Antimicrobial Stewardship Across the Continuum of Care

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Disclosure

Dr. Burns has listed no financial interest/arrangement that would be considered a conflict of interest

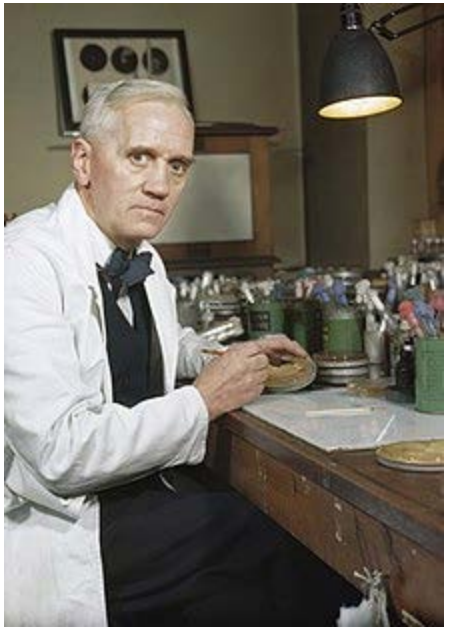
Objectives

- Define 3 objectives of an antibiotic stewardship program for inpatient and outpatient facilities
- Identify 3 barriers to judicious antibiotic use for UTI treatment and the "jurisdiction" of the Infection Preventionist
- Identify 3 model initiatives that could be undertaken by a developing antimicrobial stewardship team
- Enumerate 5 typical interventions of an inpatient antibiotic stewardship program

Birth of Antimicrobial Stewardship

- "the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out ... In such cases the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted."

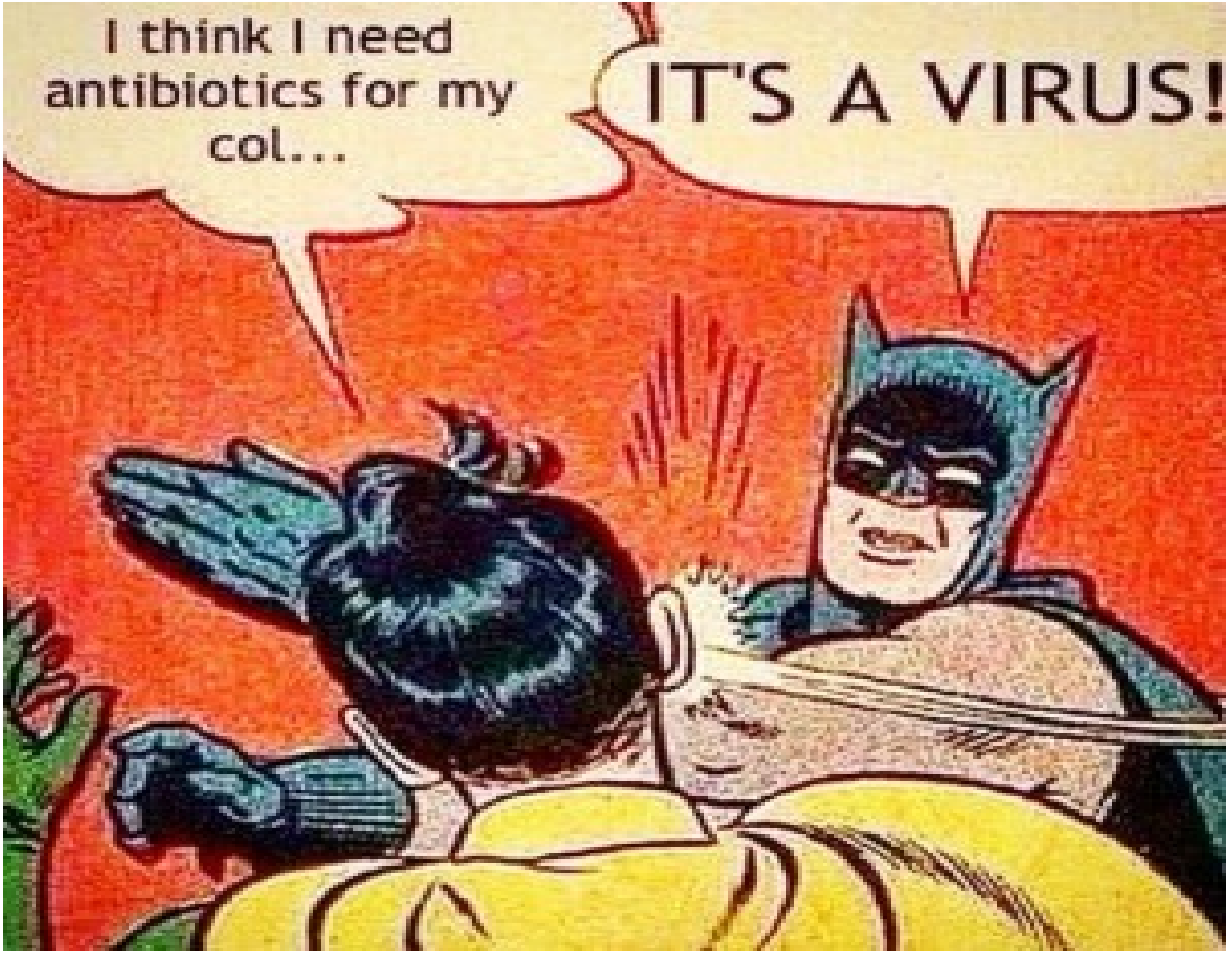
  - Sir Alexander Fleming, June 26, 1945



