Antimicrobial Stewardship (AMS) Essentials

LARRY PINEDA, PHARMD, BCPS, AAHIVP

CLINICAL PHARMACIST – INFECTIOUS DISEASES/ANTIMICROBIAL STEWARDSHIP

Learning Objectives

Recognize the importance of leadership commitment in a successful antimicrobial stewardship program

Perform a regulatory standards gap analysis to help identify areas for improvement

Utilize an antibiogram to select the most appropriate empiric antimicrobial treatment

Describe the general principles of antimicrobial susceptibility testing

Life Saving Benefits of Antimicrobials

Pre-antibiotic era

- Countless deaths due to simple infections

Modern era of antibiotics began with discovery of penicillin in 1929 by Sir Alexander Fleming

Millions of lives have been saved

Allow for major advances in medicine

- Complex surgery
- Transplants
- Cancer therapies

Power of Antibiotics

Disease	Pre-Antibiotic Death Rate	Death with Antibiotics	Change in Death
Community Pneumonia	~35	~10	-25%
Hospital Pneumonia	~60	~30	-30%
Heart Infection	~100	~25	-75%
Gram Negative Bacteremia	~80	~10	-70%
Brain Infection	>80	<20%	-60%
Skin Infection	**11%**	<0.5%	-10%
Comparison: Lancet. 1988.2(8607):349-60 *Study of aspirin or fibrinolytic drugs for acute myocardial infarction* *In control arm of this study (placebo) had mortality of **12%***			*-3%*

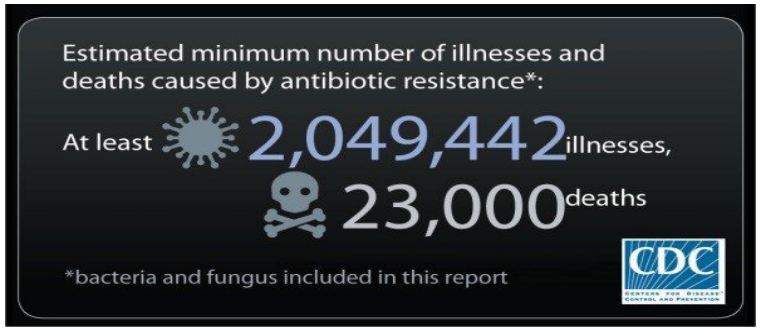
Emergence of Resistance

Most serious and growing threats to public health[1]

CDC estimates > two million antibiotic-resistant infections resulting in ~23,000 deaths annually[2]

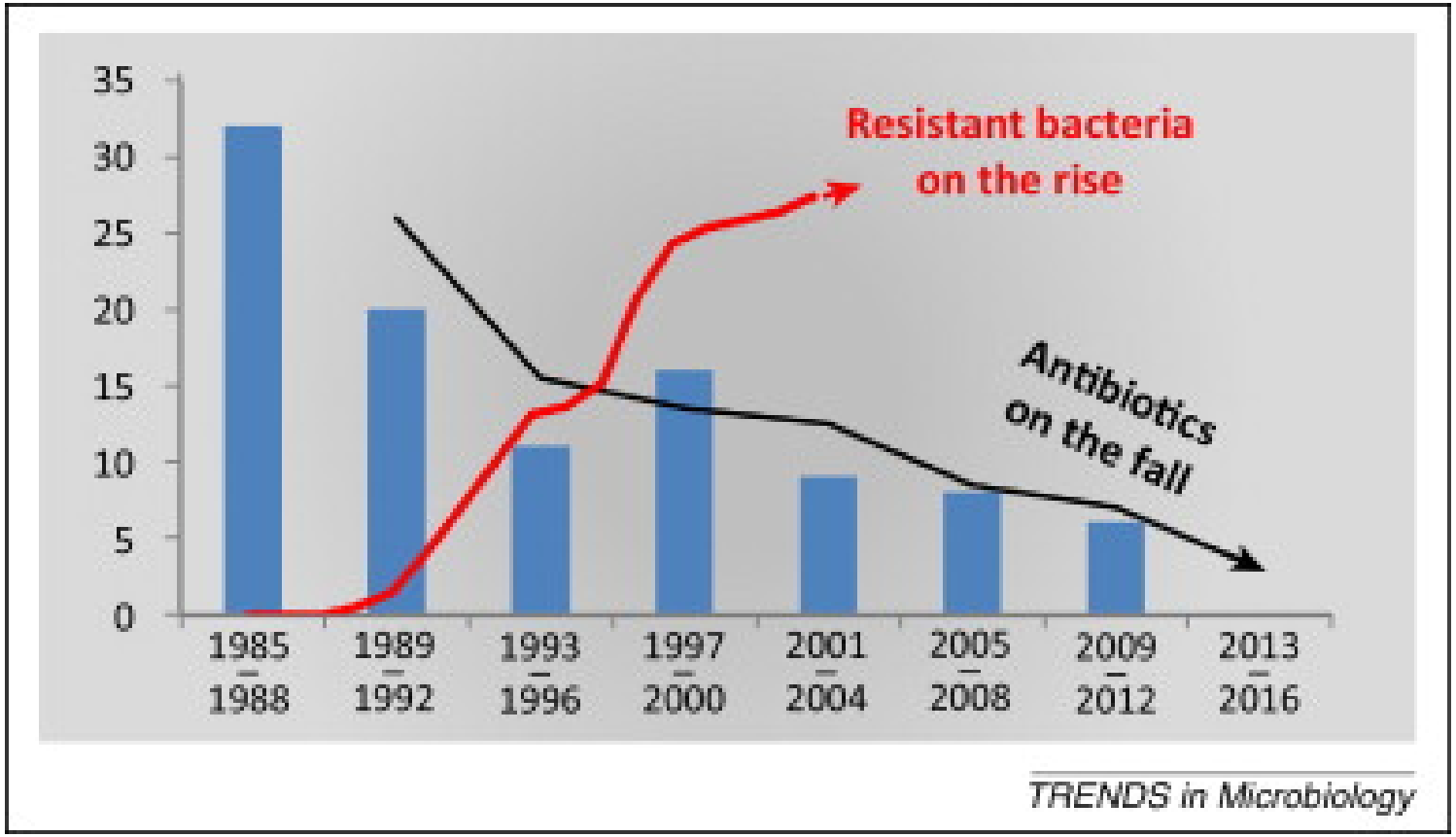
$20 billion in excess direct healthcare costs annually

