I glanced up from Amanda Wolf’s chart as the emergency department nurse, followed by the lab technician (tech), followed by the electrocardiogram (ECG) tech flowed into cubicle No. 5. John Benner, MD, pulled up a chair to review the case with me at the nursing station.

“Here’s what we’ve got. Thirteen-year-old girl with a one-week history of diffuse aches and pains, fever, chest pain, now with a rash on her lower legs. She’s short of breath; her oxygen (O₂) saturation when she arrived was 90%, normalized to 96% on 2 liters/minute O₂. Hey, thanks for coming down. I heard you were in-house. Your tie, it’s got an ugly spot on it.”

I looked down at an unidentifiable brown smudge and succeeded in smearing it more prominently with a wet finger. Dr. Benner silently handed me an alcohol swab. “Anyway, her breath sounds are diminished in the right lung base. No murmur, but her heart sounds are distant. It was a tough exam; she cried everywhere I touched her. Dad carried her in from the car. The rash is wrong for rheumatic fever; it’s mostly on the lower legs, with clusters of angry red lesions, but her face and chest are flushed as well. We’re going to continue on page 10.

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THE MYSTERY OF LUPUS

THE CASE OF A 13-YEAR-OLD GIRL WITH LIFE-THREATENING ONSET OF SLE

BY CHARLES RADIS, DO

Men work harder than women.

My mother is a pediatrician, and I have two sisters—one is a dermatologist, and one is a real estate attorney. Therefore, I think understandably, this message took me by surprise. Of late, I have been particularly awed by my lawyer-sister, with whom I catch up when she is taking the 7:45 p.m. commuter train home to care for her two children. By that time, I am often already home with my feet up, drinking a beer.

The message, however, was unavoidable. My cell phone was experiencing status epilepticus, vibrating urgently with updates regarding the initial message—and then with rapid-fire commentary regarding that initial message.

The Dallas Medical Journal is the primary publication of the Dallas County Medical Society, which counts the majority of physicians practicing in the Dallas area among its members. According to its website, the Dallas Medical Journal “includes practical advice regarding the business of medicine, profiles on member physicians, legislative updates ...” In September, in honor of Women in Medicine month, the editors elected to dedicate the issue to women in medicine, focusing on “cracking the glass ceiling” and “pay inequality between the sexes.”

Big mistake.

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RHEUMINATIONS

The First Step

Pay equity in medicine

BY PHILIP SEO, MD, MHS

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PEDIATRIC ARTHRITIS

More Than S’mores: Juvenile Arthritis Camps

PAGE 61
The Mystery of Lupus

In Brief
A case of life-threatening lupus is presented. As a classic autoimmune disease, systemic lupus erythematosus is a case of mistaken identity writ large. The immune system in lupus patients is in chronic overdrive, effectively performing its primary job—protecting the body from infection—while cross-reacting against normal body tissues & proteins.

culture her up. It could be a viral syndrome. Maybe it’s one of your diseases?” He paused.

I didn’t have enough data to comment. Around us was controlled chaos; our community hospital emergency department hummed with activity.

Labs
Amanda’s nurse flung open the ringed curtain and reached for an IV bag off a nearby supply cart. She cradled the bag against her chest and grabbed several test tubes from the cart. “Grab an extra red-topped tube for me, will you?” I yelled so that she could hear me above the din. “Are there any green topped tubes on the cart? We don’t want to draw her twice. Oh, and add a sed rate [sedimentation rate], ANA [anti-nuclear antibody], ASO [anti-streptolysin], and a C3 and C4 [complements] to the routine lab Dr. Benner ordered.”

She scowled—an “I only have two hands” look—before she tucked the extra tubes into her back pocket, and applied a tourniquet to Amanda’s right arm.

First Impressions
In the moment before the scene was obscured, I focused my attention on Amanda. Her shallow breathing was punctuated by stifl whispering. She wore loose-fitting, pink-flowered pajamas and floppy white slippers. Her mom—they shared the same jet-black, pageboy haircut, the whispering in her ear. The lab tech released a lever on the stretcher to lay Amanda flat in preparation for the blood draw.

Amanda shrieked and flailed to remain upright, as if lying down were akin to drowning, I glanced at my watch and silently counted her respiratory rate over 15 seconds. Way too high. Pain? Anxiety?

“Welcome to my world,” Dr. Benner deadpanned. “We don’t see rheumatologists down here very often.” The lab tech... BP… crunch... BP… crunch... BP… crunch. I closed my eyes and concentrated. There it was again, a pericardial rub, a distinctive sound associated with inflammation in the smallest blood vessels. They’re rarely seen in self-limited viral infections. I turned the hands palm up. A bumpy, red rash extended from the fingers to midway up the forearm.

History of Present Illness
I turned my attention to Amanda’s mom. “What was the first thing you noticed out of the ordinary?” I consciously kept my voice even, unhurried.