Why Do We Need Antimicrobial Stewardship?

- 20 – 50% of antibiotics in acute care hospitals are unnecessary or inappropriate
- *C. difficile* and other adverse reactions
- Antibiotic resistance is increasing
- Antimicrobial stewardship programs optimize treatments and reduce adverse events

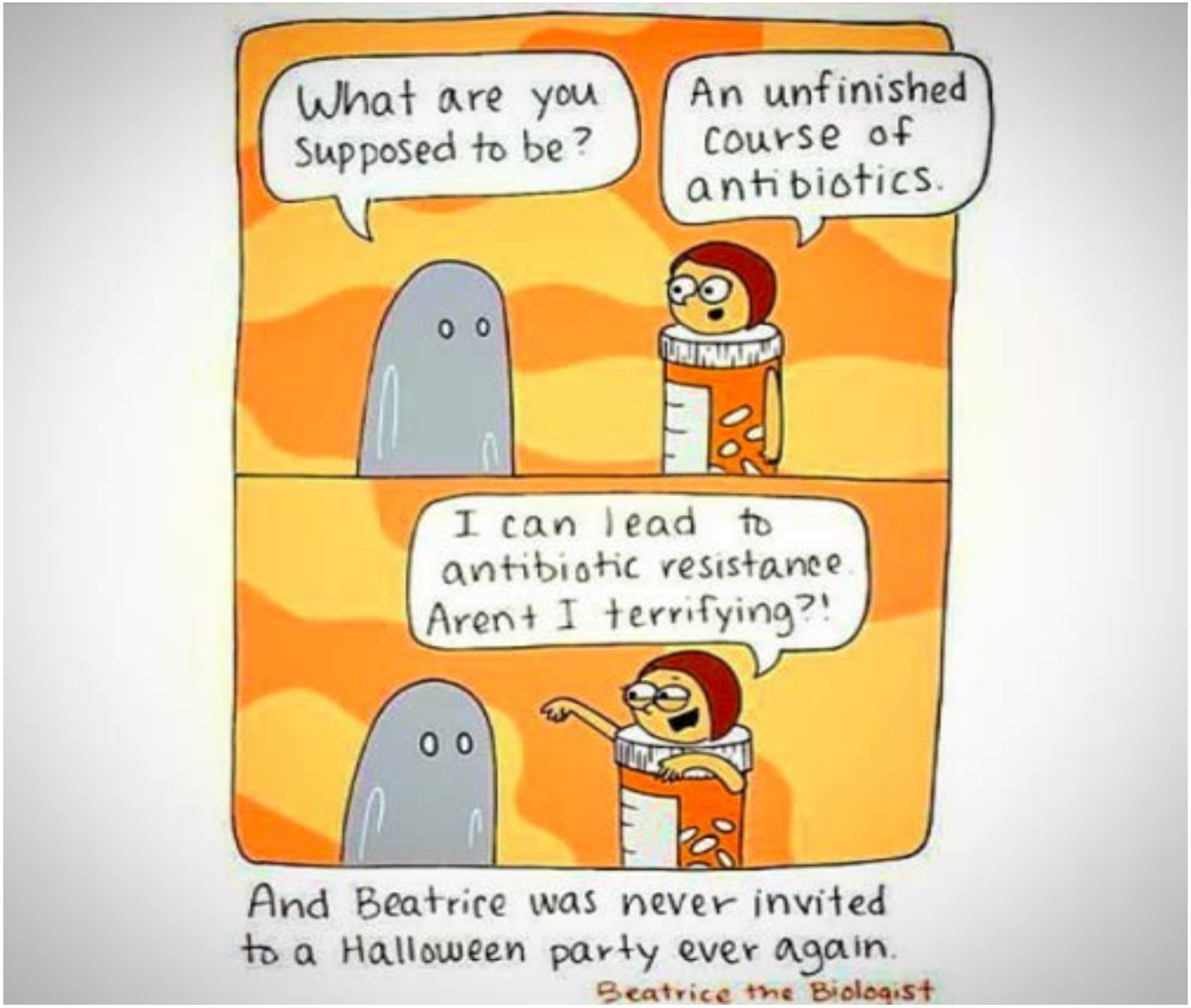
CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html


