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VITAL SIGNS

Six compelling stories from the frontiers of medicine
A body scan reveals a lemon-size mass in the chest of a 16-month-old boy. Fearing cancer, surgeons perform a risky operation to save his life.

I was reviewing my emails late in the day when I found a message flagged “Important” in the subject line. It was from Kelsey, one of our hospital’s new pediatric surgeons. “Consulted regarding a 16-month-old with a middle mediastinal mass,” her message read. “Compression of trachea. Would love your thoughts.”

The mass Kelsey referred to in her email was in an area where a lot of things can go wrong, what we call the mediastinum—the middle of the chest between the lungs, where several important organs, such as the heart, trachea, and esophagus, reside.

As a thoracic surgeon, I specialize in operating on organs in this area and often review cases with colleagues.

I responded that I’d be happy to speak with her, and in less than 15 minutes she was tapping on my door. Kelsey was obviously very concerned about this one, so I quickly pulled the CT scan of the mass up on the computer as she relayed the details of the case. The patient was a 16-month-old boy who was developing normally but had recently been diagnosed with asthma.

He had been admitted to the hospital because of increasing stridor, a high-pitched sound made during inhalation. Stridor indicates a narrowing somewhere in the main, or proximal, airways—the area of the respiratory tract between the vocal cords high in the neck and where the trachea, or windpipe, branches to meet the two lungs. Stridor is often thought to indicate asthma, but it usually doesn’t. Asthmatics make a different sound: a wheeze. Wheezes occur during exhalation and imply obstruction of the smaller airways that are in the lungs themselves.

The boy’s name was Ian, and it was clear that his breathing problems were not caused by asthma. The CT images showed a five-centimeter mass—about the size of a lemon—narrowing his trachea by more than half and encasing the adjacent esophagus, which carries food from the mouth to the stomach. It looked as if malevolent bees had built a rounded, ill-formed hive in Ian’s chest.

I took in a deep breath: “That looks bad, Kelsey.”

“Yeah,” she replied. “It may be malignant. I’m worried about a sarcoma.”

We knew that about half of mediastinal tumors in children are malignant—aggressive cancers that grow into surrounding organs. Such tumors can take various forms. Sarcomas are malignant tumors of connective tissues such as muscle and bone. Tumors can also form in the lymph glands, the small organs of the immune system that filter bacteria from the bloodstream. Mediastinal tumors are rare, however. A total of 10,000 children are diagnosed with cancer every year in the United States, and mediastinal tumors account for about 100 of those cases.

“If not a tumor, I guess this could be a fistula,” Kelsey said, “with a chicken bone or something lodged there and causing an infection.”

A fistula is an abnormal connection of tissue between two organs. There are a group of congenital fistulas that can connect the trachea and esophagus, which grow from the same embryonic tissue. If a child swallows an object that lodges in the fistula, it can trigger an infection that may result in an inflamed mass. But Kelsey said that Ian’s white blood cell count and other tests that would indicate an infection were normal.

I considered whether we should get other tests, such as a biopsy or an MRI. “We could,” Kelsey replied. “But if the mass enlarges, it will block the trachea completely. I think we just have to go for it.”

We discussed the challenges of removing Ian’s mass surgically. If it was attached to the esophagus extensively, we would have to remove much of the organ and replace it with a section of the stomach. The tracheal part of the procedure could get even more complex. The trachea does not heal as reliably as the esophagus, and only a small amount of tissue can be removed from it for reconstruction, giving us a narrower margin of error in the event of damage and subsequent repair. The complexities and risks were so great that Kelsey and I sought the input of other doctors as well. Kelsey called her mentor at the pediatric surgical program where she had trained, and I called a pediatric surgeon who had trained with me years earlier. These colleagues felt surgery was unavoidable.

We scheduled Ian’s operation and went to see him and his family in the pediatric ward. While we talked, Ian stood in his crib, sucking his pacifier.

We did our best to assuage the parents’ fears, but this was a lot of surgery for a little person, and it

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involved a great deal of risk. Whether or not we found a malignancy, the outcome might be bad.

**AFTER A NIGHT OF LITTLE SLEEP** for me, and most likely less for Ian’s parents, the morning of the surgery arrived. In the operating room, nurses carefully inserted a breathing tube into Ian’s narrowed airway. He was then anesthetized, positioned with his right side up, and cleaned with an antiseptic solution. Drapes covered his tiny body, exposing only the operative field.

We made an incision in his chest and placed retractors to make room between his ribs. The mass was immediately evident. It was oval-shaped, with an irregular contour, like the surface of a reddish-tan rock. We both felt it. “It’s fixed and firm,” said Kelsey, not needing to mention that this was consistent with a cancerous tumor. We began by working our way around the mass with surgical scissors to the back wall of the esophagus. It was a struggle.

