pennsylvania
DEPARTMENT OF HEALTH

The Steward

A partnership in reducing antimicrobial resistance through antimicrobial stewardship

December 2019 **Volume 1, Number 5**

In This Issue

Implementing Antibiotic Stewardship (AS) Policies and Interventions to Improve Antibiotic Use

By: Christine L. Mulgrew, MPH, PhD

Policies lie at the heart of all antibiotic stewardship programs (ASP). Without them, patients are more likely to be prescribed the wrong antibiotic, dose or duration and the chances of an outbreak of antibiotic resistant organisms, including *C. difficile*, may increase.

Every acute care hospital in Pennsylvania has implemented at least one AS policy to meet this core element--most have implemented three or more. As shown in the table below, ASPs labeled as "good" by the National Quality Forum (2016) have implemented a set of systemwide interventions. It is recommended that facilities develop a set of systemwide policies to form the foundation of your ASP. The list may vary from facility to facility. From there, an ASP should add AS policies that target patients and certain medical conditions. "Better" programs will have implemented patient-specific interventions such as developing guidance on dose adjustment for cases of organ dysfunction. "Best" programs will develop diagnosis and infection-specific interventions such as evidence-based methods to improve antibiotic use for urinary tract infections or surgical site infections.

As ASPs develop an array of policies, it is natural for staff to become disengaged or feel overburdened. To avoid these problems, involve staff when both developing the AS policy and deciding the area in which to develop a new AS policy. The staff can help create a more comprehensive policy and may also champion it among their peers. It is recommended to stagger implementation of new AS policies, this means introducing one policy before releasing the next one to the same staff.

Three of the other five CDC core elements work in unison with policies and interventions to support complete implementation of the policies. The AS education core element is met after staff are trained and competency is proven. Competency assessment will be a CMS requirement starting March 2020. The tracking core element may be met by measuring the implementation of some of the AS policies. Including the uptake metrics, such as competency results, in a report can augment the reporting core

News You Can Use

Center for Infectious Disease Research and Policy (CIDRAP): Experts urge better antimicrobial resistance messaging – 5 principles included for improved communications

Check out CDC's recently released report, Antibiotic Resistance Threats in the United States, 2019, which lists 18 bacteria and fungi based on level of concern to human health.

Read and share the updated Core Elements of Hospital Antibiotic Stewardship Programs, which incorporates recent literature and best practices to improve antibiotic prescribing in hospitals.

element. When developing each policy, plan to educate, track and report from the beginning. Build the education, competency and tracking components into your ASP simultaneously for each new policy as it is being developed.

Examples of AS Policies that Classify ASPs into Categories

	Good	Better	Best
Use real time, rapid diagnostics and biomarkers to improve appropriate antibiotic use			✓
Assure timely and appropriate culture collection and transport			✓
Realize important evidence-based opportunities and methods to improve antibiotic use for several infections and or situations			✓
Discussion of patient care during rounds includes antibiotics		✓	✓
Develop protocols for antibiotic treatment of suspected sepsis cases		✓	✓
Implement automated, time sensitive stop orders for specified antibiotics		✓	✓
Build alerts into EMR for duplicative drug therapy		✓	✓
Develop dose optimization recommendations, especially for organisms with reduced susceptibility		✓	✓
Establish guidance on dose adjustment for cases of organ dysfunction		✓	✓
Change from IV to oral dosing in certain situations		✓	✓
Antibiotic Time Out		✓	✓
Prior Approval Policy	✓	✓	✓
Documentation of drug, indication, dose and duration of all antibiotic orders is required	✓	✓	✓
Development of facility specific treatment recommendations	✓	✓	✓
Standardized order sets for common clinical syndromes based on facility guidelines	✓	✓	✓
Guidance for antibiotic allergy assessment	✓	✓	✓

ASPs may consider developing education, tracking and reporting policies. If a tracking policy is developed, list the metrics that are being measured and the time frame in which they are measured. If a reporting policy is developed, determine which process and outcome metrics to include, the audience for the report, the distribution method, and the frequency of the reports. For an education policy, describe the process of providing education, the method of assessing competency, plans for re-education, the targeted staff, and the timeframes to re-assess competency.