I think I need antibiotics for my col...
IT'S A VIRUS!

Why Do We Care About Improving Antibiotic Use?

- Misuse of antibiotics in humans and animals is accelerating the natural process of antibiotic resistance
- Antibiotics are the only class of drugs that can affect the health of people who aren't even exposed to the drugs
  - Resistant bugs cause 23,000 deaths in the US annually
- Improves patient outcomes and saves money
- World Health Organization (WHO) considers antibiotic resistance a threat to global health, food security, and development

World Health Organization Antibiotic Resistance: http://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance


What are you supposed to be?
An unfinished course of antibiotics.
I can lead to antibiotic resistance. Arent I terrifying?!
And Beatrice was never invited to a Halloween party ever again.
Beatrice the Biologist

Resistance Facts

- Antimicrobial resistance could wipe out many medical breakthroughs from the past century
  - Previously curable infectious diseases may become untreatable and spread rampantly
- Overuse, underuse, and misuse all contribute to the problem
- Sub-therapeutic doses of antibiotics used in animal-rearing is a source of resistant microorganisms that can spread to humans
- Hospitalized patients are a main reservoir for resistant organisms
- Weak surveillance systems contribute to the spread

World Health Organization Antibiotic Resistance: http://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance

Why Not Just Develop New Antibiotics?

- The antibiotic pipeline is very limited
  - As of December 2017, 45 antibiotics in development
    - 16 in Phase I, 14 in Phase II, 15 in Phase III
    - 20 possibly or do have activity against resistant gram negative ESKAPE pathogens
    - 25 possibly or do have activity against CDC urgent or WHO critical threat pathogens
- Typically about 1 in 5 pipeline drugs make it to market

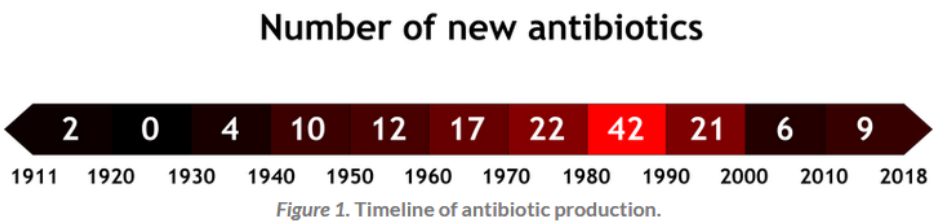


Figure 1. Timeline of antibiotic production.

Antibiotics Currently in Global Clinical Development February 2018. http://www.pewtrusts.org/-/media/assets/2018/03/antibiotics_clinical_dev_table_february2018.pdf
http://sitn.hms.harvard.edu/flash/2018/less-rebooting-antibiotic-pipeline/

