





Practically Implementing Antimicrobial Stewardship in an Evolving Landscape







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Objectives

- Review the data to support antimicrobial stewardship programs (ASP)
- Review evolving landscape in ASP
- Describe practical ASP of activities ("inside & outside the box")



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What is Antimicrobial Stewardship (ASP)?

- A healthcare institutional program to improve appropriateness of antimicrobial prescribing to:
 - Optimize clinical outcomes
 - Reduce adverse events
 - Reduce healthcare costs while maintaining quality of care
- ✓ Who are we?
 - Multidisciplinary team of ID trained physicians and pharmacists
 - Liaisons throughout the Healthcare System





http://www.cdc.gov/getsmart/healthcare

Why Stewardship?

- Up to 50% of all human antibiotic use is unnecessary or "inappropriate"
- Drug-resistant bacteria cause 23K deaths and 2M illnesses per year in the US
- FY 2016 federal budget for combating antibiotic resistance = \$1.2 billion
- Goal by 2020:
 - All acute care hospitals will have ASP
 - ASP will cover all healthcare settings
 - 30% reduction of "Inappropriate" Abx use





"Meaningful Use" of Antibiotics

- "Appropriate" means...
 - -Antibiotic Indicated?
 - -Right Drug?
 - -Right Dose and Interval?
 - -Right Route?
 - -Right Duration?



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Combating Antibiotic Resistance PCAST 9/2014



- 1) Slow the Emergence & Spread of Resistant Bacteria with help from ANTIMICROBIAL STEWARDSHIP
- 2) Strengthen National Surveillance Efforts
- 3) Advance Rapid Diagnostics
- 4) Research for New Antibiotics
- 5) Improve International Collaboration





CMS Infection Control Recent Worksheet

Centers for Medicare & Medicaid Services

Hospital Infection Control Worksheet

Name of State Agency:

Instructions: The following is a list of items that must be assessed during the on-site survey, in order to determine compliance with the Infection Control Condition of Participation. Items are to be assessed by a combination of observation, interviews with hospital staff, patients and their family/support persons, review of medical records, and a review of any necessary infection control program documentation. **During the survey, observations or concerns may prompt** the surveyor to request and review specific hospital policies and procedures. Surveyors are expected to use their judgment and review only those documents necessary to investigate their concern(s) or to validate their observations.

The interviews should be performed with the most appropriate staff person(s) for the items of interest, as well as with patients, family members, and support persons.

Interpreted
Interpret

It is unclear how each will be interpreted

CDC's ASP Core Measures – How Do We Measure Up?

- Leadership commitment
- Accountability
- Drug Expertise
- Action
- Tracking & Reporting
- Education





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Stewardship Interventions

- Dose optimization
- □ IV to PO conversion
- □ Streamlining & de-escalation
- Adjusting durations in accordance with guidelines
- Clinical pathways and treatment algorithms
- Maximizing functionality of electronic medical record (EMR)





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Guidelines, Not One Size Fits All



"Tailor" to your own reality (needs, size and resources)



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ASP Strategies Varies By Campus

Campus	Resources	Restrictions *	Audit**	Highlights
Moses (2008-)	~~~	~ ~	~ /	-ER (CAP, Sepsis) -Zosyn Time Out
Einstein (2008-)	~~	~ ~	~ ~	-ER ID Consults - Surgical prophylaxis bundles
Wakefield (2013-)	✓ ✓No fellows	 Modified at 72 hrs 	~~~	-Hospitalist De-escalation
Children's (2013-)	shared ID PharmD	🖌 Peds List	< </th <th>-Antiviral/antifungal appropriateness, -Dosing</th>	-Antiviral/antifungal appropriateness, -Dosing
Ambulatory (2016)	~	N/A	~	-Pilot for adult respiratory

Case #1:

58 y.o. female smoker from with habitual alcohol intake presents to the ER in August with fever to 102F, myalgias, and diarrhea for 4 days. She is found to have a large left sided consolidation on X-ray. Urine Legionella antigen is positive as is culture of bronchial fluid.





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Which interventions can facilitate appropriate antibiotic management of patients with community acquired pneumonia (CAP)?

