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This is the podcast from *Clinical Chemistry*. I am Bob Barrett. Although it has been 8 years since the mailing of letters containing *Bacillus Anthracis*, the causative agent of anthrax, the United States is failing to address biological weapon proliferation and biological terrorism. That's according to an October 2009 interim report released by the Commission for the Prevention of Weapons of Mass Destruction Proliferation.

While technology and capabilities have improved since 2001, newer, potentially faster, and more sensitive technologies, based on concepts like nanowires, quantum dots, microcantilevers, and hand-held spectrometers, are reported to be available or near availability, but most still require significant amounts of testing and validation under conditions replicating actual use.

In the January issue of *Clinical Chemistry*, three experts in the field of bioweapon detection answered questions about the current status of biothreat detection technology.

Our guest in this podcast, Bonnie Rubin, Associate Director of the State Hygienic Laboratory, Iowa's Public and Environmental Health Laboratory, and a member of the APHL Emergency Preparedness and Response Committee, continues their discussion.

Ms. Rubin, in the series of questions and answers that appeared in print, the role of so-called LRN Laboratories was discussed. What exactly are LRN Laboratories, and why should identification and confirmation be done by them?

Bonnie Rubin:

The Laboratory Response Network or LRN, as described on the CDC website, was established by the Department of Health and Human Services, the Centers for Disease Control and Prevention, CDC, in accordance with Presidential Decision Directive 39, which outline national anti-terrorism policies and assign specific missions to Federal Departments and Agencies.

Through a collaborative effort, involving LRN founding partners, the FBI, and the Association of Public Health Laboratories, or the APHL, the LRN became operational in August 1999.

Its objective was to ensure an effective laboratory response to bioterrorism, by helping to improve the nation's public health laboratory infrastructure, which at that time had limited ability to respond to bioterrorism.

The mission of the LRN and its partners is to maintain an integrated national and international network of laboratories that are fully equipped to respond quickly to acts of

chemical or biological terrorism, emerging infectious disease, and other public health threats and emergencies.

We consider this or call this an “All-Hazards” response approach. Today, the LRN is charged with the task of maintaining an integrated network of state and local public health, federal, military, and international laboratories, that can respond to bioterrorism, chemical terrorism, and other public health emergencies.

The LRN is a unique asset in the nation’s growing preparedness for biological and chemical terrorism.

The linking of state and local public health laboratories, veterinary, agricultural, military, and water and food testing laboratories, is unprecedented in the history of laboratory systems in the United States.

For suspect biological agents in clinical samples, such as blood, urine, or wound cultures, the LRN can be represented by a three-tiered pyramid.

At the base of the pyramid are what we call the “Sentinel Laboratories.” These are the hospital-based and independent clinical laboratories, and we consider these our laboratories at the front line.

The Sentinel Laboratories are responsible for ruling out or referring suspect agent samples to the next tier or the Reference Laboratories. Our acronym for that activity is ROAR, Rule Out And Refer.

The Reference Laboratories are the state and local Public Health Laboratories that are responsible by a mandate from the US Congress to serve as a confirmatory laboratories for most biological agents. And these laboratories are required to use the same CDC methods, including real-time PCR, in order to assure common sensitivity and specificity nationwide and with other international LRN Reference Laboratories.

Now, if the agents can’t be identified at the Reference Laboratories, or we do determine them to be positive, the samples are then sent on to the next tier or the National Laboratories. These are the CDC, USAMRID, and the Naval Medical Research Center. And these laboratories are at this level able to DNA fingerprint the organisms we sent them.

Now, the LRN system is designed such that member Reference Laboratories are using the same testing methods, and in many cases the same instrumentation, to assure that when an organism is identified or suspected, all states and national agencies are comparing apples to apples on the test

results. And this is really important in the epidemiological evaluations and predictions we use to respond and mitigate to any event.

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Host: Well, now, you have described how the LRN responds to biological agents in clinical samples, what about environmental samples, such as white powders that the first responders encounter, how are these handled?

Bonnie Rubin: Well, you know, although the LRN was originally designed to handle biological agents in clinical samples, the network has expanded, and we actually had to expand to include chemical, radiological, food, and water testing laboratories.

However, as stated in the interviews, there is not yet a national strategy on how biothreats should be evaluated and tested.

The algorithms for testing, that is who does what, when, are currently addressed at the state levels, and these protocols do vary from state to state.

