

Definitions

- Superbugs are organisms that are resistant to medications used to treat the infections they cause
- Antibiotic resistance is what happens when germs develop the ability to defeat the drugs designed to kill them
- MDRO (multidrug resistant organism) is a germ that is resistant to many antibiotics



Superbugs

• Most “concerning” bacteria from CDC in their 2019 Antibiotic Threats Report

- Four categories: Urgent Threats, Serious Threats, Concerning Threats, Watch List
- Urgent threats:
 - Carbapenem-resistant *Acinetobacter*
 - Pneumonia, wound, blood-borne and UTI
 - 2017 hospitalizations: 9,500
 - 2017 deaths (estimated): 700
 - Drug-resistant *Candida auris*
 - Looks like fungal infections but doesn't respond to therapy and enters the blood stream
 - *Clostridioides difficile* (*C. difficile*)
 - Life-threatening diarrhea, inflammation of the colon.
 - Mostly when received medical care and antibiotics
 - High degree of recurrence



Superbugs

• Most “concerning” bacteria from CDC in their 2019 Antibiotic Threats Report

- Urgent threats - continued:
 - Carbapenem-resistant Enterobacteriales (CRE)
 - Large family of bacteria
 - Resistant to nearly all antibiotics
 - Leaving more toxic and less effective
 - May not leave any options
 - 2017 estimated deaths: 1,100
 - Drug-resistant *Neisseria gonorrhoeae* (*N. gonorrhoeae*)
 - Sexually transmitted
 - Has become harder to treat over time



Antibiotic Resistance

- Antibiotic resistance development
 - Survival of the fittest
 - Mutations
 - DNA exchange between bacteria
 - Rapid reproduction



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Antibiotic Resistance and Reactions

- Antibiotic resistance
 - Each year in US – 2 million people become infected with antibiotic resistant bacteria, at least 23,000 die
 - Lack of new antibiotics in development
 - Excessive health care costs
- Preventable adverse drug reactions (ADRs)
 - Antibiotics cause 142,000 ER visits yearly for ADRs

MMWR August 21, 2015



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Excessive Health Care Costs

- ER visits due to adverse effects of antibiotics
- Costs associated with antibiotic use when not necessary
- Costs associated with the treatment of Clostridium difficile infections (CDI)



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Preventable Adverse Effects

- Antibiotics
 - 19.3% of all drug related adverse events
 - 78.7% allergic events
 - 19.2% other (diarrhea, vomiting)
- Approximately 6% require hospitalization

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Shahab N et al. Clin Infect Dis. 2008;47:735

Antibiotic Drug Interactions

- The effects of drug interactions
 - Absorption
 - Distribution
 - Metabolism
 - Elimination
- Results
 - Decreased efficacy
 - Increased potential for adverse consequences

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Rational antibiotics have major effect on INR

Supratherapeutic Bleed Risk	
Metronidazole	Erythromycin
Moxifloxacin	Isoniazid
Sulfamethoxazole	Levofloxacin
Azithromycin	Tetracycline
Ciprofloxacin	Doxycycline
Clarithromycin	
Cloxacillin	
Doxycycline	
Patient-Specific Therapeutic INR Range	
Terbinafine <small>(an increase in INR)</small>	Subtherapeutic Clot Risk
Rifampin	

Fig. 1 Antibiotic directional effects on INR

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<https://www.contemporaryinr.com/view/antibiotic-and-anticoagulation-watching-warfarin-levels>

Excessive Health Care Costs - CDI

- Hospital-acquired/hospital onset:
 - 165,000 cases
 - \$1.3 billion in excess costs
 - 9,000 deaths annually
- Hospital-acquired/post discharge (up to 4 weeks)
 - 50,000 cases
 - \$0.3 billion in excess costs
 - 3,000 deaths annually
- Nursing home onset
 - 265,000 cases
 - \$2.2 billion in excess costs
 - 16,500 death annually

Campbell et al. Infect Control Hosp Epidemiol. 2009;30:523-33
Tchobanov et al. Clin Infect Dis. 2009;48:497-504

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Antibiotics - Unnecessary Use

- 2021 World Congress on Gastrointestinal Cancer
 - Unnecessary antibiotic use may cause increased risk of colon cancer in patients under 50
 - Background –
 - from 2000-2015 antibiotic consumption increased 65%
 - Over that time Colon Cancer also significantly increased in less those <50yo
 - Compared over 50 and under 50 vs antibiotic usage
 - Scottish primary care database (2 million people)
 - Reviewed 8000 patients with bowel cancer (Colon and rectum) vs 30,018 without

<https://www.cancernetwork.com/view/unnecessary-use-of-antibiotics-may-lead-to-early-onset-crc-in-patients-under-50-years>

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Antibiotics - Unnecessary Use

- 2021 World Congress on Gastrointestinal Cancer - continued
 - In both age groups colon cancer risk was increased but more in the <50 than over 50
 - Greater risk with quinolones and sulfamethoxazole/trimethoprim
 - Findings suggest:
 - Antibiotics “may” be related to colon tumor formation in all age groups
 - This is particularly true in those <50
 - With additional confirmation this is an additional reason to limit frequent and unnecessary prescribing