Unlike other medications, antibiotics can adversely impact the health of patients who are not even exposed to them



1. 2014 WHO ANTIMICROBIAL RESISTANCE GLOBAL REPORT ON SURVEILLANCE
2. HTTP://WWW.CDC.GOV/DRUGRESISTANCE/THREAT-REPORT-2013

Post Antibiotic Era



VIM-CRPA in Lubbock

Resistance gene that is being reported with increasing frequency

- Largest cluster in US

This gene makes it more difficult to treat some infections caused by *P. aeruginosa*

VIM = VERONA INTERGRON ENCODED METALLO-BETA-LACTAMASE
CRPA = CARBAPENEM RESISTANT *PSEUDOMONAS AERUGINOSA*
HTTPS://CI.LUBBOCK.TX.US/DEPARTMENTS/HEALTH-DEPARTMENT/DISEASE-SURVEILLANCE/VIM-RESOURCES

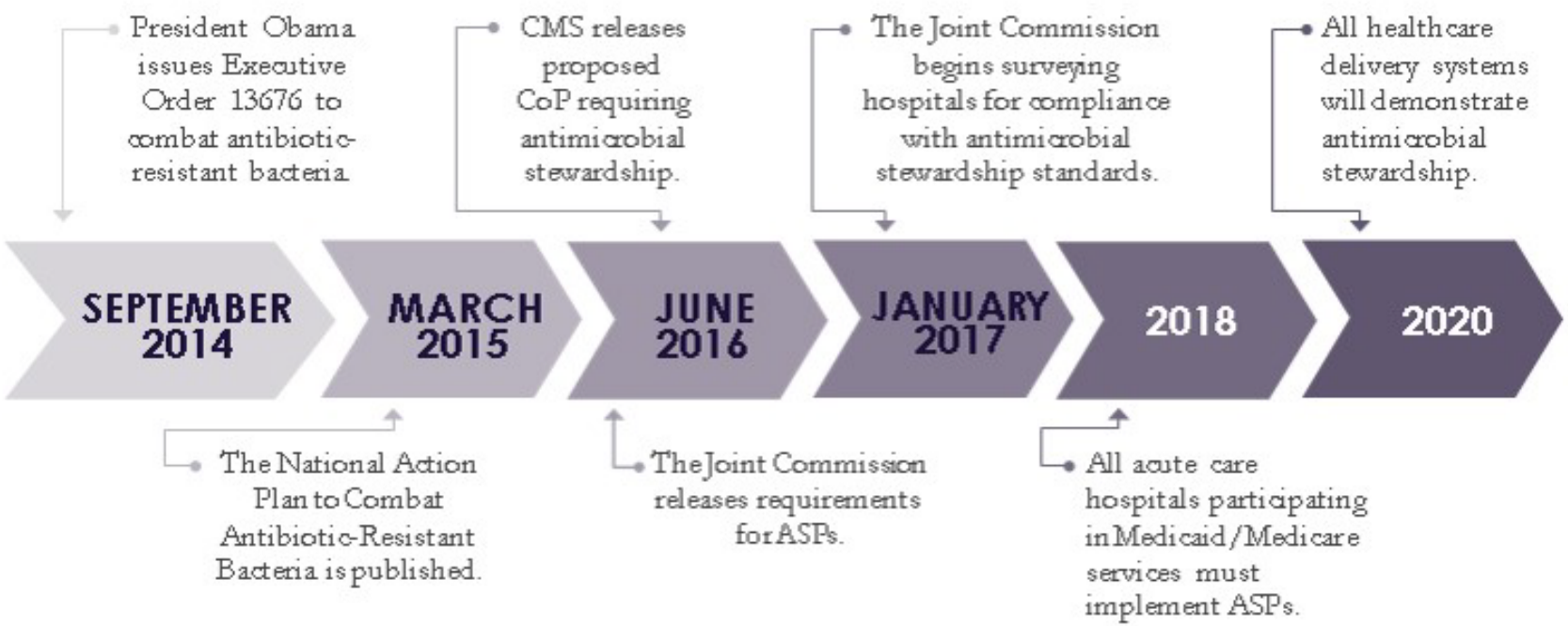
Antimicrobial Stewardship

Coordinated program which promotes appropriate use of antimicrobials

Goal is to optimize clinical outcomes & minimize unintended consequences of antimicrobial use

National Timeline

Figure. National Timeline for Implementing Antimicrobial Stewardship Programs



ASPs, antimicrobial stewardship programs; CMS, Centers for Medicare & Medicaid Services; CoP, Conditions of participation

Where to Start?

CDC Core Elements of ASPs

1. **Leadership Commitment:** Dedicating necessary human, financial, and information technology resources (identify physician leader –or- facility/clinic leader)
2. **Accountability:** Appointing a single leader responsible for program activities and outcomes (must have support of leader)
3. **Drug Expertise:** Appointing a single pharmacist leader responsible for working to improve antibiotic use
4. **Action:** Implementing at least one antibiotic use improvement action
5. **Tracking:** Monitoring prescribing and resistance patterns
6. **Reporting:** Regular reporting information on antibiotic use and resistance to all caregivers
7. **Education:** Educating caregivers and patients/families about optimal antibiotic use and resistance

CDC Core Elements of Outpatient AMS

Commitment: demonstrated dedication to and accountability for optimizing antibiotic prescribing and patient safety

Action for policy and practice: implement at least one policy or practice to improve antibiotic prescribing, assess whether it is working, and modify as needed

Tracking and reporting: monitor antibiotic prescribing practices and offer regular feedback to clinicians or have clinicians assess their own antibiotic use

Education and expertise: provide educational resources to clinicians and patients on antibiotic prescribing and ensure access to needed expertise on antibiotic prescribing

