



## **ANTIBIOGRAM SURVEILLANCE METHOD USING CUMULATIVE SUSCEPTIBILITY DATA**

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### **1. Description of Method**

Many hospital laboratories routinely perform antimicrobial susceptibility testing for *Streptococcus pneumoniae* and other bacterial pathogens. Cumulative susceptibility testing results are often organized into a summary table, or antibiogram, which may be used by clinicians, pharmacists, infection control personnel and microbiologists as a reference guide to community or hospital-specific resistance patterns. Antibiograms lend information that can be used to raise awareness of resistance problems, support the use of optimal empiric therapy, and identify opportunities to reduce inappropriate antibiotic

usage and to ascertain success of such efforts (1-3). A typical antibiogram displays the total number of bacterial isolates tested against a range of antimicrobials and includes the percentage of bacterial isolates susceptible or resistant to each antimicrobial agent tested (See Figure 1). The time period covered by most antibiograms is six to twelve months. Antibiograms may summarize susceptibility testing results for an entire hospital by inpatient, outpatient, and intensive care units or by individual wards (1).

Figure 1: Sample antibiogram using NCCLS approved guidelines for analysis and presentation of cumulative susceptibility data

Antibiotic Susceptibility	Isolates	Ampicillin	Ceftriaxone <sup>b</sup>	Ceftriaxone <sup>b</sup> -CSF	Cefazolin	Clindamycin	Erythromycin	Gentamycin	Linezolid	Methacillin	Nitroxoline <sup>c</sup>	Levofloxacin	Penicillin	Rifampin	Streptomycin	Tetracycline	Trimeth/Sulfa	Vancomycin
<b>Gram Positive Cocci</b>		Percentage of Isolates that are Susceptible <sup>a</sup>																
<i>Enterococcus spp.</i>	248	95						33 <sup>d</sup>	100		99	65	91		25	28		100
<i>Enterococcus faecalis</i>	74	100						21 <sup>d</sup>	100		100	68	98		20	35		99
<i>Enterococcus faecium</i>	281	10						23 <sup>d</sup>	100		92	9	6		95	27		20
<i>Staphylococcus aureus</i>	894				61	73	45	97		61	100	65	8	98		94	98	100
<i>Staphylococcus epidermidis</i>	92				25	70	29	68		23		39	5	93		84	66	100
<i>Staphylococcus coag. neg.</i>	402				20	68	28	74		20		44	5	97		77	64	100
<i>Streptococcus pneumoniae</i>	129		98	92		86	62					96	55			77		

Shading indicates "Not Tested"

a - Minimum Inhibitory Concentration (MIC) breakpoint is defined for each bacterial species or genus by NCCLS. The MIC is the lowest concentration of a drug which inhibits growth in vitro.

b - As of Jan 2002 NCCLS has 2 breakpoints for ceftriaxone-susceptible *S. pneumoniae*. CSF isolates are considered susceptible at <0.5mcg/ml & other isolates at <1 mcg/ml.

c - Antibiotics tested only on urine isolates.

d - Aminoglycosides are tested at high levels with *Enterococcus* spp. to indicate synergy with cell wall active agents.

For state health department personnel interested in collecting community-specific proportions of antimicrobial resistant *S. pneumoniae*, surveillance using aggregated antibiogram data is a simpler and less expensive option compared to methods that collect

information on individual episodes (please see sections: Population-based Surveillance and Sentinel Surveillance Methods). Although yielding less detailed information than other methods, antibiograms are adequate at estimating the prevalence of resistance among pneumococci to penicillin, erythromycin, and third-generation cephalosporins (2), as well as other antimicrobials such as trimethoprim-sulfamethoxazole (3). Antibiogram aggregation might be a useful surveillance method in communities where hospital antibiogram data are readily available and more intensive surveillance is impractical due to a lack of financial or personnel resources. Those using this surveillance method can improve their results by working with local hospitals to develop a consistent susceptibility-testing regimen and reporting format that facilitates aggregation of data obtained from multiple hospitals and laboratories (2, 3). Consistency among facilities can be attained by following NCCLS guidelines and performance standards for antimicrobial susceptibility testing (4, 5).

