

The Rise of Antibiotic Resistance: Is It Too Late?

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DISCLOSURES

•None

THE PROBLEM

- “Antibiotic resistance is one of the biggest public health challenges of our time.” *CDC*
- In US:
 - at least 2 million people get an antibiotic-resistant infection
 - at least 23,000 people die

THE PROBLEM

- **Worldwide**
 - 700,000 people die each year from antibiotic resistant infections
 - Projected to be >10 million/yr in 2050
- **Bacteria exposed to antibiotics quickly develop resistance**
- **Much antimicrobial use in the hospital is either unnecessary or inappropriate**

THE CURRENT ISSUES

- **Antibiotics are effective**

POWER OF ANTIBIOTICS

Disease	Pre-Abx Death Rate	With Abx Death Rate	Change
CAP	~35%	~10%	-25%
HAP	~60%	~30%	-30%
Endocarditis	~100%	~25%	-75%
Meningitis	~80%	<20%	-60%
Skin Infection	11%	<0.5%	-10%

THE CURRENT ISSUES

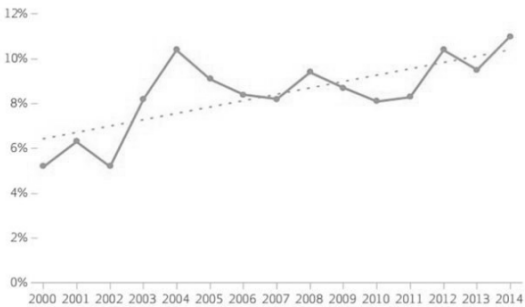
- Antibiotics are effective
- Resistance to antibiotics is growing

ANTIBIOTIC RESISTANCE

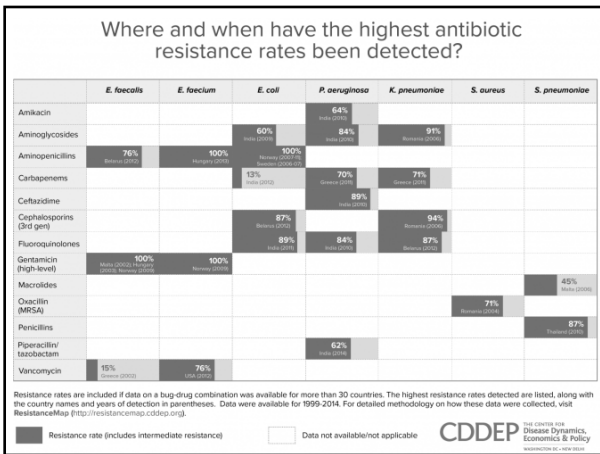
- In US, rates of antibiotic-resistant infections have roughly doubled since 2002

EXHIBIT 2

Percentages of bacterial infections with antibiotic resistance, actual and linear trend, 2000-14



SOURCE Authors' analysis of data for 2000-14 from the Medical Expenditure Panel Survey-Household Component files.



CDC: URGENT THREATS

- *Clostridium difficile*
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant *Neisseria gonorrhoeae*

CDC: SERIOUS THREATS

- Multidrug-resistant *Acinetobacter*
- Drug-resistant *Campylobacter*
- Fluconazole-resistant *Candida*
- ESBL producing Enterobacteriaceae
- Vancomycin-resistant Enterococcus (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa*