“Let’s definitely involving the esophagus,” I said. “Let’s try the trachea.” Kelsey was a skilled young surgeon, but using a variety of tools, including an electric scalpel, we could not free the mass from either structure. It was too firmly attached. While working around the mass, we spotted an enlarged lymph node nearby. “That’s not a good sign,” I murmured. “Might have spread there.”

We worked without speaking—four adult hands in a small space. A sense of foreboding was accumulating in the room around us like fog.

Finally, I made a desperate suggestion. “Let’s divide the mass,” I said. “Maybe we can save some of the trachea that way, make the repair easier.”

I took a scalpel and carefully incised the mass. After a couple of passes, it cracked open. Ian’s heartbeat, a beep on the anesthesia monitor, registered five times before either of us spoke. There was something dark and linear at the center. It looked horrifyingly like a slug. “What is that?” Kelsey asked.

I reached down and grasped it with a pair of forceps. “It’s firm,” I said. Kelsey adjusted the light overhead—there was a glint of reflection. “Metal?” I asked. I carefully pulled the object free. It was dark gray, oval, and covered in a layer of mucus. I held it up in the light between us. It was a leaf.

“A leaf?” Kelsey asked. “A leaf?” Her eyes were squinting above her mask, and her forehead wrinkled in disbelief. Suddenly it was clear. The mass formed to protect Ian’s body from the leaf and had taken on a life of its own. We both started laughing. The nurses clapped. There was no cancer; Ian was going to survive.

During the rest of the operation, we found that the leaf was nestled in a place where the normally cylindrical esophageal wall bulged out—a diverticulum in medical jargon. It all added up. Ian had swallowed an oak leaf months before, and it had lodged in the diverticulum, unable to pass. The leaf’s tip had eroded into the trachea and eventually, after white blood cells homed in on the region to heal the lesion, a scar formed around both the inflamed tissue and the leaf.

The young mother and father were incredibly relieved at the news, which Kelsey and I delivered immediately following the operation. They hugged each other, and after several moments, Kelsey and I left the room quietly, the two of them still embracing. Ian left the hospital after a few days. He was going to be fine.

The fact that the mass was not a malignant tumor didn’t change the urgency behind the operation. If Ian’s diagnosis of stridor and the surgery had been delayed, the mass could have led to the complete obstruction of the airway and sudden suffocation, or a leakage of esophageal contents, laden with bacteria from the mouth. If leaked into the trachea, these contents could have led to pneumonia, or if into the mediastinum, to sepsis and vascular collapse. We were relieved to find that the mass was not cancer, but left untreated, a simple leaf could very well have ended Ian’s life.
JERRY WAS IN FINE FORM AS HE STOOD AT CENTER STAGE, HIS HAND RESTING on the microphone stand, waiting for the laughter to subside. He had invited me to watch him perform stand-up at this West Los Angeles comedy club, and he didn’t disappoint. But his wife, Sandy, wasn’t laughing. She leaned across the small cabaret table we were sharing and said, “I need to talk to you about Jerry.” They had both been patients of mine for many years. Both were late middle-aged, and neither had ever had a serious medical problem. I looked at her quizzically and she said, “His breath.” I leaned closer and asked, “What about his breath?” “It’s different. Not bad, but it’s changed. Something’s not right.” “How long?” “Maybe three months.”

I asked if anyone else had mentioned anything, and she shook her head. “Nothing. Frankly, I wasn’t sure that...” She shook her head vigorously and said, “I am not crazy,” she insisted. “I am not crazy,” she insisted. “I’m sure.”

I nodded and said, “See him again tomorrow.”

The nasal passages and sinuses...
esophagus, stomach, or intestine.” Undaunted, she repeated, “Something’s wrong.”

I thought for a moment and then said: “Fair enough. You know, sometimes conditions in the lungs can cause the breath to be bad. Let’s do a chest X-ray.” Even though I was certain that the yield on the X-ray would be small, I wanted to be able to tell her we had turned over every stone in search of the cause of Jerry’s nonproblem.

So even though Sandy was the only one who thought her husband’s breath was bad; even though Jerry had no symptoms, findings, or risk factors whatsoever; and even though his lungs had sounded clear when I listened to them at his first visit, I had my medical assistant walk him down the hall for the chest film.

SEVERAL MINUTES LATER MY ASSISTANT put the X-ray up on the view box in my office. I took one look and had to suppress an expletive. Sitting in Jerry’s right midlung was a rounded density with a central cavity containing air and fluid. It was the radiographic signature of an abscess.

Amazingly, Jerry had been harboring a chronic infection in his right lung, but it had not been accompanied by any of the typical symptoms of an abscess—fever, cough, sputum production, sweats, and weight loss. He’d had none of them. None, that is, except for an odor on his breath. The smell of purulent sputum incubating deep within a lung may waft its way up the bronchial tree, resulting in serious halitosis. But in Jerry’s case the odor was so subtle that it took the exquisitely sensitive olfactory memory of his wife to pick up the change. The “ghosts” she smelled were real, and antibiotics were exactly what it was going to take to get rid of them.

