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No answers yet for prostate biopsy infection

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January 2016—When Kimberle Chapin, MD, learned in 2014 that Lifespan's urologists in Rhode Island wanted to begin screening transrectal prostate needle biopsy specimens for fluoroquinolone-resistant *Escherichia coli*, her first reaction was: *"What?"*

Turns out that the urologists had heard of a new safety initiative being promoted by the CMS Surgical Care Improvement Project, one that could in time become a quality measure: prophylactically administering targeted antimicrobials for prostate biopsy based on rectal swab culture.

"It was going to be on a checklist, so everyone got concerned about how this was going to be accomplished," says Dr. Chapin, who is director of microbiology and infectious diseases molecular diagnostics at Lifespan Academic Medical Centers and professor of medicine and pathology at Brown University's Warren Alpert Medical School in Providence. "I'm like, 'Okay, we don't even have a standardized way to screen for that. That's not doable in our lab outside of a major validation.'"

As Dr. Chapin told the story in a Nov. 4, 2015 Association for Molecular Pathology workshop sponsored by GeneWeave, titled "What's Missing in Molecular Diagnostics," that conundrum—must screen, can't screen—led her and her laboratory down a rabbit hole of trying to follow the CMS initiative while maintaining efficient testing processes and not contributing to antibiotic resistance. As she noted in her remarks, and in an interview with CAP TODAY, the experience was frustrating but illuminating.

The transrectal ultrasound-guided biopsy procedure "means you're going through a contaminated area," Dr. Chapin says, "and so it's considered a contaminated classification of surgical wounds. There is a significant risk of infection post-biopsy, anywhere from 0.5 to six percent of patients, and that's increased over the past 10 years." UTIs, prostatitis, and bacteremia are the possible complications, and the major pathogen associated with these post infections is fluoroquinolone-resistant *E. coli* (FRE). She explains: "Part of the issue is that fluoroquinolones are also the most common periprocedure prophylaxis, and increased resistance has followed. In addition, because there is no routine screening protocol currently performed, providers end up using the standard-of-care antibiotics." They treat longer or they use more combination therapy, or both. "We really don't want additional or inappropriate antibiotics," she says.

Hence the CMS Surgical Care Improvement Project decision to allow administration of targeted antimicrobials for prostate biopsy prophylaxis if the choice is based on a rectal swab culture. "The problem is," Dr. Chapin says, "microbiology does not perform rectal culture sensitivity or screening tests for FRE. There is no standard validated test

available, and yet I had compliance people coming to me saying, ‘This is going to be a benchmark. The lab has to be doing this so it can be measured.’”


Dr. Chapin

No standard validated test meant using what was known to be done outside of current standardized testing—getting a rectal swab a month before surgery, setting it up on a MacConkey plate with ciprofloxacin at 24 hours, identifying and subbing the organisms that grow, and performing susceptibility testing, with the entire process taking 48 to 72 hours. “This would be a nightmare to us to do in the lab,” Dr. Chapin says. “It’s a multistep process, it’s very labor-intensive, and it isn’t standardized…we would have to validate this whole process.” Then, too, “It’s an additional screening test and an added cost.”

Given the taxing nature of that process, it’s small wonder that she found herself asking: “Is there really a need for FRE screening?” and seeking data that might point her in one direction or another. The Michigan Urologic Surgery Improvement Collaborative, she discovered, looked at data from 6,300 prostate biopsies and found that up to four to six percent of patients were readmitted within 30 days after biopsy, with 91 percent of those readmitted due to infection. Ninety percent of those readmitted had received perioperative antibiotics, while 70 percent of infections were due to fluoroquinolone-resistant bacteria. “So the problem was not due to compliance of the right antibiotic prophylaxis,” Dr. Chapin says, “but to antibiotic resistance.”

As a result of those findings, the Michigan Urologic Surgery Improvement Collaborative developed two paths to address fluoroquinolone resistance. In the first, rectal swabs are obtained before the biopsy and screened for fluoroquinolone-resistant organisms, to allow for antibiotic prophylaxis with culture-directed agents. In the second, no rectal swabs are obtained. Instead, fluoroquinolone-resistant organisms are simply assumed to be present, and a second antimicrobial is added to the standard fluoroquinolone prophylaxis. (The full protocol is available at www.musicurology.com/prostate-biopsy.) The Michigan collaborative reports that its early results have demonstrated a relative reduction in prostate biopsy-related hospitalizations of nearly 50 percent.