Leadership Commitment

Stewardship is not a task, it is a culture

Culture change comes from changes in leadership behavior

Culture Change: It Starts At The Top

Grant Freeland Contributor ⓘ

Leadership Strategy

I am a BCG senior partner writing on the future of leadership and work

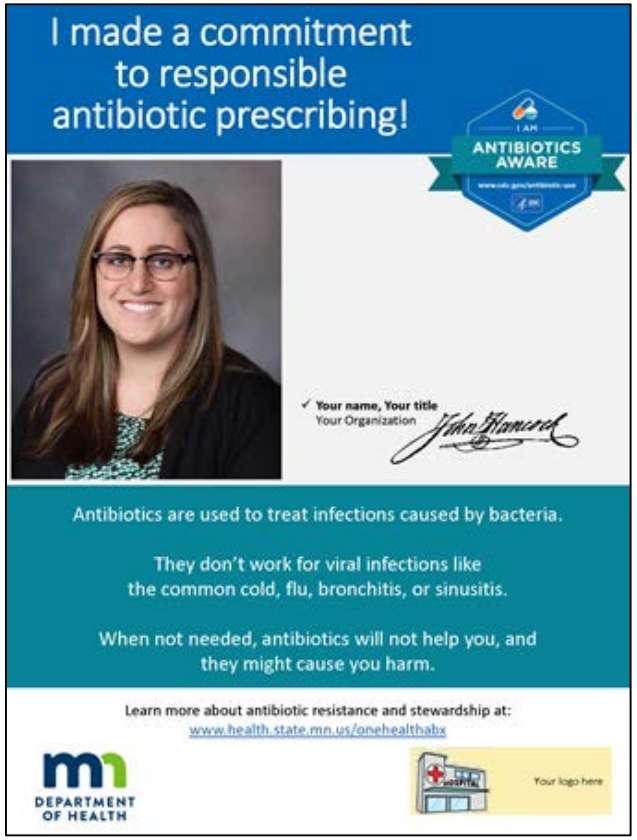
Commit Your Leader

Engage key leadership

- Ensure your medical director has an invitation to the meeting
- Leadership should approve and sign all AMS policies
- Create a formal agreement (policy) that identifies the leader
  - https://www.telligenqinqio.com/resource/our-work/core-element-2-action/core-element-2-action-resources/outpatient-antibiotic-stewardship-sample-policies/

Make your leaders the 'face' of stewardship

- Write and display public commitments in support of stewardship
  - Placed in exam rooms have been shown to reduce inappropriate antibiotic prescriptions[1]
- Poster templates available online
  - https://www.health.state.mn.us/diseases/antibioticresistance/hcp/commitkit/index.html
  - http://www.hqi.solutions/wp-content/uploads/2017/09/Safe-use-of-antibiotic_MD_flyer_FINAL2_071717.pdf
  - https://www.cdc.gov/antibiotic-use/week/pdfs/Commitment-Poster-english-11x17.pdf



1. NUDGING GUIDELINE-CONCORDANT ANTIBIOTIC PRESCRIBING. *JAMA INTERN MED.* 2014;174(3):425-431

Leadership Commitment Pearls

Modify job descriptions to incorporate antibiotic stewardship roles and responsibilities

- Make it a part of yearly performance evaluation process

Incorporate AMS roles and responsibilities into multiple leadership positions to ensure sustainability despite turn-over and prevent program collapse due to loss of a single “champion”

- Infection prevention
- Consultant pharmacist
- Co-champions

Educate all staff on importance of AMS

- Keep yearly education log
- Have a place holder for AMS in staff meetings

Pearls Continued

MAKE STEWARDSHIP DESIRABLE!

- Not just a regulatory requirement

Provide leadership with AMS benefits literature

- https://www.cdc.gov/antibiotic-use/community/pdfs/16_268900-A_CoreElementsOutpatient_appendix_508.pdf
- Sometimes you have to focus on the $$$$$

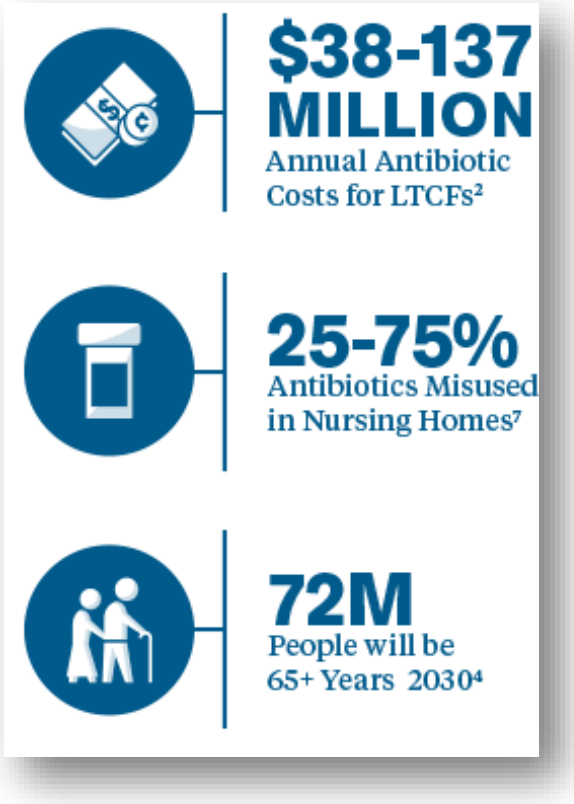
Don't expect a giant over hall, culture changes take time

- Only have to implement 1 action to get started

Don't reinvent the wheel

- Use external resources: others are willing to share

Take ACTION: Ask to join a local antibiotic stewardship collaborative



GRAPHIC: HTTPS://WWW.MCKESSON.COM/BLOG/ANTIBIOTIC-STEWARDSHIP-PROGRAMS/

Take Action

Find Your Gaps

First step is to assess your current state

- Not all AMS programs look the same
- Gap analysis will help identify where to start
- Also identifies activities already underway in your facility