Adding to my surprise was the fact that Jerry had none of the risk factors associated with a lung abscess. Among patients with intact immune systems (not compromised by HIV or chemotherapy, for example), lung abscesses occur most frequently in those with conditions that impair the swallowing mechanism and allow for the aspiration of food or saliva into the lungs. Disorders such as strokes or neurodegenerative disease and conditions that depress consciousness like alcoholism, seizures, and drug abuse can all predispose to oral contents “going down the wrong pipe.” When coupled with poor dental hygiene, which can lead to the buildup of bacteria, these disorders set people up for aspiration pneumonias, infections that can smolder and destroy normal lung tissue, literally rotting out a “dead zone” in the lung.

But in a small number of cases, lung abscesses may arise in the absence of any identifiable risk factor. It is possible that Jerry had a congenital anomaly in his bronchial tree that led to the pooling of mucus, and eventually to infection, but it is impossible to know for certain.

In the pre-antibiotic era, lung abscesses were fatal one-third of the time and left another third with lifelong debilitating lung disease. The introduction of lobectomy, the surgical removal of part of the lung, improved these numbers, but an extended course of antibiotics long ago replaced surgery as the mainstay of treatment for these infections.

In consultation with an infectious-disease expert, I started Jerry on clindamycin, a potent antibiotic effective against the anaerobic (non-oxygen-consuming) bacteria that most frequently populate this type of infected cavity. After six weeks, an X-ray showed the abscess had shrunk down to a stable and probably permanent scar on Jerry’s lung. There was no reason to expect any recurrence. But had Jerry’s abscess gone undiagnosed, it might well have continued to grow and could have eventually necessitated the surgical removal of part of his lung.

At a visit shortly after finishing the antibiotic course, Jerry told me he had gained new respect for both his wife’s dogged persistence and her uniquely talented nose. Then he said he was considering adding a bit to his stand-up routine about hiring his wife out to the bomb squad at the Los Angeles International Airport.

“Or,” I suggested, “maybe you could just get her a bouquet of sweet-smelling flowers and take her out to a nice dinner.”
A patient’s heart tumor is all but inaccessible to his surgeons. The only way to deal with it: Remove the heart and operate on it outside the body.

I was in the middle of a normal clinic day, seeing candidates for surgery, when a nurse told me that one of them had arrived with a diagnostic video. When I had a free moment, I walked over to a computer and put the CD into the drive. As the program booted up, I noticed that the video was a cardiac MRI (magnetic resonance imaging) study. I clicked through the images, and what I saw was frightening. A large mass was growing in the patient’s heart, in the back wall of the left atrial chamber, perhaps the worst possible place to have a problem like this. The right atrium and both ventricles are somewhat accessible to the surgeon’s knife. But the left atrium at the back of the heart next to the spine is a difficult, if not impossible, area to reach.

As I watched the video, more details emerged. As the left atrium attempted to pump blood, the wall opposite the growth ballooned out awkwardly instead of contracting with the rest of the chamber, its movement altered by the growth. The mass also took up a lot of space and was impeding blood flow. If it got just 5 percent larger, the chamber would be almost completely obstructed, resulting in a high risk of sudden death.

I called one of my cardiac surgery colleagues, Mike Reardon, and asked him to take a look.

“Oh, man,” Mike said, “that’s a tumor, all right—and in a bad place.”

My own heart sank. Primary tumors, which originate in tissues rather than spreading there from some other place in the body, are uncommon in the heart. They occur in less than 0.05 percent of autopsies. Seventy-five percent of them are benign, but this one did not look harmless. Benign tumors typically grow out from the surface of the cardiac wall like a mushroom on a stalk; malignant tumors look more like a bulge of varying thickness in the wall. Most cardiac surgeons will encounter only a few benign primary tumors in a career, and many will never deal with a malignant one.

“If we were to think about removing it,” I asked, “how would we approach it?”

“How old is the patient?”

“Thirty-seven,” I answered.

“How old?” I asked quickly.

“Any history of coronary disease?”

“Okay…wow,” was all I could say.

“We normally quote a 1 to 5 percent risk of dying for heart surgery,” I continued, “but your risk will be higher. The best-case scenario, if all goes well, is perhaps a 10 percent risk, and the worst case would be maybe five times that.”

There was no hesitation. “Let’s do this,” Mr. Johnson said.

Two days later we were in the operating room, where I would assist Mike. As the anesthetizing medications were administered, Mr. Johnson’s blood pressure dropped dangerously. The anesthesia team quickly gave him epinephrine to bring it back up. “Not much blood getting into that left side,” the anesthesiologist said as he looked at the

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monitor. "That’s why his pressure dropped. Good thing you didn’t wait too much longer."

We divided Johnson’s sternum and placed retractors to open up the chest. We then cut into the pericardium, the outer sac protecting the heart, and inserted tubing into the large vessels entering and leaving the heart to allow blood to bypass the organ.