These four core elements (policies and interventions, education, tracking and reporting) work together to build a robust and effective ASP, but it takes time. Since most facilities have implemented all seven core elements, take this opportunity to ensure the foundation of the program is effective. Measure and report the success. Re-educate as needed. Then build onto the program slowly and methodically.

Do You Have a Success Story Related to Your Work in AS/AR?

We would love to feature your facility or lab as a success story in a future edition of The Steward! Please send a brief summary related to preventing antimicrobial resistance or promoting stewardship activities to our resource mailbox at RA-DHHAI@pa.gov

Antimicrobial Resistance Threats, 2019 Quarter 3 Data

Pennsylvania Department of Health

Carbapenemase mechanism	Quarter 3 Count 7/1/2019 – 9/30/2019	2019 Year-to-Date
KPC	36	102
NDM	7	14
IMP	0	0
OXA-23	3	3
OXA-48	1	1
VIM	1	1
mCIM positive with no genotype detected	0	1

Resistance mechanism	Quarter 3 Count 7/1/2019 – 9/30/2019	2019 Year-to-Date
mcr-1 gene	2	2
mcr-2 gene	0	0
Any novel resistance gene	0	0

Footnote: The cases identified below were captured through voluntary reporting by healthcare facilities and laboratories, including the PA Bureau of Laboratories. Carbapenemase-producing organisms are not yet reportable throughout PA.

Philadelphia Department of Public Health

Carbapenemase mechanism	Quarter 3 Count (7/1/2019 – 9/30/2019)	2019 YTD (1/1/2019-9/30/2019
KPC	29	81
NDM	4	9
IMP	1	1
OXA-23	3	3
OXA-48	1	2
VIM	1	1
mCIM positive with no genotype detected*	1	3

Resistance mechanism	Quarter 3 Count (7/1/2019 – 9/30/2019)	2019 YTD (1/1/2019-9/30/2019
mcr-1 gene	0	1
mcr-2 gene	0	0
Any novel resistance gene	0	0

Footnote: *Philadelphia's number for mCIM positive with no genotype detected includes CRE isolates that were tested for carbapenemase production in clinical laboratories but were not submitted for mechanism testing by PDPH due to limitations in testing capacity and/or availability of isolate. These isolates may have tested positive for carbapenemase production via methods other than mCIM (i.e. MHT, Carba-NP).

Do You Know About TRAIN PA?

TRAIN PA is a learning management system and is the most comprehensive catalog of public health training opportunities for professionals. TRAIN is a free service for learners. TRAIN contains courses from CDC and health departments across the United States. You will find live and prerecorded trainings here as well as a searchable course catalog. There is also a built-in tracking system to track your learning on TRAIN PA. Many courses offered include continuing education credits.

To access TRAIN PA, just go to:
https//www.train.org/pa/
Click on the "Create an Account" button found on the left side of the screen.

Once you are logged in, use the search tool to locate training topics or if you have a course ID, you can enter that number.

