Antimicrobial Stewardship: What, Why, and How

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Objectives

- Understand the rationale and goals of antimicrobial stewardship
- Discuss primary drivers of timely and appropriate antimicrobial utilization
- Review strategies and success stories to improve antimicrobial use

Concern is Not New

1928

- ...the microbes are educated to resist penicillin

1945

- ...a thoughtless person is morally responsible for the death of a man who finally succumbs to infection with a penicillin-resistant organism

(Quote to NYTimes, June 26, 1945)
Antimicrobial Stewardship: A Rose by Any Other Name?

- Antimicrobial stewardship refers to strategic efforts to optimize antimicrobial prescribing.

- The “name” has evolved over time:
  - Antibiotic control
  - Antibiotic management
  - Antibiotic stewardship
  - Antibiotic safety

Overall Goal

- Right drug
- Right dose
- Right duration

  Recognize when not needed

Antibiotic Misuse

- Between 20-50% of antibiotic prescriptions are either unnecessary or inappropriate:
  - Given when they are not needed
  - The wrong antibiotic is chosen to treat an infection
  - Continued when they are no longer necessary
  - Given at the wrong dose
  - Broad spectrum agents are used to treat very susceptible bacteria

The Challenge

- Antibiotics are commonly used “just in case”
  - Broad coverage
  - Unclear criteria
  - Uncertain duration

- General perception that there is (almost) no risk and (almost) all benefit to giving an antibiotic

Consequences of Inappropriate Use

- Antibiotics can harm patients
  - C. difficile infections
  - Adverse effects

- Resistance can lead to higher mortality and health care costs

Clostridium difficile Infections

Antibiotic exposure is the single most important risk factor

- Exposure to antibiotics increases the risk of C. diff infection by at least 3 fold for at least a month
- Up to 85% of patients with C. diff infection have antibiotic exposure in the 28 days before infection

Deaths due to *C. difficile* Infections

- 14,000 deaths in the US each year
- Deaths increased 400% between 2000 and 2007
- A stronger (hypervirulent) strain has emerged

Source: CDC National Center for Health Statistics, 2012

Antibiotic-Related Adverse Events

- Antibiotics account for nearly 1 in 5 (19.3%) drug-related adverse events
  - >140,000 ER visits/year due to adverse effect of antibiotics
  - Admission required for 6.1% of adverse events

- Side Effects: Fluoroquinolones (an example)
  - Increased INR
  - QT interval prolongation
  - Tendon rupture
  - Risk of hypo- and hyperglycemia

Antibiotic Use Drives Resistance

For individuals

- Getting an antibiotic increases a patient’s chance of becoming colonized or infected with a resistant organism
- Risk of death higher for resistant infections


Effect of Antibiotic Use in Individuals Susceptible / Resistant

At 1 month

Up to 3 months

Up to 6 months

Up to 1 year

Increased resistance right of line

Higher Mortality due to Resistance

- Methicillin resistant vs. susceptible *S. aureus* (MRSA vs. MSSA)
  - Mortality is nearly double\(^1\,^2\)

- Carbapenam resistant *Klebsiella pneumoniae* (CRKP vs. CSKP)
  - Mortality is 4-5 times higher\(^3\)

\(^1\) CDC. Infect. Dis.36(1),53–59 (2003);
\(^2\) Infect. Control Hosp. Epidemiol.28(3),273–279 (2007);

Antibiotic Use Drives Resistance

Within healthcare settings

- Increasing use of antibiotics increases the prevalence of resistant bacteria in hospitals

**Vancomycin-resistant enterococci (VRE)**

- Increased with Vancomycin Use

**Imipenem-resistant P. aeruginosa**

- Increased with carbapenem use rate

**Antimicrobial Resistance**

- “Imminent crisis in the control of infectious diseases”
- Joint statement on antibiotic resistance from 25 national health organizations and the CDC, 2012
- Antibiotic resistance is among CDC’s top concerns
Reason for Concern: Declining New Antimicrobials in the U.S.

- Drug development takes 10 years
- ~$400-800 million per approved agent
- No new gram (-) coverage in the pipeline

Joint Statement on Antibiotic Resistance from 25 National Health Organization and the CDC

- "The development of resistance is an inevitable byproduct of exposure to antibiotics."
- "...the way we use antibiotics today impacts how effective they will be in the future in other patients."
- "We jointly recognize our collective responsibility to protect to effectiveness of all antibiotic."

