

# Cardiovascular Report

NEWS FOR PHYSICIANS FROM JOHNS HOPKINS MEDICINE

Spring 2015

## A Cesarean Delivery With the Patient on ECMO



**Ashish Shah:** “Advanced mechanical support may be a viable option for critical illness of pregnancy.”

It could have been a case straight out of *House*, the TV drama known for depicting astoundingly complex if often far-fetched clinical scenarios.

In January 2014, 37-year-old Peggy Chung, four months pregnant and previously healthy, went to her local emergency room with persistent fever, cough and shortness of breath. Within hours, she developed severe hypotension and hypoxemia and was transferred to the hospital’s ICU with acute respiratory distress. Chung was then airlifted to The Johns Hopkins Hospital, where additional workup revealed flu infection and diffuse bleeding in her lungs.

Critical care specialists led by ARDS expert and intensive care unit director **Roy Brower** initiated respiratory support and treatment with antivirals, but Chung’s fever was unrelenting, her pulmonary bleeding worsened and one of her lungs collapsed. Clinicians then initiated steroid treatment and ordered a CT scan.

What the scan showed was a true zebra case. Chung had multiple bilateral cysts on her lungs, a clue that led to further testing and the presumptive diagnosis of lymphangiomyomatosis (LAM), a rare lung disease with a predilection for women of childbearing age that’s characterized by the abnormal proliferation of smooth-muscle cells in the lungs or other organs. Yet, figuring out the diagnosis was only half the battle.

“This patient was in fulminant lung failure with severe airway bleeding, and conventional techniques were failing badly,” says cardiac surgeon **Ashish Shah**, who oversaw Chung’s care together with Brower and maternal fetal medicine fellow **Arthur Jason Vaught**. “We knew that extracorporeal life support—ECMO—was her only chance.”

Although Chung was stabilized on ECMO, her airway bleeding continued. The clinicians resorted to spraying the blood-clotting protein recombinant Factor VII directly into the patient’s airway, which stopped the bleeding.

But as if the case couldn’t get any more complicated, Chung’s blood pressure began to rise, steadily and relentlessly. Within days, she developed proteinuria, the hallmark of preeclampsia.

Waiting any longer could kill both mom and baby, so at just 24 weeks into her pregnancy and 11 days after going on ECMO, Chung was wheeled into the OR for a cesarean delivery. She gave birth to a 650-gram baby girl. A lung biopsy on Chung was done at the same time and confirmed the LAM diagnosis.

Following delivery, Chung’s condition improved rapidly. Within three days she was taken off ECMO, and two days later she was breathing on her own.

The newborn, however, faced her own set of challenges: a patent ductus arteriosus, which pediatric cardiac surgeon **Luca Vricella** closed a month after her birth; a bout with mild necrotizing enterocolitis, promptly nipped with antibiotics; and retinopathy of prematurity that regressed with photocoagulation therapy.

Believed to be only the second instance of a live delivery on ECMO, the case highlights a cascade of nearly catastrophic complications, but also how the orchestration of care among specialists from cardiac surgery, pulmonary critical care, obstetrics and neonatology helped both mom and baby overcome seemingly unbeatable odds.

Or as Shah puts it, “This case powerfully illustrates the intersection of high-tech medicine, Oslerian attention to detail and, above all, the good judgment of dedicated and smart clinicians.” ■



### Case Discussion

To watch cardiac surgeon Ashish Shah and maternal fetal medicine fellow Arthur Jason Vaught talk about how they and colleagues managed this patient’s care, scan the code or visit <http://bit.ly/CesareanOnECMO>.

# Endarterectomy in Patients Over 70

**A**t 94, Doris Russell has a workout routine that puts to shame most people half her age. She swims laps three times a week and competes annually in the Maryland Senior Olympics and YMCA Nationals. But three years ago, Russell had a series of transient ischemic attacks. Because these mini-strokes are forerunners of full-blown ischemic stroke, they could not only derail Russell's workouts but also precipitate devastating neurologic injury. So when the spry nonagenarian ended up in the office of Johns Hopkins vascular surgeon

**Bruce Perler**, the decision to proceed with carotid endarterectomy was a no-brainer.

"Strokes are particularly debilitating in the elderly due to their lower physiologic reserve, but also because the aging brain tends to have preexisting microvascular damage, so the effects of a stroke can be more extensive and clinically severe," Perler says.