Periodically (standing agenda item) review and update progress

Will review 3 examples (many more available)

- Joint Commission standards analysis
- CDC checklist
- Current state assessment - Washington State DOH

Excel Joint Commission Gap Analysis

Gap Analysis	Standard 1	Standard 2	Standard 3	Standard 4	Standard 5
Facility	Does your facility have a formal, written statement of support from leadership that supports efforts to improve antibiotic use (antibiotic stewardship)?	Does your facility receive any budgeted financial support for antibiotic stewardship activities (e.g., support for salary, training, or IT support)?	Is there a physician leader responsible for program outcomes of stewardship activities at your facility?	Is there a pharmacist leader responsible for working to improve antibiotic use at your facility?	Continued…
A					…
B					…
C					…
D					…

Yes

No

In progress

Joint Commission – Outpatient Facilities

Effective January 1, 2020, new antimicrobial stewardship requirements will be applicable to Joint Commission accredited ambulatory health care organizations that routinely prescribe antimicrobial medications

- Pick an individual responsible for developing and monitoring appropriate prescribing practices **[commitment]**
- Create at least one goal each year related to antimicrobial stewardship **[action & commitment]**
- Use evidence-based guidelines to complete the goal **[action]**
- Educate staff and licensed independent practitioners on the organization's goal and appropriate prescribing practices **[education]**
- Collecting and analyzing data related to antimicrobial stewardship **[tracking & reporting]**

Regulatory Requirements

Joint Commission standards do not apply to all

Centers for Medicare & Medicaid Services

- Medicare Access and CHIP Reauthorization Act of 2015 (MACRA)
- Quality Payment Program (QPP)
- Merit-based Incentive Payment System (MIPS)

Stewardship is not avoidable: not a matter of if, but when

Good news: If you are fulfilling all CDC elements, no need to sweat the regulatory stuff

Adult Sinusitis: Antibiotic Prescribed for Acute Sinusitis (Overuse)
Adult Sinusitis: Appropriate Choice of Antibiotic: Amoxicillin With or Without Clavulanate Prescribed for Patients with Acute Bacterial Sinusitis (Appropriate Use)
Appropriate Testing for Children with Pharyngitis
Appropriate Treatment for Children with Upper Respiratory Infection (URI)
Appropriate Treatment of Methicillin-Sensitive Staphylococcus Aureus (MSSA) Bacteremia
Avoidance of Antibiotic Treatment in Adults With Acute Bronchitis
Documentation of Current Medications in the Medical Record
Use of High-Risk Medications in the Elderly

TABLE: HTTPS://WWW.HSAG.COM/CONTENTASSETS/003BE6B0A7884614B652807DB59FD20F/MIPSOVERVIEWANTIBISTWRDSHIP508.PDF

CDC Clinician Checklist for Core Elements of Outpatient Antibiotic Stewardship

COMMITMENT

1. Can you demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety related to antibiotics? ❑ Yes ❑ No

If yes, indicate which of the following are in place (select all that apply)

- ❑ Write and display public commitments in support of antibiotic stewardship.

ACTION

2. Have you implemented at least one practice to improve antibiotic prescribing? ❑ Yes ❑ No

If yes, indicate which practices which you use. (Select all that apply.)

- ❑ Use evidence-based diagnostic criteria and treatment recommendations.
- ❑ Use delayed prescribing practices or watchful waiting, when appropriate.

TRACKING AND REPORTING

3. Do you monitor at least one aspect of antibiotic prescribing? ❑ Yes ❑ No

If yes, indicate which of the following are being tracked. (Select all that apply.)

- ❑ Self-evaluate antibiotic prescribing practices.
- ❑ Participate in continuing medical education and quality improvement activities to track and improve antibiotic prescribing.

EDUCATION AND EXPERTISE

4. Do you provide education to patients and seek out continuing education on antibiotic prescribing? ❑ Yes ❑ No

If yes, indicate how you provide antibiotic stewardship education. (Select all that apply.)