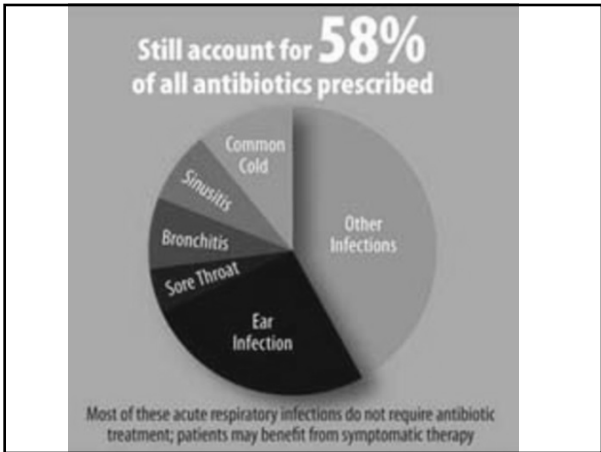
CDC: SERIOUS THREATS

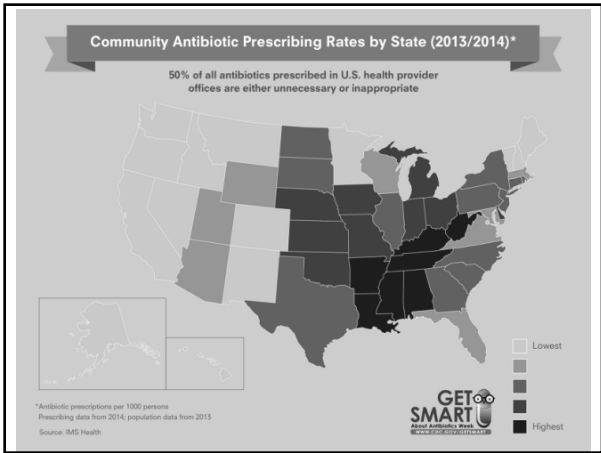
- Drug-resistant *Salmonella*
 - non-typhoidal strains
 - Serotype Typhi
- Drug-resistant *Shigella*
- MRSA
- Drug-resistant *Strep pneumoniae*
- Drug-resistant Tuberculosis

WHY IS THERE SUCH AN INCREASE IN ANTIBIOTIC RESISTANCE?

ECOLOGICAL TIDAL WAVE OF ANTIBIOTIC USE

- In 2014, 15.3 million kg (34 million pounds = 17,000 tons) used in animals
- In 2013, 3.5 million kg (7.7 million pounds = 4,000 tons) used in humans
- Animal use *increased 20%* from 2009-2014

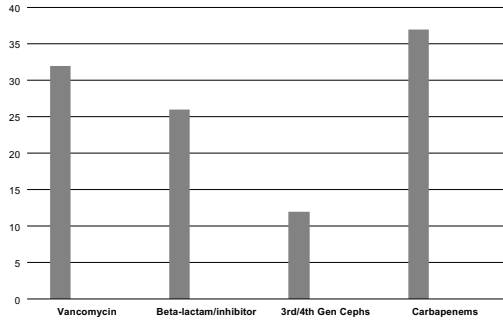




ACUTE CARE HOSPITALS

- Overall rates of antibiotic use in U.S. hospitals did not change from 2006-2012
- >50% of patients received antibiotics during hospital stay
- One third of antibiotic prescriptions were inappropriate
- Increasing use of broad spectrum antibiotics

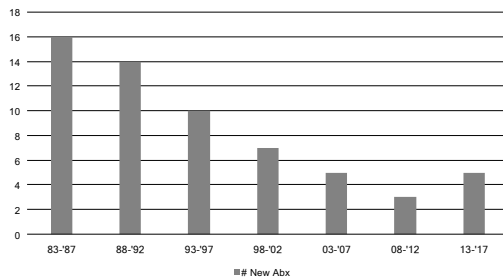
Abx Classes with Largest Increase in Use 2006-2012



THE CURRENT ISSUES

- Antibiotics are effective
- Resistance to antibiotics is growing
- New antibiotics are not keeping up with the demand

NEW ANTIMICROBIAL AGENTS RELEASED IN THE US



ANTIMICROBIAL MARKET FAILURE: CAUSES

- **Science**
 - Low hanging fruit plucked
- **Economics**
 - Antibiotics are not a good investment
 - Short courses
 - Short life span
- **Regulatory**
 - R&D is too risky and expensive