## **2. Level of Precision**

Two published studies have compared the estimates of community-specific *S. pneumoniae* susceptibility testing from antibiograms to that obtained from active, population-based surveillance that collected data on individual cases. In Portland, Oregon, the percent of *S. pneumoniae* susceptible to penicillin, cefotaxime, trimethoprim-sulfamethoxazole and erythromycin were statistically comparable to results of active surveillance for the twelve hospitals studied except for one hospital's erythromycin susceptibility results where antibiograms underestimated susceptibility (3). In a multisite study, performed among eight geographically diverse sites in the United States using data from CDC's Active Bacterial Core surveillance (ABCs), the proportions of penicillin-,

erythromycin-, and third-generation cephalosporin-resistant *S. pneumoniae* estimated by aggregated antibiograms were compared to levels of antimicrobial resistance estimated by active population-based surveillance for invasive pneumococcal disease (defined as cases with isolates from sterile body sites) (2). In each of the eight sites, the proportions of penicillin-nonsusceptible isolates from antibiograms were within 10 percentage points of those obtained through active surveillance; for six sites, the difference in nonsusceptibility was within 5 percentage points. When proportions of local nonsusceptibility to third-generation cephalosporins as estimated by antibiograms were compared to those obtained from active surveillance, all but one site was within 10 percentage points. Similarly, proportions of pneumococcal isolates nonsusceptible to erythromycin as estimated by antibiograms were within 10 percentage points of proportions estimated by active surveillance in all ABCs sites. No significant differences in the two surveillance methods were noted between geographic areas of high and low penicillin resistance (2). Results were consistent even though the antibiogram data included results from both sterile and non-sterile site isolates and used clinical laboratory susceptibility testing results whereas the ABCs data included only sterile site isolates that were tested for susceptibility in reference laboratories.

### **3. Resources Required**

*Participating Laboratories* Public health personnel may select any number of clinical laboratories serving the population under surveillance when using this method. As with all surveillance systems, including more hospitals and therefore collecting data for more isolates (i.e., a larger sample area that matches the catchment area's population characteristics) increases the system's representativeness and the degree to which

inferences may be drawn from the sample to the community at large. If a subset of clinical laboratories is used, obtaining data from the laboratories that provide service to the most representative healthcare facilities is desirable; for example, surveillance personnel may choose participating laboratories based on whether they serve large academic centers, small or children's hospitals, long term care, outpatient, or urgent care facilities, depending on the population they would like represented. Considering which population subgroups might be over-represented or excluded when selecting hospitals is important for designing the surveillance system (6). For example, children's hospitals are more likely to have a higher percentage of penicillin-nonsusceptible pneumococci than other hospitals and could overestimate the community's resistance levels (7). Because most clinical laboratories routinely generate antibiograms and others can generate them on request, obtaining antibiograms from all or nearly all clinical laboratories serving a population is feasible and likely to provide the best results.

Three published antibiogram analyses used specific criteria to facilitate antibiogram aggregation (2, 3, 8). Two or more antibiograms may be aggregated and used to summarize pneumococcal resistance in a specified community if each of the individual antibiograms: 1) cover similar time periods (e.g., 6 or 12 months), 2) include susceptibility testing results for the same antimicrobials, and 3) list both the total number of pneumococcal isolates tested against the antimicrobials in question and the percent of isolates that are nonsusceptible (or susceptible). A demonstration of how data from multiple antibiograms are combined to estimate nonsusceptibility of a bacterial pathogen to an antimicrobial in one community is shown in Figure 2 below. The total number of nonsusceptible isolates (column E) obtained from five hospital laboratory antibiograms is

divided by the total number of isolates tested (column B) to give the proportion of isolates nonsusceptible to the antimicrobial of interest in the community under study. The information in columns D and E may not be listed in the individual laboratory's antibiogram but may be calculated from the information in columns B and C.

Figure 2: An example of how data from antibiograms can be aggregated for a pathogen to estimate nonsusceptibility in a community.

A	B	C	D	E
Hospital	No. of isolates	% susceptible	No. susceptible (B x C)	No. non-susceptible (B - D)
1	14	78.6	11	3
2	12	83.3	10	2
3	18	77.8	14	4
4	36	77.8	28	8
5	23	82.6	19	4
<b>All 5 hospitals combined</b>	<b>103</b>	<b>79.6</b>	<b>82</b>	<b>21</b>

% susceptible isolates among 5 hospitals =  $82/103 = 79.6\%$   
 % non-susceptible isolates among 5 hospitals =  $21/103 = 20.4\%$   
 or  $100\% - 79.6\% = 20.4\%$

Susceptibility data from some laboratories should be excluded if the number of pneumococcal isolates tested for the antimicrobial in question (e.g., a macrolide or cephalosporin) is only a *subset* of isolates tested for susceptibility to penicillin (2, 8). Often a hospital or reference laboratory will only test penicillin-nonsusceptible isolates for susceptibility to other antimicrobials. Because penicillin-nonsusceptible isolates are more likely to be nonsusceptible to other antimicrobial agents than are penicillin-susceptible isolates (9), resistance to the additional antimicrobials might be overestimated. An example is shown in Figure 3.

Figure 3. Sample antibiogram. Note that not all antimicrobials are tested per pathogen. Penicillin is tested against 68 *S. pneumoniae* isolates, but only two are tested against the other antimicrobials.