- a) Placement of PO azithromycin in ER
 Pyxis MedStation[™]
- b) Automated stop duration of 14 days for CAP regimens
- c) Upfront restriction of IV piperacillin/tazobactam
- d) Developing CAP order sets in EMR
- All but b)



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- Multidisciplinary task force to improve compliance with CMS CAP measures (QI, ASP, ED)
- Quasi-experimental, before-and-after study, QI methodology ("plan, do, check, act") w/ a bundled intervention:
 - 1. Treatment algorithm for ED providers
 - 2. "CAP Kit" with first line antibiotics and dosing
 - 3. Preloaded ER Pyxis with regimens, access audited





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Results

Site	Appropriateness Before (2008)	Appropriateness After (2011)	P- value
Pilot ED	54.9%	93.4%	P = .001
2 nd ED	64.6%	91.3%	P = .004

- In an interrupted time-series logistic regression analysis, intervention was statistically associated with improved prescribing
- Antibiotic administration w/in 6 hours not statistically different before and after

Ostrowsky, B., et al. (2013). Antimicrobial Stewardship and Automated Pharmacy Technology Improve Antibiotic Appropriateness for Community-Acquired Pneumonia. <i>Infection Control &Hospital Epidemiology (6), 566-572. doi:10.1086/670623





Interventions for CAP

Pre- authorization	Formulary Restriction	Audit & Feedback	Education
Upfront restriction of IV azithromycin and fluoroquinolones	Levofloxacin as Respiratory Fluoroquinolone of choice	Antibiotic orders by medicine house staff and hospitalist services	First line CAP regimens
			Allergy regimens
72h authorization of IV vancomycin	Ceftaroline non- formulary, restricted to ID consultation	Ambulatory antibiotic prescriptions for acute respiratory tract infections	Newer literature on durations

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Case #2

A 75-year-old female with COPD and active tobacco use presents with 3 days of productive cough and fevers. The patient has a remote history of rash due to penicillin given for an STD at age 18. She was hospitalized 6 weeks ago for community acquired pneumonia (CAP) and treated with levofloxacin. On exam, she is febrile and tachycardic. She is also frail, weighing only 45kg. CXR shows a right sided consolidation. WBC count is 13. Serum creatinine is 1.6mg/dL.

The patient is started on broad spectrum antibiotics and feels much improved 48 hours later.



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Identify opportunities for pharmacydriven interventions presented in the scenario

- a) Debunking allergy history
- b) Optimizing dose for host factors
- c) Duration adjustment per newer guidelines
- d) Bug-drug match by respiratory culture
- e) De-escalation from broad spectrum regimen
- All of the above





Clinical Infectious Diseases Advance Access published July 14, 2016

IDSA GUIDELINE



Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society

- 1 in 10 ventilated patients get VAP,
 - 13% mortality rate
 - Increases ventilator days and $LOS \ge 3$ days
- 7 day course of therapy for hospital-acquired or ventilator-associated pneumonia (HAP, VAP) is sufficient
- Shorter course does not reduce benefits or therapy and may reduce antibiotic-associated adverse events





Penicillin Allergies



- Only 2-15% of patients with reported penicillin allergy have a positive skin test
- 80% loss of IgE occurs after 10 years
- These patients receive suboptimal, more broad, and more toxic agents
 - Associated with increased resistance, cost, hospital LOS, and mortality
 - In matched cohort study higher rates of *C. diff*, MRSA, and increased hospital LOS

Lee CE et al. Ann Intern Med 2000 Macy E et al. Allergy Clin Immunol 2013 Unger NR et al. Pharmacotherapy 2013





Using Antibiogram Data for Teaching Campus 1 &2







Educational Intervention: Cases and Prescribing Tools

70 year old male with DM, active tobacco and EtOH use presents with 48 hours of cough with dark sputum, fevers up to 101F and rigors. On exam, he appears ill and has rhonchi at the R. base. CXR confirms an infiltrate. He reports a remote penicillin allergy when he was treated for syphilis in the army. Which of the following is true about penicillin allergies?

- a. Up to 10% of patients report penicillin allergies
- b. Skin testing shows that most are not IgE mediated
- c. Loss of IgE titers occurs with each decade of life
- d. Most patients can be successfully challenged with Beta-lactam antibiotics
- e.
- All of the above

Aspiration Serial CRR, CBC, sputum outure

If treatment required Ampicilin/subactain 1.5-3g OR Clindamycin 600mg

Community Acquired Pneumonia

OBC, CXR, Unre Ag for Legionella/5, preumoniae, sputum culture, influenza sweb if in season

Hospitalized, non-severe Cethiaxone 1g IV + Asimonyon 500mg PO (stop if agomila Ag reg); texofoxacin 500mg PO if anachelasa to Penicilin