“Two weeks ago, the fevers started up. Every night, just over 100, then the muscle aching,” Mom replied.

“How about the rash last month?” Amanda’s dad patted his daughter’s ankle and took a seat on the other side of the stretcher. “Same one she has now, but it faded after four or five days. It came on a day after she spent the afternoon at Fun Town with her friends. It seemed different than a sunburn—you know, not red all over—and that was the first time her muscles ached. I thought she had some kind of bug. Did we take her temp that night?” he looked at his wife, who shook her head.

Physical Exam
I methodically went through my exam. Inside Amanda’s mouth I identified two large ulcers on the edge of her tongue and another on the inner cheek. I noticed that above the right ear was a bare patch of pink scalp. Amanda reached up and grabbed my hand. “I hate my hair. Don’t touch it.”

I scanned her face from the side, saying nothing. The slightly raised rash extended across the nose and onto the cheeks, sparing the outer edge of the nostrils. With her mother’s help, I pulled up Amanda’s pajamas to assess the lower extremities. From the mid-calves to the ankles, the skin was peppered with angry red spots. It was the wrong rash for parvovirus, the coxackie virus, and the wrong rash for measles or mononucleosis. This was much more worrisome, a vasculitic rash, an immune-mediated inflammation of the venules and capillaries nourishing the skin.

The left knee was warm, perhaps minimally swollen, and it was Amanda’s whimper when I asked her to bend it slightly. “I’m not going to bend your knee; I just need feel if there’s fluid inside it. Okay?”

“Just don’t lay me down,” she answered, grabbing my side rails. A telltale budge sign was present in the knee, evidence of a small effusion.

“Okay, time to listen to your heart.” I tapped the diaphragm side of the stethoscope to ensure it was clicked into the correct position, and allowed it to drop down the front of her chest beneath her P.J.s. The background din of the emergency department faded as I placed the ear buds firmly in place and raised a finger to Amanda’s father, who was talking on his cell phone.

I filtered out the steady shhhhhhh of oxygen flowing into Amanda’s nose and listened. There. A faint leathery sound kept beat with her racing heart, filling in what is normally a silent pause between beats. BP... crunch... BP... crunch... BP... crunch. I closed my eyes and concentrated. There it was again, a pericardial rub, a distinctive sound associated with inflammation of the sack surrounding the heart.

Without a word, I wrapped a blood pressure cuff around Amanda’s right arm and squeezed the bulb up to 150 mmHg before slowly releasing the pressure. Nursing had previously charted her blood pressure. I was interested in something else. At 106 mmHg the faint tapping of Amanda’s pressure could be heard, but only intermitently. That’s odd. The top number, the systolic blood pressure, is usually steady or coxing a metronome. I adjusted the earplugs and listened intently. When I held the blood pressure cuff steady at 106 mm, I heard the tap, tap, tap of the blood pressure only as she exhaled.

Breathing in, the rhythmic tapping disappeared. As she breathed out, the pulse...
rebounded. I released the pressure on the cuff ever so slowly and the pattern persisted. Finally, at 88 mm, I heard the heart rate throughout her respiratory cycle.

The hair on the back of my neck tingled. The lab tech handed me the initial results of Amanda’s complete blood count (CBC): low white blood count and lower red blood cell count; platelets—critically low.

The curtain parted, and Dr. Benner motioned to me, “Dr. Radis, can I borrow you for a moment?” On the instrument tray next to the nursing station he reviewed the printout of Amanda’s ECG with me. “Classic pericarditis. Low voltage, diffuse ST segment elevation. This is pretty unusual for a teenager.”

“Listen, John,” I replied. “If it were just pericarditis, we could take our time and work out the details. But we need to move on this. She has systemic lupus—I mean, a true lupus, life-threatening lupus. The full house. She needs a gram of Solu-Medrol [methylprednisolone sodium succinate] STAT, and we need to transfer her over to the medical center, like, 30 minutes ago. Check me out on this, but I think with the pericarditis, she has tamponade with a huge pulsus paradoxus. I measured it at 18.”

“Eighteen?” Dr. Benner repeated slowly. The X-ray tech flipped the view box on and hung Amanda’s CXR on the screen. The size of the heart was breathtaking, taking up nearly three-fourths of the lower chest. We both knew the enlargement of the heart was primarily an inflammatory fluid within the sac surrounding the heart. The pressure from the fluid was slowly squeezing the heart like an external fist, triggering the abnormal pulse pressures and making it less and less effective at maintaining an effective blood pressure. I leaned forward from my seat and looked over my glasses at Amanda’s blood pressure on the cardiac monitor had dropped to 96. We reflexively turned back to where we could see Amanda through the edge of the exam curtain. She sat bolt-upright, her breaths increasing into shallow panicky gasps. No wonder the poor kid can’t lie down; that feeling of drowning was real.

