Public health laboratories (PHLs) have an important role in detecting and reporting antimicrobial resistance by providing antimicrobial susceptibility testing (AST) on organisms of public health significance. AST directs the clinical use of antimicrobials by predicting the drug susceptibility of an organism to a particular antimicrobial agent, and is performed on a wide range of bacteria, including *Mycobacterium tuberculosis* and *Staphylococcus aureus*, as well as some viruses and fungi. The results from these tests often inform the appropriate clinical course of treatment and provide data to determine trends in drug resistance for public health surveillance. As antimicrobial resistance emerges, it is critical that laboratorians are well trained to perform, troubleshoot and interpret the results of AST. They must also learn to recognize novel resistance, which can be challenging. While it is well known that AST is conducted in PHLs, specific capacities and capabilities have been undocumented. In order to gain a better perspective on current AST practices in state public health laboratories (SPHLs), the Association of Public Health Laboratories (APHL) in coordination with the Centers for Disease Control and Prevention (CDC) launched the 2009 Antimicrobial Susceptibility Testing Survey.
METHODS
APHL periodically surveys its member laboratories to assess their testing capacities, capabilities and practices. With increasing concerns surrounding antimicrobial resistance, CDC and APHL launched an Antimicrobial Susceptibility Testing Survey in 2009 to gain an understanding of the capabilities of SPHLs to perform AST on pathogens of public health importance. This survey was developed by AST subject matter experts from public health laboratories, APHL and CDC, and administered through MRInterview, a web-based survey instrument. The survey was issued to 51 SPHLs including the District of Columbia. Respondents were asked to provide information about their AST practices from January 1, 2008 – December 31, 2008 including data regarding funding sources, organism-specific methodologies, barriers to identifying and reporting resistant organisms, standards and guidelines employed, and reporting methods.

ANTIMICROBIAL SUSCEPTIBILITY TESTING IN STATE PUBLIC HEALTH LABORATORIES
Forty-eight (94%) of the 51 SPHLs invited to participate responded to the survey. Overall, 45 (94%) of the respondents provide some type of AST on bacteria, fungi or viruses. Three (6%) of the respondents do not provide any AST.

Of the 48 laboratories that offer AST, the majority of SPHLs (n=40; 83%) offer some level of AST for *Mycobacterium* spp. (see Table 1). Additionally, 16 respondents provided confirmatory testing of unusual resistance patterns in Mycobacteria, and 9 respondents provide AST to support surveillance of this resistance.

SPHLs reported varying levels of AST of non-TB bacterial isolates. Illustrating the range of services across SPHLs, 10 respondents who provide AST (22%) provide routine diagnostic testing of non-TB bacterial isolates, including testing of *Group B Streptococcus* for patients allergic to penicillin. Twenty-one of 45 (47%) reported providing confirmatory testing of unusual resistance patterns. Twenty-five respondents (56%) reported conducting surveillance for resistance among bacterial isolates.
Table 1: Number of SPHLs offering various types of AST for bacteria and fungi, categorized by purpose

<table>
<thead>
<tr>
<th>TESTING CATEGORIES*</th>
<th>BACTERIA</th>
<th>MYCOBACTERIA</th>
<th>YEASTS/MOLDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>(number of labs, N=45)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Routine diagnostic testing</td>
<td>10 (22%)</td>
<td>40 (89%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Confirmatory testing</td>
<td>21 (47%)</td>
<td>16 (36%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Surveillance</td>
<td>25 (56%)</td>
<td>9 (20%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (11%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

*Not mutually exclusive categories

**ORGANISM-SPECIFIC AST**

The number of organisms tested in SPHLs ranges from 0 (3 SPHLs) to 30 (1 SPHL). On average, SPHLs responding to this survey perform AST on four organisms. First-line drug testing for *Mycobacterium tuberculosis* was the most common type of AST provided by survey respondents (43 of 45; 96%). Twenty-two of 45 (49%) respondents reported performing AST to confirm vancomycin-resistant *Staphylococcus aureus* (VRSA) isolates, vancomycin-intermediate *Staphylococcus aureus* (VISA), and second-line drug testing for *Mycobacterium tuberculosis* (see Figure 1). Forty percent of laboratories (18 of 45) perform AST for Methicillin-resistant *Staphylococcus aureus* (MRSA), and 17 laboratories (38%) for *Neisseria gonorrhoeae*. Approximately one third of SPHLs perform AST on these organisms: *Salmonella*, *Shigella*, vancomycin-resistant enterococcus (VRE), multiple drug resistance gram-negative rods, *Klebsiella pneumonia*-producing carbapenamase (KPC), *Acinetobacter*, *Streptococcus pneumoniae*, Group A and Group B Streptococcus.
Figure 1: Percentage of SPHLs that provide AST for specific organisms (% of labs, N=45)
AST METHODS AND STANDARDS

