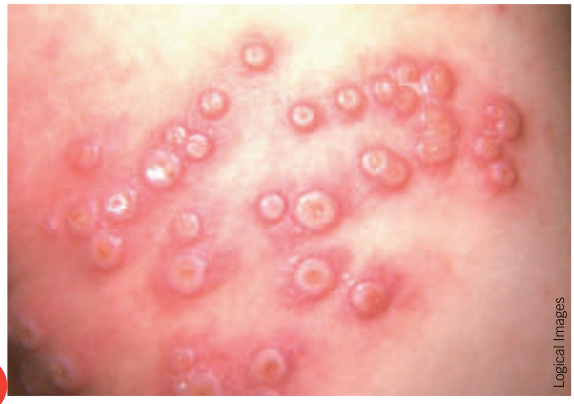
Dramatic rescue relieves rare case of smallpox infection

The American soldier came home in mid-February to see his wife and two-year-old son. Three weeks earlier, he had been vaccinated for smallpox, but he followed instructions and kept the injection site covered to prevent virus shedding. Even when his wife asked for a peek, he refused.

That should have been the end of it.

Two weeks later, his son presented with symptoms of eczema vaccinatum, a rare and dangerous skin infection caused by the vaccinia virus used in the vaccine. The case is the first in the new era of vaccination, which began in 2002 when fears of bioterrorism prompted the military to vaccinate all its personnel, more than a million so far.

The child's reaction, rare even in the days of regular smallpox vaccination, triggered a cruel rash over 80% of his body. Only a coordinated effort from several agencies, health departments and institutions, a Hollywood actor and the dramatic private-jet delivery of an untested drug saved his life.



Logical Images

Over reaction: Virus shed from a soldier's vaccine site triggered symptoms of eczema vaccinatum in his son.

The single case may have lasting effects on the military's vaccination campaign and the government's plans to prepare for a bioterror attack. It may also give an early boost to a new drug candidate.

Interestingly, the boy's mother also acquired the rare condition, in an apparent case of secondary transmission–a previously unknown phenomenon.

Since it began the vaccinations, the US Department of Defense has waged a careful education campaign. People with eczema, also known as atopic dermatitis, are not inoculated as they are the ones most likely to develop the illness.

"I think this is the first case since 1990," says John Marcinak, the doctor who treated the child at the University of Chicago Comer Children's Hospital.

As soon as the boy reached the hospital in the first week of March, the Centers for Disease Control and Prevention (CDC), the Department of Defense and others organized a conference call and shared photos and lab results.

The child was initially treated with Canada-based Cangene Corporation's Vaccinia Immuno Globulin (VIG), the once-standard antibody treatment for eczema vaccinatum. When that wasn't enough, doctors tried the antiviral drug cidofovir, which turned out to be too toxic. Then the CDC's Inger Damon thought of SIGA Technologies' ST-246, a drug designed to combat pox viruses, including smallpox and vaccinia, which had only been through one safety trial in people.

On 10 March, a Saturday afternoon, the US Food and Drug Administration granted an emergency permit to use ST-246. "Frankly, it was amazing to me that the federal government was able to move that quickly," says Dennis Hruby, SIGA's chief scientific officer.

"The initial plan was to send the drug by FedEx to get it there Sunday at 5 p.m.," says Marcinak. "But Eric Rose of SIGA ended up getting on this private jet and was in our inpatient pharmacy by 4 a.m." That jet was courtesy of the actor Ron Perlman, one of SIGA's investors.

With the parents' consent, the child was on the drug by 9 a.m. Sunday and immediately began to improve. His kidney failure reversed, his skin began to clear and he was moved off the respirator. By 12 April, he had been transferred from intensive care to the general ward.

SIGA's officials are naturally pleased with the outcome. If ST-246 proves safe and effective in further trials, the government might want to stockpile it in case of a bioterror attack. Discussions about whether this would be sensible are simmering in public health circles, in advance of formal publications on the case.

Some say stocking the drug would be frivolous, given the rarity of the complication. Others add that the window in which an anti-pox drug would be effective ends before the symptoms appear. "That was the dogma in the literature, but all our data say that that is not so," counters Hruby. "I don't think that's true."

Emma Marris, Washington DC

monitored by a doctor. Cheating on the diet—such as eating a candy bar—can bring on a seizure in minutes.

The diet enhances the protective role of energy-, or ATP-, dependent potassium channels in the brain, which control the electrical firing of neurons that release the neurotransmitter gamma-aminobutyric acid (GABA) in a region of the brain called substantia nigra pars reticulata, the researchers found. Those neurons are known to be associated with seizure control, says lead investigator Gary Yellen, professor of neurobiology at Harvard.

Examining the channels in mouse brains, the researchers infused brain slices with ketone bodies, chemicals produced by the liver when the body is on the ketogenic diet. When the channels are intact, the ketone bodies reduce electrical firing, but when the channels are eliminated by genetic alterations or drugs, the effect is lost, suggesting the channels' importance.

Experts say the explanation makes sense, but must be tested in a whole mouse, rather than in brain slices. The diet may also cause many other changes in the body, some of which may be more important than the effect on the potassium channels.

"The diet affects multiple metabolic features," notes Philip Schwartzkroin, a neuroscientist at the University of California, Davis. "Some are related to antiepileptic effects of the diet and some are irrelevant."

Schwartzkroin says there are many other cells in the brain that have energy-sensitive potassium channels that might be affected by the diet. "How that might be integrated is not even discussed," he says.

The diet is so complex, in fact, that doctors have seen benefits in people with other neurological diseases, such as Alzheimer's and Parkinson's diseases.

The researchers next plan to study the role of energy-dependent potassium channels in other parts of the brain. And a second group,at the University of Wisconsin in Madison is investigating how blocking glycolysis, or the breakdown of sugars, may delay the progression of epilepsy.

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