The Melville, NY-based Advanced Urology Centers of New York, Dr. Chapin learned, takes a different approach. There, every prostate biopsy patient receives two orally administered antibiotics two to three days before the procedure and IV therapy one hour before it, as well as an enema the evening before the procedure, the morning of the procedure, or both. That’s how they could keep their infection rate to about one percent, Dr. Chapin says, “and the goal is to get it to 0.5 percent.”

“They didn’t really do any screening. They just decided they were going to give cipro, but they were also going to give other antibiotics in case there was cipro resistance,” she says. “That’s just overkill and overuse of antibiotics. I would say that while they find their infection rate maybe isn’t as high, they aren’t really going to be able to target where there’s a problem, and then they may create additional problems in terms of antibiotic resistance.”

In January 2014, the American Urological Association held a Quality Improvement Summit with the aim of reducing infectious complications of transrectal needle biopsy. Out of that summit came four recommendations. First, urologists should monitor their practice’s prostate biopsy infection rates and consult the current local antibiogram. Second, physicians should query patients to assess whether they are at high risk for fecal carriage of resistant coliform organisms, an identified risk for a transrectal prostate needle biopsy complication. Third, individuals at high risk for resistant coliforms may be identified by recent antibiotic usage (within six months), foreign travel, and exposure to health care environments as an employee or patient. Last, when a patient is deemed high risk for resistant organisms, prophylactic protocols might be intensified; a rectal swab might be considered, or the antibiotic coverage may be augmented.

Dr. Chapin’s reaction? “We do our antibiogram once a year, so that’s not exactly real-time data,” she says. “And ‘assess risk for exposure to antibiotics, a hospital environment, or foreign travel’? I don’t know anybody who wouldn’t fall in some of those categories. Bottom line is, anybody getting a biopsy, you’re at risk.”

While Dr. Chapin and others wait for the AUA to hold another summit on this topic with updates on current antibiotic resistance rates and potential new screening methods, she's looking to a technology called GeneWeave as a potential solution.

"It's both a molecular and phenotypic detection method," she explains. "It uses something called Smarticles, which are basically a bacteria phage-type DNA product that gets into the specific host organism. So, for example, I would have to specifically have a Smarticle that targeted *E. coli* and cipro resistance. Then, if the organism is alive and resistant, you would see no signal, but if there was *E. coli* there and susceptible to quinolone, you would see the signal. If you have live organisms expressing resistance, you're going to be able to have a functional test and know what's really there, as opposed to looking at a gene target and not knowing if that resistance is being expressed or not. That's the current problem with some of the resistance markers in some of the current blood detection systems or CRE assays that look for a gene target."

"The bottom line is," she says, "the technology doesn't work unless you have live organisms, and that's the real power of this particular technology. It's very different than just molecular alone."

Dr. Chapin sees at least one potential downside to GeneWeave: "You have to know exactly which particle you're going to develop and what your target is going to be, because that's how that test is developed," she says. "But are they going to go to something broader, like an all-bacterial or an all-Gram-positive? I don't know. Am I going to have a storeroom full of different Smarticle assays? That could be an inventory nightmare. But GeneWeave has the potential to really be something different for us in the lab. And it is good in that you can target specific things that nobody's going to go out and make a big panel for."

Recently purchased by Roche, GeneWeave does not yet have a diagnostic product or a screening product available. "They're very close to starting clinical trials. I believe they're going to start with MRSA," Dr. Chapin says. "It will be interesting to see where they go now that they are part of Roche."

What's different with Roche, she says, is that it currently uses only amplified technology. "GeneWeave is different because it involves specific genetics but also requires there to be live organisms, so that's really live microbiology. And while everyone knows Roche to be a molecular company, we don't really think of it as being a microbiology, grow-things-on-plates kind of company. It's definitely a different kind of technology for them, and that's something they're going to have to make clear: What differentiates this from other molecular technologies is that it does require live organisms for the resistance expression to be known."

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