- ❑ Use effective communications strategies to educate patients about when antibiotics are and are not needed.
- ❑ Educate about the potential harms of antibiotic treatment.
- ❑ Provide patient education materials

Current State of Prescribing Documentation

Facility Profile	
Last Calendar Year or Last 12 months	**Write in**
Number of office visits	
Number of unique prescribers	
Average number daily office visits per prescriber	
What are the three most common infectious syndromes treated in your clinic?	
Name 3 clinical practice guidelines for infectious syndromes that are *regularly* followed in your facility?	
Of the guidelines listed above, for which is clinician adherence to the guideline monitored in your facility?	
What proportion of office visits result in an antibiotic prescription?	
What proportion of **acute bronchitis** cases in persons without COPD are treated with an antibiotic?	
What are the three most common antibiotics prescribed **for acute bronchitis** in persons without COPD?	
What proportion of **acute sinusitis** cases are treated with an antibiotic?	
What are the three most common antibiotics prescribed for **acute sinusitis**?	
What proportion of **acute URI** cases are treated with an antibiotic?	
What are the three most common antibiotics prescribed for **acute URI**?	
Does your clinic require chart documentation of indication for each antibiotic prescription?	

Improve Prescribing

ACTION

2. Have you implemented at least one practice to improve antibiotic prescribing?

If yes, indicate which practices which you use. (Select all that apply.)

- ❑ Use evidence-based diagnostic criteria and treatment recommendations.
- ❑ Use delayed prescribing practices or watchful waiting, when appropriate.

Antibiogram

Tool used to guide empiric antibiotic prescribing

- Estimates the prevalence of antibiotic susceptibilities for common pathogens

Helpful for tracking resistance trends

Most commonly used in hospitals to encourage responsible prescribing uponadmission

Valuable tool for outpatient facilities, but difficult to create

- Limited number of isolates
- Cultures not collected for most mild infections
- Urine culture most common, but extrapolation can be risky
- Lack of resources to develop

South Plains Regional Antibiogram

Collaborative between University Medical Center and Covenant Health System antimicrobial stewardship programs

Outpatient clinics only

- Excluded:
  - Rural hospitals
  - Long term care facilities
  - Wound care clinics

Only include pathogens which commonly cause community-acquired infections

Only include antibiotics available for outpatient use

Will be available for all on Lubbock Department of Health website

Components

SOUTH PLAINS REGIONAL ANTIBIOGRAM

Trifold

C	B	A

Component A

Introduction

- *An antibiogram is an antibiotic prescribing tool that summarizes the percent of individual bacterial pathogens isolated in microbiological cultures which are susceptible to different antimicrobial agents.*
- *Included is data from **over 50 outpatient clinics** who send specimens to the region's two largest medical center microbiology laboratories. It is the goal of the Lubbock Area Antimicrobial Stewardship Collaborative to assist with judicial use of antimicrobials in all outpatient healthcare settings throughout the South Plains region.*

Disclaimers

- *This antibiogram has been prepared according to standards established by the Clinical and Laboratory Standards Institute.*
- *It should only be used to **guide empiric therapy and should not replace clinical judgment**. Once available, refer to microbiology results for the specific susceptibility of individual isolates.*
- *This antibiogram is not generalizable to settings outside of the depicted region.*

Contact Information

Component B

For South Plains Region Use for **2019**

Questions?
Covenant Microbiology
(806)725-4262
UMC Microbiology
(806) 775-8375

Values in boxes represent percent susceptible
Blank boxes = insufficient data or drug is not tested

BACTERIUM (# of isolates)		BETA-LACTAMS	Amoxicillin†	Amoxicillin/Clavulanate†	Ampicillin†	Oxacillin	Penicillin†	CEPHALOSPORINS	Cefazolin (1st)†	Cefoxitin (2nd)†	Ceftriaxone (3rd)	FLUOROQUINOLONES	Ciprofloxacin†	Levofloxacin†	OTHERS	Clindamycin†	Erythromycin	Nitrofurantoin²	Tetracycline†	Trimethoprim/Sulfa†
	Gram positive	*S. aureus¹(658)*					54	7		52					63		77	42		93	98
		S.epidermidis(89)					37	10							69		62	23		89	
		*S. pneumonia (23)**		87				82				83			96		78	56		74	70
		E. faecalis(48)				96		96							50			19			
		*E. faecium(29)**				90		90										21			
	Gram negative	*E. cloacae(29*)*										79		100	100					100	100
		E. coli(85)			59	33				61	88	80		69	69					61	64
		*E. coli † (5591)***			81	50				75	94	91		73	73				97	70	69
		*K. pneumonia(30)**			83					80	93	87		90	90					90	87
		*K. pneumonia † (975)***			91					82	93	92		91	96				34	79	85
		*P. mirabillis(33)**			88	73				76	97	94		82	85						91

(*) Decreased statistical validity with < 30 bacterial isolates, exercise discretion in interpretation of susceptibility (**) Urine Isolates ONLY (†) adjust dose in renal impairment (1) 46 % of isolates represent methacillin-resistant strains (MRSA) (2) Avoid if CrCl ≤60 ml/min

