Antimicrobial Stewardship

Presented By: Neha Nanda, MD
   Associate Professor of Clinical Medicine
   Medical Director of Antimicrobial Stewardship
   Hospital Epidemiologist
   Keck Medicine of USC

Date: November 4th, 2019
Agenda

• Background

• Current Status - How did we get here?

• Efforts to Optimize use - What can we do about it?

• Antimicrobial Stewardship Program

• Future directions
Emma Jones beams a weak smile at her newborn son, cradled in her husband’s arms at a hospital in New York. She is recovering from a severe bacterial infection that she contracted during her Caesarean section. The infection had begun to shut down her organs; doctors put her in a coma and hooked her up to a breathing machine. Ms. Jones is lucky. She is one of a handful of people to have been treated with parvomycin, the first new antibiotic to become available since 2024.
In Western countries the rise in deadly infections has been primarily in hospitals. Back when antibiotics still worked, they were used preventively in almost all operations. In 2015 surgical-wound infections occurred in less than 5% of cases; by 2040 the rate had leapt to nearly 30% for some operations. Caesarean sections, which at their peak made up one-third of births in America in 2019, are now carried out only when there is no other option.
Some hospitals no longer perform elective surgeries, such as hip and knee replacements, because so few patients are willing to take the risk of post-operative infection. But surgeons are busier with amputations. The lack of effective antibiotics means that amputating a limb is sometimes the only way to treat an infected skin ulcer in a diabetic patient.

At a New York Hospital, most heartbreakingly are the paediatric wards. They are full of children recovering from amputations, many as a result of sepsis. “It often starts with just a scrape, a bug bite or a strep throat,” says Dr Velasquez, “things that take-home antibiotics easily cleared up 20 years ago.”
Antibiotic 'apocalypse' warning

By James Gallagher
Health and science reporter, BBC News

The rise in drug resistant infections is comparable to the threat of global warming, according to the chief medical officer for England.

Prof Dame Sally Davies said bacteria were becoming resistant to current drugs fast, and there is a very real possibility of a 'superbug' apocalypse in the future.

Drug resistance is spreading rapidly around the world: in India, there is now a strain of totally drug-resistant TB. "We're doomed if that spreads," she said.

There are some drugs that are still effective. One of the most powerful is Colistin: "It's a last resort antibiotic," said Davies. But its use is also being reduced as bacteria evolve to become resistant to it.

"If you look at the timeline," she said, "we are reaching a point where many of our antibiotics aren't effective anymore."
HOW DID WE GET HERE?
Acute care hospitals

• >50% of patients received antibiotics during hospital stay
• One third of antibiotic prescriptions were inappropriate
• Increasing use of broad spectrum antibiotics
Antimicrobials with Largest Increase in Use 2006-2012

- Vancomycin
- Beta-lactam/inhibitor
- 3rd/4th Gen Cephs
- Carbapenems
In 2016, 270 million antibiotic prescriptions were dispensed in the outpatient areas, i.e., 836 per 1,000 population.

Antibiotic Use in Outpatient Areas

At least 30% of antibiotic prescriptions written in offices and emergency departments are unnecessary.
After Steady Increases, Sales of Medically Important Antibiotics for Use in U.S. Food-Producing Animals Fell for the First Time in 2016


© 2018 The Pew Charitable Trusts
Antibiotic Resistance of *Klebsiella pneumoniae* in Pacific

% Resistant (invasive isolates)

- Aminoglycosides
- Cephalosporins (3rd gen)
- Piperacillin-tazobactam
- Carbapenems
- Fluoroquinolones

Center for Disease Dynamics, Economics & Policy (cddep.org)
Antibiotic Resistance of *Escherichia coli* in Pacific

% Resistant (invasive isolates)

- **Aminoglycosides**
- **Carbapenems**
- **Cephalosporins (3rd gen)**
- **Fluoroquinolones**
- **Aminopenicillins**
- **Piperacillin-tazobactam**

Center for Disease Dynamics, Economics & Policy (cddep.org)
Agenda

• Background

• Current Status - How did we get here?

• Efforts to Optimize use - What can we do about it?

• Antimicrobial Stewardship Program

• Future directions
WHAT CAN WE DO ABOUT IT?
A) MANUFACTURE NEW ANTIBIOTICS

Figure 1. Timeline of antibiotic production.
B) ALTERNATIVE WAYS TO KILL BACTERIA

**Bacteriophages**
- Infect specific bacteria by injecting their genome into the cell, producing new phages, and lysing the cell.

**Polymers**
- Physically shear open bacteria, rather than targeting one specific protein or enzyme in the cell.

**Engineered nanoparticles**
- Can be designed to perform many chemical functions to kill bacteria. For instance, they can form reactive oxygen species that damage the cell membrane.

*Figure 2: New ways to kill bacteria.* Scientists have been developing alternative ways to kill bacteria, such as the use of bacteriophages, polymers, and other kinds of engineered nanoparticles.
C) STEWARDSHIP OF CURRENT RESOURCES (ANTIMICROBIALS)

- This was the fourth time a health issue has been taken up by UN General Assembly (HIV, non-communicable disease and Ebola).
- Centre of Disease Control and Prevention (CDC) recommended all hospitals should have an Antimicrobial Stewardship Program.
ANTIMICROBIAL STEWARDSHIP CONT.