<https://www.cancernetwork.com/view/unnecessary-use-of-antibiotics-may-lead-to-early-onset-crc-in-patients-under-50-years>

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Closer to "Home"

- According to the commentary on the reform to the CMS regulations, there are 1.6 – 3.8 million Hospital Acquired infections in LTC annually
 - Estimated 150,000 hospitalizations
 - 388,000 deaths
 - Healthcare costs from \$673 million to \$2 billion

8/18/2020



Purpose of Antibiotic Stewardship

- Limit inappropriate and excessive antibiotic use
- Improve and optimize therapy and clinical outcomes for patients



Goals of Antibiotic Stewardship

- Reduce antibiotic consumption and inappropriate use
- Reduce CDI
- Improve patient outcomes
- Increase adherence/utilization of treatment guidelines
- Reduce adverse drug events
- Decrease or limit antibiotic resistance



CMS Changes

- Appendix PP
- Revised F-Tags
- Training Resources
- Five Star Implications
- Enforcement
 - Fines and Nursing Home Compare
- Survey Process



Core Elements of an Antibiotic Stewardship Program

- Leadership commitment – to support training and education
- Accountability – someone to be responsible for the program
- Expertise – rely on input from physicians, pharmacists, lab, etc.



Core Elements of an Antibiotic Stewardship Program

- Action –
 - Implement policies to document dose, duration and indication of antibiotics
 - Develop facility- specific treatment recommendations for common infections
 - Implement interventions based upon needs of facility
 - Provide education to staff and physicians



Core Elements of an Antibiotic Stewardship Program

- Tracking and Reporting
 - Conduct retrospective chart reviews for periodic assessments of antibiotic use
 - Establish benchmarking
 - Track clinical outcomes
 - Report resistance trends



Where to Start . . .

- Develop an antibiotic stewardship team within the facility
 - The leader of this committee will have significant duties for monitoring this program
- Contact pharmacist and physician for input regarding the development of the program



Where to Start . . .

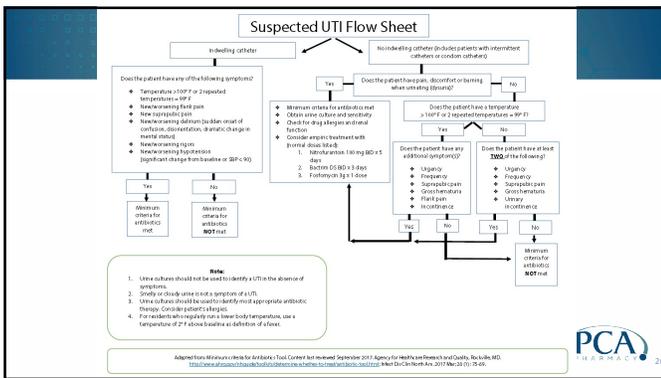
- Review the Phase II Regulations
- Educate
 - Staff
 - Family
 - Prescribers
- Policy and Procedures
- Protocols for Antibiotic Use
- Organized structure



Where to Start . . .

- Develop policies/protocols for ordering diagnostic tests for common suspected infections
- Develop policies/protocols for clinical criteria needed for diagnosis of infection





Suspected Lower Respiratory Infection (LRI)	Suspected Lower Respiratory Infection (Moderate)
<p>Febrile > 100°F</p> <p>AND at least one of the following:</p> <ul style="list-style-type: none"> • Productive cough • Respiratory rate > 25 <p>Febrile > 100°F</p> <p>AND at least one of the following:</p> <ul style="list-style-type: none"> • Productive cough • Respiratory rate > 25 • Pulse > 100 • Rales • Rhonchi • Respiratory rate > 25 <p>At least one of the following:</p> <ul style="list-style-type: none"> • New infiltrate on chest X-ray thought to represent pneumonia and at least one of the following: <ul style="list-style-type: none"> • Fever > 100°F • Pulse > 100 • Respiratory rate > 25 • Productive cough <p>Check X-ray and complete cell count with differential leukocyte count for patients with fever, cough, and/or tachypnea</p> <ul style="list-style-type: none"> • Pulse > 100 • Respiratory rate > 25 • Rales 	<p>Pneumonia (at least one of the following):</p> <ol style="list-style-type: none"> 1. Intermittent or a chest radiograph demonstrating pneumonia or the presence of a new infiltrate. 2. At least 1 of the following respiratory criteria: <ul style="list-style-type: none"> • New or increased cough • New or increased sputum production • O₂ saturation < 90% on room air or a fraction of O₂ saturation of > 3% from baseline • New or changed lung examination • Abnormal chest X-ray • Pleuritic chest pain • Respiratory rate of > 20 breaths/min 3. At least 1 of the constitutional criteria: <ul style="list-style-type: none"> • Fever: <ul style="list-style-type: none"> - Single oral temperature > 37.8°C (100°F) OR - Rectal or oral temperature > 37.2°C (99°F) for 2 consecutive days • Single temperature > 1.1°C (2°F) over baseline from any site (oral, tympanic, axillary) <ul style="list-style-type: none"> • Leukocytosis: <ul style="list-style-type: none"> - Neutrophils (>16,000 leukocytes/mm³) OR - Lymphocytes (< 4% bands or < 1500 bands/mm³) • Abnormal changes in mental status from baseline (all criteria must be present): <ul style="list-style-type: none"> - Fluctuating course - Inattention <p>AND Either disorganized thinking or altered level of consciousness OR Abnormal bedside reflexes</p> <p>4. A new 3-point increase in total activities of daily living (ADL) score from baseline, based on the following? (ADL score is based on 10 ADL dependent to a 10-item dependence)</p> <ul style="list-style-type: none"> • Bed mobility • Transfer • Locomotion within LTCF • Dressing

