

Iowa Mumps Outbreak Spreads to Nearby States

BY MIRIAM E. TUCKER AND
HEIDI SPLETE
Senior Writers

More than 1,000 cases of mumps in nine states have been confirmed in the nation's largest mumps outbreak in decades, announced Dr. Julie Gerberding, director of the Centers for Disease Control and Prevention, Atlanta.

The outbreak began in Iowa in December 2005 among college students, whose close living conditions make them susceptible to the virus, Dr. Gerberding said in a press briefing. By comparison, a yearly average of 265 mumps cases have been reported for the entire country since 2001, while Iowa previously averaged just 5 cases per year since 1996, the CDC reported (MMWR [Dispatch] 2006;55:1-3).

"As clinicians become more aware of what we are looking for, we expect more cases will be diagnosed," Dr. Gerberding said. "A lot of clinicians have never seen a case of mumps. Not everyone presents with swollen glands."

Most cases occurred in people aged 18-25 years, many of whom had received either one or two doses of the mumps vaccine. Cases are under investigation in Illinois, Indiana, Kansas, Michigan, Minnesota, Missouri, Nebraska, and Wisconsin. Dr. Gerberding declined to name additional states in which suspected but unconfirmed cases are under investigation.

In addition, two individuals have been

identified in Iowa who were potentially infectious during nine different commercial flights between March 26 and April 2, to or from cities outside the Midwest, including Tucson, Ariz.; Dallas; and Washington, the CDC said in an official health advisory issued on April 14.

Mumps, an acute viral upper respiratory infection, may present initially with nonspecific symptoms such as myalgia, anorexia, malaise, headache, and fever, and

progress to acute onset of unilateral or bilateral tenderness and swelling of parotid or other salivary glands. About 30%-70% of unvaccinated people develop typical acute parotitis, but up to 20% of infections are asymptomatic; nearly 50% are associated with nonspecific symptoms or symptoms that are primarily respiratory, with or without parotitis. Severe complications can include deafness, orchitis, oophoritis, mastitis, meningitis/encephalitis, and spontaneous abortion.

Most people with mumps are ill for about a week, and they can be contagious from 3 days before symptoms appear until about 9 days after the appearance of symptoms, according to the CDC.

"It's very important for health care workers to have a second dose of the MMR vaccine," Dr. Gerberding emphasized.

In affected areas, the MMR vaccine should be offered to individuals without evidence of immunity, including all unvaccinated persons born after 1957.

Health care providers in affected areas are advised to offer the MMR vaccine to individuals without evidence of immunity, including all unvaccinated persons born after 1957. In addition, a second dose is recommended for school-age children, college students, and other high-risk groups. Most children have received both doses, but vaccine coverage rates vary with location and population, Dr. Gerberding said.

The supply of MMR vaccine is adequate to cope with the outbreak, she said. The CDC will assist states with vaccine supplies as needed, and Merck has donated 25,000 doses to the CDC's stockpile.

The problem, Dr. Gerberding said, is a lack of complete coverage with a vaccine that is not 100% effective. About 10% of people who receive both doses simply fail to respond and remain susceptible to mumps.

Individuals suspected to have mumps should be tested and any positive cases reported immediately to local public health officials. Such individuals should be isolated for 9 days after symptom onset, the CDC advised.

Physicians should familiarize themselves with the clinical presentations of mumps, infectious disease specialist Dr. Mary Anne Jackson told this newspaper. Some pa-

tients complain of pain at the corner of the jaw, or of an earache that can be confused with otitis. Ovarian inflammation, which may occur in up to 5% of infected postpubertal females, may be confused with appendicitis.

Symptomatic meningitis, which occurs in up to 15% of cases, is associated with a lymphocytic pleocytosis (inflammatory cells in the spinal fluid) that is typical of viral meningitis, but with a low CSF glucose level. Typical summertime enterovirus meningitis is usually associated with normal or low-normal CSF glucose levels, typically around 40%-50% of peripheral glucose. With mumps meningitis, those levels might be 10%-25%. It's important to rule out bacterial meningitis, which a low CSF glucose might suggest, said Dr. Jackson, chief of infectious disease at Children's Mercy Hospital, Kansas City, Mo.

When mumps is suspected, options include culturing the nasopharynx, throat, or urine or testing for serum IgM antibodies. Standard shell vial culture could miss mumps, so ensure that your laboratory's culture will identify mumps, she advised.

At the time of the press briefing, no deaths related to the mumps outbreak had been reported, Dr. Gerberding said. "We hope the containment steps that are being taken at the state levels will help to slow things down," she said.

