



Handling Infectious Disease

How Wisconsin
copes with
monkeypox
and more

*By Marc Kennedy
special to WMJ*

Wisconsin is no stranger to exotic infectious diseases. Legionnaire's disease and La Crosse encephalitis in the 1970s; toxic shock syndrome (TSS) and Lyme disease in the late 1970s and 1980s; and West Nile virus since 2000 are just a few of the more prominent culprits.

So, when a few unusual cases began appearing in north central Wisconsin and outside of Milwaukee that did not fit the pattern of any recognized illness, health care officials were more intrigued than surprised. The surprise came when they found out what it really was.

"We had never seen it before in the United States," said Jeff Davis, MD, Chief Medical Officer and State Epidemiologist for Communicable Diseases with the Wisconsin Division of Public Health (DPH). "Human cases of monkeypox virus infection had occurred only in parts of Africa. And some clusters occurred in zoo animals in Europe. So when this was first discovered north of Marshfield by physicians and laboratory experts, they did an excellent job in delineating what happened."

After a young girl was bitten on the finger by her pet prairie dog, physicians at Marshfield Clinic began

the process of identifying the subsequent illness, ruling out known pathogens along the way: smallpox, plague and tularemia.

"There was a small localized infection at first," said Kurt Reed, MD, Infectious Disease Pathologist and Director of Clinical Research at the Marshfield Clinical Research Foundation. "Animal bites are common, but we don't have much experience with people being bitten by prairie dogs."

The girl was seen as an outpatient and given antibiotics, but she didn't improve and was eventually hospitalized. Meanwhile the prairie dog died and the girl's mother developed a similar type of lesion on her hand, according to Reed.

"Although some of the lesions were similar to those seen with smallpox, right from the start we had strong clinical indications it was something else," Reed said. Bioterrorism was ruled out since the two isolated cases were so strongly linked to prairie dog exposure, and dermatologist John Melski, MD, was convinced it was a viral infection, but not one he had seen before.

Undaunted, Reed and his colleagues kept looking.

“A biopsy taken from the mother looked suspiciously like a viral infection,” Reed continued. “Using an electron microscope, we found that it appeared to be a pox virus, but it was still difficult to determine exactly which type. Meanwhile, the girl was out of the hospital, and was recovering well, along with her mother, who was never admitted.

“Over the weekend the virus from the mother’s biopsy grew in culture, something we had never isolated in our laboratory before. By June 3, there was enough of a change in the cultured cells to use a different technique, negative staining, which would enable us to see the entire surface of the virus, which would in turn help us identify the type. We found it was an orthopox virus, but we searched the literature and didn’t come up with much linking prairie dogs and pox virus.”

Monkeypox was a surprise but shouldn’t have been, considering the risks of keeping exotic animals or native wildlife as pets.

At that point, all they knew was that the same virus was found in the girl, her mother and the now deceased prairie dog. Reed prepared pictures of the virus to send to the State Laboratory of Hygiene in Madison when they got the news of other cases near Milwaukee involving prairie dogs—and something else.

“When we heard that the prairie dogs near Milwaukee had been exposed to exotic African animals, Gambian Giant Rats, it all then came into focus: an Old World virus is now in the New World,” Reed said.

Reed credits the cooperation of health care agencies across the state and the nation for helping them quickly diagnose the source of the illness as well as implementing measures to prevent the disease from spreading further. The state epidemiologist signed an emergency order to prevent import, movement, and sale of prairie dogs in Wisconsin, and the Centers for Disease Control and Prevention (CDC) moved quickly to ban importing seven species of rodents from Africa and to restrict the inter- and intrastate transporting of prairie dogs.

“It was amazing how rapidly the state’s Division of Public Health and the CDC got moving on this once we figured out how the monkeypox was being spread,” Reed added.

Knowledge of old diseases helps prepare for the new
Fast action is nothing new for the Wisconsin Depart-

ment of Health and Family Services, according to Davis, who has been involved in any emerging infectious disease outbreaks since he became chief in 1978.

“At that time, Legionnaire’s disease was not new but it had happened recently,” recalled Davis. “Within my first nine months on the job we got involved in a large Legionnaire’s disease investigation.”

