Public Health Issues in Antimicrobial Susceptibility Testing

Background

Many different clinical laboratories perform Antimicrobial Susceptibility Testing (AST). It is very important that all laboratories use methods that are comparable, so that results from one institution would be equvalent to results from any other institution.

For years, there has been a professional organization, CLSI (Clinical and Laboratory Standards Institute) that was formerly known as NCCLS (National Committee on Clinical Laboratory Standards) that created standards for performance of AST tests.

All clinical laboratories performing testing for antimicrobial susceptibility should have access to current guidelines and adopt them. This assures that clinicians use appropriate antibiotic therapy when necessary.

This document will provide information on AST for several reportable diseases in an effort to assure valid performance and data collection. It is not a comprehensive listing of information about AST. Please visit the reference section at the end for additional information.

BT agents (including *B. anthracis, Y. pestis, Burkholderia mallei,* and *Burkholderia pseudomallei*)

Drugs to test and report:

B. anthracis: Penicillin, Doxycycline or Tetracycline, and Ciprofloxacin.
Y. pestis: Gentamicin, Streptomycin, Doxycycline or Tetracycline, Ciprofloxacin, Chloramphenicol, and Trimethoprim-sulfamethoxazole.
Burkholderia mallei: Ceftazidime, Doxycycline or Tetracycline, Imipenem
Burkholderia pseudomallei: Amoxicillin-clavulanic acid, Ceftazidime, Doxycycline or Tetracycline, Imipenem, Trimethoprim-sulfamethoxazole.

Enterococcus (including VRE)

How to test:

If you are using disk diffusion testing for *Staphylococci*, ensure that you measure zones using transmitted light, not reflected light.

Do not report:

It is important that all laboratories note that aminoglycosides (except high concentration), cephalosporins, clindamycin, and trimethoprim-sulfamethoxazole should never be reported as susceptibile for *Enterococcus*. These antibiotics may appear to be active in the laboratory, but they are not effective clinically.

Unusual results that should initiate supervisory review:

Enterococcus:

- Daptomycin R or I
- Linezolid. R or I

***Enterobacteriaceae* (ESBL)**

ESBL (Extended Spectrum Beta Lactamase):

Strains of *Klebsiella* sp. and *E. coli* that produce ESBLs may be clinically resistant to therapy with penicillins, cephalosporins, or aztreonam, despite apparent *in vitro* susceptibility to these agents.

What to report:

All confirmed ESBL strains should be reported as resistant to all penicillins, cephalosporins, and aztreonam.

Unusual results that should initiate supervisory review:

Enterobacteriaceae:

- Carbapenem R or I

E. coli:

- ESBL confirmed positive

Klebsiella sp:

- ESBL confirmed positive

Haemophilus influenzae

Drugs to test:

For CSF isolates of *Haemophilus influenza*, only ampicillin, a third-generation cephalosporin, chloramphenicol, and meropenem should be routinely tested and reported.

Unusual results that should initiate supervisory review:

Haemophilus influenza:

- Aztreonam R or I
- Carbapenem R or I
- 3rd generation cephalosporins R or I
- Fluoroquinolone R or I

Neisseria gonorrhoeae

Unusual results that should initiate supervisory review:

Neisseria gonorrhoeae:

- 3rd generation cephalosporin R

***Salmonella/Shigella* species:**

Drugs to test and report:

For fecal isolates of *Salmonella/Shigella*, only ampicillin, a fluoroquinolone, and trimethoprim-sulfamethoxazole should be routinely tested and reported. If organism is resistant to a fluoroquinolone, please note this on the slip when the organism is sent to the Utah Public Health Laboratory.

Do not report:

It is important that all laboratories note that 1st and 2nd generation cephalosporins and all aminoglycosides should never be reported as susceptible for these organisms. These antibiotics may appear to be active in the laboratory, but they are not effective clinically.

Staphylococcus aureus (including MRSA and VRSA)

Drugs to test:

Penicillin/oxacillin:

To determine resistance to the penicillin class of drugs, you need only test for penicillin and oxicillin resistance.