Russell is among a growing number of people over 70 who undergo both therapeutic and preventive carotid endarterectomies. In fact, about 40 percent of the nearly 2,000 carotid patients Perler has operated on are in their 70s, 80s and 90s. Performing

carotid surgery among elderly patients with symptomatic disease—marked by TIAs and notable carotid occlusion—is not controversial, Perler says.

"Between 30 and 40 percent of people who have a mini stroke go on to have a full-blown stroke," Perler says. "Doing nothing poses a grave risk."

However, performing surgery for asymptomatic disease in this advanced-age group remains debatable because the risk-benefit ratio is less clear. Yet, Perler says, when done correctly, the procedure—gently peeling away the calcified atherosclerotic plaque from the arterial wall—is both safe and justified.

Older symptom-free patients with substantial carotid occlusion—80 to 90 percent or more—stand to benefit from preemptive surgery because the risk of full-blown stroke looms large.

Perler cites the case of a 90-year-old man who initially presented with 90 percent stenosis of the right carotid and opted for medical therapy and watchful observation. Six years later, his right carotid, by then completely occluded, was no longer operable, and he'd developed 95 percent blockage in his left carotid. That finding moved the needle. The patient went ahead with a left carotid endarterectomy, becoming Perler's—and possibly Johns Hopkins'—oldest endarterectomy patient.

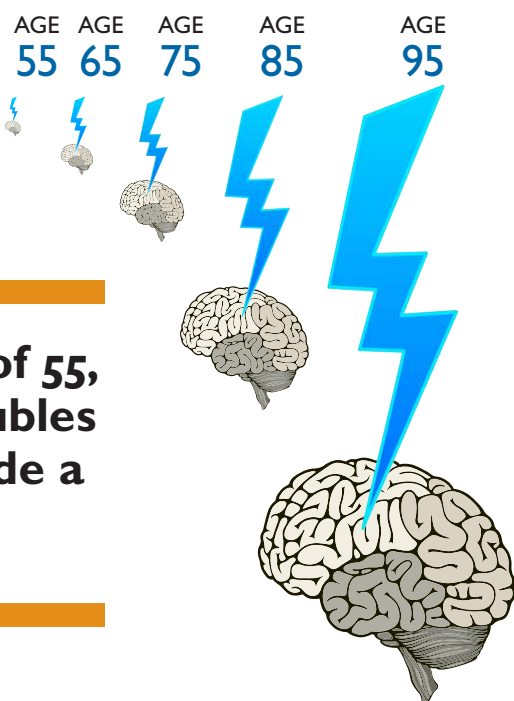
Tailoring intraoperative and postoperative care to the physiologic needs of elderly people can minimize risk and so can careful patient selection, Perler says.

For example, Johns Hopkins anesthesiologists use minimal sedation,



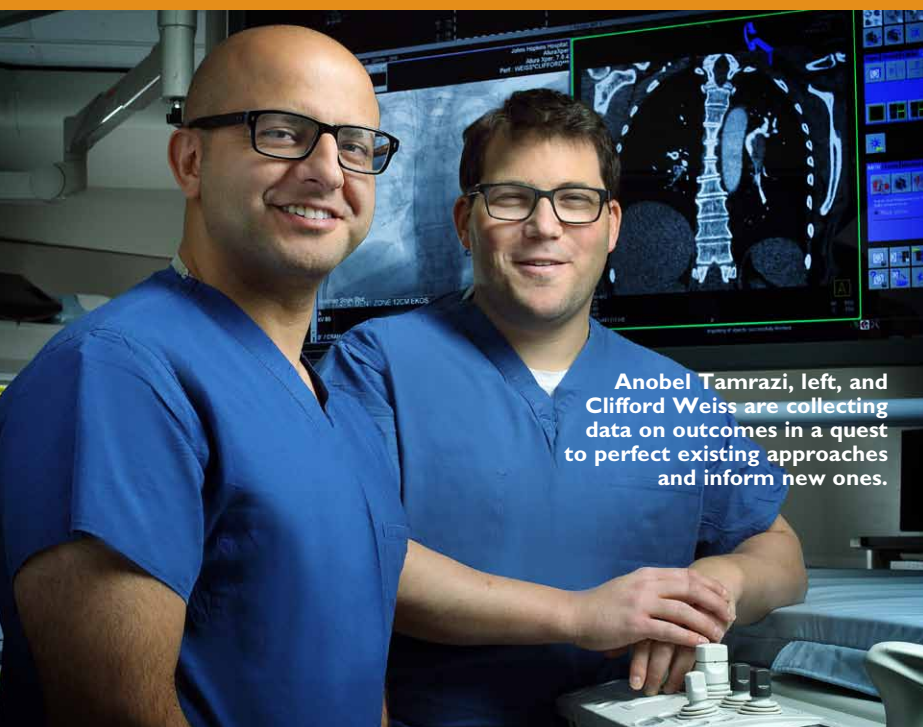
The key to patient selection, says Bruce Perler, is to focus not on chronologic age but on physiological age and overall health: "If you think about it, you've got to be pretty healthy overall to get to 80 or 90."