“Go on bypass,” Mike said, loudly enough for the technicians managing the pump behind us to hear. The heart began to empty of blood.

We put a cold saline slush around the organ to help put it into a kind of suspended animation. Then Mike and I went to work, using surgical scissors and scalpels to sever the vessels entering and leaving the heart. Once the large vessels and other attachments were cut, Mike lifted the organ out of the body.

I looked into Mr. Johnson’s open chest as Mike placed this cold, now flaccid heart on an operating table a few feet away. Where his heart should have been was a void with tubes leaving it from the margins.

The only other time a doctor has this view is during a heart transplant, after the removal of the diseased organ and immediately before placing a donor heart into the recipient’s chest. The difference in this situation, however, was critical. During a transplant, we never take out the diseased heart until we have the new one in the room. In this case, there was no new heart and a chance we wouldn’t be able to fix the one we had taken out.

Mike and I worked quickly at the table, using our scalpels to remove the tumor.

“It’s bigger than it looked in the images,” Mike said, “but I think we got all of it.”

We placed the tumor and the portion of the fleshy heart wall that we removed in a small plastic bucket to transfer to a pathologist. He would check the tissue to make sure that we had removed the entire mass.

A few moments later, the pathologist called into the room. “There is some microscopic tumor at the margin,” he said.

Mike stared down at the opening in the back of the heart where the tumor had been.

“If we take any more,” he said, “we may not be able to reconstruct it.”

“We can try chemotherapy,” I replied. “It has a better chance of working with microscopic disease. Better to have a chance than not to leave the O.R.”

“I agree,” he said. “We don’t have much time. We need to get this organ back in there.”

He sewed a piece of bovine pericardium—the heart sac from a cow—into the opening left by the removed tumor. We then carried the heart back over to the patient and placed it in the void.

We sewed the large vessels back together and allowed the heart to gradually warm. We knew that a healthy organ will often start to beat once it is warmed, even without a blood supply reestablished.

But nothing happened.

We continued to work, completing the suture lines. Blood began to flow back into the coronary vessels.

“No action here,” the anesthesiologist said, watching the electrocardiogram.

Mike inserted a small needle into the muscle to measure the temperature. “Should be working; the temp is good,” he said.

Several more seconds passed. Still nothing.

Then we noticed a quiver near the apex of the heart, followed by another, and then the heart sprang back to life, beating vigorously. We removed the tubes and closed Mr. Johnson’s sternum.

Our patient made a good recovery and was discharged from the hospital several days later. After a regimen of chemotherapy to treat the microscopic tumor left on the heart, he had a good chance of complete remission and possibly even a cure.
The Inverted Patient

A doctor is baffled: Why did a giant man walk into the ER holding a tiny woman by her feet?

The emergency room was busy that afternoon. I had just started my shift and was making my way through a scrum of frantic doctors, nurses, and orderlies when I heard yelling coming from the ambulance bay entrance.

“Put her down now!” I recognized the stern voice of Herb, one of our security guards.

“Get a stretcher, stat,” said Ellie, the head nurse.

“You’re hurting her,” a woman yelled.

I ran to the ambulance bay, rounded a corner, and saw a huge man, seven-foot-something, holding a petite woman, maybe five feet tall, by her feet, her head dangling down. “I have to hold her this way,” the man insisted.

“I’m fine,” said the woman through her dangling long black hair. “I feel ok now.”

Herb grabbed at the man’s muscular arms, attempting to free the woman.

“This is my wife,” the giant shouted. “Let go of me.” He glared at Herb, who kept pulling at his biceps and wrists. A large group of ER personnel was now watching them from a distance.

“Let’s everybody take a deep breath here,” I said, leaning over, trying to see her face. “What’s your name, sir?”

Herb released his grip on the man and took a step back.

“Jason,” he said, more calmly now. “Okay, Jason,” I said. “Why are you carrying your wife by her feet?”

“Hi, Dr. Janeira,” said the upside-down woman. “Remember me?”

“No,” I said. “Have we met?”

“Yes, I was here yesterday,” she said. “Remember? With the slow heartbeat?”

And then it came to me. Her name was Mary, a woman in her mid-60s. She had arrived at the ER the day before with complete heart block, caused when the electrical system connecting the atria to the ventricles fails because of scarring, infection, or heart attack. As a result, the heart slows dramatically. Mary’s heart rate had been under 40 beats per minute instead of the 60 to 80 that would be considered normal in her age group. She was having recurrent fainting spells and seizures. This giant hadn’t been with her then, and I had called a colleague for urgent implantation of a pacemaker, which generates rhythmic electrical pulses that prevent slowing of the heartbeat. Within minutes she had been taken from my ER to a laboratory where she was fitted for the device.

I approached the couple slowly.

“I didn’t expect to see you so soon,” I said, leaning over, trying to see her face. “Didn’t you have your pacemaker implanted yesterday?”