Severe CAPICU Celtriacare 1g IV + Addresmych Sköng IV + Vancamich 1g IV

Severe CAP, Anaphylaxis to Penicillin

110

Asthromycin 500 mg IV + Astronam 1-2g IV + Vancomycin 1g IV (Asthromycin can be replaced with Levelowcin 500mg IV(PO)

COPD Exacerbation

Criteria for Antibiotics

1) 3 cardinal symptoms (increased sputum volume, purvient sputum, dyspree) OR 2) 33 cardinal symptoms (including sputum purviewa) OR 3) Severe decase requiring positive pressure werklakin

Wid: Dovovsine QR Aphromycin

Moderate: PO Anoxic Bridowulanate, OR N Ampolitishubactam, Celhiavone, Levofloxecin (severs Penicilin allergy)

Severe + RF for MDRDs: Anti-previousla S-lactam (La. Colegime, PipiTaz; see below), OR levoloxacin TSOmp IV (severe Periodin allergy)

Healthcare Associated Pneumonia

Sputum culture, senial COR, +/- Legionetia Ag (// nosocomial outbreak suspected)

ATS-IDSA Risk Factors for HDRDs:

- Abs in preceding 80d
 current impatient stay at least 5d
- hospitalized at least 2d in prior 90d
 voin 600mg
 Nihlextended care residence
 - Innurosuppressive disease or therapy

Mid Disease/Limited Healthcare Exposure Celtrisione 1g +/Vancomycin 1g IV

Severe Disease/VAP

Vanconycon 1g IV + either Celepine 1-3g IV ON Piperacilinitazobacian 2.25-4.5g IV: can add antroglycoside for severe sepsis or hito MORD

Anaphylaxia to Periotiller: start Varconycin 1g IV + either Aztrocram 1-2g IV OR Captificacin 400mg IV, can add aminoglycoside for severe sepsis or No MDRO

infuenza

concerts)

Repid influenzes swatt, +1-RVP and PCR, CXR d with

Treatment: Osotantivr 75mg PO (Q12h dosing if OrCl of 30 and above)

Intra-abdominal Infection

CBC, abdominal stay, US or CT, UFTs, amylaselipase, stool C.dlf and culture I damhes

Community Acquired/Non-severe Healthcare

Acquired [Cethrakone 1g1V CR Cetoxitin 1g1V CR Confloxacie 500mg PO(400mg IV) + Methonidazole 500mg PO(IV

"Diproflokacin reserved for severe allergy to Penicillin

Severe healthcare acquired Celepine 1g IV + Meteniclassie Silling IV, OR Pperschlivtlasotactare 225-4 5g IV (add Meteniclassie 500mg IVPO anly If C. cifficile is a

Evidence Based Antibiotic Dutations

Syndrome	Duration
OPD fair with orderia for antibiotics	37 DAVS
incomplicated GAP	5-7 days
Complicated CAP (empyeria, bacterenic , 8: sureus RVA, adacese, legionella)	Duration variable (ID consult recommended)
CAPIVAP (nd MRSA, P. aetuginosa, A. baumani, agionelia)	7 days 7-10 days for legionella but can vary 2 14 days for 1953A, Pseudomonas, Acinetabacter (10 consult recommended)
CAPIVAP el MISA, P. sergirosa, A. baumani	14 days due to increased tisk of recurrence (ID consult recommended)
lacterial Meeinglis	7-21 days depending on organism isolated (ID consult recommended)
Gr Enconalita	1421 days
Catheter-related Bioodolinuum infection (cutheter emoved recommended for source control)	CoNS: 1-7 days S. autoux: 4-9 weeks, shorter if certain orders met. (10 canual recommender) CARB: 7-14 days Candica aso: 14 days from finit registive BCx
fuerza	5 taya
iyelonophrits Jocomplicated UTI	7.14 daja 36 days
ts-abbrind	4.7 days if source controlled
នា	Pathopenicase specific; for non-healing leaters, unaual exposure: atgocal organisms; compromised host – ID consult recommended
Autoperic lever	Hold Abx once afebrie 2 48h with negative suitures and readiving readropenia ; If documented source, treat accordingly for site and organism
C officia collin	Initial opsocie: 10-14 days 1st recumence: 10-14 days 2nd recumence: PO Vanconycin x 15-14 days, then taper up to 8 weeks - see 10 homepage for details