****It is a general recommendation to avoid agents with >15-20%% resistance for empiric therapy****

Component C

Table of select adverse events

Most common

Most serious

Listed in order of antibiogram information

Bolded footnote regarding *C. difficile* risk

SELECT ANTIBIOTIC ADVERSE EFFECTS

BETA-LACTAMS

Amoxicillin, amoxicillin/clavulanate, ampicillin, oxacillin, penicillin
Adverse effects: rash, hypersensitivity, GI disturbances, drug fever

CEPHALOSPORINS

1st G: Cefazolin, cephalexin
2nd G: Cefoxitin, cefaclor, ceforozil, cefuroxime
3rd G: Ceftriaxone, cefdinir, cefixime
Adverse effects: rash, hypersensitivity, GI disturbances, leukopenia

FLUOROQUINOLONES

Ciprofloxacin, levofloxacin, moxifloxacin
Adverse effects: GI disturbances, headache, tendinopathy/rupture (esp. in elderly), photosensitivity, QT interval prolongation, hypoglycemia (esp. in diabetics)

OTHERS

Clindamycin
Adverse effects: GI disturbances, rash, hypersensitivity, jaundice
Nitrofurantoin
Adverse effects: GI disturbances, rash, urine discoloration (brown)
Linezolid
Adverse effects: GI disturbances, thrombocytopenia, rash, leukopenia, serotonin syndrome (with concurrent serotonergic agents)
Tetracycline (doxycycline, minocycline)
Adverse effects: GI disturbances, photosensitivity, bone/dental effects in children (avoid in age < 8y)
Trimethoprim/Sulfamethoxazole
Adverse effects: GI disturbances, rash, hypersensitivity, electrolyte imbalance, renal toxicity, neutropenia

All antibiotics can increase the risk of C. difficile diarrhea through disruption of normal gut microflora. Risk increases with longer antibiotic durations and exposure to multiple (or broad spectrum) antibiotics.

Reverse Side

Table of recommended antimicrobials for selected outpatient infectious diseases

Provides guidance for empiric therapy based on most recent guidelines

- Upper respiratory tract infections (bronchitis, pharyngitis, rhinosinusitis, colds)
- Community-acquired pneumonia (influenza separate)
- Urinary tract infections
- Skin and soft tissue infections
- Acute otitis media

Disclaimers

- Serves as a guide and should not replace clinical judgment
- All doses assume normal renal function, adjust as indicated

Antibiogram in Action

A 21-year-old female college student presents to your medical office with a 3-day history of dysuria and frequency. She denies any fever or back pain and is otherwise healthly. She tells you she has self-medicated with cranberry juice and pyridium that her roommate gave her. She takes no other medications and has not taken antibiotics for over a year.

An in-office urine dipstick analysis reveals **(+) nitrite** and **(+) leukocyte esterase**.

Does this patient meet criteria for antimicrobial therapy?

A. Yes, patient has urinary tract infection
B. No, this is asymptomatic bacteriuria which does not require treatment
C. Yes, patient needs hospital admission for intravenous antibiotic therapy
D. No, patient already taking pyridium

Urinary Tract Infection Treatment

Uncomplicated UTI

- Lower urinary symptoms (dysuria, frequency, and urgency) in otherwise healthy non-pregnant women

Most common pathogens:

- *E. coli* (most frequent, 75-95% cases)
- Staphylococcus saprophyticus
- Other *Enterobacteriacae* (*Klebsiella pneumoniae* and *Proteus mirabilis*)

Based on the South Plains community antibiogram, what would best choice for empiric antimicrobial therapy?

- *Note: Infectious Diseases Society of America UTI guidelines recommend 20% as the resistance prevalence threshold at which an agent is no longer recommended for empirical treatment of acute cystitis*

For South Plains Region Use for **2019**

Questions?
Covenant Microbiology
(806)725-4262
UMC Microbiology
(806) 775-8375

Values in boxes represent percent susceptible
Blank boxes = insufficient data or drug is not tested