In 1979, DPH began working on TSS, and then Lyme disease came to the forefront.

“When something is reported, and we don’t know what it is, we pursue it as an unknown, gathering pertinent information from clinicians: time, place and persons involved,” said Davis. “As we collect a lot of data, we look at the clinical illness, what might be in the differential diagnosis. It takes a certain amount of data including collecting appropriate specimens to ensure we validate

the diagnosis. That’s how we structure our investigation. We have to see the big picture. If we don’t know what is, or see how rapidly it’s occurring, it isn’t possible to prevent new cases.” Davis added that one of DPH’s roles is to support local health departments’ investigations.

“With an emerging pathogen, we get involved early,” said Davis. “We work closely with local health resources where the illness occurs, as well as other laboratories and physicians in the state.

Wisconsin physicians can keep up-to-date by logging on to the Health Alert Network (HAN). HAN is a health department Internet system for sharing information about activities and events related to bioterrorism preparedness, emerging infectious disease, and other conditions. (*See sidebar.*)

The HAN system, plus availability of professionals who are well experienced in addressing emerging diseases, gives Wisconsin a substantial boost when new infectious diseases emerge.

“We were able to deal with Lyme disease with a stride,” Davis explained. “However, given what was known in 1979 regarding the ecology of Lyme disease and the terrain in the Northwoods and its popularity with hikers, campers, and hunters, investigating the occurrence of Lyme disease in Wisconsin posed substantial logistical challenges. It required much work and cooperation to delineate its occurrence statewide and create an action plan for dealing with it.”

Davis reiterated the importance of coordination and response by physicians across the state in reporting emerging infectious diseases.

“Wisconsin physicians have been extraordinary about reporting cases,” he said. “They have been very responsive when we’ve had new conditions emerge.

Once they became aware of TSS, reporting was stellar. This allowed us to conduct case control studies that associated menstrual TSS with tampon use. Physicians in the state also allowed us to generate studies of appropriate power by recognizing these diseases, particularly Lyme disease.”

Prevention and control are keys

Having experienced and well-connected health care professionals in the state is an important component in responding to crises related to infectious diseases. But preventing the outbreaks from occurring at all is also a primary concern, and in the case of monkeypox, this involves banning the importation of exotic animals.

“This virus, monkeypox, was not previously detected in the Western Hemisphere,” said Davis. “Unless something changes, opportunities to introduce new pathogens through importing of exotic animals will continue. It’s a matter of maintaining surveillance. If we know a problem exists, and we know what we need to do to prevent it, it would be prudent to stop it.”

Davis advocates limiting the importation and exportation of certain species by determining what types of animals are appropriate pets considering the health risks for humans and other animals. “Clearly,” says Davis, “exotic pets such as Gambian Giant Rats are inappropriate pets for various reasons.”

“These steps are necessary, but we need a placeholder far broader than this,” added Davis. “The federal import bans on African rodents occurred quickly once monkeypox was recognized in the US, but there are other species that might have been spreading the disease as well.”

Mammals aren’t the only problem.

“We see illness in humans associated with reptiles kept as pets, such as snakes, lizards, iguanas, turtles, etc.,” Davis added. “An example is reptile-related salmonella infection, especially in young children.”

While the experts know a great deal about how certain diseases are transmitted from one species to another, what they don’t know concerns them as well.

“We know about a lot of transmissible diseases,” said Reed, “and clearly we’re finding new infectious agents regularly. But there is still so much more we don’t know. For example, with Ebola virus we have no idea about how many animal reservoirs carry it. Common sense tells you that it’s a bad idea to import animals from areas of the world where diseases like that exist. You can quarantine animals but even if they look healthy, what if they are asymptomatic and still harbor the disease? Plus you can’t test for diseases that you don’t even know exist yet.”

Health Alert Network

Wisconsin health care professionals who discover something unusual while treating patients should keep in mind a resource that is close at hand: HAN, the Health Alert Network. Established and maintained by the State Department of Health and funded by a grant from the US Centers for Disease Control and Prevention, HAN provides a secure and rapid way to share information pertaining to bioterrorism, emerging infectious diseases and other public health threats.

