In praise of the path less traveled: public health labs

Jan Bowers

July 2016—For those who crave variety in their work and have a penchant for the unusual, Paul Bachner, MD, has a career message: Don't overlook public health.



Dr. Bachner

As medical director of the Division of Laboratory Services for Kentucky's public health department from 2013 to July 2015, Dr. Bachner expected the unexpected, whether it was an outbreak of food contamination, a suspected case of Ebola, or a newborn with a life-threatening metabolic disorder. "We would begin the day with a meeting of all the supervisors of laboratory sections and talk about what kind of testing we were doing that's out of the ordinary," says Dr. Bachner, who is now a consultant to the health department. "For example, we may have been informed by our colleagues in epidemiology that there was a *Salmonella* outbreak in a particular county; we needed to confirm that, identify the strain, and track down the source. We had alerts involving tuberculosis within the past year."

Although the state laboratory is not routinely staffed at night, Dr. Bachner says they're prepared to test at any time for agents of potential bioterrorism, always with more than one person present. "We periodically have a white powder event, in which a suspicious-looking substance is sent to someone in government," he says. "More often than not, it turns out to be talcum."

Dr. Bachner is a professor of pathology and laboratory medicine, University of Kentucky, and director of laboratories at UK HealthCare. Three years ago, the state contracted with the university to provide a director of laboratory services, an arrangement Dr. Bachner calls uncommon. "Public health is a wonderful career path, but I believe one of the reasons the state was interested in having us provide the directorship is that it's difficult to find pathologists who know about this opportunity."

(C. Darrell Jennings, MD, chair of pathology at UK, and Julie Ribes, MD, PhD, UK professor and director of clinical microbiology, UK HealthCare, served with Dr. Bachner as associate directors and are now consultants. Jeremy Hart, MD, an assistant professor of pathology and laboratory medicine at UK, is now the medical director. "He's doing a great job with many complex issues," Dr. Bachner says, "not least of which has been to implement a test for Zika in record time.")

Much of what public health laboratories do is related to microbiology, Dr. Bachner notes. "But there is also the environmental testing and newborn screening, a scientifically fascinating and complex field that is transforming from a biochemically based science to one that is molecular testing based."

The evolution of newborn screening was responsible in part for drawing an anatomic pathologist out of private practice and into the public health arena more than a dozen years ago. Stephanie Mayfield Gibson, MD, who would eventually become the first woman and the first African-American to serve as Kentucky's commissioner of public health, fully intended to turn down an unsolicited offer to become director of the state's public health laboratory. "I got the call from the former commissioner of public health," she recalls. "I drove out to meet him, out of respect, to tell him no. When I got there, he said, 'There's something exciting going on here.' And he sold me on the mission."



Dr. Gibson

At the time, the state was preparing to expand its panel of screening tests for newborns from four disorders to 26, as a result of recent test approvals by the U.S. secretary of Health and Human Services. "I didn't know if I wanted to give up my anatomic work, but I do like new things and intense things, and this was both," Dr. Gibson says. "These tests would primarily be done by mass spectrometry. I had to get instruments, we had to build an IT system, and I had to get staff to work on weekends. This involved moving to a different culture." Once the instruments were validated and the IT system was in place, Dr. Gibson went to Mayo Clinic laboratories for training in biochemical molecular genetics and how to interpret test results. "We managed to go live a month ahead of the target implementation date set by the governor."

The new testing was designed to diagnose life-threatening diseases such as medium- and long-chain acyl-CoA dehydrogenase deficiencies, Dr. Gibson says, adding that Kentucky had the highest rate in the nation of some of these disorders—one in every 100,000 babies—and one of the highest rates in the world. Today, the Kentucky public health laboratory performs about 50 tests on about 62,000 specimens from newborns each year.

After a decade as director of Kentucky's public health laboratory, Dr. Gibson was recruited to become commissioner, the state's top public health position. There, she says, she learned to "walk an apolitical line" as she targeted some of Kentucky's most urgent public health challenges. With the highest rate of acute hepatitis C in the nation, largely attributable to intravenous drug abuse, "we needed a program that would allow drug users to exchange syringes," Dr. Gibson says. Kentucky law permitted communities to establish their own needle-exchange programs, but there were no guidelines to help implement the programs. Dr. Gibson and her staff developed evidence-based guidelines in collaboration with the Centers for Disease Control and Prevention, the state universities of Kentucky, and some local health departments. In addition to needle exchange, the guidelines cover screening for infectious diseases, referring drug users to treatment programs, and administering naloxone for overdoses.