Starting the Process

- Develop policies/protocols regarding antibiotic selection/dose/duration for the most common infections in the elderly
 - UTI
 - Recurrent UTI
 - Pneumonia
 - Bronchitis
 - Skin/wound
 - C. Diff



Starting the Process

- Educate all staff, physicians and families on the new policies and program
- Educate all staff on timely and accurate recognition, assessment, communication and documentation of a change in residents condition
- Ensure protocols are easily accessible to nursing staff when contacting physicians



Starting the Process

- Develop tracking tools to monitor infections, antibiotic use and adherence to the established protocols



Basic Tenets of Antimicrobial Stewardship and Pearls



Factors to Consider When Selecting an Antibiotic

- Spectrum of coverage
- Patterns of resistance
- Evidence or track record for the specified infection
- Achievable serum, tissue or body fluid concentration
- Allergy
- Toxicity
- Formulation (IV vs PO)
- Adherence/convenience
- Cost



Antibiograms

- What is an antibiogram?
 - An overview of susceptibility of microorganisms to antimicrobials
- How will the antibiogram be created?
 - Aggregate data from C&S's
- Why are antibiograms important?
 - Shows development of resistance - regionally
- What is the potential impact of using antibiograms?
 - Less drug resistance by using more susceptible drug
- How are antibiograms used?
 - Look for your microbe – then look for a drug with a high percent of susceptibility



Antibiograms

Organism	No. Strains	% Susceptible								
		CLI	DOX	ERY	GEN	OXA	PEN	RIF	SXT	VAN
All <i>S. aureus</i>	1317	80	98	50	93	68	13	98	96	100
Oxacillin-resistant <i>S. aureus</i> (MRSA)	449	44	96	4	79	0	0	95	94	100
Oxacillin-susceptible <i>S. aureus</i> (MSSA)	904	97	99	72	99	100	18	99	97	100

- Other things to consider
 - Location of infection
 - Example: Bone infection vs Soft Tissue
 - Route of administration
 - IV vs PO
 - Other medications and comorbidities
 - Allergies
 - Renal or liver impairment
 - Drug interactions
 - Should be used while waiting for the C&S



Tenets of Appropriate Antibiotic Use

- Treat bacterial infection, not colonization (Ex: asymptomatic bacteriuria)
 - 10,000 colony forming units is often used as a diagnostic criteria for positive urine culture – which means the culture is not likely due to contamination or colonization
 - Pyuria is also not predictive on its own
 - It's the presence of symptoms AND pyuria AND bacteriuria that denotes infection



Tenets of Appropriate Antibiotic Use

- Do not treat sterile inflammation or abnormal imaging without infection
 - X-rays can be difficult to interpret. Infiltrates may be due to non-infectious causes such as atelectasis, malignancy, hemorrhage, pulmonary edema
 - Pneumonia is not present in up to 30% of patients treated
 - Do not treat abnormal X-rays with antibiotics if the patient does not have systemic evidence of inflammation (fever, WBC elevation, sputum production etc)



Tenets of Appropriate Antibiotic Use

- Do not treat viral infections with antibiotics
 - Acute bronchitis
 - Common Colds
 - Sinusitis with symptoms less than 7 days
 - Pharyngitis not due to Group A Strep



Tenets of Appropriate Antibiotic Use

- Limit duration of antibiotic therapy to the appropriate length based upon published guidelines
 - 10 days is not always needed
- If empiric therapy started, re-evaluate after lab results obtained



Pearls

- Wash your hands!
- Get Vaccinated
- Review admission histories
 - Other facilities
 - Travel abroad
 - Vaccine history
 - Colonization
- Educate
 - Staff
 - Residents
 - Families



Pearls

- When there is an outbreak
 - Contain infections
 - Notification
 - Staff
 - Family
 - Resident
 - Disaster plan



Conclusion

- Balance the therapeutic benefit of antibiotics with the unintended adverse consequences
- Inappropriate antibiotic use is associated with increased antibiotic resistance, adverse drug effects and Clostridium difficile infection
- Antibiotic stewardship is important for preserving existing antibiotics and improving patient outcomes
- Antibiotic prescribing should be prudent, thoughtful and rational



Resources

- Minnesota Department of Health has developed a tool kit for implementation of an antibiotic stewardship program
<http://www.health.state.mn.us/divs/idepc/dtopics/antibioticresistance/asp/ltc/index.html>
- www.dobugsneeddrugs.org
- CDC