“Yes,” she said. “I had the surgery yesterday. Everything went well, and I went home this morning.”

“Everything was good until about half an hour ago,” Jason said. “She coughed and then collapsed.”

“But I don’t understand why you’re keeping her upside down,” I said.

“I picked her up and put her on our bed,” Jason explained. “She regained consciousness for a few seconds. She tried to get up but went out again and fell behind the bed. I picked her up by her ankles and she came to.”

“I still don’t get it,” I said.

“If Jason puts me in bed or upright, I faint again,” Mary told me. “We’ve tried it four times now, and every time he changes my position, I go to la-la land.”

“So you’re conscious upside down but not right side up?” I asked.

Mary’s upside-down head nodded vigorously.

An Urgent Diagnosis

My mind raced through the possibilities. Mary could have something obstructing the blood flow from her heart to her brain that was overcome when her head was down. Or her blood pressure could be so low that blood reached the brain only when she was upside down. Blood pressure that low could have been triggered by an allergic reaction, anaphylactic shock, or severe dehydration.

Another possibility was that Mary was suffering from cardiac tamponade, a compression of the heart caused by a buildup of blood in the sac covering the organ. If her heart had been perforated during the pacemaker implantation and blood had seeped out into the sac around it, it might be that her ventricles were now being squeezed by this accumulating blood, lowering her cardiac output. That condition could improve when she was upside down by increasing blood flow to the brain.

The first thing to do was to check Mary’s vital signs. “Bring her into a room,” I said. “Let’s get her on a monitor.”
I pointed the way, and Jason carried her into the cardiac room, an entourage of curious ER personnel trailing behind us.

Even once in the cardiac room, Jason was unconvinced that he should let go of her ankles and put her on the bed. “When I put her down, she’ll go out on us,” he said.

I paused for a moment. “We’ll do an assessment of the vital signs first while Mary is upside down. Then we’ll put her in bed and see if and how things change, ok?”

Jason nodded. Mary’s long black hair waved back and forth, which I took for agreement from her, too. Ellie then placed heart monitor electrodes on her chest.

“Normal-paced rhythm,” I said, watching the monitor. “The pacemaker is working perfectly fine right now.”

“And I feel perfectly fine,” said Mary. “Well, except that I’m upside down and have been for about 30 minutes now.”

Ellie wrapped a blood pressure cuff around her arm. “It’s 120 over 66,” said Ellie. “Pretty good.”

“Ok, slowly get her on her back,” I said. Jason walked closer to the bed and Ellie and I eased Mary down onto it. The only sound came from the heart monitor: beep, beep, beep, steady at 60 times a minute. We all held our breath.

Then the cardiac monitor showed a sudden change. The alarm began screaming.

“Here I go,” said Mary. “It’s happened…” Her words dissolved into nothingness.

“No heart rhythm,” Ellie called out. “Pacemaker failure.”

“Get me epinephrine,” I yelled. Also known as adrenaline, epinephrine is a hormone that can constrict blood vessels and get a stalled heart beating again.

“But we don’t have an IV in yet,” said Ellie.

“Out of my way,” said Jason, pushing us aside to get to Mary’s feet. “I told you this would happen.” The big man grabbed Mary’s ankles and pulled them up in the air. Moments after Mary was upside down again, the heart monitor resumed steadily beeping.

“I’m back,” said Mary.

Something must have gone wrong with her operation yesterday, I thought. Then suddenly it hit me. “The pacemaker lead, the wire going from the pacemaker generator to your right ventricle, must have disconnected. Your coughing spell could have done it,” I said. “Somehow, the lead reconnects when you are upside down and continues to stimulate the heart.”

Pacemakers are made up of two main components, a generator and a lead that carries electrical impulses to the heart. Often the lead tip is screwed directly into the heart muscle, but in rare cases it can dislodge and cease to stimulate the heart. Data from St. Jude Medical, one of the largest pacemaker manufacturers, show that out of about 220,000 implants of the company’s most popular lead attached directly to the heart, only 97 dislodged within 30 days of implantation. Apparently, Mary was one of the rare cases.

Getting The Patient Upright

“How are we going to fix this, doc?” Jason wanted to know.

“You’ll need to go back to surgery to reattach the lead,” I said to Mary. “Let’s page your electrophysiologist stat.” I looked at Jason and sighed. “Meanwhile, keep her upside down.”

We inserted an IV in Mary’s arm and hooked her up to an external pacing device. But pacing her heart through her chest wall gave her severe discomfort and was not a good option, even in the short term. Moreover, it turned out that Mary’s slow beat did not respond at all to medications, including intravenous epinephrine. So she was quickly transported to the electrophysiology laboratory, dangling by her ankles, carried by the only man around with enough strength to do it. And my ER shift continued.

The next day I was back on duty. As I came out of a room after examining a small child with a fever, I heard a familiar voice behind me.

“Dr. Janeira, it’s me, Mary. I’m all fixed up.”