To date, the guidelines have been used to implement needle-exchange programs in Louisville and Lexington. Other communities are still in the development phase. "We're second highest in the nation for drug overdoses," Dr. Gibson says. "We have a lot to work on. It's not going to happen overnight, but we feel like we're trending in the right direction."

Dr. Gibson joined KentuckyOne Health early this year as the health system's vice president of population health. She is also chief medical officer for KentuckyOne Partners, an accountable care organization. "Being part of history, implementing the Affordable Care Act and the Food Safety Modernization Act in our state, has been a thrill," Dr. Gibson says. "Being commissioner of public health is a natural fit for a pathologist. I would love to see another pathologist in this position."

Unusual situations keep public health laboratory work challenging and unpredictable, say two microbiologists who spoke with CAP TODAY recently and presented at the 2015 meeting of the American Society for Microbiology, where they told stories on things as disparate as geoduck and cheese.

When China suddenly banned the import of geoducks, which are large clams, from the U.S. in 2013, it sent shock waves through the shellfish industry, reports William Glover, PhD, who oversees testing services as director of science and technology at Washington State Public Health Laboratories. "They're a high-value export for our area, and China is the largest consumer," he says, noting the Chinese pay exporters more than \$100 per pound for the giant clams. Geoducks (pronounced "gooey ducks") can grow to 3 kg and live for more than 100 years. "They're

considered a delicacy in Asian countries," Dr. Glover says. "They grow naturally along the shoreline from the low tide level to 100 feet of water, and there are hundreds of rows of geoduck farms here in the Pacific Northwest."

In a surprise move, the Chinese government informed the National Oceanic and Atmospheric Administration about a new standard for acceptable levels of inorganic arsenic in geoducks, and the information was passed along to exporters and to public health departments in the affected states. Previously, "inorganic arsenic levels didn't have any standard we knew of," Dr. Glover explains. "So our environmental laboratory, along with its federal, state, and commercial partners, had to come up with methods to test and certify that all geoduck clams exported to China were below this inorganic arsenic limit." The challenge was extracting, separating, and measuring organic and inorganic arsenic, the latter being the more toxic of the two and the former being more abundant in the animals.

"It's not unusual to have to come up with a new test, but the speed with which we had to do this was unusual," Dr. Glover says. "People gave up their Christmas vacations. It was an urgent matter."

The expertise needed to develop and validate the test was spread throughout different laboratories within the Washington State Public Health Laboratories' office of environmental laboratory sciences, which worked in conjunction with federal, state, and commercial partners, Dr. Glover says. "The shellfish biotoxin lab knew how to shuck, skin, separate, and homogenize the geoducks. The radiation laboratory had expertise in cryo-grinding [freezing and then grinding the sample]. The chemical incident response laboratory had expertise in the extraction of arsenic because they do that in food. And then the biomonitoring group had experience in the arsenic speciation method because they had developed the method for urine, apple juice, and brown rice testing."

Those groups developed and validated the protocol, then turned the assay over to the shellfish biotoxin laboratory to perform, Dr. Glover says. "They came up with a test very quickly, the data generated by validation of the study was deemed sufficient by the Chinese government, and ultimately the ban was lifted. And the people in environmental laboratory sciences who worked on the test got a call from the governor."

In contrast to the rapid development of the test for inorganic arsenic, the development of a PCR assay for *Vibrio parahaemolyticus* has been a slower process. "Our assay has evolved over time due to the fact that *Vibrio parahaemolyticus* serotypes that cause human illnesses in Washington state vary," Dr. Glover says. Vibrio is a halophilic bacterium that occurs naturally in Washington coastal waters, with levels rising during the warmer months. *Vibrio parahaemolyticus*, in particular, is often the culprit when people become ill after consuming raw oysters.