Antibiotic Development

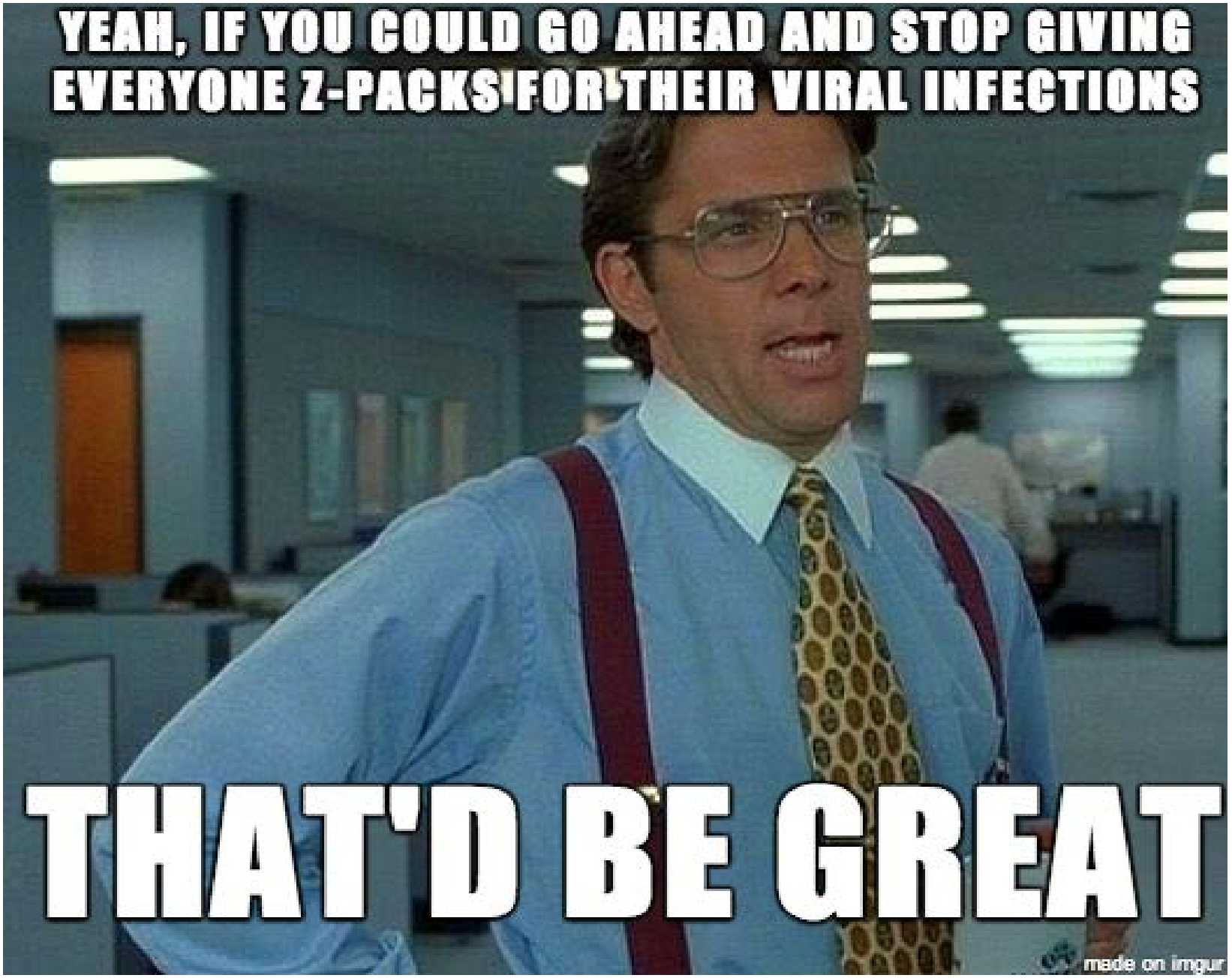
- The basic strategy has been to use the same basic drug classes with modification to bypass resistance mechanisms
  - Of 15 new drugs since 2000, only 4 with new mechanisms
  - Approval can be faster, targets are known, side effects mostly known
  - Fuels resistance by repeatedly introducing similar drugs
- Drug development costs several billion dollars before the drug gets to market
  - Several large companies dropped antibiotics from development due to the rapid development of resistance to new agents
- Generating Antibiotics Incentives Now Act (GAIN) 2012
  - Financial incentives to conduct antibiotic development

http://sitn.hms.harvard.edu/flash/2018/less-rebooting-antibiotic-pipeline/

Core Elements of Outpatient Antibiotic Stewardship

- Commitment
  - Commit to improving antibiotic practices
- Action for policy and practice
  - Implement at least 1 policy or practice aimed at antibiotic prescribing
- Tracking and reporting
  - Track prescribing practices and report back to clinicians
- Education and expertise
  - Provide educational resources to patients and families on appropriate antibiotic use
  - Educate clinicians on antibiotic prescribing

CDC: https://www.cdc.gov/antibiotic-use/community/pdfs/16_268900-A_CoreElementsOutpatient_508.pdf