and the patient is awake promptly after surgery, which lasts about an hour. Most go home the following day. A careful preop exam and ultrasound can pinpoint the occlusion—usually at the carotid bifurcation—and ensure a smaller incision. And since carotid stenosis is fueled chiefly by atherosclerotic plaque, all patients should be on statins, Perler adds, because those who take them fare better overall. "If they are not already on a statin," he says, "we make sure they start taking one, ideally at least a month before surgery." ■



**After the age of 55, stroke risk doubles for every decade a person is alive.**

## INTERVENTIONAL RADIOLOGY



Anobel Tamrazi, left, and Clifford Weiss are collecting data on outcomes in a quest to perfect existing approaches and inform new ones.

# Precision-Targeted Low-Dose

**T**he patient, a woman in her 50s, had a history of deep vein thrombosis in the legs, so when she developed fatigue and shortness of breath in the fall of 2013, she prudently went to the local emergency room. Her physical exam was unremarkable and her blood work came back normal, so the patient was discharged with instructions to rest.

But a few months later, the episode repeated itself—this time rather more dramatically. The woman could barely climb a flight of stairs; the short walk

from her office to the car left her gasping for breath. An ECG performed in her primary physician's office showed nonspecific changes, made more ominous in the context of another finding—oxygen saturation in the mid-80s. An echocardiogram showed an enlarged and dysfunctional right ventricle and elevated pulmonary artery pressures.

The patient was transferred to Johns Hopkins, where a CT scan revealed two large emboli lodged in the left and right pulmonary arteries. Cardiologist **Steven Schulman**, knowing time was of the



# The Curious Case of the ‘Nervous Heart’

It started with mild palpitations, sporadic at first, then increasingly frequent and bothersome. Next came chest discomfort, spikes in blood pressure, tremors and a jittery, something-is-not-right sensation the patient described as a “nervous heart.”

For three years, the mystifying spells—lasting from a few minutes to an hour—plagued the 42-year-old Northern European man, sending him to various specialists across three countries and two continents. Full-body CT and MRI scans, renal artery studies, repeat ECGs, and stress and transthoracic echocardiograms turned up nothing. Blood chemistries were completely normal. Yet, the symptoms persisted. Most worrisome of all, the man’s blood pressure went up and down, at times topping 200/100.

When the patient ended up in the care of Miami cardiologist and former Johns Hopkins fellow Juan Rivera, the physician knew it was time to call on **Oscar Cingolani**, a Johns Hopkins cardiologist with expertise in treatment-resistant hypertension and a knack for cracking hard-to-solve cases.

The years’ worth of clinical notes and medical tests gave Cingolani no clues. But the physical exam pointed to a possible culprit. Palpating the abdomen, Cingolani noticed the man’s fingers turned cyanotic, his heart rate shooting up. He sweated profusely and experienced a flurry of premature atrial and ventricular contractions. Then, in a matter of minutes, the symptoms subsided.

Even though a previous CT scan had shown normal adrenal glands, Cingolani immediately suspected adrenal trouble, most likely caused by a pheochromocytoma. Yet, when a blood test showed normal chromogranin-A values, the plot thickened. Then something else caught Cingolani’s attention: the mildly elevated metanephrine levels of a blood



**Oscar Cingolani co-directs the multidisciplinary Hypertension Center at Johns Hopkins, designed to prevent gaps in care by bringing together specialists from cardiology, internal medicine and nephrology.**

test obtained shortly after the patient’s spell, a finding suggestive of another kind of adrenal mischief. Then a smoking gun: A radioisotopic scan showed a hyperactive zone in the left adrenal medulla, consistent with adrenal hyperplasia. Following a laparoscopic adrenalectomy, the patient’s symptoms vanished rapidly. His improvement was dramatic, Cingolani says.

Isolated adrenal hyperplasia is rare, Cingolani says, often mimicking the symptoms of its more common cousin, pheochromocytoma.

Perhaps more importantly, he says, the condition can also present as stable hypertension, a relatively common scenario within the population that Cingolani treats: those with resistant hypertension.

