Human Antibiotic Use

Historical Perspective:
A challenge for medicine and public health

U.S. Pork Industry Antibiotic Seminar
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Bottom Line Up Front

• Medical and public health approach to AMR is rapidly evolving
• Emerging science and technology are providing new solutions
• We know enough information to act effectively, but not enough to resolve every argument
• Education without systems change will not work
• Sophisticated communication and effective marketing of ideas are prerequisites to change
• Multisectoral leadership coalescing around core principles is critical
Presentation Outline

• Overview
• A longstanding problem
• Why the problem has been so hard to fix
• New science and technology offers a new approach
• Next steps
Estimates of Burden of Antibacterial Resistance

**European Union**
- Population 500m
- 25,000 deaths per year
- 2.5m extra hospital days
- **Overall societal costs**
  - (€ 900 million, hosp. days)
  - Approx. €1.5 billion per year

**Thailand**
- Population 70m
- >38,000 deaths
- >3.2m hospital days
- **Overall societal costs**
  - US$ 84.6–202.8 mill. direct
  - >US$1.3 billion indirect

**United States**
- Population 300m
- >23,000 deaths
- >2.0m illnesses
- **Overall societal costs**
  - Up to $20 billion direct
  - Up to $35 billion indirect

*Source: ECDC 2007*

*Source: Pumart et al 2012*

*Source: US CDC 2013*

Global information is insufficient to show complete disease burden impact and costs
• Deaths increased 400% between 2000 and 2007.
• A stronger (hypervirulent) strain has emerged.

Antibiotic Use Drives Resistance

Animals get antibiotics and develop resistant bacteria in their guts.

Drug-resistant bacteria can remain on meat from animals. When not handled or cooked properly, the bacteria can spread to humans.

Fertilizer or water containing animal feces and drug-resistant bacteria is used on food crops.

Drug-resistant bacteria in the animal feces can remain on crops and be eaten. These bacteria can remain in the human gut.

George gets antibiotics and develops resistant bacteria in his gut.

George stays at home and in the general community. Spreads resistant bacteria.

George gets care at a hospital, nursing home or other inpatient care facility.

Resistant germs spread directly to other patients or indirectly on unclean hands of healthcare providers.

Patients go home.

Resistant bacteria spread to other patients from surfaces within the healthcare facility.

Simply using antibiotics creates resistance. These drugs should only be used to treat infections.

www.cdc.gov
Antibiotic Use in Hospitals

• About 50% of all hospital patients receive an antibiotic
• Prescribing rates in some hospitals are three times that in other hospitals
• Patients on broad-spectrum antibiotics are three times more likely to get a new infection with a more resistant bacteria
• A 30% decrease in high-risk antibiotics would decrease new *C. difficile* infections by 26%
Antibiotic Use in Outpatients

- Antibiotics are prescribed in about 10% of all outpatient visits (>100 million visits/year)
- Over 20% of all pediatric visits result in an antibiotic prescription (~50 million prescriptions/year)
- $10.7 billion per year spent on antibiotics
  - $6.5 b outpatient
  - $4.2 b inpatient ($3.6 b hospital, $0.4 b long-term care)
- Despite improvements, about 50% of visits for acute RTI (common cold) still result in antibiotic prescriptions
Dwindling therapeutic options:
A decline in new antibiotics in recent years

Goal: Slow emergence and spread of AMR to buy time for development of new therapies

Consumers and the Media are Engaged
Many Action Plans
A longstanding problem

The status quo has been resilient
Last week, at the annual meeting of the American Association for the Advancement of Science in San Francisco, microbiologist Alexander Tomasz of Rockefeller University warned that many common bacteria are evolving resistance to more and more antibiotics. As a result, we are facing "nothing short of a medical disaster." he said.
A longstanding problem

“Indiscriminate prescribing of antibiotics, whether inside or outside hospitals, adds needlessly to the mounting pressures for selection of resistant organisms”


“At the present time, hundreds of thousands of patients may be unnecessarily exposed to the hazards of antibiotics because of their inappropriate use”

Simmons HE, Stolley PD. This is Medical Progress? Trends and Consequences of Antibiotic Use in the United States. JAMA. 1974
A longstanding problem

Alternatively, it may be possible to discover new antibiotics that would eradicate, or at least inhibit, species that have been emerging and spreading and have been the cause of antibiotic-resistant infections. The spread of resistant species also calls for the development of technics of prevention; such methods have, thus far, been either inadequate or not pursued with sufficient vigor.
Timeline