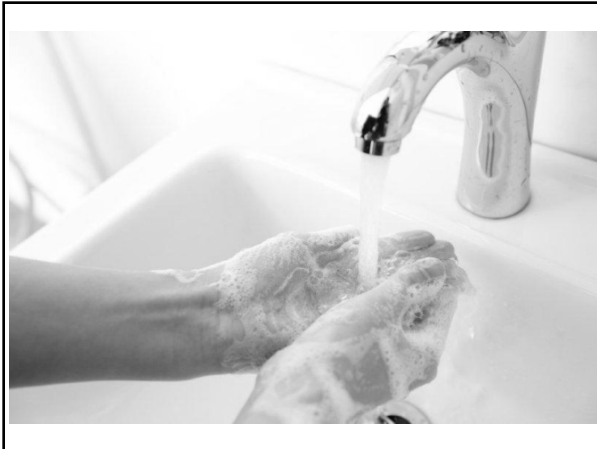
TREATMENT OF HIGHLY RESISTANT GRAM-NEGATIVES

- *New York Times* (11/6/10) report on antibiotic resistant infections, concludes:
“For these infections, we’re back to dancing around a bubbling cauldron while rubbing two chicken bones together”

WHAT CAN WE DO?

**CDC's
4 STRATEGIES TO COMBAT
ABX RESISTANCE**

- Preventing Infections, Preventing The Spread Of Resistance
 - AKA "Infection Prevention and Control"



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**CDC's
4 STRATEGIES TO COMBAT
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- Preventing Infections, Preventing The Spread Of Resistance
 - AKA "Infection Prevention and Control"
- Tracking
- Improving Antibiotic Prescribing And Use
 - AKA "Stewardship"

ANTIBIOTIC 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, *NY Times*, June 1945

ANTIBIOTIC STEWARDSHIP

- We need to recognize that antibiotics are unique among drugs
 - Only they have transmissible resistance
- Those that work today won't work in the future—they must be continually replaced

ANTIBIOTIC STEWARDSHIP

- Every person's use affects everyone else's
- Antibiotics are a shared societal trust—not true of any other type of drug

Antibiotics and Entitlement

No one has a right to waste antibiotics—wasting them hurts everyone.

PRINCIPLES OF ANTIBIOTIC STEWARDSHIP

- Make sure what you're treating is actually an infection!

BASIC PRINCIPLE

- Culture results \neq Infection
 - Do not treat asymptomatic patients
 - Do not send swabs from chronic ulcers for culture!
 - Never send a urine culture without also sending a urinalysis!

PRINCIPLES OF ANTIBIOTIC STEWARDSHIP

- Make sure what you're treating is actually an infection!
- SHORTER = BETTER
 - We are treating for too long

Stewardship: Shorter = Better

Diagnosis	Short (d)	Long (d)	Result
CAP	3 or 5	7, 8, or 10	Equal
HAP	7	10-15	Equal
VAP	8	15	Equal
Pyelonephritis	7 or 5	14 or 10	Equal
Intra-abd	4	10	Equal
AECB	≤ 5	≥ 7	Equal
Cellulitis	5-6	10	Equal
Osteomyelitis	42	84	Equal
Neutropenic Fever	AF x 72 h	+ANC > 500	Equal

**PRINCIPLES OF
ANTIBIOTIC STEWARDSHIP**

- **Make sure what you're treating is actually an infection!**
- **SHORTER = BETTER**
 - We are treating for too long
- **Use narrow-spectrum drugs when possible**

**What is
Antibiotic Stewardship?**

- **Coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting selection of optimal:**
 - Antimicrobial drug regimen
 - Dosage
 - Duration of therapy
 - Route of administration

GOALS OF PROGRAM

- **Improve patient health outcomes**
- **Minimize toxicity and other adverse events**
- **Limit the selection for antimicrobial resistant strains**

What is Antibiotic Stewardship?