Dr. Glover

"When I came on board in 2013, we were getting requests from the office of shellfish and water protection to provide them with results on a new marker of virulence that had been reported in the literature, a gene called TDH-related hemolysin [*trh*]," says Dr. Glover. Previously, "we were detecting only the thermostable direct hemolysin [*tdh*], a different gene. We have *Vibrio* strains in Washington that are *tdh*-negative but *trh*-positive, so it was important to incorporate that marker into the assay." As it turned out, "That marker is one of the trickiest targets to develop an assay for because of the sequence variations." Updating the assay for trh required a year of testing and another year of validation. The Interstate Shellfish Sanitation Conference, which reviews and approves tests for incorporation into state regulatory programs, has granted the assay emergency use authorization.

"We know from our experience here that there are other *Vibrio* species in the water that can cause human illness. It's very important that all *Vibrio* clinical isolates in Washington state are submitted to us, because if we see something new causing illness in people eating shellfish, it may indicate we need to modify our assay."

In Utah, an alert microbiologist working in the state public health laboratory noticed an unusual pattern in *Salmonella* samples the lab was receiving and notified the bureau of epidemiology. Her email sparked a multiyear investigation that led to an unlocked barn door and a man the lab staff dubbed "Mr. Cheese." Robyn Atkinson-Dunn, PhD, director of the Utah Public Health Laboratory, points to the Mr. Cheese saga as an example of a food safety incident "that wouldn't have made it to anyone's radar if the lab hadn't been doing what the lab does."

The public health laboratory serotypes the *Salmonella* isolates sent to it and performs pulsed-field gel electrophoresis to obtain the DNA fingerprint of the *Salmonella* organism. The lab began seeing sporadic samples of *Salmonella* Newport during the summer of 2009. "If you start to see three or four, this raises the interest of the lab," Dr. Atkinson-Dunn says. "It's a commonish pattern, but we shouldn't be seeing it this often. Our microbiologist thought this was a little strange; we keep seeing *Salmonella* Newport with the same PFGE pattern month after month. In her mind, something was going on."

The samples were clustered in the same largely Hispanic neighborhood. The epidemiology department's first investigation yielded no clues. When more cases appeared in the summers of 2010 and 2011, epidemiologists stepped up their efforts. "As they interviewed people in the neighborhood, they heard stories of a gentleman selling cheese from the trunk of his car," says Dr. Atkinson-Dunn. An epidemiologist staff member visited restaurants and asked where they were buying their cheese.

"One restaurant owner said, yes, he was buying queso fresco cheese from a gentleman who came to the restaurant. We were dealing with a close-knit community, and no one wanted to identify the individual. But we finally tracked down 'Mr. Cheese.'" A site investigation of the home revealed he was making cheese in his kitchen. "We sent a lab staff member to swab the kitchen for Salmonella. We didn't find any but did find several obvious health violations. So the department of agriculture gave him a cease-and-desist order, which meant that until he got a proper food-grade kitchen, he needed to stop selling cheese."

The agriculture department, which Dr. Atkinson-Dunn characterizes as "small-farmer and small-business friendly," helped Mr. Cheese locate a proper kitchen space and advised him in how to obtain certification and a proper license to sell his cheese. But the investigation wasn't over. "He was using raw milk to make the cheese. Where was he getting it? He led the department of agriculture to a single dairy farm.

"Someone on my lab staff went out there, again to help with the sampling. I learned that before you connect a cow to an automatic milker, it's common practice to milk by hand because that first milk is often contaminated or not the best milk. It turned out that someone was collecting that milk in buckets, putting it in the hallway of the barn, leaving the barn door unlocked, and telling their friends there was raw milk for the taking. The dairy farm owner had no idea."

The laboratory staff member who traveled to the farm did not find samples of the *Salmonella* strain, but it was detected in a sample of queso fresco that Mr. Cheese sold to a restaurant. "That was enough to make the connection between his practices and the illnesses we were seeing," Dr. Atkinson-Dunn says. They saw a significant drop-off in *Salmonella* cases in 2012, the year he got his official license, and since 2013 they haven't seen any cases related to him or the cheese.

For Dr. Atkinson-Dunn, much of the appeal of public health lies in its ability to affect an entire community. "In a clinical setting, it's a one-on-one relationship with a patient, and you're trying to help the physician treat that individual. In public health, you care about that individual, but we're more interested in knowing if you have disease *x*, do others in your community also have disease *x*? Did you all get it from the same place, and if you did, what can public health do to try to mitigate that so more people don't get sick?

"I like that bigger picture aspect of my work." [hr] Jan Bowers is a writer in Evanston, Ill.