Results

Time frame	Antibiotics Indicated	Appropriate Regimen by Syndrome	P-value
Pre-intervention	87%	60%	
(-1 month)	(n = 187)	(n = 187)	
Post-intervention	85%	70%	0.0496
(1 month)	(n = 163)	(n = 163)	
Post- intervention	80%	80%	P < 0.01
(20 months)	(n = 75)	(n = 75)	

- At 20 months: 92% of doses and 86% of durations were correctly chosen by house staff
- ✓ >90% of house staff were analyzed only once
- Positive impact on house staff prescribing sustained almost two years after introduction of intervention

Bhar S, Nori P, Ostrowsky B. Improving Antibiotic Use Starts with Our Trainees. IDWeek 2015 oral presentation





Antibiotic Prescribing by Syndrome

Pre-intervention vs. 20 month Post-intervention by Syndrome		e e	100% 90%			
	-1 month	20 months	P value	yndrom	80% 70%	
UTI	57% (n=42)	86% (n=28)	0.011	ie by S	60% 50%	
Respiratory	59% (n=80)	75% (n=20)	0.001	ropriat	40% 30%	- 1 month - 1 month
SSTI/OM	73% (n=22)	67% (n= 12)	0.001	% App	20% 10%	20 months
GI	50% (n= 28)	75% (n= 4)	0.34		0%	
Other	73% (n= 15)	82% (n= 11)	0.61			Respirator SS Othe
				-		` Infectious Syndrome





Antibiotic Regimens - EPIC Order Sets

Non-severe	Severe sepsis/shock
Dept/Room/Bed: MOSES KLAU 7 / K737 / Attending: Rondinel, Evely Pt Loc: MOSES DI Allergies Admit Date/Time: 02/08/2017 2340 Service: Internal Medicine Height: 1.778 m (5' Glyburide Day #: 33 Patient Class: Inpatient Weight: 112.5 kg (Glyburide Bronx RHIO: Gave Consent Treatment Team: NEURO BMI: 35.59 kg/m ² ets	Order Sets ? A These regimens are for initial regimen adult severe sepsis/septic shock patients only. Restrictions apply on subsequent doses. The regimens can not cover all clinical situations. Use clinical judgement and call ID for assistance.
Antibiotic Recommendations	Orders will be audited.
<u>Hospitalized (non severe):</u> Ceftriaxone 1gm IV + Azithromycin 500mg PO <u>For anaphylaxis to Penicillin (non severe):</u> Levofloxacin 500mg po(IV if unable to tolerate po or per tube)	C CV Catheter Associated C Intra-abdominal C Meningitis C Neutropenic Fever C Out of Hospital Cardiac Arrest
For severe CAP/ICU: Ceftriaxone 1gm IV + Azithromycin 500mg IV + Vancomycin 1gm IV For severe CAP/ICU and anaphylaxis to penicillin: Severe CAP/ICU and anaphylaxis to penicillin: Levofloxacin 500mg IV + Aztreonam 1-2gm IV + Vancomycin 1gm IV Alle	Pneumonia: Community Acquired Antibiotic Recommendations (Use Clinical Judgment) For severe CAP/ICU: Ceftriaxone 1gm IV + Azithromycin 500mg IV + Vancomycin 1gm IV For severe CAP/ICU and anaphylaxis to penicillin: For severe CAP/ICU and anaphylaxis to penicillin:
CefTRIAXone IV a zithromycin tablet 500 mg, oral, once D azithromycin tablet	CertRIAXone IV 1 gram, intravenous, once azithromycin IV
azithromycin iv 500 mg, intravenous, once vancomycin IV 1 gram, intravenous, once I levofioxacin tablet	S00 mg, intravenous, once
500 mg, oral, once levofloxacin IV 500 mg, intravenous, once aztreonam IV	aztreonam IV 1 gram, intravenous, once aztreonam IV 2 gram, intravenous, once
1 gram, intravenous, once aztreonam IV 2 gram, intravenous, once C Pneumonia: Health Care Associated	Montefiore FINSTEIN

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Maximizing Use of EMR



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Educational Tools Evolved Over Time

#Stewardship_Problems

So Many MUEs, So Much to Do...