• ~ 3 billion years ago: Bacteria appear

• ~2 – 3 billion years ago: Bacteria make antibiotics; bacteria develop resistance to antibiotics

• 105 years ago: Arsenical compounds used to treat syphilis

• 87 years ago: Discovery of penicillin

• 80 years ago: Sulfa drugs used to treat infection

• 75 years ago: IV penicillin used to treat infection
Why the problem has been hard to fix

The status quo has been resilient
Why the problem seems hard to fix

• AMR is the most complex problem in public health; *but we know enough to act*

• Bacterial resistance spreads easily; *but we know how to control it*

• Existing information systems and prevention programs are inadequate; *but we know how to fix them*

• The use of antibiotics is poorly rationalized; *and efforts to improve prescribing can be greatly enhanced*

• Communication about the problem has been confused, confusing and contradictory; *but we can be clearer about what we know and what we don’t*
AMR spreads at the speed of jet travel
Data systems for tracking AMR and AU are inadequate all over the world

• Lack of consistent definitions

• Inadequate understanding of epidemiologic priorities

• Proprietary demands to withhold vital information and control data

• Conflating clinical and public health needs

• Lack of laboratory standardization

• Limitations in laboratory capacity

• Limited informatics and IT capacity

• Conflating disease surveillance and quality metrics

Current infection control is inadequate: Infected and colonized patients move widely and easily between healthcare settings.

Inadequate Infection Control Leads to Rapid Spread

Antibiotic overuse in human medicine: Variations in prescribing demonstrates overuse

Antibiotic prescribing per 1000 persons, US, 2011

Hicks. Clin Infect Dis. 2015;60:1308
CAREFUL ANTIBIOTIC USE

Make promoting appropriate antibiotic use part of your routine clinical practice

PRACTICE TIPS

When parents ask for antibiotics to treat viral infections:

- Explain that unnecessary antibiotics can be harmful.
  Tell parents that based on the latest evidence, unnecessary antibiotics CAN be harmful, by promoting resistant organisms in their child and the community.

- Share the facts.
  Explain that bacterial infections can be cured by antibiotics, but viral infections are not.
  Explain that treating viral infections with antibiotics to prevent bacterial infections does not work.

- Build cooperation and trust.
  Convey a sense of partnership and don't dismiss the illness as 'just a viral infection.'

- Encourage active management of the illness.
  Explicitly plan treatment of symptoms with parents. Describe the expected normal time course of the illness and tell parents to come back if the symptoms persist or worsen.

- Be confident with the recommendation to use alternative treatments.
  Prescribe antacids and decongestants, if appropriate.
  Emphasize the importance of adequate nutrition and hydration.
  Consider providing “care packages” with non-antibiotic therapies.

Create an office environment to promote the reduction in antibiotic use.

- Talk about antibiotic use at 4 and 12 month well child visits.

The AAP Guidelines for Health Supervision III (1997) now include counseling on antibiotic use as an integral part of well-child care.

SIX SIMPLE AND SMART FACTS ABOUT ANTIBIOTIC USE

1. Antibiotics are life-saving drugs
   Using antibiotics wisely is the best way to preserve their strength for future bacterial illnesses.

2. Antibiotics only treat bacterial infections
   If your child has a viral infection like a cold, talk to a doctor or pharmacist about symptom relief. This may include over-the-counter medicine, a humidifier, or warm liquids.

3. Some ear infections DO NOT require an antibiotic
   A doctor can determine what kind of ear infection your child has and if antibiotics will help. The doctor may follow expert guidelines to wait a couple of days before prescribing antibiotics since your child may get better without them.

4. Most sore throats DO NOT require an antibiotic
   Only 1 in 5 children seen by a doctor for a sore throat has strep throat, which should be treated with an antibiotic. Your child’s doctor can only confirm strep by running a test.

5. Green colored mucus is NOT a sign that an antibiotic is needed
   As the body's immune system fights off an infection, mucus can change color. This is normal and does not mean your child needs an antibiotic.

6. There are potential risks when taking any prescription drug
   Antibiotic use can cause complications, ranging from an upset stomach to a serious allergic reaction. Your child's doctor will weigh the risks and benefits before prescribing an antibiotic.