The Public Health Perspective

- Antibiotics are a Shared Resource
  - Antibiotic use in one patient can impact the effectiveness in another
  - If everyone does not use antibiotics wisely, we will all suffer the consequences
  - Antibiotics are becoming a scarce resource
Rationale for Antimicrobial Stewardship

- Improve Patient Care and Safety
  - Prevent C. Diff
  - Minimize Adverse Events
- Reduce Resistance
  - Decrease deaths
  - Preserve antimicrobial effectiveness

Additional Benefit: Cost Savings

- Improving antibiotics use saves money
  - Comprehensive programs have consistently demonstrated a decrease in antimicrobial use with annual savings of $200,000 - $900,000
- Cost savings due to:
  - Less pharmacy expenditure
  - Limiting increased costs associated with resistant infections (Length of stay, Readmission)

Cost Savings from Stewardship

- Antimicrobial utilization costs fell 45.9% during program
  - $64,181 per 1000 patient days (PD) to $23,933
- Increased 32.3% within 2 years when program ended
  - $31,850 / 1000 PD
  - Equiv. to $2 million
Antimicrobial Stewardship

How?

Approaches to improving antimicrobial use

Antimicrobial Stewardship “Program”
Test and Refine Specific “Interventions”

Antimicrobial Stewardship Program

- Focus: Hospital-based
- Who (Team):
  - ID physician
  - ID-trained pharmacist
  - Administrative support
- Two Core strategies:
  - Prospective audit with intervention and feedback
  - Formulary restriction and preauthorization

Infectious Diseases Society of America / Society of Healthcare Epidemiology of America Guidelines
Prospective Audit

- An ID physician or pharmacist reviews orders and intervenes with modification of order and feedback to prescriber
- Results in improved use, decreased costs
- Caveats:
  - Time and labor intensive
  - Many settings do not have capacity
  - Providers may not be receptive

Formulary restriction and preauthorization

- Specific antibiotics cannot be ordered without authorization
- Useful in response to healthcare-associated outbreak

Impact of Fluoroquinolone Restriction on Rates of C. difficile Infection (CDI)

Formulary Restriction and Preauthorization

- **Caveats:**
  - Depends who is authorizing use
  - Impact on reducing resistance is not clear
  - Often results in increased use of other antibiotic alternatives

Limitations of the “Program” Approach

- Formally staffed stewardship programs are beyond the reach of most facilities
- Even a really good stewardship program cannot intervene on every patient getting antibiotics
- Programs create a perception that antibiotic stewardship is something that is done for you

Moving Stewardship to the Front Lines

- Every practitioner and each facility should embrace the responsibility to optimize antibiotic use
  - Not “create a stewardship program”
  - But “implement a specific intervention”
- Starting point: Identify specific ideas that people can do to improve antibiotic use
Antibiotic Driver Diagram

- CDC partnered with experts in stewardship and with the Institute for Healthcare Improvement (IHI)
- Broke the process of prescribing and administering antibiotics into discrete steps
- Determined what specific actions could improve each of those steps

Result: A “Driver Diagram and Change Package” for antibiotic use in hospitals

http://www.cdc.gov/getsmart/healthcare/learn-from-others/driver-diagram/introduction.html

What are the ‘Drivers’ of Appropriate Use?

- Appropriate initiation
  - What to treat. What not to treat.
  - Obtaining cultures
  - Choosing based on guidelines and local susceptibility

- Appropriate administration and de-escalation
  - Correct dosing, route, and timing
  - Stop or change based on culture
  - Reconciling antibiotics at all transition in care

‘Drivers’ of Appropriate Use (Continued)

- Leadership Support
- Culture of Quality Improvement
- Stewardship Infrastructure/Champions
- Data monitoring
- Availability of Expertise
Antimicrobial Stewardship

Success Stories

Antimicrobial Stewardship in a Community Hospital

- **Setting:** 535-bed community hospital in Michigan
- **Team:** 2 ID physicians, 3 critical care pharmacists
- **Intervention:**
  - Prospective audit of 8 antimicrobials
    - 3 carbapenems, 2 antifungals, daptomycin, linezolid, tigecycline
  - Pharmacist evaluated each order (M-F)
  - Feedback given to providers
    - Approve, stop, de-escalate
    - Obtain an ID consult

Malani et al. Am J Infect Control. 2012; May 9
Antimicrobial Stewardship in a Community Hospital

- **Clinical Outcomes**
  - An approximate 50% reduction in the odds of developing CDI
  - No increase in mortality at 30 days after discharge
  - No increase in readmission rate

- **Economic Outcomes**
  - Antimicrobial cost per patient-day decreased from $10.16 to $8.81
  - Antimicrobial budget decreased by 15.2% (Total savings of $228,911)
  - There was a 25.4% decrease in use of the target antimicrobials