ANTIBIOTIC SUSCEPTIBILITY REPORT										
In Vitro Antimicrobial Susceptibility of Common Aerobic Gram Positive Cocci										
Isolated During January -- December, 1997										
Data are Percent Susceptible										
ORGANISMS	No. of Strains	Ampicillin	Cefazolin	Clindamycin	Erythromycin	Nafcillin	Penicillin	Trimeth./sulfa	Vancomycin	Ciprofloxacin <sup>a</sup>
<i>E. faecium</i>	110	11							34	3
<i>E. faecalis</i>	409	100							100	22
<i>Staph aureus</i> <sup>b</sup>	338		100	96	77	100	5	96	100	84
<i>Staph epidermidis</i>	446		55	70	46	44	21	54	100	61
<i>Strep pneumoniae</i>	2	100	100	100	50		87 <sup>c</sup>	80	100	
MRSA	108			25	9	0	0	99	100	6

Shading indicates "Not Tested"

- a. Not tested against all isolates
- b. Does not include MRSA
- c. Tested against 68 isolates

*Personnel* The design of the antibiogram surveillance method allows for minimal investment in health department staff time and training. Little time is required for data aggregation once antibiograms are collected from clinical laboratories. The savings in time and training is especially evident in comparison to other surveillance methods that collect data on individual cases. Because most hospital laboratories that perform susceptibility testing will routinely generate an antibiogram, no additional effort is needed for laboratory staff to prepare and provide the data to health department staff. The antibiogram study of 12 Oregon hospitals required an estimated 20 hours of health department staff time (3). The North Carolina statewide antibiogram study spent ~ \$1000 on mailings, survey distribution, and personnel costs to aggregate data from 5 years of

surveillance (8). Health department staff are required once or twice a year to notify and recruit participating laboratories, collect and aggregate antibiogram data, and prepare reports for dissemination to clinical and public health partners. When starting an antibiogram-based surveillance program, health department staff may choose to take additional time to survey local laboratories to assess the current methods for antibiogram construction and results routinely collected and to promote consistency of methods (e.g., antimicrobials tested) used among participating laboratories. All laboratory methods should be compared to the NCCLS approved guideline for analysis and presentation of cumulative antimicrobial susceptibility test data (4).

*Materials and Supplies* Antimicrobial susceptibility testing is routinely performed by most hospital laboratories. Laboratories that are not currently generating an antibiogram can do so if they have a computer system capable of summarizing results. Traditionally, clinical laboratories have manually tabulated these data but increasingly automated methods are being utilized by various laboratory information systems. Many information technology (IT) departments at hospitals have resources to generate these data. Guidance on minimal requirements for analysis and presentation of antibiogram data has been prepared by NCCLS (4).

Surveillance personnel considering antibiogram surveillance may be able to work with local hospitals and laboratories to develop a cost-effective susceptibility testing regimen using a consistent set of antimicrobial agents and recommended testing methods. A uniform approach to susceptibility testing will increase the amount of data that can be aggregated, increasing representativeness and generalizability of results. A coordinated

approach among laboratories within a defined surveillance area will help to overcome weaknesses of this surveillance method; in past studies of the use of antibiograms, use of different antimicrobials for susceptibility testing and missing data on the total numbers of pneumococcal isolates tested were common reasons for not being able to include antibiogram results from particular laboratories (2).

Ideally, the ability to track resistance to multiple antimicrobials can be enhanced by encouraging clinical laboratories to perform routine susceptibility testing for a standard set of antimicrobial agents; however, clinical needs at the hospital level dictate which antimicrobials are tested. The clinical laboratory tests isolates against the antimicrobials that are currently in the hospital formulary and represent potential treatment options for clinicians. It is likely that the set of antimicrobials tested will differ among laboratories. NCCLS document M100 contains tables 1 and 1A which suggest drugs to test and report (5).

#### **4. Information Gained**

Community-level aggregated antibiogram information can enable providers and epidemiologists in that community to track antimicrobial resistance levels and to raise awareness of the resistance problem and the need to use optimal empiric therapy, and may be used to identify opportunities to both reduce inappropriate antimicrobial usage and to ascertain success of such efforts (1-3). As susceptibility testing of pneumococci to penicillin is fairly standard among laboratories, aggregated antibiograms may be used to estimate the community-specific proportion of penicillin-resistant *S. pneumoniae* (PRSP). If an adequate number of laboratories provide susceptibility data on other commonly used

antimicrobials such as cephalosporins, macrolides and vancomycin, susceptibility testing results to these drugs may also be aggregated. Aggregated antibiograms may also be used to track resistance to other organisms such *Staphylococcus aureus* and gram-negative bacteria if testing of these pathogens are routinely included on the local antibiograms.