Acquired and Innate Resistance Among Carbapenem Resistant Enterobacteriaceae

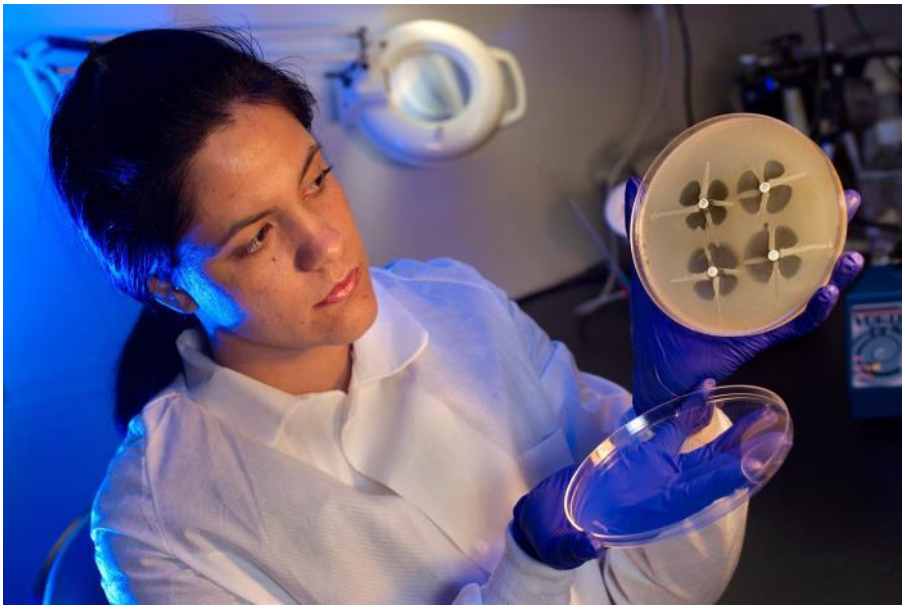
By: Julie Paoline, MA, CPHA, CIC & Jane M. Gould, MD, FAAP, FPIDS

Carbapenem resistance among Enterobacteriaceae is complex. It is unlike methicillin-resistant *Staphylococcus aureus* which, for the most part, represents one resistance mechanism in one species of bacteria. Enterobacteriaceae include more than 70 different genera and many different mechanisms which can lead to carbapenem resistance (CDC, 2019). All carbapenem-resistant Enterobacteriaceae (CRE) are multidrug-resistant organisms which require prevention and control strategies in the health care setting to prevent transmission. The primary cause of the increasing spread of CRE in the United States is believed to be attributed to carbapenemase-producing CRE (CP-CRE) as they contain an underlying carbapenemase mechanism which allows transmission to spread more easily from site-to-site, organism-to-organism and person-to-person. Therefore, CP-CRE have been targeted by public health where state and local health departments will initiate an early aggressive response at the first signal of a problem. Public health action is taken through implementation of the Centers for Disease Control and Prevention (CDC) containment strategy.

Due to limitations on resources, the most effective approach is to identify organisms that have the greatest epidemiological importance. More simply put, it is imperative to distinguish CP-CRE from non-CP-CRE. Mechanism testing can help make this distinction and is routinely used during epidemiological investigations to identify organisms that require additional public health action. Because mechanism testing is not recommended for guiding therapeutic decisions, this testing is not routinely performed in many U.S. clinical laboratories. Providers or laboratorians that wish to submit CRE isolates to the state public health laboratory may contact the Pennsylvania Bureau of Laboratories or the Bureau of Epidemiology for consultation as needed.

It is important to understand carbapenem resistance which, in general, tends to include:

- Enzymes that break down carbapenems and related antimicrobials making them ineffective, due to the production of carbapenemases (called CP-CRE) → Acquired
- A combination of mechanisms other than carbapenemase production (called non-CP-CRE), most commonly the production of beta-lactamases (e.g., AmpC) in combination with alterations in the bacteria's cell membrane (e.g., porin mutations) → Innate



The above image is of a CDC microbiologist holding up an opened Petri dish culture plate. The modified Hodge test (MHT) is a phenotypic screening test to identify carbapenemase producers **Photo Credit:** CDC Photo Library

Types of Resistance

Acquired Resistance: Some isolates of a species have acquired the ability to grow in the presence of high levels of a drug. For example, early strains, prior to the 1970's were susceptible, and after the 1970's, strains became increasingly resistant (Roberts, 2019).

Innate Resistance: All members of a species are resistant because there's no target, a modified target, they prevent entrance into a cell, or increased export of drug. For example, all members were resistant even prior to the introduction of antibiotics (Roberts, 2019).