YEAH, IF YOU COULD GO AHEAD AND STOP GIVING EVERYONE Z-PACKS FOR THEIR VIRAL INFECTIONS
THAT'D BE GREAT
made on imgur

Core Elements of Nursing Home Antibiotic Stewardship

- Leadership Commitment
- Accountability
- Drug Expertise
- Action
- Tracking and Reporting
- Education

Core Elements of Hospital Antimicrobial Stewardship Program

- Leadership Commitment
- Accountability
- Drug Expertise
- Action
- Tracking
- Reporting
- Education

CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html

Leadership Commitment

- Formal statements that facility supports efforts to improve and monitor antibiotic use
- Provide sufficient time for participation in stewardship activities
- Support training and education
- Financial support

CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html

Accountability and Drug Expertise

- Stewardship program leader responsible for program outcomes
  - Often a physician
- Pharmacy leader to co-lead the program
- Formal training in infectious diseases or antibiotic stewardship
- Does not have to be full time for smaller facilities
- Pharmacy and Therapeutics committee should not be the stewardship team, unless the role is expanded to include specific stewardship activities

CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html

Action

- Implement policies to support optimal antibiotic use
- Three major categories
  - Broad
  - Pharmacy driven
  - Infection and syndrome specific

CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html

AMS Support Beyond the Formal Team

- Clinicians
  - Support for efforts to improve antibiotic use
- IP and epidemiologists
  - Monitoring and prevention of healthcare-associated infections (HAI)
- Quality and Safety
  - Reporting and patient safety initiatives
- Lab
  - Proper use of tests and flow of results
  - Antibiogram
- Information technology
  - Integration of protocols, clinical decision support
- Nurses
  - Timing of cultures and antibiotic administration

CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html

Tracking and Reporting

- Measurement is critical
  - Process and outcome
- Antibiotic use measures
  - Days of Therapy (DOT) or Defined Daily Dose (DDD)
    - DOT preferred
    - DDD if IT infrastructure can't support DOT
  - Leverage clinical decision support and/or EHR reporting capabilities
- Standardized Antimicrobial Administration Ratio (SAAR) can be calculated by NHSN
  - Has been nationally standardized and endorsed by National Quality Forum

CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html

Caveats for Monitoring Cost Savings

- Cost savings are hard to track
  - If tracking drug costs, factor in inflation
- After initial cost savings, tend to stabilize
- Factor in the costs (personnel) to maintain any savings gained

Education

- Provide regular updates on prescribing, resistance, and management
- Share facility specific information on antibiotic use
- Not all education has to be formal, didactic programming
  - Flyers or posters, newsletters
  - Case reviews

CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html

Joint Commission Standard MM.09.01.01

- The hospital has an antimicrobial stewardship program based on current scientific literature
- Leaders establish AMS as an organizational priority
- Hospital educates staff and prescribers at hire and periodically thereafter
- Hospital has an AMS team with the following team members
  - ID physician
  - Infection preventionist
  - Pharmacist
  - Practitioner

The Joint Commission E-dition 2018 Accreditation Requirements

Joint Commission Standard MM.09.01.01

- The AMS program includes the CDC core elements
- The AMS program uses organization-approved multidisciplinary protocols
- Hospital collects, analyzes, and reports data on its AMS program
- Hospital takes action in improvement opportunities identified by its AMS program

The Joint Commission E-dition 2018 Accreditation Requirements

OUR TEAM HAS FORMED…NOW WHAT DO WE DO?

Potential AMS Team Projects for a Developing Program

- Required indication and duration on all antimicrobial orders
- Antibiotic “time out” at 48 hours
- Implementation of pharmacy or nursing driven programs
  - IV to PO conversion
  - Isolation precautions
  - Foley removal
  - Automatic stop protocols for surgical prophylaxis
  - Renal dose adjustment protocol

Potential AMS Team Projects for a Developing Program

- Order sets/clinical practice guidelines
  - Extended infusion piperacillin/tazobactam
  - Disease specific order sets
- Evaluate appropriate utilization of a target antimicrobial or antimicrobial class
  - Example – improve fluoroquinolone utilization through prospective audit and feedback
  - Example - Implement an automatic AMS review of all carbapenems or echinocandins at 24 or 48 hours
  - Example – drug utilization review of a target antimicrobial to identify potential intervention strategies