I turned and smiled at Mary and nodded at Jason, who towered massively behind her. “You were right. The pacemaker’s ventricular lead had to be re-screwed in my heart,” she said. “I’ll be having the pacemaker checked in a few days and then every three months.”


And with that, she left my ER walking upright and hand-in-hand with her giant.
Does a confused patient have a recurring case of viral meningitis, or has something else triggered his altered mental state?

I sensed a commotion rippling across the emergency room. Near the entrance, a man sporting a surgical mask and pajamas was pacing like a tethered ferret. It was 2 a.m., but as a rule most patients don’t wear their pj’s to the ER. Something was strange about this one. Heading over, I watched as Claudia, the intake nurse, tried to coax him into the triage chair. He sat for a moment, stood up, then plopped back down. “I need to see your expert,” he spat out. “I have to do this quickly.” “Do what, sir?” Claudia asked.

The patient sprang up. “I can’t feel my legs. I can’t breathe. Where’s your expert?”

His wife walked calmly over from the registration desk. “John was hospitalized uptown four days ago,” she told me. “It started then just like it did tonight, with a headache and confusion.” The spinal tap done uptown had shown a high white blood cell count, indicative of infection, but all the cultures were negative. John had stayed in the ICU and gotten better overnight—a surprise for the uptown staff, who then diagnosed viral meningitis. (Meningitis is an inflammation of the meninges, or lining of the brain and spinal cord, usually caused by bacteria or a virus; bacterial meningitis can be life threatening, but viral meningitis usually acts more like a passing flu.) In line with that diagnosis, they’d sent John home.

“Yet just before bed tonight he had a headache, then woke up babbling again,” his wife explained. “No fever, vomiting, or new medications?” I asked.

She shook her head. “It’s all right, darling,” the wife said soothingly. “This is no worse than last time.”

“I can’t stay, “ John said in a rush. “We have to go. ”

“First can I make sure you’re ok?” I pleaded. “It really would be better if you stayed,” I said in my softest please-don’t-make-me-tie-you-down voice. “See? The doctor is very nice,” the wife implored.

“See? The doctor is very nice,” I told Stacy. “Go in there and get more detail: Fever? Headache? Nightmares? Travel? Hearing voices? The weirdest part is how he got better, then bang, bad again. I’m counting on ya, kid.”

For a few minutes, all was calm. Then Stacy came trotting out of the room. “Dr. Dajer, can he have water and an Advil? He has a headache.”


Advil?

Tony Dajer is chair-
man of the depart-
ment of emergency
medicine at New
York Downtown
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In a Vital Signs column in this magazine 17 years ago, infectious-disease physician Abigail Zuger described the conundrum of a young woman with recurrent meningitis. Hospitalized four times in a matter of months, the patient exhibited high fevers, delirium, and a stiff neck—all signs of life-threatening bacterial, septic meningitis. CAT scans were normal. Spinal taps revealed high white cell counts in the cerebrospinal fluid—usually a
harbinger of severe infection—but bacterial and viral cultures grew nothing. The patient was becoming ill and then abruptly getting better. The fourth time, to general eye-rolling, a medical student was tasked with asking the woman for the umpteenth time whether she had taken anything, anything, prior to getting sick. He hit pay dirt: Advil.

Zuger’s patient hadn’t considered over-the-counter, everyday Advil a medication. It is also sold as Rufen or Motrin, and the chemical moniker is ibuprofen. Ubiquitous as this drug is, until reading Zuger’s article I hadn’t known that in rare cases it can cause meningitis.

Case reports are the lifeblood of diagnosis. The dry, reductionist, what-percent-have-cough and what-percent-have-fever lists in medical texts will put you to sleep. But good stories stick. Doctors trade odd diagnoses like baseball cards; we glean them from journals, TV, and friends, stockpiling them against the next tough diagnosis. Zuger’s story—even one old years later—primed me to jump on one small clue.

“ADVIL!” I CRIED TO STACY. “DID he take any tonight before he came in?”

“Yes, when he went to bed. Three hours ago.”

“How about four days ago?”

“I didn’t ask.”

“Well,” I smiled, “let’s.”

John was up again, still too bright-eyed and staring, but more there.

“What are the results?” he demanded. “I require transportation home.” His wife stood by warily.

“Do you remember taking any medications last time?” I asked him.

“He had a headache that night.” The wife tapped her lips. “Maybe some Advil?”

I showed my cards.

“Look,” I began, “I can’t prove this, but I think all your symptoms are due to the Advil. The best evidence is whether you took some before each episode.”

The wife’s face lit up. “Yes. He definitely took some the first time. Could that really be it?”

“It’s poorly understood,” I said. “It’s probably a hypersensitivity immune reaction. The ibuprofen may bind to specific tissues, like the meninges that line the brain, and set off an antibody attack. Most reported cases are in patients with immune disorders like lupus. But some have been in healthy people. It can happen with other anti-inflammatory drugs, like Aleve. The hallmark, besides the confusion and meningeal irritation, is that you get better quickly off the Advil.”