- It is NOT “Antibiotic Prevention”
- May reduce excessive costs attributable to suboptimal antimicrobial use

COST SAVINGS

- Effective programs show 22%-36% decrease in antimicrobial use
 - ~\$200,000-\$900,000 annual savings
- Decrease in rates of *C. difficile*
- Decrease in MDROs such as VRE

STRUCTURE OF PROGRAM

- ID Physician
- Clinical Pharmacist with ID training
- Others:
 - Clinical Microbiologist
 - Information Systems
 - Infection Prevention specialists

What is Antibiotic Stewardship?

- **New TJC standards**
 - “New Antimicrobial Stewardship Standards”
 - 8 elements of performance
 - Apply to all acute care hospitals as of January 1, 2017

PROGRAM METHODS

- **Prospective audit with intervention and feedback**
- **Formulary restriction**
- **Preauthorization requirements**

CDC's 4 STRATEGIES TO COMBAT ABX RESISTANCE

- **Preventing Infections, Preventing The Spread Of Resistance**
 - AKA “Infection Prevention and Control”
- **Tracking**
- **Improving Antibiotic Prescribing And Use**
 - AKA “Stewardship”
- **Developing New Drugs and Diagnostics**

**Stewardship:
The Power of Diagnostics**

- Fear drives inappropriate abx use
- Fear based on diagnostic uncertainty
- Rapid diagnostics provide psychological reassurance to overcome the fear

RAPID DIAGNOSTIC TESTS

- Tests that rapidly identify MDROs (MRSA, VRE, etc) after the organism is cultured in the lab

RAPID DIAGNOSTIC TESTS

- 2010 study with rapid PCR to detect MRSA/MSSA in blood cultures
 - Switch from vancomycin to nafcillin or cefazolin was 1.7 days shorter
 - Mean LOS was 6.2 days shorter
 - Hospital costs \$21,387 less per patient

Bauer et al, CID 2010;51:1074-80

RAPID DIAGNOSTIC TESTS

- Tests that rapidly identify MDROs (MRSA, VRE, etc) after the organism is cultured in the lab
- Tests that rapidly identify an organism directly from a patient specimen
 - CSF
 - Sputum
 - Stool

RAPID DIAGNOSTIC TESTS

- Issues with RDTs
 - Need for an infrastructure that can respond to rapid identifications
 - Problems with interpretation of results
 - Many respiratory tract organisms are identified, but their significance and how to manage them is not well defined

WHAT IS THE FUTURE FOR ANTIBIOTIC RESISTANCE?

- New diagnostic tests
- New antimicrobials?
- New and increasing resistance

**Human destiny is bound
to remain a gamble,
because at some
unpredictable time
and in some
unforeseeable manner,
nature will strike back.**

Mirage of Health, Rene Dubos, 1959

**THANK
YOU**

Empty rectangular box for writing.

OBJECTIVES

- Upon completion of this program, the participant should be able to:
 - Describe current practices leading to antibiotic resistance
 - Identify practices to combat the rise of antibiotic resistance
 - Implement treatment strategies that decrease the risk for antibiotic resistance

QUESTION #1

What is the greatest driver for the development of antibiotic resistance?

1. The increase in the number of immunocompromised patients
2. Not giving long enough courses of antibiotics
3. Inappropriate use of antibiotics
4. Lack of new antibiotics for resistant pathogens

QUESTION #1: ANSWER

- What is the greatest driver for the development of antibiotic resistance?
 3. Inappropriate use of antibiotics

QUESTION #2

The main reason that clinicians antibiotics inappropriately is:

1. Fear and diagnostic uncertainty
2. Knowledge of the local antibiogram
3. Evidenced-based guidelines for antibiotic treatment
4. Hospital policies for use of antibiotics

**QUESTION #2:
ANSWER**

The main reason that clinicians antibiotics inappropriately is:

1. Fear and diagnostic uncertainty