BACTERIUM (# of isolates)		BETA-LACTAMS	Amoxicillin†	Amoxicillin/Clavulanate†	Ampicillin†	Oxacillin	Penicillin†	CEPHALOSPORINS	Cefazolin (1st)†	Cefoxitin (2nd)†	Ceftriaxone (3rd)	FLUOROQUINOLONES	Ciprofloxacin†	Levofloxacin†	OTHERS	Clindamycin†	Erythromycin	Nitrofurantoin²	Tetracycline†	Trimethoprim/Sulfa†
	Gram positive																			
	S. aureus¹(658)					54	7		52					63		77	42		93	98
	S.epidermidis(89)					37	10							69		62	23		89	
	*S. pneumonia (23)**		87				82				83			96		78	56		74	70
	E. faecalis(48)				96		96							50			19			
	*E. faecium(29)**				90		90										21			
	Gram negative																			
	E. cloacae(29)*										79		100	100					100	100
	E. coli(85)			59	33				61	88	89		69	69					61	64
	*E. coli † (5591)***			81	50				75	94	91		73	73				97	70	69
	*K. pneumonia(30)**			83					80	93	87		90	90					90	87
	*K. pneumonia † (975)***			91					82	93	92		91	96				34	79	85
	*P. mirabillis(33)**			88	73				76	97	94		82	85						91

(*) Decreased statistical validity with < 30 bacterial isolates, exercise discretion in interpretation of susceptibility
(**) Urine Isolates ONLY
(†) adjust dose in renal impairment
(1) 46 % of isolates represent methacillin-resistant strains (MRSA)
(2) Avoid if CrCl ≤60 ml/min

UTI Commonly Prescribed Agents

Nitrofurantoin monohydrate/macrocrystals (Macrobid): 100 mg PO twice daily x 5 days

- Be aware of use in renal dysfunction (caution <60 ml/min; avoid <30 ml/min)
- Active against most common UTI pathogens
- Achieves high urinary concentration but does not penetrate well into the renal parenchyma; therefore, it should not be used for the treatment of pyelonephritis

Bactrim

- No longer preferred agent due to high resistance rates

Fluoroquinolones

- Overuse has lead to high E. coli resistance rates
- FDA warnings: tendon rupture, *C. difficile* infection, hypoglycemia, CNS effects, aortic dissections

Ceftriaxone IM

- Remains active against most UTI pathogens
- Reserve for pyelonephritis

Antibiotic Streamlining

DE-ESCALATION

Benefits

Improved clinical outcomes – right drug as early as possible

Reduce *C. difficile* infection risk (and other secondary infections) from broad spectrum antibiotics exposure

Minimizing antimicrobial resistance

Minimizing toxicity/adverse events

Antimicrobial Susceptibility Testing (AST)

For each culture there is a preliminary report ~ 12-24 hours with pathogen identification

Followed up by final report which includes susceptibility of isolate against common antimicrobial agents

Final AST report will be based on minimum inhibitory concentration (MIC) which represents lowest concentration of antibiotics that prevents visible growth

MICs vary based on organism-drug combination

- Lower MICs do not reflect higher potency

Accuracy depends on appropriate specimen collection!

Urgent Care Case

A 52-year-old woman with well-controlled type 2 diabetes presents to the your urgent care with burning during urination, costovertebral angle tenderness, and nausea. She reports previous UTIs but she has not had one for a few years. Patient is not allergic to any medications.

Urinalysis **(+) nitrite** and **(+) leukocyte esterase** (culture pending)

Provider assessment/plan:

Uncomplicated acute pyelonephritis

- Zofran for nausea
- Ceftriaxone x 1 dose today
- Prescription for levofloxacin PO 500 mg daily x 6 days
- Follow up with culture

Next day

Escherichia coli isolated in urine culture (preliminary)

Nurse follow up phone call with patient:

- Nausea resolved
- Urinary symptoms resolved
- Has not picked up levofloxacin prescription but planning on picking up this afternoon

Provider opts to continue as planned, patient instructed to call with any worsening

48 hours

Antimicrobial susceptibility results final

Bug/drug mismatch

- Resistant to current therapy

Deescalation – choose focused (narrow spectrum) therapy

- Augmentin (beta lactams require 10-14 days)
- 1st, 2nd, 3rd generation cephalosporins
- Avoid nitrofurantoin in pyelonephritis
- Gentamicin and piperacillin/tazobactam only available IV
- Bactrim (TMP/SMX) x 14 days

Organism: E. coli

Antibiotic	MIC	Interpretation
Amoxicillin/clavulanic acid	8/4	S
Ampicillin	>16	R
Cefazolin	2	S
Cefuroxime	<=4	S
Ceftriaxone	<=.05	S
Gentamicin	<=1	S
Levofloxacin	>4	R
Nitrofurantoin	<=16	S
Piperacillin/tazobactam	<=2/4	S
Trimethoprim/sulfamethoxazole	<0.5/9.5	S

Summary

Successful AMS starts with leadership and accountability

Communicate expectations

- Prescriber, nursing, caregiver/family

Start small and reach out for resources

Document your progress (checklist)

Celebrate success!

Questions?