

# Medicine

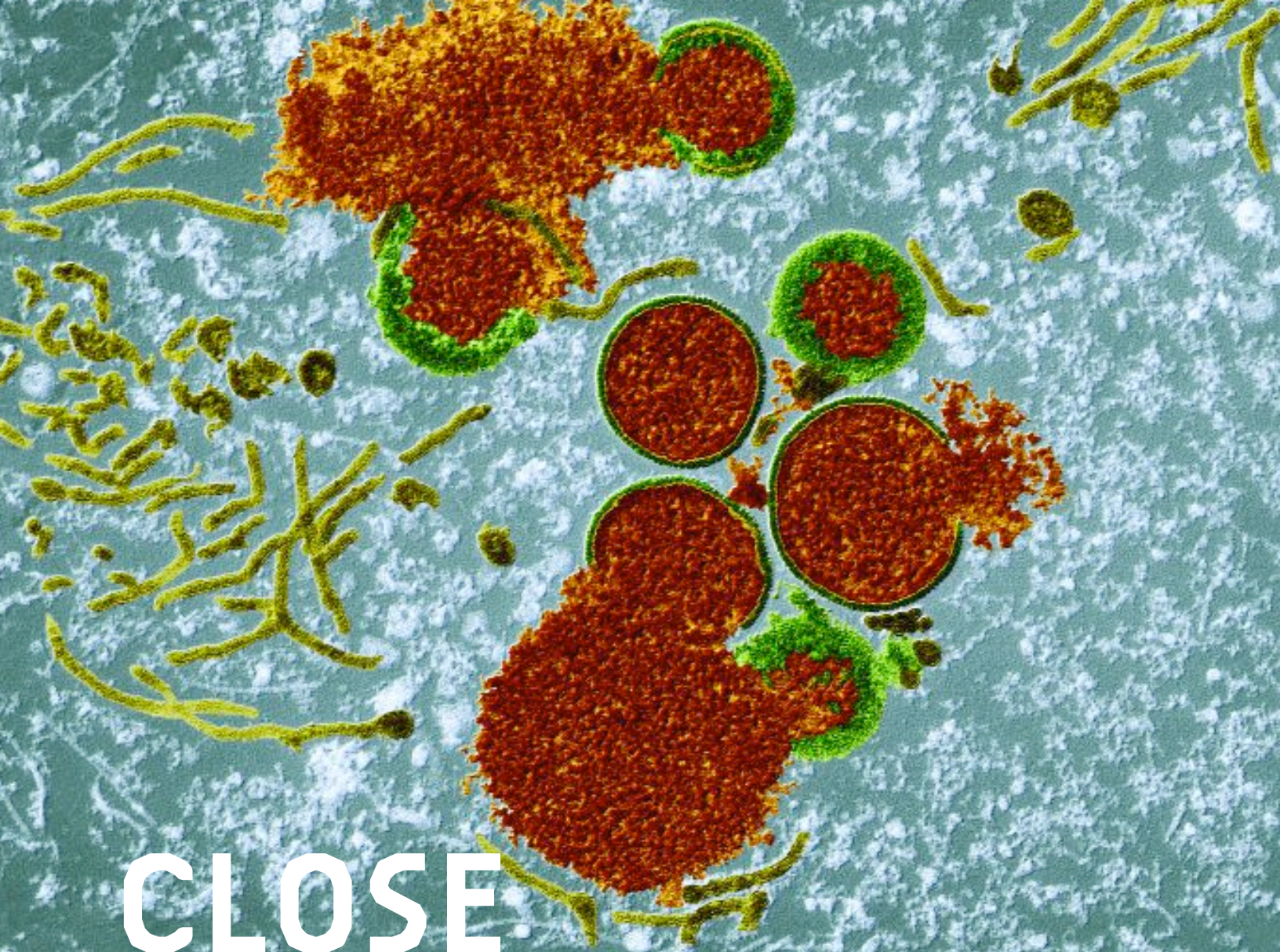
ON THE MIDWAY



What  
makes  
US  
human?