I turned to Stacy and smiled, “Nice work, Sherlock.”

She blushed. “Thanks.” (No, thank Dr. Zuger, I thought.)

To John I said, “I’m not going to scan or tap you.” I crossed my arms. “I think you’re ok.”

“You sure?” he asked.

I had an improving patient, a solid story, a negative recent workup, and a very intelligent and attentive spouse. I felt it was safe to release him.

“Go home,” I ventured. “Get some sleep and I’ll call you later this morning. Have your

she recounted, referring to a potential anticonvulsant. “But it’s making him very drowsy.”

John’s course after discharge was as I had predicted, give or take a few vague symptoms. And diagnosis of a seizure relies heavily on patient history.

A week later, his wife phoned. “I’m taking him off the Keppra.”

Eight hours later we spoke.

“Yes, dear, please,” his wife sighed.

“Better?”

John ventured.

“Still dubious, John asked, “Can I take off the mask?”

“Yes, dear, please,” his wife sighed.

A week later, his wife phoned to tell me a neurologist had decided John had a form of temporal lobe seizure. “These can cause bizarre behavior but none of the muscle clenching or loss of consciousness seen in regular grand mal seizures.”

He started John on Keppra,

There is no test that proves it. While the neurologist was trying his best to make a diagnosis based on vague, nonspecific symptoms, I was sure I had it right. I decided to be blunt.

“Look,” I told the wife, “every specialty has its default diagnosis. Seizures can do just about anything, but they don’t cause white cells in spinal taps. I truly think John is OK. It boils down to so little data, so many competing hypotheses.”

She fell silent, then finally said, “I’m taking him off the Keppra.”

A month later, he was doing fine.

No more than one hundred cases of ibuprofen-induced meningitis have been reported in the literature. But you have to wonder, given that ibuprofen is practically in the drinking water, how many more mistaken cases of “viral meningitis” are out there. 😐

—from the author
A Rip Van Winkle Virus

When her friend returns from Africa with a strange skin condition, a doctor suspects a pathogen from out of the past.

A

Y-YI-YEEE! THE PAIN RUNNING down the back of my arm—like a jolt of current traveling a frayed electric cord—caught me off guard. I had never felt a sensation quite like it. On the other hand: Why not? I had just finished a grueling week of hospital consults. My middle-aged frame was simply complaining in a new way, right? I probably just needed rest. “Move over, Ollie,” I mumbled. My dozing spaniel made space on the living room couch and I soon drifted off, pain forgotten.

Two days later, my fingers found a roughened patch of skin in the same area as that high-voltage twinge. I craned my neck but couldn’t see it. Finally, angling a mirror, I found the telltale lesion: a single nickel-size spot studded with small, fluid-filled bubbles. Aha, I thought to myself. So that explains the burning nerve. That was the moment I realized my body had won a secret battle that I had barely noticed.

But this isn’t my story—it’s Penny’s. Dr. Penny Nelson isn’t just a patient; she’s a longtime friend who has spent decades tackling malnutrition in developing countries. It’s hard to believe the lively pediatrician is now in her 80s. She still travels to a research site in western Kenya where I have no doubt, the sight of her warm smile, salt-and-pepper hair, and sturdy leather sandals is as beloved to her African coworkers as it is to her colleagues here in the United States. Most recently she has been studying the effects of high-protein foods on child growth and maturation.

Knock on wood, Penny’s health is as strong as her will to teach, trek overseas, and live a full, exciting life—and she does everything she can to keep it that way. Last year, however, something strange and disturbing happened to her. Out of the blue, a few days before leaving Kenya, she developed a low-grade fever, knifelike head pains, and one-sided hearing loss.

At first Penny thought an ear infection might be brewing. She started taking a penicillin-type antibiotic her dentist had prescribed for an aching tooth. Nonetheless, over the next 48 hours the head and ear pain worsened, and strange bumps resembling flea bites began to erupt on a cheek as well as her chin and ear. Although she couldn’t see them, she also felt bumps in her ear on the side where her hearing had been affected.

Could This Be a Tropical Disease...

By the time Penny landed in Los Angeles, several bumps had ulcerated, others had coalesced into small, scabby lakes, and a new theory had formed in her mind. Maybe chicken pox virus, which had been lying dormant in her body since she was infected in childhood, had escaped from her cells, multiplied, and started migrating down her local nerve tracts. In other words, she might have shingles—a skin eruption, commonly found on the chest and abdomen, stemming from a reawakened, often decades-old chicken pox infection. It was a logical diagnosis except for two facts. One: Shingles sufferers rarely develop lesions in their ears. And two: One year earlier, Penny had received a shingles vaccine, which re-primes aging immune systems to recognize and fight back against varicella-zoster, the virus that causes chicken pox and shingles.

