Spread of meningitis outbreak exposes lack of drug oversight in US

Kate Randall
13 October 2012

The outbreak of fungal meningitis linked to contaminated steroids continues to spread at a rapid pace. As of Thursday afternoon, the Centers for Disease Control and Prevention (CDC) reported that 184 people had contracted the illness and 14 had died. The outbreak has affected 12 states: Florida, Idaho, Indiana, Maryland, Michigan, Minnesota, New Jersey, North Carolina, Ohio, Tennessee, Texas and Virginia.

The spread of the rare form of meningitis has been linked to vials of the drug methylprednisolone acetate manufactured by a specialty compounding pharmacy, the New England Compounding Center (NECC) in Framingham, Massachusetts. NECC has voluntarily recalled lots of the suspect drug and surrendered its license to operate until a Food and Drug Administration (FDA) investigation into the contamination is complete.

NECC shipped approximately 17,000 vials of the drug to about 75 health care facilities in 23 states, beginning around May 21. About 14,000 people received injections of the drug produced by NECC, mostly to treat back pain. The CDC has determined that more than 50 vials of the steroid were contaminated by a fungus usually found in leaf mold, and more tests are underway.

Meningitis, an inflammation of the protective membranes covering the brain and spinal cord, is often fatal. Unlike meningitis caused by an infection from bacteria or a virus, the fungal form is not contagious. According to the CDC, the incubation period for fungal meningitis is usually between one and four weeks. However, the CDC says infections have been known to take hold outside of that time period.

Those who received the injections and have not yet contracted the disease must now play a harrowing waiting game. Health authorities have advised anyone who received injections of the drug to be on the lookout for signs of infection, including headache, fever, nausea, neck stiffness, confusion, dizziness and sensitivity to light. Treatment involves months-long courses of high-dose antifungal medications, usually administered intravenously in a hospital setting.

The meningitis outbreak has focused attention not only on the suspect NECC facility, but on the lack of oversight of what are called compounding pharmacies. These pharmacies combine, mix or alter ingredients to create customized drugs to meet the specific needs of individual patients, such as a smaller dose, or the removal of an ingredient that might cause an allergic reaction.

So-called compounding pharmacies began as small, community-based operations, functioning much like the corner drugstore. State pharmacy boards, many dating back to the 19th century, are tasked with regulating all pharmacies, including compounding pharmacies. The FDA, which was established in 1938, was given the authority to oversee drug manufacturers, which rapidly overtook pharmacists as the main producers of prescription medications.

In the ensuing period, however, specialty compounding pharmacies have outgrown their “corner-store” mode of operation. Instead of filling prescriptions of individual patients, many of these pharmacies have begun to mass-produce drugs, promoting their products with sales teams and distributing them widely throughout the US.

More than half of the nation’s estimated 56,000 pharmacies do some compounding, and the industry has grown into a $3 billion business with more than 7,500 large-scale pharmacies. Shortages of some popular drugs, due in part to consolidation of some pharmaceutical operations, have encouraged the growth of compounders. The compounding pharmacies also

often offer drugs similar to those produced by drug companies, but at a reduced cost, making them more attractive to health care providers.

The growing compounding industry has fought efforts to subject its profitable operations to increased oversight. The International Academy of Compounding Pharmacists has spent more than $1 million over the past decade to beat back such efforts, including a 2003 measure that would have set up an FDA advisory committee to oversee compounders.

The deadly consequences of NECC's operations have prompted renewed calls for tighter federal regulation of specialty compounding pharmacies. Despite a number of incidents, some fatal, involving products from compounding pharmacies, their operations continue to be regulated by often over-stretched state boards, with occasional rebukes from the FDA.

NECC appears to have violated Massachusetts law with its distribution of large quantities of the injectable steroid. Compounding pharmacies operating in the state are only licensed to produce medications to fill single patient prescriptions. But NECC continued to produce and ship the drug despite a 2006 warning from the FDA, which read in part: "Your firm has reportedly also told physicians' offices that using a staff member's name on the prescription would suffice."

Dr. Madeleine Biondolillo, director of the Massachusetts Bureau of Health Care Safety and Quality, commented at a news conference, "It looks like they [NECC] have violated that aspect of the state licensing regulations despite their assertion that they were operating under the regulation."

In 2004, the FDA and the Massachusetts Board of Pharmacy carried out an inspection of NECC. Two years later the FDA issued a warning letter to NECC, citing the company for opening sterile products and repackaging them in a manner that could pose health risks. In particular, the FDA cited NECC's splitting of the cancer drug Avastin into multiple doses, to be used to treat an eye condition.

The tragic unfolding of the fungal meningitis outbreak is only the latest consequence of the shoddy oversight of the compounding pharmacies, which is encouraged by the for-profit health care system as well as a lack of funding for state agencies regulating pharmacies. The state and federal agencies tasked with ensuring the safety of medicines have been beholden to the drug industry, and have often looked the other way, with deadly results.

A *USA Today* review of government records, academic journals and industry reports revealed that since 2001 more than two dozen deaths "have been linked to contaminated or mismeasured doses of medications produced by compounding pharmacies" and that "scores more patients have been badly injured, sometimes resulting in permanent disability."

Incidents uncovered by the *USA Today* review include:

March 2012: 33 patients in seven states developed eye infections after being injected with contaminated drugs from a compounding pharmacy in Florida. Three-quarters of these patients suffered vision loss, some severe.

March 2011: Nine patients died in Alabama hospitals after consuming nutritional supplements prepared by a Birmingham, Alabama compounding pharmacy. The product contained contaminated water.

March 2007: Two patients in Washington and Oregon died after receiving doses of intravenous pain medication measured improperly by a Texas compounder. A third patient in Oregon was likely the fatal victim of the same compounding error, according to the CDC.

September 2005: Three patients died at a Virginia hospital after receiving drugs from a compounding pharmacy in Maryland. The FDA discovered contamination in samples after the drug was shipped to three states and Washington, D.C.