## **5. Advantages**

Antibiogram-based surveillance is a feasible, inexpensive, relatively rapid, and accurate surveillance option for estimating prevalence and trends of pneumococcal nonsusceptibility. Using aggregated antibiograms to estimate the prevalence of antimicrobial resistance among *S. pneumoniae* and other bacteria places a relatively small burden on local public health department personnel and little to no additional work on staff in hospital or reference laboratories that have available antibiograms. Time and financial requirements for antibiogram surveillance are therefore minimal, which makes using antibiograms a feasible surveillance system for many health departments (2, 3). Hospital laboratory susceptibility testing is routinely performed and antibiograms are commonly available. If computerized summary techniques are in place, laboratory staff effort is limited to sending a current antibiogram to the health department.

Additionally, the accuracy of antibiograms in describing local prevalence of pneumococcal nonsusceptibility to penicillin has been found comparable to prevalence results from active surveillance for invasive disease by studies investigating this method as a viable option for sites. Furthermore, this method may provide opportunities for estimating *S. pneumoniae* susceptibilities to some other antimicrobial drugs, such as

macrolides and 3<sup>rd</sup> generation cephalosporins (2, 3, 8). Depending on the specific antibiograms routinely generated by local laboratories, aggregated antibiograms may also be used to track resistance among other bacteria of public health importance (2).

## **6. Disadvantages**

Antibiograms collect data at the hospital level and may estimate the proportion of drug-resistance in the population served by those hospitals. Sometimes, the population served by the hospitals does not reflect the actual neighborhoods surrounding the facility, so it is important to define the specific groups served by the hospital. Laboratories may serve as reference labs for patients whose residence is outside of the community under study.

Importantly, aggregated antibiogram data do not allow the susceptibility results to be evaluated by age or other potential variables of interest such as race or gender. The lack of patient-specific data (e.g., risk factors, demographics) and case-specific information eliminates the opportunity for more thorough analyses which might be needed to evaluate the effect of programs such as vaccination campaigns.

A recent study of antibiograms in eight different communities across the country revealed that only 23 percent of antibiograms distinguished between pneumococcal isolates that are intermediate and resistant to penicillin (2). This distinction is relevant for treatment of infections as NCCLS guidelines recommend different breakpoints by syndrome for some cephalosporins. Most hospital laboratories perform antimicrobial susceptibility testing on *S. pneumoniae* isolates from both sterile and non-sterile sites, on isolates that cause both invasive and noninvasive infections, and on multiple isolates from the same patient.

Most often, results from all isolates tested are included in an antibiogram. The inclusion

of non-sterile site isolates and multiple isolates from a single patient can influence the overall proportion of strains that are reported to be resistant (2, 3). For *S. pneumoniae*, the inclusion of non-sterile site isolates tends to increase the overall percent resistant. In addition, participating laboratories may test a limited number of antimicrobials and may use a variety of testing methods and reporting formats (2). This will limit the number of sites whose data can be aggregated. In considering the validity of information gained from antibiograms, state public health surveillance officers must keep in mind the potential for variation in susceptibility testing methods among hospital laboratories and provide training and field assessment mechanisms to ensure the validity and ultimate value of the information gained. Finally, not all laboratories may generate an antibiogram that can be aggregated because of missing information.

## **7. Appropriate Uses of Data**

State surveillance personnel are encouraged to weigh the benefits of implementing community-level antibiogram surveillance based on the advantages and limitations of this method. It has been suggested that aggregated antibiograms may be used to track trends in antimicrobial resistant infections at the community level (2). In addition to reporting trends of resistance, aggregated antibiograms can raise awareness of the local resistance problem. Incidence cannot be calculated from antibiogram data because the data are not population-based.

## **8. Goals Best Met by Surveillance Methodology**

Aggregated antibiogram data as a method for antimicrobial resistance surveillance should be used by health departments who require an inexpensive, relatively low effort, simple

yet accurate alternative for other surveillance activities. The data are usually routinely generated by local hospital laboratories, do not require a large amount of personnel time to collect, and are relatively comparable to data from active, population-based surveillance programs that collect information on individual cases. To maximize the benefits of using existing antibiograms it is necessary to understand how local antibiograms are generated to improve the consistency of antimicrobials and bacteria tested.

## **9. Examples of Aggregated Antibiogram Surveillance**

The following two examples of antibiogram surveillance studies were undertaken by the Alaska department of health and social services (example 1) and the Washington department of health (example 2). Each document displays how antibiogram data can be used and compiled.

Ex. 1: [http://www.epi.hss.state.ak.us/bulletins/docs/b2003\\_25.pdf](http://www.epi.hss.state.ak.us/bulletins/docs/b2003_25.pdf)

Ex. 2: <http://www.doh.wa.gov/topics/Antibiotics/Documents/data2003Summary.pdf>

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