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A rough, tough cough: Was it, or wasn't it, the whooping kind?

By Laura Stephenson Carter

n the spring of 2006, a number of DHMC employees began exhibiting classic signs of pertussis, or whooping cough—runny nose, watery eyes, a slight fever, and a severe, repetitive cough that can sound like a "whoop" as the person gasps for breath. The disease can even be fatal for infants or vulnerable adults, such as those with cystic fibrosis. (The vaccinations that protect children from pertussis, diphtheria, and tetanus don't begin until two months of age, and the protection wears off by adulthood. And until very recently, there was no adult booster.)

Dr. Kathryn Kirkland and her DHMC infection control team sprang into action: screening and testing almost 1,000 employees (16% of the staff); ordering ill people to stay home; giving prophylactic antibiotics to 1,300 contacts of suspected cases; and vaccinating over 4,500 people (72% of the staff) in a three-day period. There were 134 suspected cases, with 98 of them considered positive (33 definite and 65 indeterminate) based on a molecular test called polymerase chain reaction (PCR).

Cold: "Once you conclude pertussis is circulating, then any respiratory symptom has to be considered as possibly suspect pertussis," Kirkland explains, "because early in the first week of the illness, the symptoms are just cold symptoms—runny nose, runny eyes, congestion. That's the time at which people are the most contagious."

Then, months after the outbreak ended, DHMC officials announced that it might not have been pertussis after all. Follow-up testing failed to confirm the PCR results. The 27 specimens sent to the state health department for traditional culture testing were negative, and those sent to the Centers for Disease Control for PCR yielded just one positive result.

Diagnosing illnesses like pertussis is complicated, and positive results from molecular tests are hard to confirm. A culture test is still considered the gold standard, though it is less sensitive and



Photo by: Jon Gilbert Fox

Kathy Kirkland, left, and Elizabeth Talbot found a silver lining in a pertussis scare.

That swab [is] then smeared on an agar gel that has nutrients that allow the organism to grow. And the organism, if present, would multiply and ultimately would become visible."

An additional problem with culture testing is that it takes several days before the bacteria have multiplied enough to be detectable. So clinicians have begun relying on fast molecular tests. In a situation like DHMC faced, fast testing is essential to protect vulnerable patients.

"We typically do about 200 [pertussis tests] a year and we did 1,300 in a month and a half," says Dr. Gregory Tsongalis, DHMC's director of molecular pathology. "We were getting frequent pleas from the leadership to turn these tests around as quickly as possible, because so many people presented for care that we were in danger of not having enough staff to run the institution." Luckily, 90% of the screened employees tested negative for pertussis. The other 10% had either equivocal or positive findings and so had to be treated. "Equivocal results are typically associated with individuals who have low levels of infection that may not

"In any of these PCR tests you start out with what's called a primer—that is, a short length of DNA that is meant to mimic the DNA that would be found in the bacterium you're trying to identify," says AuBuchon. The bacterial DNA binds to the primer DNA, and the enzyme systems "identify this coupling and then produce more DNA that ultimately gets amplified and identified." DHMC's assay has 50 to 100 copies of the DNA target per bacterium. The CDC used an assay with only one target per organism. "So," says AuBuchon, "it was easier for us to find [pertussis] because of the 100-fold natural amplification."

Pseudo-epidemics of pertussis have occurred elsewhere, including Children's Hospital Boston; definitive tests failed to confirm the illness there, too. The molecular pathology community, which has used PCR-based pertussis testing for over 10 years, is working to further develop the tests and their interpretation. For example, DHMC is "sending blinded, unknown samples of pertussis . . . to 30 labs around the country," says Tsongalis, who is president-elect of the Association of Molecular Pathology.

may not detect individuals with mild infections.

Gel: The traditional way of "identifying a bacterial illness is to actually grow up the bacteria," says Dr. James AuBuchon, chair of pathology at DHMC. "You take a sample from whatever site would be infected with the bacterium, like the throat —nasopharynx in the case of pertussis.

be clinically significant," Tsongalis explains.

PCR tests are highly sensitive and can detect tiny numbers of bacteria even if the patient has no active infection. But they may be positive in cases where older methods do not detect disease, and the import of a positive result is not always clear.

Screen: DHMC learned a lot from the experience. "We were able to aggressively screen our health-care worker population," Kirkland says, giving her "hope for the potential for controlling the next unknown epidemic, whether that's pandemic flu or the next SARS or whatever."

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