Potential AMS Team Projects for a Developing Program

- Implement interventions to decrease healthcare acquired *C. difficile* rates
  - Antibiotic de-escalation
  - PPI stewardship
  - Audits on contact precautions and hand hygiene
  - Staff education on detection and diagnosis of *C. difficile*
- Develop a penicillin allergy assessment algorithm
- Decrease vancomycin nephrotoxicity through de-escalation and enhanced monitoring on high risk patients
  - Vancomycin and piperacillin/tazobactam
  - High BMI
  - Received contrast or other concurrent nephrotoxins

Potential AMS Team Projects for a Developing Program

- Disease specific interventions
  - Community acquired pneumonia
  - Urinary tract infections
  - Skin and soft tissue infections
- Nursing homes: Develop a communication tool for residents suspected of having an infection

Precautions

- Don’t implement too many initiatives at once
- Choose interventions based on facility size and available expertise

CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html

Role of the Infection Preventionist

- Coordinate facility-wide monitoring and prevention of healthcare-associated infections
- Auditing, analyzing, and reporting data
- Monitoring and reporting of resistance and *C. difficile* trends
- Educating staff on the importance of appropriate antibiotic use
- Implementing strategies to optimize the use of antibiotics

CDC: https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html

Typical Antimicrobial Stewardship Pharmacist Interventions

- De-escalation of antibiotics
- Drug-bug mismatch
- Antimicrobial dose or days of therapy adjustments
- Initiation of antibiotics
- IV to PO conversion
- Order sets/clinical practice guidelines

AMS INTERVENTIONS FOR UTI

IP Professionals Impact UTI Treatment

- Education and development of policy/procedure
  - Proper urine specimen collection technique
  - Assure that an indication exists
    - Odor and frequency aren't an indication for a specimen
  - Foley removal protocol and appropriate use of foleys

Case 1

- 95 year old male presented to the ER with fevers and altered mental status. Lives at area nursing home. UA suggested urinary tract infection.
- Patient started on empiric ceftriaxone for UTI treatment.
- On day 3, escherichia coli (10,000 colonies/mL) and enterococcus faecalis (100,000 colonies/mL) were isolated on urine culture.
- In attempt to prepare patient for discharge, provider changed antibiotic from ceftriaxone to ciprofloxacin PO on day 3 of admission

Susceptibility

	Escherichia coli (1)	
		SUSCEPTIBILITY
Amoxicillin + Clavulanate	<8/4	**Susceptible**
Amp-Sulbactam	<8/4	**Susceptible**
Ampicillin	<8	**Susceptible**
Cefazolin	<8	**Susceptible**
Cefepime	<4	**Susceptible**
Cefotaxime	<2	**Susceptible**
Ceftazidime	<1	**Susceptible**
Ceftriaxone	<8	**Susceptible**
Cefuroxime	8	**Susceptible**
Ciprofloxacin	<1	**Susceptible**
Gentamicin	<4	**Susceptible**
Levofloxacin	<2	**Susceptible**
Meropenem	<1	**Susceptible**
Nitrofurantoin	<32	**Susceptible**
Piperacillin + Tazobactam	<16	**Susceptible**
Tetracycline	<4	**Susceptible**
Ticarcillin + Clavulanic Acid	<16	**Susceptible**
Tobramycin	<4	**Susceptible**
Trimeth/Sulfa	<2/38	**Susceptible**

Susceptibility

	Enterococcus faecalis (2)	
		SUSCEPTIBILITY
Ampicillin	<2	**Susceptible**
Ciprofloxacin	>2	**Resistant**
Levofloxacin	>4	**Resistant**
Nitrofurantoin	<32	**Susceptible**
Penicillin	2	**Susceptible**
Rifampin	<1	**Susceptible**
Tetracycline	>8	**Resistant**
Vancomycin	1	**Susceptible** [1]

[1] S = Susceptible I = Intermediate R = Resistant

Case 1 AMS Intervention

- Enterococcus isolate was resistant to fluoroquinolones
- Provider did not see enterococcus isolate
- Fluoroquinolones are not effective therapy for most enterococcus infections
- Changed antibiotic to more narrow antibiotic option, amoxicillin, to cover enterococcus UTI.