**Immediate Treatment**

“Katen,” Dr. Benner’s voice was sharp and focused. Gone was the laid-back, you’ve got a stain on your tie repartee. He clicked out a series of orders. “Turn her O₂ up to 6 L/minute. Switch her IV to normal saline, and let’s give this young lady a liter of normal saline wide open over the next 15 minutes. Start another wide-bore IV in the opposite arm. We don’t want to get caught without IV access if a line infiltrates. Get Maine Medical Center life-saving lupus hanging on the phone. Turn around the Buxton ambulance that left five minutes ago. It’s too late to call in the ultrasound tech to verify there’s a big effusion around the heart. We need a transfer, now.” He shot me an uncertain, questioning look. “How much Solu-Medrol was that?”

“A gram of Solu-Medrol,” I repeated. “Make that a gram of Solu-Medrol. Send Tom up to the pharmacy. I know we don’t have that much down here. STAT. Let’s get that Solu-Medrol infused before the transfer…”

**Additional Lab Results**

The lab tech was hovering, unsure who to give the remaining lab results to. I took the sheet from her, and the results were a splash of red, critically abnormal numbers. Okay, concentrate.

Off to one side, I reviewed where we stood in Amanda’s work-up and treatment, aware that in another half hour, another team of physicians was going to evaluate Amanda, and I wanted to ensure we weren’t overlooking any critical data that required immediate attention. The diagnosis of systemic lupus erythematosus was removed, a pericardial effusion discovered, and a drain placed to prevent the fluid from reaccumulating to critical levels. Her blood pressure immediately rebounded to 118/78, her pulse dropped to 96. The immediacy of her death was averted.

**Discussion**

The term lupus—derived from the Latin word for wolf—refers to the disfiguring facial rash of lupus patients. And to transfer her true case of lupus may occasionally be suggestive of a predator’s bite, in many patients, the skin is entirely spared. The variability of the disease is breathtaking. The diagnosis may be readily apparent at the onset of the disease, as it was in Amanda, or elude diagnosis, sometimes for years. In medical school, I was taught that lupus and syphilis were the Great Imposters, meaning their signs and symptoms mimic a host of more common disorders. On medical rounds, it was always a safe bet to exclude lupus in the broad differential diagnosis of any perplexing case.

In contrast to rheumatoid arthritis, in which the joints are the primary target and serositis of the lung and pericardium are uncommon, diverse organ inflammation is the rule in lupus. The lungs, heart, blood, joints, skin, kidneys, liver, eyes and central nervous system of patients may all be targeted simultaneously in a critically ill patient, or symptoms and laboratory abnormalities may unfold over decades.

But what is lupus? As a classic autoimmune disease, systemic lupus erythematosus (SLE) is a case of mistaken identity with large. The immune system in lupus patients is in chronic overdrive, effectively performing its primary job—protecting the body from infection, while cross-reacting against normal body tissues and proteins. Ninety-nine percent of SLE patients develop anti-nuclear antibodies. Many patients have additional antibodies to proteins within the nucleus: anti-DSDNA, anti-RNP, anti-Sm, anti-histone antibodies. The list is long and growing.1

In medical school, I was taught that lupus & syphilis were the Great Imposters, meaning their signs & symptoms mimic a host of more common disorders. On medical rounds, it was always a safe bet to include lupus in the broad differential diagnosis of any perplexing case.
The Mystery of Lupus

The immune system may turn against components of blood. The resultant low white blood counts predispose patients to infection, the low platelets to bleeding gums or recurrent nose bleeds. Anti-bodies directed to the outer membrane of red blood cells may trigger life-threatening hemolytic anemia, giving rise to pale, ghost-like victims.

The exact sequence of events leading to lupus is unclear, but like so many immunologic disorders, the disease has both a genetic predisposition and suspect environmental and infectious triggers. This much is clear. Lupus is primarily a disease of women in the child-bearing years. For every 10 cases of lupus, nine are women.2

Back to Our Patient

The next day, Amanda’s kidneys hovered between catastrophic failure and reversible injury. Her urine output slowed to a trickle. A nephrologist consulted and performed a kidney biopsy. It confirmed two more days of high-dose Solu-Medrol, and in my notes indicated she would require a long-term immunosuppressive drug, depending on the results of the kidney biopsy.

Amanda’s urine output increased ever so slightly—the precious golden fluid draining through her Foley catheter into the collection bag at the bedside. A hematologist consulted on her autoimmune hemolytic anemia. A cardiologist weighed in on the pericarditis. An infectious disease specialist suggested that because of Amanda’s high fevers and critical illness, antibiotics should be continued until infection could be excluded.