Most patients with resistant hypertension have essential hypertension, but a fair number harbor underlying pathologies that fuel secondary hypertension.

“Such patients could be easily chalked up as suffering from primary resistant hypertension,” says Cingolani, “when in fact they have correctible conditions such as renal artery stenosis, thyroid

## Resistant HTN or Something Else?

Defined as the inability to achieve blood pressure below 140/90 mm/Hg despite the concurrent use of three antihypertensive agents (one of which is a diuretic), resistant hypertension affects one in 10 patients with chronically elevated blood pressure.

Nine out of 10 hypertensive patients have essential hypertension, but among those with resistant forms of the disease, about 30 percent might have hypertension secondary to identifiable causes.

There’s no magic algorithm for differentiating between the two groups, and a test that makes perfect sense in one patient can turn out to be a dead-end diagnostic pursuit in another.

In such clinically challenging cases, Oscar Cingolani first rules out pseudo-resistant hypertension caused by medication noncompliance, inadequate BP-measuring technique, or “white-coat syndrome.” To do so, he spends up to an hour in the exam room during first visits, asking probing questions about lifestyles and hobbies and taking repeat BP measurements.

“If the patient appears to have genuine resistance,” he says, “then the question becomes, What’s causing it?”

Once underlying pathologies are ruled out, the most likely culprit behind treatment-resistant hypertension is, well, suboptimal treatment.

disease, obstructive sleep apnea or primary aldosteronism.”

Such underlying disorders, he adds, are by no means the prime suspects in all cases of treatment-defying hypertension, but they are possible culprits that ought to remain on every diagnostician’s differential.

“Then the million-dollar question becomes how far to go and whom to test,” Cingolani says. ■

# Treatment for Large Clots in the Lungs

essence, conferred with interventional radiologist **Clifford Weiss**, who had recently started using a new transcatheter treatment for patients with large emboli: ultrasound-enhanced lysis that drives thrombolytic agents directly into the clot. Because the system’s cardinal feature is precision-targeted lysis, it is best suited for patients with massive clots, particularly those already exhibiting signs of right ventricular strain or those in full-blown respiratory or cardiac failure. The approach is rapidly emerging as a more efficient and safer alternative to traditional catheter-based treatment or high-dose intravenous clot-busting therapy for massive emboli and may have similar promise

for large yet submassive clots. High-dose intravenous tPA—used for massive clots—can cause brain bleeds in 3 to 5 percent of patients, but the use of ultrasound-enhanced lysis can cut the total tPA dose from 100 milligrams to 12 to 24 milligrams, Weiss explains.

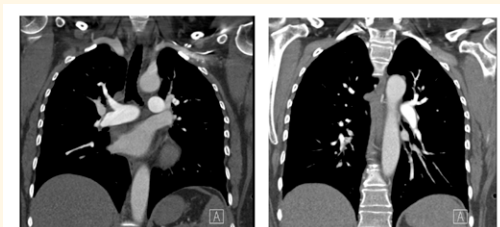
“We’re plumbers. We like treating the problem directly and locally,” adds Weiss’s colleague, interventional radiologist **Anobel Tamrazi**. “It’s precision-targeting at its best, and the response we see is rather remarkable.”

After the treatment, the patient’s pulmonary artery pressure dropped from 82/37 to 42/12

*(continued on back page)*



**One presentation with submassive pulmonary embolism**



**Months later, thrombus clear, patient taking an anticoagulant**

## Precision-Targeted Low-Dose Treatment for Large Clots in the Lungs *(continued from page 3)*

mm Hg in a matter of hours and continued to decrease slowly over the next day.

“We restored the pulmonary vasculature, allowing the body to take care of the rest,” Weiss says. “In less than 12 hours, we took this patient from critically ill to stable and, most importantly, we gave her rapidly decompensating heart a new life.”

Weiss and Tamrazi have used the treatment in about 20 people thus far—all of them with excellent results.

Now, says Tamrazi, “we’re gathering biomarker information that reveals the tipping point at which critically ill patients become stable following treatment. Knowing the trajectory of recovery can help us optimize dose titration and tweak treatment in real time.” ■

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# CardiovascularReport

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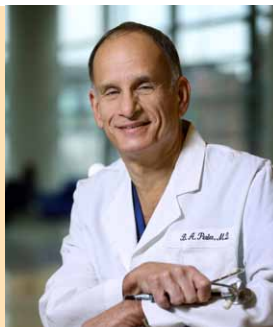
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