Further information from the CDC is available at www.cdc.gov/nip/diseases/mumps/mumps-outbreak.htm. ■

Aerosol Amphotericin B in the Works as Fungal Prophylaxis

BY NANCY WALSH
New York Bureau

LAS VEGAS — An inhaled formulation of amphotericin B in clinical development may answer the unmet need for antifungal prophylaxis in immunocompromised patients, said Michael J. Weickert, Ph.D.

Regimens that protect against bacterial, viral, and yeast infections are widely used for patients undergoing chemotherapy to prepare for bone marrow or stem cell transplantation, prevent rejection of a solid organ transplant, treat hematologic malignancy, or control graft vs. host disease.

These patients—about 150,000 in the United States and Europe—remain susceptible to infections with molds such as *Aspergillus fumigatus*, and mortality is high, reportedly between 44% and 87%.

To meet the need for antifungal prophylaxis, a dry powder aerosol formulation of amphotericin B has been developed, and a multidose clinical study is underway, said Dr. Weickert, who is an employee of and shareholder in Nektar Therapeutics, the manufacturer.

The powder is packed into a capsule that is inserted into a small pulmonary delivery device. The drug is delivered to the lungs during a single inhalation. The particles, which have the same aerodynamic properties as fungal spores, distribute to the

same sites that the spores would if inhaled, Dr. Weickert explained at a meeting on fungal infections sponsored by Imedex.

In the regimens being tested, a loading dose is given on day zero that would achieve a concentration of the drug in the lung many times higher than the minimum inhibitory concentration (MIC) required during the early, high-risk period for colonization and infection with *Aspergillus*.

The loading dose is followed by a lower maintenance dose that is self-administered at weekly intervals to maintain an adequate MIC long term, he said.

Systemic levels of the drug are expected to be very low, and the hope is that the toxicities that have long prevented the use of intravenous amphotericin B prophylactically will be avoided, he said.

The drug has been tested in doses of 5 mg, 10 mg, and 25 mg. For the 25-mg dose, the peak systemic level of the drug was 20 ng/mL, which is about 2% of the level generally regarded as the threshold of toxicity for amphotericin B, Dr. Weickert said.

Adverse events, such as cough, headache, and taste distortions, were not serious. "In general [amphotericin B] has been very well tolerated," he said.

The product received orphan drug designation on Dec. 15, 2005, and a phase III trial is expected to begin within the next year. ■

Probiotics May Undo Immune Deficiency in Fatigued Athletes

BY MARY ANN MOON
Contributing Writer

Elite athletes with a syndrome of fatigue, recurrent sore throat, and shedding of Epstein-Barr virus in the saliva appear to have an exercise-induced defect of mucosal T-cell immunity that can be reversed with probiotic therapy, said Dr. R.L. Clancy of the University of Newcastle, Australia, and associates.

This is the first study to report reduced gamma interferon secretion in athletes with the fatigue syndrome, and the first to suggest a possible treatment. Further study is needed to clarify the mechanisms of the immune impairment and the therapy. Future research should also assess whether the findings can be applied to patients with other chronic fatigue illnesses, Dr. Clancy and associates said.

The researchers noted that protracted, intense training can cause recurrent upper respiratory tract symptoms and fatigue along with the appearance of Epstein-Barr virus (EBV) DNA in the saliva. They reasoned that intensive exercise, like other stressors, can impair T-cell-mediated immunity, which in turn impairs the containment of latent EBV infection and leads to viral reactivation.

They assessed saliva and blood samples in 9 athletes (mean age 25 years) with fa-

tigue and recurrent sore throat and in 18 healthy volunteer athletes (mean age 26) who served as control subjects.

Gamma interferon levels from CD4 cells in blood samples were significantly lower in the fatigued athletes. Eight of the nine (90%) also were seropositive for previous EBV infection, and five of these eight subjects (63%) were actively shedding EBV DNA in their saliva.

After observing that isolates of *Lactobacillus acidophilus* enhanced T-cell function and protected against mucosal infection in mouse studies, the researchers treated the fatigued athletes with daily capsules of the organism for 4 weeks. This treatment raised gamma interferon secretion in the fatigued athletes to levels comparable to those in the control group (Br. J. Sports Med. 2006;40:351-4).

Before treatment, 6 of 24 saliva samples (25%) from fatigued athletes had detectable levels of EBV DNA; after treatment only 1 of 24 samples (4%) did.

The findings "suggest that a subtle T-cell defect in control mechanisms contributes to EBV reactivation and virus shedding," and that probiotic therapy reverses the defect. The results must be confirmed in a larger study so clinicians can devise treatment strategies for affected athletes and possibly for patients with other fatigue syndromes, they said. ■