“The interest and vigilance of doctors across the state is key,” said Jeff Davis, MD, Chief Medical Officer and State Epidemiologist for Communicable Diseases with the Wisconsin Division of Public Health. “As soon as they find out something odd or suspect we want to know, the Wisconsin Health Alert Network is a great tool for communicating this information and for learning from others who are dealing with emerging illnesses.”

Physicians also can receive planning and training materials, and Davis says web courses may be offered in the future.

Physicians can access the secured site, <http://www.han.wisc.edu>, by submitting a profile to open an account. This site is limited to physicians who can use the high-speed Internet to connect with local and state public health agencies to share information and send emergency messages. For the public, there is a general access site at <http://www.dhfs.state.wi.us>.

“We provide all kinds of information on infectious diseases,” added Davis. “And we’ve gotten positive and constructive feedback from doctors as well. HAN is great for communicating what’s happening with monkeypox, SARS and other new diseases in the state.”

Reed warns that there may have been isolated cases earlier that went unreported.

“It might have happened that someone got a funny rash and got better on their own without reporting it. We really wouldn’t know,” he said. “But the big question now is ‘did this virus get out to our wild animal population?’ How far will it spread? With West Nile virus, everyone was hoping when winter came it would kill off the mosquitoes, thereby limiting the range. Obviously that didn’t happen and now West Nile virus is a problem from coast to coast. It’s affecting wild bird populations and what’s next? We don’t know. It’s way too early to know about the long-term impact of monkeypox.”

Small world getting smaller

The ability to transfer human beings and animals around the world in a matter of days has exacerbated the issue of infectious diseases and the problems health care professionals face today.

“The globalization phenomenon has really been very important for those of us in public health as epidemiologists,” said Davis. “The rapid movement from place to place, whether it’s people, food or animals, is incredible. Certainly the global experience with SARS is very striking. The disease hit hard and it took an extraordinary effort by the CDC and numerous international agencies cooperating in China, Hong Kong, Canada, Singapore, and other nations to respond so quickly. This cooperation helped officials make decisions with significant ramifications economically and socially that called for isolation and quarantine to contain illnesses.”

Extraordinary technological advances have also aided scientists in isolating and sequencing viruses, and high speed communication has allowed them to share this medical information in near real time.

“The up-to-the-minute capability to share current information is striking,” said Davis. “It helps us share information and make decisions quickly. This change is very exciting and is affecting all areas of medicine. If anything, this increases our guard and enables us to take rapid action.”

“We can take an organism and see DNA patterns and post that data electronically and see whether you have the same organism in another state or country,” he added. “One of the reasons for this rapid response is all of the preparation for bioterrorism. So when these new diseases occur, we’ve been able to mobilize the resources already available that we would use for bioterrorism attacks. It’s a dual-use capability. We use it every day, not just for larger events.”

Twenty-first century science offers capabilities undreamed of decades ago, but historical events still provide valuable examples of how to react to epidemics.

“Lessons learned in the worldwide influenza epidemic in 1918 are still very germane today,” Davis said. “This was before antibiotics were available. There were no vaccines. Now when something emerges, we still won’t have a vaccine right away, but if we can mobilize rapidly we can generate resources to control it. Modern science enables us to be more thorough and rapid, but the principles are still the same.”

Just a month ago, few had ever heard of monkeypox or SARS. What’s next? No one can be sure, but Davis is certain that new diseases are bound to emerge, and familiar ones will re-emerge.

For more information, contact Kurt Reed, MD at Marshfield Clinic: 715.387.5511, reed.kurt@marshfieldclinic.org, and Jeff Davis, MD, at the Wisconsin State Department of Health, 608.267.9006; davisjp@dhsf.state.wi.us.

“It is not a matter of whether a new pandemic influenza outbreak will happen,” Davis warns grimly, “It’s a matter of when.”

Though the SARS and monkeypox scares seem to have abated, Davis, Reed and other infectious disease experts know it’s far from over.

“Now it is extremely important to plan as though these epidemics will happen again,” said Reed.

“Monkeypox was a surprise but shouldn’t have been, considering the risks of keeping exotic animals or native wildlife as pets,” added Davis. “This practice of domesticating wildlife and exotic animals is dangerous to humans and to animals. Juxtaposing these situations is like a time bomb waiting to go off.”



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