The methods employed by respondents are shown in Figures 2a-2d. To confirm unusual resistance among non-tuberculous bacterial isolates, the majority of SPHLs (21 of 31; 68%) utilize manual methods, such as Etest and CLSI Reference Disk Diffusion. Despite advances in the ability of automated systems to produce reliable susceptibility data in a short period of time, distinct limitations still exist in their ability to reliably detect novel resistance. Until such resistance has been well-researched and the ability of automated systems to detect it is well-documented, traditional manual methods are required for confirmation and surveillance of emerging resistance. Predominantly, laboratories reported the use of two systems for susceptibility testing of Mycobacteria: BD BACTEC MGIT 960 (24 of 43; 56%) and BD BACTEC 460TB (17 of 43; 40%). One drawback to the use of the BACTEC 460TB system has been its dependence upon a radioactive indicator of growth. The manufacturer of this instrument, Becton Dickinson, has indicated they will no longer manufacture the media and reagents for the BACTEC 460TB by September 2011, which will likely result in a shift of those users to either the BACTEC MGIT 960 or the VersaTREK system.

Figure 2a: AST methods for non-TB bacteria in SPHLs (% of labs, N=31)
Figure 2b: AST methods for TB in SPHLs (% of labs, N=43)

AST METHODS: TB (% OF LABS, N=43)

- MGIT: 56%
- Bactec: 40%
- Agar Proportion: 37%
- Other: 7%
- VersaTREK: 7%
- Molecular (commercial method): 5%
- Etest: 2%
- Trek Manual: 2%
- Molecular (in-house method): 2%

Figure 2c: AST methods for non-TB Mycobacteria in SPHLs

AST METHODS: NON TB MYCOBACTERIA (% OF LABS, N=8)

- Agar Proportion: 63%
- MGIT: 38%
- Bactec: 25%
- CLSI Reference Disk Diffusion: 13%
- Trek Manual: 13%
Due to the clinical and public health implications of AST results, the Clinical and Laboratory Standards Institute (CLSI) issues performance standards and guidance documents for AST. Laboratories should have the latest updates of these documents and assure their methods adhere to these standards. To gain an understanding of standards employed by SPHLs, laboratories performing AST were asked to report which AST-related CLSI standards were available and used. Reflecting the complexity of AST, PHLs reported multiple sources of guidance for AST practices.

Twenty-seven percent of respondents reported employing CLSI documents exclusively; the remaining 73% reported utilizing a variety of other additional sources for protocols and guidelines, predominantly CDC and instrument manufacturers. The cost of maintaining current documents is in itself a continuing financial challenge. One SPHL did not report having any guidance documents on-hand or on order despite performing AST; misunderstanding of the question cannot be excluded as the reason for this response.
REPORTING AND OUTREACH

Seventy-three percent (33 of 45) of respondents performing any AST did not generate AST surveillance data, perhaps reflecting the difficulties and expense of collecting or generating representative data. Reports were generated for CDC for various programs (e.g., GISP, TB, and NARMS) by a reported 13% of respondents. Nine percent (4 of 45) of respondents published a statewide antibiogram, and an equal percent posted AST data to a website, with 4% (4 of 45) publishing results in a public health newsletter. These categories are not mutually exclusive; those PHLs who communicated their data utilized multiple means. It cannot be determined from these survey questions if the data reported publicly are from internal testing or generated from clinical antibiograms. Eleven percent (5 of 45) of respondents reported collecting cumulative antibiogram data from their clinical microbiology laboratories.