One thing that appears to be common in successful state-level responses to the biothreats is that, there is an established partnership between the first responders, which are primarily the HazMat teams, the public health laboratory, and the state's civil support team. Each state and territory of the United States has a National Guard Weapons of Mass Destruction Civil Support Team, or we call them the CSTs.

These teams have a mobile Analytical Laboratory System, that they call an ALS, that provides a standardized mobile laboratory, that combines benchtop analytical equipment, with support systems and engineering controls for sample processing. Because of their mission to be on call to support civil authorities at potential or actual incident sites, CSTs are likely to be on-site of incidents where samples requiring LRN analysis will originate.

If they are not on-site, they are still available by phone to provide analytical and technical advice to the HazMat teams.

With their first response time, standardized training and sample collection, close coordination with FBI, and on-site characterization, they can provide LRN Laboratories with really predictable samples from incident sites, and that's really important to us.

In a Joint Position Paper being drafted by the National Guard, CST, and the APHL, we state that the CSTs represent

the preferred entry point of initial samples from terrorist events into the LRN.

Now, field instruments and type of testing used by the first responders varies, not only from state to state, but unfortunately from team to team. As mentioned earlier, there currently is no national strategy for first responders, which is an issue that's being addressed at all levels of preparedness.

In the 2009 Hazardous Materials Roundtable Strategic Planning Report, sponsored by the International Association of Fire Chiefs, one of the several important emerging issues is the need for improved biosampling capabilities.

A recent GAO report cited shortcomings in the sampling, detection, and concept of operations for biological threats that first responders use. Each year first responders receive a list of approved field detection systems that can be purchased by their federal funds. However, there are no guidelines regarding what level of sensitivity and specificity are required from these instruments.

Some state's HazMat teams coordinate their purchases to standardize their tools and others don't. Many Public Health Laboratories, in partnership with their CSTs, have developed training programs and guidelines for their first responders, and we provide consultation prior to the purchase of any field equipment, so that all the response family knows what's being used in the field.

Host: Okay. With that in mind, the instruments used in the clinical laboratory have to go through a lot of hoops before they can be marketed to the public. Are there any similar requirements for biological field detection devices?

Bonnie Rubin: No, and that is what the Public Health Laboratories see as one of the major problems with these devices. As most listeners know, and have lived through, clinical laboratory instruments are subject to 21 CFR 800, the medical device rule, with the FDA mandating to assure that medical devices, such as clinical laboratory instrumentation, are safe and effective, and "where the benefits outweigh the risk."

They are defined in expected performance standards and validation criteria to demonstrate how the manufacturer has met these criteria. However, there are no industry-wide performance criteria, nor are there any designated organizations or agencies responsible to assure that these field devices meet any specified standards.

In February 2007, the APHL approved a position statement recommended by their Emergency Preparedness Response

Committee, on the need for standardized validation of screening kits and devices for use in the field to identify any hazardous biological and chemical agent in order to reduce the likelihood of erroneous field test results.

It's pointed out in the statement that while these kits and devices are not designed to give definitive results like medical devices, they still need to be reliable in terms of expectancy, sensitivity, and specificity.

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Concern regarding this lack of field standardization and validation has resulted in a statement by the US Department of Health and Human Services, recommending against the use of field screening kits, such as hand-held devices, to evaluate and respond to incidents involving unknown powders suspected to contain *Bacillus Anthracis* and other biological agents.

This need to standardize and validate field screening kits and devices is supported by the CDC, FBI, APHL, and by state and local LRN Laboratories.

In the journal, *CQ Homeland Security*, the October 2003 article, by Lipowicz and Starks, it's entitled, "Where Are Standards? Almost Nowhere, Say Rescue Units, Struggling to Buy the Right Stuff."

The position is also stated by public officials, who must make decisions regarding purchase and use of these devices. This is really a critical issue for public safety, public health, and homeland security.

Every partner in the Preparedness Response Program, including the Public Health Laboratories, we really want first responders to have the ability to detect in the field. However, currently most kits and devices on the market were originally designed for military applications to be used in very specific instances, with defined and prescribed responses. These devices need to be subjected to a standardized criteria for the type of field processes being used within the states, recognizing that the Public Health Labs and the CSTs are really critical partners in this process.

Host: Now, Cheryl Gauthier mentions BioWatch and the USPS Biohazard Detection System as two types of detect to warn systems in the US. Have these systems been effective?