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# CLOSE ENCOUNTER

## A disease not seen since the early 1990s brings a 2-year-old boy to within inches of death

by Katie Scarlett Brandt

She felt no fear, Madelyn Kahana said, as she peered down at the tiny boy barely conscious and wrapped in blankets in his pediatric ICU bed. Despite the pustules covering his face, arms, legs and hands—teeming like hundreds of bees on a keeper—Kahana, MD, chief of pediatric critical care, and nurse Jamie Harrison remained focused on their patient rather than the potential catastrophe his infection threatened.

“Right or wrong,” she said, “we had no fear.”

But they had reason to fear.

This boy would be the University of Chicago Medical Center’s first chance to manage what could have turned into a widespread, national medical emergency. His case mobilized the medical community: dozens of physicians, nurses, pharmacists, environmental services personnel, food services and infection control staff, social workers, the Centers for Disease Control and Prevention—and even the Department of Defense.

When Kahana and Harrison first met the boy, he’d been in the hospital for five days, after being transferred from another



hospital and admitted to the general pediatrics floor with a flare of eczema on Saturday, March 3. He wouldn't leave the medical center for 48 days. Most of that time he spent intubated, drugged and on a ventilator. For a typical case of eczema, this would have been extreme, but the rash consuming the boy's skin was anything but typical.

On his first day in Comer Children's Hospital, the 2-year-old had cuddled up to his mother, then pulled away when doctors and nurses came too close. When pediatric infectious disease specialists John Marcinak, MD, and Surabhi Vora, MD, first checked in on him, the boy was sitting up in his crib, pointing at a cup just out of reach through the crib's bars. "Cup, cup, cup," he chanted. At this point, Marcinak said, the patient had no IV for fluids; it was clear that the virus ravishing the boy's body was already dehydrating him.

That first weekend, hospitalist Barret Fromme, MD, saw the boy. Pediatric dermatologist Sarah Stein, MD, met him on Monday, March 5. She agreed with the working diagnosis of eczema herpeticum and recommended typical antimicrobial and skin care for such cases. Despite such care, his condition worsened—the rash growing in complexity and extent, his awareness levels dropping—as physicians struggled to decipher the cause.

By Wednesday the lesions covering his arms and legs and the skin around his mouth had changed. Juicy pus oozed from them, and they now resembled craters—red blisters with indentations in their centers that resembled some form of pox infection. Stein and Fromme reassessed the situation.

"What are we missing?" they asked each other. Their treatments were failing; the boy clearly was growing sicker, seemingly each time they looked at him. That was when something occurred to Fromme and Stein: Had the boy been in contact with a member of the military? Could he have contracted a virus from someone's small pox vaccination, which is required of people in the service?

## A LIVE VIRUS

Why yes, his mother said. The boy's father was in the military, recently deployed to Iraq, and had been vaccinated at the end of January.

Fromme and Stein knew that the chances of the boy having smallpox were slim to none. They also knew that the smallpox vaccination used a live-virus vaccine, and that people with eczema or compromised immune systems—those with HIV, for instance, or who have undergone organ transplants—are especially prone to contracting eczema vaccinatum, a rare smallpox-like infection, if they came into contact with the virus.

The physicians suddenly realized what they were facing. "We were fired up when we made the diagnosis. Now we knew: That's why he's not getting better," Stein said. "But then the reality set in of what this meant for the patient."

Smallpox is a vicious, deadly and extremely contagious virus that by 1980 had been eradicated by universal vaccinations; however, small stockpiles of the virus still exist in government labs, and many physicians fear that it could someday re-emerge as a bio-terrorism agent.

Kahana's first thought when she saw the boy was a drawn out, "Oh-my-God," she said. "It's no wonder so many people died. [The boy's rash] looked exactly like textbook pictures of smallpox." His hands surprised her most. "He had so many lesions, mounds and mounds. The density spread his fingers," she said.