Malani et al. Am J Infect Control. 2012; May 9

Antimicrobial Stewardship in a Rural Hospital

- **Setting:** 141-bed community hospital in rural Northwest
- **Team:** Pharmacist-led (non-ID), Remotely located ID physician
- **Intervention:**
  - Targeted review of six antimicrobials
  - Piperacillin/tazobactam, imipenem, cilastatin, ertapenem, vancomycin, linezolid, daptomycin
  - Weekly teleconference "rounding" with ID physician
  - Streamlined Therapy
    - Eliminated unnecessary combinations
    - Recommended more narrow spectrum
  - Dose optimization


Antimicrobial Stewardship in a Rural Hospital

- **Outcomes**
  - Number of interventions increased from 2 to 7 per week
  - Streamlining was most common intervention
    - 44% before program, 96% after program began
  - C. diff infections decreased from 5.5 to 1.6 (cases/10,000 pt days)
  - Antimicrobial purchase costs decreased
    - $13,521 per 1,000 pt days (baseline) to
    - $ 9,756 (2010) to
    - $ 6,583 (2011 Quarter 1-2)

Yam et al. Am J of Health-System Pharm. 2012; (69):1142-8
An Antibiotic ‘Time Out’

- The ‘time out’ concept is borrowed from surgery
- A concrete point in time dedicated to reviewing antimicrobial choice and duration
  - Reappraise therapy when more clinical data are available (usually in 48-72 hours)
  - Decide about continuation, narrowing therapy and specify a duration
- Recommended changes are better received and more likely to be followed at a later time point

ICU Antibiotic ‘Time Out’

- Setting: 3 ICUs in tertiary-care medical center
- Person: Pharmacist
- Intervention:
  - Record review of all ICU patient on antibiotics at days 3 & 10 of therapy
    - 3rd gen cephalosporin, carbapenems, p/piao, fluoroquinolone
  - Recommendation for optimization given by progress note and verbal feedback
  - Acceptance of recommendation by ICU attending

ICU Antibiotic ‘Time Out’ Results

- Broad spectrum use decreased
  - 644 to 503 days of therapy/1,000 pt days
  - Cost savings of $95,000/year
- C. diff infections
  - ICU: Decreased 11 to 6 cases
  - Control wards: Increased 87 to 116 cases
- Meropenem susceptibility increased from 78.2% to 83.4% in ICU isolates
Low Hanging Fruit
Transition from IV-to-oral

- VA Hospital reviewed their use of fluoroquinolone by route of administration
  - Of all IV fluoroquinolone prescriptions, 90.9% could have been converted to oral route
  - Avoidable IV fluoroquinolone use accounted for 46.8% of all fluoroquinolone use


Low Hanging Fruit
Eliminate double anaerobic coverage

- Double coverage: metronidazole given with another agent that covers anaerobes
  - Excluding courses given for C. diff, cholangitis, and cholecystitis treatment
  - Reviewed metronidazole use from 2006-2010 at 128 acute-care VA facilities
  - Of 781,708 days of therapy, nearly 1 in 4 orders (23.5%) fulfilled criteria for possible redundancy


Measurement

- Antibiotic Use Module
  - National Healthcare Safety Network (NHSN) module
  - Provides facilities a mechanism to report and analyze antimicrobial use
  - Antimicrobial use is captured by pharmacy information software
    - Launched, but in early stages of uptake
    - Dependent on pharmacy IT vendors to provide service

http://www.sidp.org/Resources/Documents/SIDP_Stewardship_Vendor_List_9_5_12.pdf
Conclusions

Antimicrobial Stewardship

Antimicrobial Prescribing is Complex

- Knowledge in microbiology, infectious diseases, and pharmacology is required
- Information for decisions is available at different time points (and may change)
- Many different people and departments are involved

Prescribing: An Act within a System

An individual may prescribe appropriately but what about...
- New clinical information
- Care transitions and hand-offs

Successful approaches to achieve appropriate use reach beyond the prescriber
Take-Home Points

- Appropriate antimicrobial use is important for healthcare quality and safety

- Many opportunities exist to improve antimicrobial prescribing
  - Education is not enough
  - Stewardship doesn’t need to be a program
  - Small interventions can have big impact

Antimicrobial Stewardship

Where to find resources?

Resources on Get Smart for Healthcare Website – For your use!

- Fact sheets and fast facts
- Slide sets
- Tools to start a program
- Press kit to raise awareness
Thank you!

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For more information please contact Centers for Disease Control and Prevention.

Thank you!

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