SPHLs, perhaps responding to the expectations of the National Laboratory System or to the needs of their clinical partners, have implemented outreach involving consultation, training, and provision of technical reference resources. Just over half of the respondents who performed AST (23 of 45) provided training or outreach specifically related to AST practices to clinical laboratories. Most commonly this training is through provision of expert consultation from SPHL subject matter experts (78%; 18 of 23). Additionally, 48% (11 of 23) provided reference material specific to AST, such as CLSI documents, 43% (10 of 23) provided in-person lectures and 30% (7 of 23) conducted teleconferences specific to AST practices.

Twenty six of the 45 (58%) SPHLs conducting AST do not provide training to their clinical laboratories specific to antimicrobial resistance surveillance. Among those who do provide this training, the majority, 13 of 19 (68%), provided expert consultation upon request. To a lesser extent, SPHLs offered teleconferences, provided reference materials, such as CLSI documents, and conducted in-person lectures.

TRAINING METHODS FOR STAFF

Due to the complexity of AST and the importance of interpreting and reporting accurate results, it is important for staff to maintain competency in current AST practices. When asked to reflect on training methods, SPHLs reported multiple means. Most commonly, respondents indicated staff was trained by other staff members proficient in AST (33 of 45; 73%).

National Laboratory Training Network (NLTN) training was utilized by just over half of respondents (53%), and CLSI AST teleconference and instrument manufacturer training by 42% each. These categories are not mutually exclusive, with labs employing multiple strategies.
BARRIERS

SPHLs reported several barriers to performing AST. Lack of demand for in-house AST was the primary reason for the three SPHLs who do not perform any AST. All three of these laboratories reported that this role was fulfilled by their clinical laboratory partners; however, an SPHL’s role in AST is not clearly defined and needs to be elucidated. Two of the three laboratories (67%) also cited inadequate funding as a barrier to offering AST, and one of the three laboratories reported AST not being in the scope of their laboratory’s mission.

For those SPHLs who do perform AST, 42% (10 of 24) identified inadequate funding as the primary barrier to testing additional organisms for antimicrobial susceptibility (see Figure 4). Similarly, inadequate staffing was indicated by 38% (9 of 24) of SPHLs as a secondary reason for not adding additional organisms (data not shown). Seventeen percent (4 of 24) of laboratories cited that adding AST capabilities was not in the scope of their mission. The cost of sustaining regulatory requirements for verification, validation, quality control and proficiency testing was reported as a barrier by 13% (3 of 24) of laboratories.

Figure 4: SPHL barriers to offering additional AST
Conclusions

This survey provides insight to AST practices in SPHLs. The fact that the majority of SPHLs provide AST for at least one organism indicates that APHL should explore areas to involve member laboratories in activities, such as training, to expand their capabilities.

Given the great variation in the size, organization, funding and mission of SPHLs, it is not surprising that there is a wide range of diversity in AST practices. This survey demonstrates that the practices of one SPHL cannot be used to predict those of another. The most common finding is that most SPHLs offer testing of at least Mycobacterium tuberculosis. Only two that offer any AST services do not offer at least some testing for this agent.

Adequate funding to support AST remains a challenge to public health laboratories. Few states, only 7 (16%), have funding specifically directed to AST; it is not clear from this survey if that funding totally supported this service.

The majority of state public health laboratories rely on general or federal funds to support AST. Both of these funding sources may have suffered significant budget cuts with the recent economic downturn.

With continued concerns surrounding antimicrobial resistance and the public health implications of drug resistance in organisms such as Neisseria gonorrhoeae and Mycobacterium tuberculosis, it is evident that PHLs have a role in AST that needs to be more clearly defined. The role of SPHLs in providing surveillance for emerging resistance, identifying and reporting novel mechanisms of drug resistance, providing reference testing services not provided by most clinical laboratories, and maintaining reference methods are critical functions that need to be explored and expanded upon by PHLs. In the future, APHL will continue to seek opportunities to collaborate with federal, state, local and other partners to address AST challenges and improve AST practices in the nation’s public health laboratories.
REFERENCES


The Association of Public Health Laboratories (APHL) is a national non-profit organization dedicated to working with members to strengthen governmental laboratories that perform testing of public health significance. By promoting effective programs and public policy, APHL strives to provide member laboratories with the resources and infrastructure needed to protect the health of US residents and to prevent and control disease globally.

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