Antibiotics Aren’t Always the Answer

National Center for Immunization and Respiratory Diseases
Division of Bacterial Diseases

http://www.cdc.gov/getsmart/week/educational-resources/index.html
Interventions to improve physicians’ prescribing can be effective

Decreasing antibiotic prescribing for acute respiratory tract infections in children

But the effects are transient

Gerber. JAMA. 2014;312:2569-70
Emerging science and technology are providing new solutions

• Take advantage of advances in informatics, human and bacterial genomics, epidemiology and statistics, behavioral psychology, and in communication and information science

• Take advantage of growing awareness and a world-wide focus on the problem

• Take advantage of a better understanding of AMR complexity and the need for broad-based and inclusive collaboration
Genomics and bioinformatics--
Powerful new tools that can:

- Better diagnostics: identify resistance very rapidly for both clinical and public health purposes
- Conduct public health surveillance of urgent and serious threats in near real-time
- Follow the evolution of bacterial strains in near real-time
- Trace patterns of spread of AMR bacteria with great precision
- Focus on epidemiologic priorities for intervention and to evaluate and improve interventions
The microbiome

A tool for promoting antibiotic safety and personalizing risk:

• The “ecological community of …microorganisms that literally share our body space”
• 90% of all the cells associated with the human body; the other 10% are human cells

Personalizing Excess Prescribing Risks: avoiding the “tragedy of the commons”

- Disruption of the human microbiome
  - Associated conditions: susceptibility to infection, obesity, IBD, asthma, allergies, neurological illness
  - *C. difficile* infection: >250,000 infections, 14,000 death/yr

- Antibiotic-related adverse events (side effects, allergies, drug-drug interactions)
  - 19.3% of all ED visits for drug-related AE
  - >38,000 pediatric ED visits/yr for abx-related rxns

“Nudged” Prescriber Behavior

- Using EHRs, informatics can be used to implement behavioral approaches (computer-assisted physician order entry)
  - Real-time feedback to each provider at the time of prescribing
  - Restructure online menus to match local conditions
  - Tailor messages and channels to each audience—”optimal prescribing”

“Optimal prescribing” as a complement to “antimicrobial stewardship”

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<th>Optimal prescribing</th>
<th>Antimicrobial stewardship</th>
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<td>• Focuses on the act of prescribing in the moment of prescribing</td>
<td>• Focuses on a broader, distantly realized public good</td>
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<td>• Focuses on immediate risks and benefits to the patient being treated</td>
<td>• Focuses on societal benefits</td>
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<td>• Communicates personal and professional accountability</td>
<td>• Communicates a shared responsibility, including outside of medicine</td>
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<td>• Invokes patient safety</td>
<td>• Appeals to respect for the common welfare</td>
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<td>• Outcomes can be measured directly</td>
<td>• Outcomes require additional measurement</td>
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Improve Infection Control to Prevent Transmission: Local solutions

- Adopt outcome-focused, real-time, data-driven continuous rapid cycle improvement in all settings
  - The precise, ideal menu of interventions for each setting (from hospital to community) will vary and may be hard to predict in advance

- Implement a regional approach
  - Individual facilities can control AMR only to a certain point
  - Public health and health care must collaborate to assure availability and sharing of data and technical assistance
An Ongoing National Intervention to Contain the Spread of Carbapenem-Resistant Enterobacteriaceae

Monthly incidence of carbapenem-resistant Enterobacteriaceae detected by clinical culture per 100 000 patient-days, January 2005–May 2008.

The Value of Statistical Modeling

- Economic impact of AMR
  - Micro vs macroeconomics -- €900 million vs $55 billion vs $10 trillion
- Prioritizing interventions
  - Where: hospitals, nursing homes, community
  - Which ones: infection control, antibiotic management
- New antibiotic development
  - Which bacteria
  - Which incentives
Comparing antibiotic use in humans and animals in the EU: corrected by biomass

Controversies

We need to prioritize action over argument

- Diagnostics: Genomic testing vs traditional AST
- New antibiotic development: Delinkage vs regulatory reform, etc.
- Surveillance: PH surveillance vs quality improvement, counting cases vs tracking trends
- Interventions: Stewardship vs decontamination vs screening + isolation, etc.
- Implementation: Payment reform vs regulation vs public-private partnership vs public reporting
- Etc.
Summary: From action plans to action (1)

Enhance measurement methods and metrics:

• Use informatics, genomics, diagnostics to make (near) real-time data and information available to decision-makers from doctors’ offices to national health agencies.

• Use statistical modeling to open up the “black box” of complex systems where inputs (actions to prevent emergence and spread of AMR) are transformed into outputs (decreased AMR infections).
Summary: from action plans to action (2)

Change individual and organizational behaviors:

• Use emerging sciences and sophisticated communications and marketing tools to personalize risks to patients and accountability to prescribers

• Encourage outcomes-based programs under local control with public access to data

• Facilitate implementation and management of interventions at multiple levels—medical practice, healthcare facility, community, state
Thank you.

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