Case 2

- 65 year old female admitted for sepsis secondary to UTI. UA from the ER resulted with +3 leukocytes and + nitrites
- Patient started on UTI sepsis pathway with IV ceftriaxone and IV levofloxacin
- Urine culture grew pseudomonas aeruginosa isolate on day 2 of admission

Case 2 AMS Intervention

- Ceftriaxone has no activity against pseudomonas infection
- Blood cultures were negative at 48 hours
- Discontinued the ceftriaxone and transitioned the patient to levofloxacin PO
- Sensitivities resulted the next day with pan-sensitive pseudomonas sensitive to levofloxacin

Case 3

- 64 year old female with chief complaint of syncope
- AKI on admission (SCr 2.4, baseline 0.9)
- UA resulted with +1 leukocyte esterase, many epithelial cells
- Started on ceftriaxone 1g IV Q24H empirically

Case 3 AMS Intervention

- Urine culture grew mixed culture with 4 colony types on day 2
- Patient was not experiencing any UTI symptoms
  - No dysuria, polyuria, etc.
- WBC normal and no fevers
- Recommended to discontinue the ceftriaxone on day 2

Case 4

- Received orders for a 75 year old male to receive ertapenem in the outpatient infusion center
- Indication was pseudomonas UTI
- Ertapenem has little to no activity against pseudomonas
- Pseudomonas UTI was resistant to fluoroquinolones

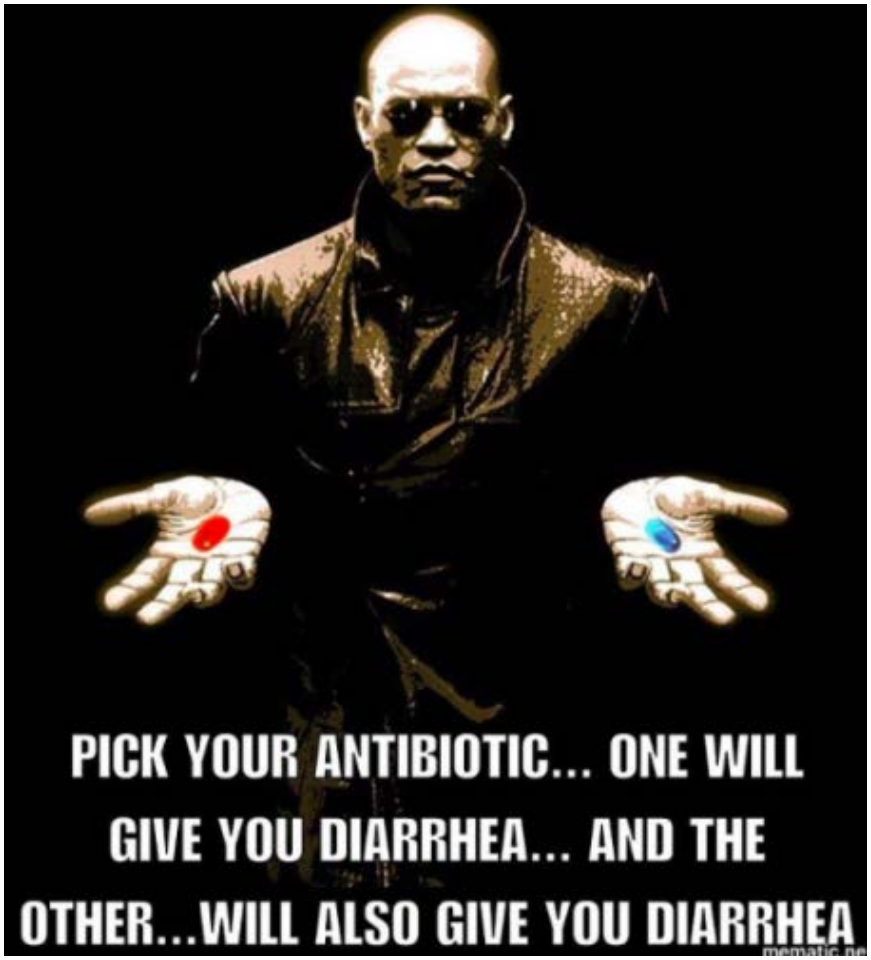
Case 4 AMS Intervention

- Changed antibiotic to cefepime 1g IV Q12H
- Carbapenems should be reserved for ESBL infections and critically ill patients in the majority of cases
- Meropenem has activity against pseudomonas compared to ertapenem that does not

Conclusion

- Antibiotic resistance is a real and present threat
- A formal program to assure appropriate antibiotic use is a CDC recommendation for all types of healthcare facilities
  - Mandatory for Joint Commission accredited
- The specific interventions chosen to implement should be based on facility size and available resources

Questions



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