As she ate breakfast on her third day in the intensive care unit, Amanda’s eyes suddenly rolled back, and she suffered a grand mal seizure—a known complication of lupus. The force of the seizure ripped the IV from her forearm, splattering blood and IV fluid onto the bed sheet and floor. The oxygen line snapped off the wall mount, and Amanda’s oxygen level plummeted. Fortunately, the cathe- ter extending from her chest wall into the pericardium of the heart was pinned to her hospital gown and remained in place.

The IV was re-inserted, and an infusion of Vialum (diazepam) and Ditanin (phey- nytoin) terminated the seizure. A portable CXR confirmed the worst; half her right lung was a blotchy whiteout. She’d aspirated a portion of her breakfast. An attending intubated her, and her vital signs were compromised. A rapid response team arrived at the same time. We sat down with the nephrologist and neurologist on call to perform a spinal tap. The neurologist on call performed a spinal tap. The computed tomography (CT) scan of the brain, ICU attending intubated her, and her vital signs stabilized. Histology was not my forte in medical school. I figured (correctly) that’s why you have pathologists. But even I could see the normal architecture on the kidney biopsy was distorted almost beyond recognition.

“Diffuse membranoproliferative glomerulonephritis—Class IV SLE nephritis,” the pathologist said finally, perusing over her glasses. “What a shame. Thirteen years old!”

That morning, Dr. Parker and I met with Amanda’s parents in the family room off to the side of the ICU. They were still shell-shocked. Amanda had gone from a goofy, hyperactive teen to a critically ill, unstable lupus patient, seemingly overnight. But at least she was off the ventilator. Dr. Parker explained that just as rapidly dividing cancer cells are sensitive to chemotheraphy, the overactive immune system cells responsible for Amanda’s lupus kidney damage were susceptible to chemotheraphy as well.

“What’s more,” I added, “we now have the ability to protect other organs from the effects of chemotherapy. An injectable drug called Luronin can shield the ovaries from the side effects of chemotherapy and preserve fertility.”

Dr. Parker and I believed in her recovery, and pregnancy could still be in Amanda’s future if her lupus came under control. After a few minutes, Amanda’s parents gave their consent.

With her system bathed in the immunosuppressive effects of high-dose steroids and an infusion of cyclophosphamide, Amanda’s kidneys stabilized just short of requiring dialysis. The cyclophosphamide and high-dose steroids slashed the production of antibodies directed against her blood cells, and the bone marrow responded by pouring out new red and white cells and platelets. Her kidney numbers steadily improved, the pericordial drain was pulled, her supplemental oxygen discontinued.

Ten days after she was admitted, Amanda was able to get to the bathroom.
Lupus is primarily a disease of women in the child-bearing years. For every 10 cases of lupus, nine are women.

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Without assistance. The constricting pain of pericarditis and the tortuous pain in her muscles and joints slowly dissipated. It was as if a malignant finger were lifted from every organ system.

**Life with Lupus**

Through her teenage years, Amanda’s care remained a challenge. Her parents separated and subsequently divorced. She sulked, became depressed and, for a while, probably didn’t take her medications at all. She was a no-show at four consecutive office visits.

Following a night of binge drinking, she suffered another seizure and was admitted in kidney failure. This triggered another six-month course of cyclophosphamide and high-dose steroids. Miraculously, the disease was beaten back and the kidneys recovered.

Then, a few days before her high school prom, she decided to go to a tanning booth—with predictable results: dozens of blisters erupted over her back and upper chest. The open sores became secondarily infected and, a few days later, she was found by her father lying on the kitchen floor, unconscious, in septic shock. Somehow, she survived.

That was the last time she was hospitalized. Over time, she stuck with the medications, even the prednisone, which she hated more than anything. Then one day, six years after the disease first settled in, and with significant trepidation, I discontinued the last 1 mg of prednisone. Nothing happened.

Not that she was cured. Lupus isn’t cured, it goes into remission. And it wasn’t as if Amanda was off all medications. She kept a pillbox to manage the daily assortment of pills required for high blood pressure, gastritis, depression and anxiety. And of course, I never stopped the hydroxychloroquine or low-dose mycophenolate. Like a good insurance policy, they quietly protected her from lupus rashes and kidney inflammation, and she knew it.

Several years later, Amanda went on to college and returned that fall break to inform me, “Depression is about the past. Anxiety is about the future. If you’re at peace, you’re living in the now,” and then she laughed until tears ran down her cheeks. “No, really, that’s what my psychology professor said last week.” She held up two fingers in a V. “Peace,” and collapsed again in a fit of laughter. She slumped deeper into her chair, twirling a pen. I waited.

“Lupus sucks,” she said. “I know that it sucked when I was 13, and it sucks now, and it’ll suck when—and if—I make it to 30.” She straightened up, half smiling. “But you know, I’m okay with that. Deal me in. You know what I mean? Deal me in.”

And I think I did.

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**References**