Characteristics of Resistance (Adapted from Roberts, 2019)

Acquired	Innate
High level resistance	Low/moderate resistance
Transfer to unrelated species/genera	Requires multiple mutations
Adds new genes and proteins	Changes existing structures
Usually on mobile elements; transfer by conjugation, transduction, transformation	Transferred to daughter cells; limited transfer to other strains
Often linked to multiple antibiotic resistance genes, and/or genes for virulence, toxins, heavy metal resistance	Clinical importance varies with drug and bacteria

Carbapenem susceptibility results should be reported to include all classes of antibiotics tested along with the appropriate indicators for interpretation. Results from phenotypic or genotypic tests that detect carbapenemase-production should not be used to change the interpretation of a carbapenem susceptibility result. A carbapenemase test result (see the Deciphering the CRE

Acronyms chart on the next page) should be reported to infection prevention and control and those requesting epidemiological information, including state or local surveillance programs. As the use of mechanism testing increases with the development and dissemination of new technologies, and as the epidemiology of CRE is better defined, CDC will re-evaluate prevention and control strategies.

Deciphering the CRE Acronyms (adapted from Gniadek, 2016)

Acronym	Definition	Laboratory Result	Carba ^{R} Mechanism
CRE	Carbapenem Resistant Enterobacteriaceae	Carbapenem resistant result in disk diffusion or MIC test using current CLSI breakpoints	All possible carbapenem resistance mechanisms (carbapenemase or production of AmpC[1] or ESBL[2] with altered permeability due to porin mutation[3] or efflux pumps[4])
Non-CP-CRE	Non-Carbapenemase producing Carbapenem Resistant Enterobacteriaceae	Carbapenem resistant result in disk diffusion of MIC test using current CLSI breakpoints AND negative carbapenemase result	Production of AmpC or ESBL with altered permeability due to porin mutations or efflux pumps
CP-CRE	Carbapenemase producing Enterobacteriaceae	Carbapenem resistant result in disk diffusion or MIC test using current CLSI breakpoints AND positive results on carbapenemase test[5]	Production of a carbapenemase (ex. KPC, NDM, VIM, IMP, OXA-48, OXA-23)

Deciphering the CRE Acronyms (cont.)

Acronym	Definition	Laboratory Result	Carba ^{R} Mechanism
KPC	Klebsiella producing carbapenemase	Carbapenem resistant result in disk diffusion or MIC test using current CLSI breakpoints AND positive result on carbapenemase test* AND positive result on PCR test for genetic mechanism	Serine containing carbapenemase
NDM	New Delhi metallo-β-lactamase	Same as above	Zinc containing carbapenemase
VIM	Verona integron-encoded metallo-β lactamase	Same as above	Zinc containing carbapenemase
IMP	Imipenemase metallo-β lactamase	Same as above	Zinc containing carbapenemase
OXA-48	Oxacillinase-48-like carbapenemase	Same as above	Serine containing carbapenemase
OXA-23	Oxacillinase-23-like carbapenemase	Same as above	Serine containing carbapenemase

[1]AmpC= ampC β-lactamase

[2]ESBL= extended spectrum β- lactamase

[3]Reduced porin expression (ex. OmpK35 or K36 mutations)

[4]Overexpression of efflux pumps (ex. AcrAB-TolC efflux pump)

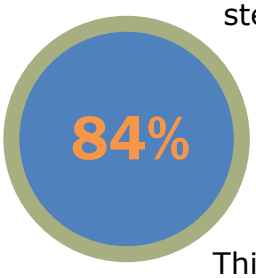
Carbapenemase tests= Modified Hodge Test (MHT), carba NP, modified carbapenem inactivation method (mCIM)

Uptake of Core Elements

By: Christine L. Mulgrew, MPH, PhD

We commend the 178 PA hospitals that have met all seven core elements of an antibiotic stewardship program (ASP). These programs help combat the development of new antibiotic resistant organisms and promote appropriate use of antibiotics.

Hospitals were surveyed about implementation of CDC's antibiotic stewardship core elements through NHSN's annual survey in early 2019. Analysis of the 212 acute care hospitals that are required to have antibiotic stewardship programs showed that 84 percent had met all seven of CDC's core elements. This is a 10 percent improvement from the previous year.



This metric required just one of seven policies be implemented to meet the "action" core element. A letter of support from the leadership meets the "leadership" requirement. Neither financial or IT support are necessary. Educating staff or nurses or pharmacists once per year meets the "education" requirement. These are the bare minimum expectations of an ASP.