Though the boy's father was supposed to ship out to Iraq soon after the vaccination, his deployment was delayed, and he went home for a brief visit in February to see his wife and three kids. "Last time we saw him was in July of last year," the boy's mother said in an interview with the *Northwest Indiana Times*, the only interview she granted. "Of course we wanted to see him before he left [for Iraq] because you never know what's going to happen."

The father had no intention of exposing his family to his vaccination. He kept that part of his skin—his upper left arm—



**Pediatric infectious disease specialist John Marcinak was a key player in a team of more than 50 health care providers that saved a 2-year-old boy from dying from eczema vaccinatum. Photo by Dan Dry**

**Opposite page: the vaccinia virus. Photo by Eye of Science/Photo Researchers Inc.**

completely covered and wouldn't even show it to his wife when she asked.

"This dad had no idea of the risk," Kahana said, citing Page 4 of a Defense Department document about the vaccine that didn't go any further than mentioning a "risk for people with eczema."

Two weeks after the father left, the boy's skin broke out in a rash, and his mother took him to St. Catherine's Hospital in East Chicago, Ind. "The doctor at St. Catherine's said he'd never seen anything like it before. Over three to four days, lesions spread over most of his body," the boy's mother told the newspaper.

From there, the boy and his mother traveled to the University of Chicago, not knowing that they wouldn't return home for almost seven weeks.

## NO RELIEF

By the time the *Chicago Tribune* broke the story on March 17, the boy was in critical condition. He was unconscious and quarantined in a special negative pressure room at Comer. Hospital planners included the room for situations exactly like this one. Its design kept the virus contained, allowing hospital air to flow into the room, but not back out. The boy was extremely ill, on the brink of death, and contagious. And because nobody had seen a case of eczema vaccinatum since at least 1990, they took every precaution.

Once it occurred to the doctors that the boy could have eczema vaccinatum, caused by the vaccinia virus, they sent both his and his mother's tissue samples to the Illinois Department of Public

milder form. She'd contracted it through close contact with her son. A dozen lesions surrounded her mouth. "It started like a headache, flu-like symptoms as if I was coming down with a real bad cold I might get over in a few days...but I didn't expect this in a million years," she said.



The inner right leg (top), and abdomen and chest of the 2-year-old boy with a rash of dimpled lesions caused by eczema vaccinatum—a rare severe adverse reaction caused by exposure to the vaccinia virus. Photos courtesy of John Marcinak

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—Sarah Stein, MD, Assistant Professor of Medicine

morning drew nationwide attention. The media in general handled the story appropriately, emphasizing the clever detective work, and being careful not to alarm their readers. As other news outlets picked up the story, reporters dutifully explained that the boy did not have smallpox and his virus

was under control at the medical center, quelling public fear that the infection could spread.

Kahana's own father needed reminding that his daughter, a physician for 28 years, was not treating smallpox. "He was freaked out, but I take risks every day. If I were scared all the time, it would be paralyzing," she said, likening her job to that of soldiers who can't let a fear of gunfire keep them from the front lines. "I think a doctor has to do that. It's a little boy. He needs your help."

And the Marcinak-Kahana team provided just that. Once the boy was officially diagnosed and transferred to the PICU, Kahana became a central member of the team. For 14 days, she and Marcinak spent several hours a day in his room. Marcinak and Vora spent many

extra hours each day on the phone with colleagues at the CDC.

But there were no easy answers, despite a clear diagnosis. By the Sunday after his diagnosis, the boy had progressed to multi-system organ failure. "He was in a lot of trouble," Kahana said.

Marcinak and Vora held daily conference calls from 11 a.m. to noon with infectious disease specialists at the CDC, the Department of Defense, the Food and Drug Administration, the National Institutes of Health, pharmaceutical companies and city and state public health departments from Illinois and Indiana.

The mother was confined to her son's hospital room, unable to see her other children. "She had to be there the whole time because she was infected too," Stein said. "She was remarkably calm, never antagonistic."