Problem/Antimicrobial	Action			
Adult				
Quinolones	Restriction changes			
Daptomycin	De-escalating to other alternatives			
Ganciclovir/Foscarnet	Presenting institution specific data to oncology department			
Ceftaroline	Monitor appropriateness			
Ceftolozane/tazobactam, Ceftazidime/avibactam	Monitor appropriateness			
Pediatric				
Palivizumab	Restriction/tracking/batching			
Meropenem	Restricting to NICU			
Antifungals	Ongoing monitoring			
Others				
CAP Treatment guidelines	Reducing inappropriate antibiotic use			
Surgical prophylaxis guidelines	Reducing inappropriate antibiotic use			
High risk or last resort antimicrobials	Ongoing monitoring			

Core Stewardship Team & Extended Family

- 1. ID pharmacy manager at each campus
- 2. Systems director, medical directors, ASP fellow
- 3. New ID/ASP CCM service
- 4. Data analyst
- 5. On-site clinical microbiology lab

Hyun et al JAMA 2013

Partner with Microbiology

• Early:

Creation and dissemination of Antibiograms
Creation of testing and reporting cascades

Intermediate:

- New viral and influenza testing platforms
- Sensitive Clostridium difficile testing

<u>Complex:</u>

 Introduction rapid diagnostics (e.g., MALDI-TOF)

Preliminary Outcomes for Severe Sepsis/Shock (conventional vs MALDI- TOF)

	March-April 2013 (n=96)	March-April 2014 (n=69)
Gram-negative + S.aureus*		
Time to Org ID (hours)	51.8	31.8
Time to Streamlined Susceptible Regimen (hours)	74.2	58.1
Time to ID consultation (hours)	35.1	16.3
Time to microbiological clearance (hours)	69.2	55.9
Unadjusted mortality (%)	23.9	18.8
Length of Stay (days)	10.6	10.1

Relationship holds when subgrouped by Gram-negative or *S.aureus* Park *et al.* IDweek abstract, 2015

Let the Debate Begin... Use the Data

- Attended Hematology/Oncology QI meeting
- ASP and ID went as team with data

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Making a Persuasive ASP Case Using Pilot days of therapy (DOT) data

Antimicrobial Utilization by Agent and Hospital

Antimicrobial Utilization by Nursing Units

This is Not a New Finding...

2011

Pip/tazo: Piperacillin/tazobactam

Action Plan

Piperacillin/tazobactam De-escalation

Review Patient List			
Identify patients on	EMR Chart Review		
pip/tazo therapy for >72 hours without ID consult.	Review indication, dosing, duration, culture results and clinical progress	Contact Primary Team Have a meaningful discussion with house	
		and make appropriate recommendations.	

Results (May-July 2013, n=60)

Type of Intervention

- Shorter Duration
- Narrow Therapy
- Discontinuation
- ID consult
- Switch to Oral Regimen
- Continue Therapy
- Others

Collaboratives—Working Together in NYS on CDI*

Dates	Facilities	Collaborators	Interventions	Outcomes
2008- 2009 ¹	35	NYS DOH +GNYHA/ UHF	-IPC & Cleaning Bundles -Education	
2010- 2012, ^{2,3}	10	GNYHA/ UHF + AHRQ/ CDC + Montefiore	-CDI directed ASP -Education	 ✔ CDI Targeted antibiotics AHRQ CDI Toolkit
2015- on	80	GNYHA/ UHF + NYSCHSP + Montefiore	-ASP Course -ASP survey -CDI Point Prevalence -CDI ASP Posters	<u>Facilities (n)</u> 80 61 53 16

GYNHA/ UHF=Greater NY Hospital Association/ United Hospital Fund, NYSCHSP= NYS Council Health Systems Pharmacists, HO-CDI= Hospital onset CDI

1) Koll. J. Healthcare Quality. 2013: 36 (3): 35-45.

2) Ostrowsky. ICHE. 2014: suppl 3:S86-95.

3) AHRQ Toolkit Available at: http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/cdifftoolkit/index.html#

* Addition NYSDOH collaborative LTCF and CDI

Additional Montefiore ASP Activities

Stewardship Program "Timeout"

- 1. Examine your routine activities
- 2. Take credit for strategies already in place
- 3. Address new federal regulations with well documented policies
- Perform a needs assessment and ask "what am I not yet doing?"

Take Home Lessons

- CDC Core ASP Strategies are resources
- ASP needs to be tailored to your facility.
- ASP development & implementation takes time
- ASP is a team sport
- ASP activities:
 - Likely already exist
 - Can start simple, grow/ expand with the program
 - Must do because regulated (should do because it is important for your patients)
- Learn from other ASPs (we can be your resources)

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