Moving forward, CDC and leaders in the field are considering other ways to assess the effectiveness, depth and breadth of ASPs. The Nebraska Department of Health and Human Services used stricter criteria to assess whether the action, tracking, reporting and education core elements are met. (See Table.)

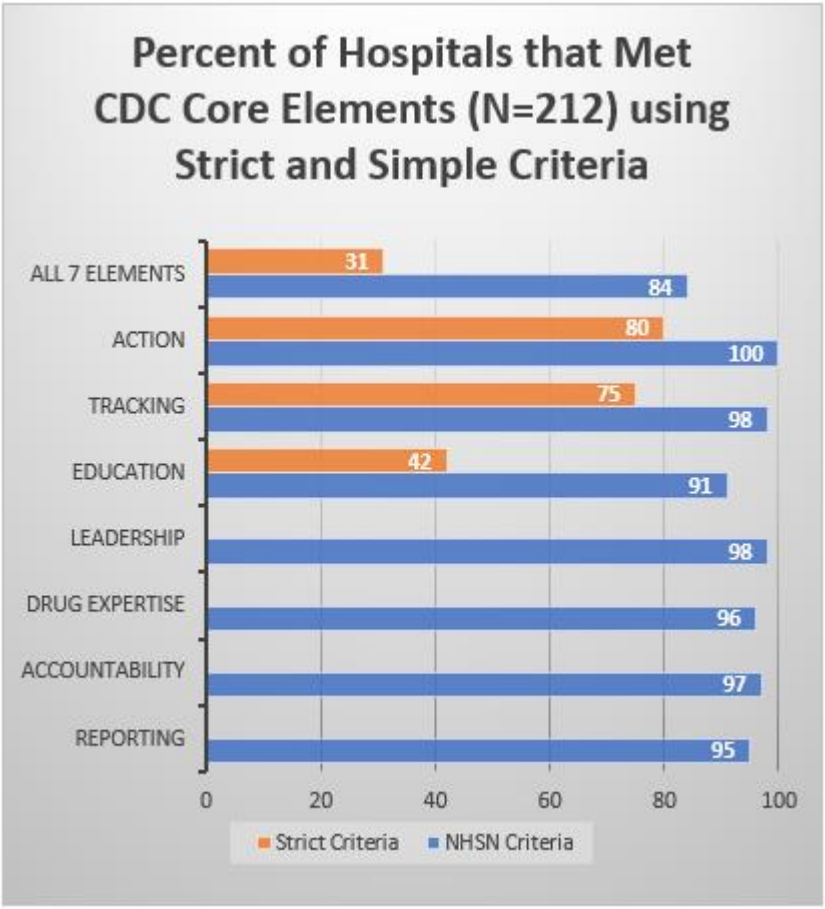
Two Methods of Assessing Coherence to Four ASP Core Elements

Core Element	Simple Criteria	Strict Criteria
Action	1 of 7 policies	Antibiotic time-out policy or prospective audit and feedback
Tracking	Either antibiotic use OR antibiotic resistance	Both antibiotic use AND antibiotic resistance
Reporting	Either antibiotic use OR antibiotic resistance	Both antibiotic use AND antibiotic resistance
Education	Prescribers, nurses OR pharmacists	Prescribers AND other relevant staff

31%

If the PA hospitals were reevaluated using three of these four strict criteria, the results would be significantly different. As shown in the below chart, the percent of hospitals meeting all seven core elements drop to 31 percent. This is mainly attributed to the "education" core element. However, the "action" core element decreases from 100 percent to 80 percent and the "tracking" core element decreases from 98 percent to 75 percent. The "reporting" core element could not be assessed because the survey didn't ask about reporting antibiotic resistant data.

Given the urgent threat of multidrug resistant organisms, it is expected that ASPs will remain a critical required program to combat this growing problem. The ASP activity expectations have recently been expanded through federal rules that go into effect in March 2020. CDC recently released the updated list of hospital core elements (available here).



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