- Disk Diffusion - For *Staphylococcus aureus* it is easier to read a cefoxitin disk than an oxacillin disk, and the results are comparable. Therefore, for disk diffusion tests - it is preferable to use a penicillin disk and a cefoxitin disk. IF you use an oxacillin disk – and the results are intermediate, then you should perform an alternate test, such as mec A, PBP2a, cefoxitin disk test, oxacillin MIC test, or oxacillin-salt agar screening test, rather than reporting the intermediate result.
- MIC tests – use penicillin and oxacillin.

For *Staphylococcus* species, penicillin resistance and methicillin resistance are separate. Organisms can be susceptible to penicillin and methicillin, OR resistant to penicillin but susceptible to methicillin, OR resistant to both.

If you perform *mec*A or PBP2 testing, you can report all positives as methicillin (oxacillin) resistant. *Staphylococci* with oxacillin MIC's ≥ 4 ug/ml are oxacillin resistant.

Vancomycin:

Vancomycin intermediate or resistant *Staphylococcus aureus* is very rare and presents infection control challenges. All *Staphylococcus aureus* isolates with a vancomycin MIC ≥ 4 ug/ml should be reported to public health and infection control immediately. The isolate should be sent to a reference lab as soon as possible.

Clindamycin:

If *Staphylococcus aureus* is resistant to erythromycin, but susceptible to clindamycin, do NOT report the clindamycin results before performing a test for inducible clindamycin resistance. This is a D zone test, performed by placing a 2 ug clindamycin disk 15-26 mm away from the edge of a 15 ug erythromycin disk. Any flattening of the susceptibility zone (D-shaped) would indicate inducible clindamycin resistance and should be reported as "resistant" not susceptible.

How to test:

- CDC has created a fact sheet that answers questions laboratorians may have about how to test and the significance of results of vancomycin

intermediate or resistant *Staphylococcus aureus* isolates. CDC also has created a testing algorithm that describes appropriate testing strategies.

- If you are using disk diffusion testing for staphylococci, ensure that you measure zones using transmitted light, not reflected light.

Do not report for MRSA:
All methicillin/oxacillin resistant *Staphylococcus aureus* are ALSO resistant to all penems, cephems, and other beta-lactams such as amoxicillin-clavulanic acid, piperacillin-tazobactam, and imipenem. These antibiotics may appear to be active in the laboratory, but they are not effective clinically.

Unusual results that should initiate supervisory review:
Staphylococcus aureus:

- Linezolid R or I
- Quinupristin-dalfopristin R or I
- Daptomycin R or I
- Vancomycin R or I (if this result is confirmed, immediately notify the Utah Department of Health, the clinician, and your infection control practitioner).

Streptococcus pneumoniae

Drugs to test:
For CSF isolates of *Streptococcus pneumoniae*: penicillin, cefotaxime, ceftriaxone, vancomycin, and meropenem (if on your formulary) should be routinely tested by MIC and reported.

Unusual results that should initiate supervisory review:
Streptococcus pneumoniae:

- Fluoroquinolone R or I

***Streptococcus* (Beta hemolytic)**

Drugs to test:
Beta hemolytic streptococci do not require susceptibility testing for penicillin, other beta-lactams, or vancomycin as all are uniformly susceptible.

Unusual results that should initiate supervisory review:
Beta hemolytic Streptococci:

- Penicillin or ampicillin R or I

References*

1. The MASTER website (self-training) for AST:
http://www.phppo.cdc.gov/dls/master/default.aspx

2. Fact sheets from CDC on laboratory issues, including AST:
http://www.cdc.gov/ncidod/hip/Lab/LAB.HTM

3. Web site for CLSI (can purchase current guidelines):
http://www.nccls.org/

Guidelines appropriate for AST include:

- M2-A8 (M2) 2003 – Performance standards for antimicrobial disk susceptibility tests. Eighth edition. Approved Standard.
- M7-A6 (M7) 2003 – Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. Sixth edition. Approved Standard.
- M100-S15 (M100) 2005 – Performance standards for antimicrobial susceptibility testing. Fifteenth informational supplement.

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