Bonnie Rubin: In December 2009, the National Academy of Science, Institute of Medicine, and National Research Council, they released a report entitled "BioWatch and Public Health Surveillance: Evaluating Systems for the Early Detection of

Biological Threats.” The authors of the report made several important recommendations stating that the current BioWatch system requires better testing to establish its effectiveness and better collaboration with public health systems to improve its usefulness.

By 2009, BioWatch air sampling devices have been deployed in more than 30 major US cities. What this is, is air samples are tested daily in contracted Public Health Reference Laboratories for the presence of genetic material, consistent with the biological agents the system monitors.

Now, the Biohazard Detection System, or referred to frequently as the BDS, is used by the United States' postal system and processing and distribution centers across the US.

The BDS uses sophisticated DNA matching to detect the presence of anthrax, *Bacillus Anthracis*, in the mail by testing air samples from mail-canceling equipment.

All the BDS processes are automated, and the equipment collects samples of air as the mail goes through the canceling machine. It absorbs the airborne particles into a sterile water base, and then this creates a liquid sample that can be tested.

The liquid sample is injected into a cartridge, and the PCR test for a DNA matching is performed. If there is a suspect positive by this testing, the tests are sampled and sent to your LRN Public Health Laboratory and is confirmed there.

The Executive Office of the President's Office of Science and Technology Policy created an interagency working group that revealed the performance of the BDS, and confirmed with their own test that the BDS is consistent with the state-of-the-art, laboratory-based detection systems, and is sufficient to perform the task stipulated by the postal service.

The detection, conformation, and result communication processes for both these systems, the Biohazard Detection System and BioWatch have worked well enough, but as stated in the IOM evaluation, there are still improvements to be made.

Host:

Well, it sounds like there has been and still is a lot being done throughout the US, at the federal, state, and local levels, to provide biological agent detection and identification testing. But is being able to test for these agents enough, what else needs to be in place to reduce the risk of biothreats to the public?

Bonnie Rubin: Having worked in this area for several years, my experience is that having working partnership at the federal, state, and local levels are the most important systems to have in place, to really assure a successful response of mitigation of any emergency event. For testing a response, not only is it critical for local responders, the state's LRN Reference Labs, and the CSTs to be working together on a routine basis, but it's essential that the entire public health and healthcare systems have been included in the preparedness program from the start.

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A common statement we have in the preparedness arena is, an emergency event is not the time to be exchanging business cards. The IOM Report brief has succinctly stated our future needs in bio preparedness.

In principle, BioWatch, the BDS, the LRN systems, and Infectious Disease Surveillance through the public and healthcare systems, all should be complimentary. While all these detection systems have the potential to provide a timelier event or alert than the public health and healthcare systems, the promise still remains theoretical.

For example, warning from these systems could be more timely, but it would have to be under very specific circumstances, such as a large-scale aerosol attack, that's using a certain biological agent we already test for that occurs where a BioWatch system is.

While surveillance through the public health and healthcare systems need improvement, it's an integral part of daily public health activities across the country, at the local, state, and federal levels.

These surveillance activities are broader and more flexible than detection systems, permitting detection of a wider range of infectious diseases, and diseases resulting from sources to exposure that testing devices are not necessarily designed to detect.

State and local authorities have legal responsibilities, as well as knowledge of endemic health risk that make them essential and valuable partners in the emergency preparedness efforts.

Together our resources need to be better linked to a broader and more effective national biosurveillance framework that will help provide state and local public health authorities and the healthcare systems with the information needed to determine the appropriate response to biological threats.

The public health and healthcare systems, we face many challenges meeting preparedness goals and needs, and these include improving the effectiveness of our Infectious Disease Surveillance, and testing, developing better capabilities for analysis, and importantly, having the ability to exchange information in a timely manner.

The differences in capabilities across local and state health departments, including the laboratories, currently contributes to inefficiencies, and to the potential for surveillance gaps.

Although emergency preparedness has improved significantly since 2001, further improvements are needed, but unfortunately, federal funding has and will continue to decline since the initial post-2001 increases that we saw.

Host:

Bonnie Rubin is Associate Director of the State Hygienic Laboratory, Iowa's Public and Environmental Health Laboratory, and a member of the APHL Emergency Preparedness and Response Committee, and has been our guest in this podcast from *Clinical Chemistry*. I am Bob Barrett. Thanks for listening.

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