## WITHOUT A MAP OR A GUIDE

Nobody is quite sure how, but a reporter at the St. Paul/Minneapolis's *Star Tribune* found out about the story. His editor, seeing no local angle, killed it. But the reporter called a colleague at the *Chicago Tribune*, and a Page One story the next

Health and lesion photographs to the Department of Defense and the CDC. Both the IDPH and CDC confirmed the vaccinia virus infection.

Each day it seemed like there was more precautions to comply with before entering the boy's room. Stein said she wasn't scared, but slightly perplexed. First she wore only gloves; then gloves and a mask; then gloves, a mask and a gown. "Each time it was like, 'But what about yesterday? We didn't have to do that yesterday,'" she said.

Before long, physicians discovered that the boy's mother also was suffering from the vaccinia infection, though a considerably





The boy was kept in a special negative pressure room (similar to one at left) in Comer Children's Hospital, designed to keep the virus contained and allowing hospital air to flow into the room, but not out.  
*Photo by Dan Dry*

Those calls focused on the boy's clinical care; another series of calls took place on Mondays, Wednesdays and Fridays to trace the virus' epidemiology.

One reason for the calls was orchestrating use of a drug known as VIGIV, short for vaccinia immune globulin intravenous. Experts consider VIGIV the first-line treatment for vaccinia; the CDC keeps a stockpile in case universal smallpox vaccination becomes necessary. U.S. marshals brought it in by plane on the boy's sixth day in the hospital.

During the conference calls, experts also decided to try cidofovir, an antiviral drug recognized as a second line of treatment, and the experimental ST246, which physicians had never before used in a human. Chief of the CDC's Poxvirus Laboratory, Inger Damon, MD, PhD, convened a Saturday afternoon conference call with Marcinak and the manufacturers of ST246 to discuss its use. Only hours after physicians agreed they wanted to try it, the Food and Drug Administration approved emergency use of ST246 in this case. But ultimately the boy's parents faced the decision of whether or not to use it on their son.

"We had no guide," Marcinak said. "We had to take it one day at a time."

## GOODBYES, HIGH-FIVES

The parents opted to use ST246. SIGA Technologies Inc., who developed and had begun phase-1 testing of the drug, arranged to fly it to Chicago from Oregon on Saturday via a private jet that billionaire and SIGA investor Ron Perelman paid for. It arrived at 4 a.m. Sunday and was administered to the child the same morning. By the next day, although the boy looked worse, his health was improving. He remained on a ventilator and unconscious, but the oozing pustules coating his body were beginning to scab—first red, then black.

The physicians and nurses provided treatment akin to that given to a burn victim. Nurses from the burn unit pitched in when they could, coaching the boy's PICU nurses on how to keep the skin moist. "It was unbelievable," Kahana said. "Every time we changed his wraps, I thought I was watching time-lapse photography."

The plastic surgeons, who soon would cover parts of the boy with cadaver skin, or allografts, knew they first had to debride (or "pick") the boy's scabs in order to keep his skin moist for optimum healing. "They grafted his arms, hands, chin, neck. That had never been done before," Marcinak said.

Kahana said the case was worse than any similar infection she had seen in her almost three decades as a physician. "Not even the worst case of chicken pox" looked this bad, she said, "and I saw one child die from that."

As his 30th day in the medical center approached, Kahana extubated the boy. However, he remained in the hospital for two more weeks. "We kept him here a long time after [he was well enough to go home] because we wanted to make sure he wasn't shedding the virus," Stein said.

With the tube out and a healthier, happier boy laughing with nurses and physicians as they visited, only a farewell party stood between him and his return trip home.

"He looked good. My guess is he'll grow up healthy and strong," Kahana said. "It was tremendous, the collaboration and work that went into saving this child's life."

When she last saw him, he was eating the icing from his cupcakes, and he gave Kahana a high-five. Perhaps the party served as closure, too, for all the people who took care of the boy—whether they faced their fears in doing so or didn't even recognize fright as an option.