Also weighing on Penny’s mind was the sheer number of exotic blights, from sleeping sickness to snail fever, that a person could contract in the part of Africa’s Rift Valley where she was working. After all, when an illness starts in the bush, you can’t help but worry. While overseas, Penny was exposed to people, insects, and livestock, all of which can harbor some pretty strange microbial stowaways. What if it wasn’t shingles but something more exotic? Because of this nagging worry, within 24 hours of Penny’s return, I received an email from her savvy internist, Joan Grant. Suspecting varicella-zoster, Grant had already prescribed acyclovir, an antiviral remedy. But she and Penny wanted a second opinion.

“Penny!” I cried the next morning after meeting my intrepid pal in my outpatient exam room. “Poor you!” Meanwhile, my eyes swept her face and my brain skidded through a list of skin infections both common and rare: crusty impetigo, an inflammatory infection caused by staph or strep bacteria; a rash caused by tick-borne parasitic bacteria called rickettsia; ulcerating sores from the bites of a sand fly laden with microscopic leishmania parasites. For a heartbeat I even considered anthrax acquired from handling infected animal hides, or orf, a pox virus that can pass from sheep and goats to humans.

As my mind whirred, Penny screwed her mouth into a wry smile...
and raised her eyebrows. "What do you make of this?" she asked, sticking out her tongue. Reddish lesions, like bumps on a pickle, dotted the tongue’s front two-thirds on the same side as her blistered cheek. Along with the pocks in her ear, the lesions were the giveaway. To reach those two disparate sites, varicella-zoster virus must have traveled specific branches of the facial nerve. Penny had shingles, all right—but in a far-from-ordinary location.

"Ramsay Hunt syndrome," I breathed, "straight from the textbook. I haven’t seen it in years."

...Or Something Much Rarer?

In 1907, James Ramsay Hunt, a neurologist at Cornell Medical College, published a seminal paper in The Journal of Nervous and Mental Disease. In it he noted that virus-induced inflammation of a knot of nerves ("the geniculate ganglion") near the auditory canal yields a facial eruption in the exact pattern revealed by Penny’s exam.

Today, the National Organization for Rare Disorders estimates some 15,000 people experience Ramsay Hunt syndrome in the United States each year. For contrast, an estimated 1 million Americans come down with shingles each year.

Penny remained perplexed. "Why did I get it now? And why here, of all places?" she asked, pointing to her ear. "I was immunized last year."

"Some patients still break out in a modified rash," I mused. "But this is not a place I would expect a vaccinee to develop lesions."

I paused and thought harder. "Did something else stir up the dormant virus near your facial nerve, I wonder?"

That’s when an "aha!" look lit Penny’s eyes. "How about major dental work?" she offered. "Earlier this spring, I had several implants done."

Of course—it was a perfect, recent trigger. The deep bite of the dental drill and fixing of the titanium “roots” of the implanted teeth would have rattled Penny’s immune system, explaining the reactivation of decades-old varicella-zoster virus. It all added up. Now I could safely skip an imaging study of Penny’s head and diagnostic scrapings of her blisters to rule out the various tropical diseases.

Sure enough, two weeks later, after she completed the antiviral treatment prescribed by her internist, Penny’s lesions were gone. We were both relieved. Without prompt, effective treatment, I estimate that Penny’s chance of complete recovery would have been 50-50 or less. Permanent hearing loss, facial weakness, and ongoing pain are common complications of Ramsay Hunt syndrome. Thankfully, my friend experienced none of these.

Now for the coda.

A Dormant Virus Awakes

As soon as I spied the bubbly patch on the back of my arm, I realized I had a “forme fruste”—another modified version—of shingles.

For one thing, the jangling, electric-shock sensation I had felt two days before was typical of an acutely inflamed nerve. The pièce de résistance was the cluster of blisters atop my skin lesion—the hallmark of varicella-zoster and its close relative, herpes simplex, the virus that causes cold sores and genital herpes.

Most people don’t realize that shingles can present with a subtle footprint, or even with only nerve pain by itself. "Zoster sine herpete" (roughly translated from the Latin, “shingles minus creeping eruption”) is medical lingo for the second syndrome.

In zoster sine herpete, human immune cells quash the virus before it infects the nerve. Accordingly, sufferers fail to develop blisters and scabs but still experience the burning spurts of pain associated with full-blown shingles. Proving that varicella-zoster is to blame is not easy. There’s still no simple test for the virus if the patient doesn’t develop lesions, although many doctors know that varicella-zoster virus is one of the leading culprits for such pain.

My patients often ask if a major or minor case of shingles protects them against subsequent outbreaks. Not necessarily, unfortunately; varicella-zoster remains in the body’s cells even after attacks are treated or resolve on their own. Therefore, the shingles vaccine is currently recommended for healthy people over 60 (today, many experts even say over 50), whether or not they have a history of the disease.

I’m a case in point. Will I stick out my arm for the vaccine after reaching age 60? Absolutely.
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