fact that possibly safer and more effective covered stents are barely on the regulatory radar in this country (they've been widely and successfully used in Europe), and the kerfuffle increases even more.

And, that's what has motivated Ringel to spearhead the largest, most rigorous trial ever to look at stents for coarctation in children and adults.

"Ultimately," he says, "we want to better define the safety and effectiveness of aortic stenting and make covered stents available in this country." But, even touching covered stents means first focusing the trial—called COAST—on a comparison of bare metal stents to surgery, a requirement of the FDA. As part of the study design, though, the trial



Richard Ringel, on a mission to get hard evidence.

also allows for compassionate and emergency use of covered stents. It's already a huge benefit, says Ringel.

Each of the 18 centers participating in the COAST trial has access to covered stents for high-risk patients or emergency situations. That data also will be used to support a future covered stent trial.

"We want a better device here, and that's going to help patients," says Ringel. "But we need to first statistically demonstrate the overall worthiness of stents to surgeons, cardiologists and the FDA." ■

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410-955-2800

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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.

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