• The Joint Commission required all acute care hospitals to have an Antimicrobial Stewardship Program by Jan 1\textsuperscript{st}, 2017

• All acute care hospitals were expected to meet the 7 Elements of Performance (EPs)
ELEMENTS OF PERFORMANCE FOR ASP

• Leadership commitment from administration
• Single leader responsible for outcomes (ID Physician)
• Single pharmacy leader (ID Pharmacist)
• Antibiotic use tracking
• Regular reporting on antibiotic use and resistance
• Educating providers on use and resistance
• Specific improvement interventions
ASP Interventions

• Prospective audit with intervention and feedback
• Formulary restriction
• Preauthorization requirements
Antimicrobial Stewardship Operations (ASP team and Pharmacists)

- Daily audit with Intervention and Feedback -
  
  - Performed by ASP Pharmacist and ID Attending Physicians (M - F) in the form of daily clinical rounds
  
  - Select drugs reviewed at 72 hours (Meropenem, Vancomycin, Micafungin, Linezolid and Zosyn)

- Daily Rounds with ASP Pharmacist & ID attending
Antimicrobial Stewardship Operations contd.

- Antimicrobial Restriction – (restricted to approval by Infectious Diseases Consult)
  - Daptomycin  - Tigecycline  - Ceftaroline  - Ceftolozane/tazo
  - Isavuconazole - Fidaxomicin - Quinupristin/Dalfopristin
  - Ceftazidime/Avibactam

- Pharmacy will dispense up to 24 hour supply – after hours, weekends

- Unit Pharmacist will inform ID consult of formal consultation
Review of other antimicrobials

- Other antimicrobials include Cephalosporins, Quinolones, Aminoglycosides, Colistin, Polymixin B and Unasyn

- Reviewed at 48-72 hours by unit pharmacists

- Challenging cases reviewed by ID Pharmacist
ASP Overview at Keck Medical Center of USC

**All Antibiotics**

- To ensure timeout at 48-72 hours (for durations >24 hours for OR pharmacy) and assess appropriateness of antibiotic use
- **ALL Pharmacists to discuss challenging antibiotic therapy cases with AST on an as-needed basis**

**Decentralized Pharmacies**
- Vancomycin (ICU rounds)
- Cefepime
- Ceftazidime
- Ceftriaxone
- Ciprofloxacin
- Levofloxacin
- Ampicillin-sulbactam
- Aminoglycosides (amikacin, tobramycin, gentamicin)
- Colistin and polymyxin B

**Antimicrobial Stewardship Team (AST)**

**OR Pharmacy**

**Prior Authorization Required**
- Ceftaroline
- Ceftolozane/tazobactam
- Daptomycin
- Isavuconazonium sulfate
- Tigecycline
- Fidaxomicin
- Quinupristin-dalfopristin

**Daily Review:**
- Carbapenems, piperacillin-tazobactam, aztreonam, linezolid, vancomycin (non-ICU) and micafungin

**For Treatment Durations >24 Hours**
- Cefazolin
- Cefoxitin
- Clindamycin
Social Determinants of Antibiotic Prescribing

- Medical sociologists and anthropologists believe – prescribing a drug is a highly social as well as a clinical act

- Social factors
  - Relationship between Clinicians
  - Emotional response (fear, anxiety)
  - Environmental factors
  - Perception of the problem

Social Determinants of Antibiotic Prescribing contd.

• Social factors need to be considered in implementing stewardship interventions

• Appreciation of environmental and emotional factors

• Relationship between clinicians will be best addressed in collaboration with respective professional societies

• Adoption of Culture of Safety in antimicrobial stewardship
Antimicrobial Stewardship Initiatives at Keck

• Aim: Modification of behavior with positive reinforcement

• Collaboration and Leadership in Antimicrobial Stewardship-CLASS Initiative at Keck and Norris

• Antimicrobial orders are reviewed daily

• Antimicrobial Stewardship team identify providers who are top prescribers, i.e., choose their antibiotics wisely and ensure a drug-bug match
Appreciating efforts for appropriate antibiotic usage

• Monthly communication is sent to providers

• As a part of CLASS initiative, we have recognized and rewarded 26 providers thus far
Appropriate Usage of Antimicrobials

- Carbapenems 84% (baseline) → 96%
- Vancomycin 72% (baseline) → 92%
- Zosyn 74% (baseline) → 83%
Current Status at Keck Medical Center

VRE Rate per 1000 patient days

Appropriate Vancomycin Use
Extended Spectrum beta-lactamase producers

ESBL rate per 1000 patient days

Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 2016 2016 2016 2016 2017 2017 2017 2017 2018 2018 2018 2018

Appropriate Zosyn Use

Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 2017 2017 2017 2017 2018 2018 2018 2018
C. Difficile and Gram Negative Utilization

CDI rate per 1000 patient days

Gram Negative Utilization (DOT per 1000 patient days)
Agenda

• Background

• Current Status - How did we get here?

• Efforts to Optimize use - What can we do about it?

• Antimicrobial Stewardship Program

• Future directions
FUTURE OF ANTIMICROBIAL STEWARDSHIP

• Expansion of ASP in non-hospital settings

• Curtailing use of antimicrobials in food producing animals

• Increasing emphasis on diagnostics

• Incentivizing pharmaceutical companies to manufacture new antimicrobials
“IF WE FAIL TO ACT, WE ARE LOOKING AT AN ALMOST UNTHINKABLE SCENARIO, WHERE ANTIBIOTICS NO LONGER WORK AND WE ARE CAST BACK INTO THE DARK AGES OF MEDICINE”

David Cameron, former UK Prime Minister
THANK YOU

NEHA.NANDA@MED.USC.EDU