One Health Antibiotic Stewardship: A Collaborative Approach

Ruth Lynfield, MD
State Epidemiologist and Medical Director, Minnesota Department of Health
“For most of the infectious diseases on the wards of Boston City Hospital in 1937, there was nothing to be done beyond bed rest and good nursing care.”

Lewis Thomas. *The Youngest Science*
“I remember the astonishment when the first cases of pneumococcal and streptococcal septicemia were treated in Boston in 1937. The phenomenon was almost beyond belief. Here were moribund patients, who would surely have died without treatment, improving in their appearance within a matter of hours of being given the medicine and feeling entirely well within the next day or so....we became convinced, overnight, that nothing lay beyond reach for the future. Medicine was off and running.”

Lewis Thomas. *The Youngest Science*
## The Power of Effective Antibiotics

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pre-Antibiotic Death Rate</th>
<th>Death with Antibiotics</th>
<th>Change in Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Pneumonia¹</td>
<td>~35%</td>
<td>~10%</td>
<td>-25%</td>
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<tr>
<td>Hospital Pneumonia²</td>
<td>~60%</td>
<td>~30%</td>
<td>-30%</td>
</tr>
<tr>
<td>Heart Infection³</td>
<td>~100%</td>
<td>~25%</td>
<td>-75%</td>
</tr>
<tr>
<td>Brain Infection⁴</td>
<td>&gt;80%</td>
<td>&lt;20%</td>
<td>-60%</td>
</tr>
<tr>
<td>Skin Infection⁵</td>
<td>11%</td>
<td>&lt;0.5%</td>
<td>-10%</td>
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</table>

By comparison…treatment of heart attacks with aspirin or clot busting drugs⁶ -3%


B. Spellberg
Emergence of Antibiotic Resistance

Susceptible Bacteria

Mutations

Resistance Gene Transfer

Resistant Bacteria

New Resistant Bacteria
Selective Pressure

- When bacteria are exposed to an antibiotic, susceptible cells die
- Those that are resistant (or acquire resistance through mutation, genetic rearrangement or acquisition of genes) survive
- With reduced competition from susceptible bacteria, resistant bacteria thrive and outcompete others
- Antibiotics also impact “normal flora” which otherwise could limit the expansion of pathogens
  - Non-pathogenic but resistant bacteria can impact the microbial niche by increasing the reservoir of resistance genes
The new generation of resistant infections is almost impossible to treat

Jerome Groopman, August 11, 2008

In August, 2000, Dr. Roger Wetherbee, an infectious-disease expert at New York University’s Tisch Hospital, received a disturbing call from the hospital’s microbiology laboratory. At the time, Wetherbee was in charge of handling outbreaks of dangerous microbes in the hospital, and the laboratory had isolated a bacterium called *Klebsiella pneumoniae* from a patient in an intensive-care unit. “It was literally resistant to every meaningful antibiotic that we had.”
US woman killed by superbug resistant to every available antibiotic

Notes from the Field

Pan-Resistant New Delhi Metallo-Beta-Lactamase-Producing Klebsiella pneumoniae — Washoe County, Nevada, 2016

Lei Chen, PhD1; Randall Todd, DrPH1; Julia Kiehlbauch, PhD2-3; Maroya Walters, PhD4; Alexander Kallen, MD4

On August 25, 2016, the Washoe County Health District in Reno, Nevada, was notified of a patient at an acute care hospital with carbapenem-resistant Enterobacteriaceae (CRE) that was resistant to all available antimicrobial drugs. The specific CRE, Klebsiella pneumoniae, was isolated from a wound specimen collected on August 19, 2016. After CRE was identified, the
‘Superbugs’ Kill India’s Babies and Pose an Overseas Threat

By GARDINER HARRIS  DEC 3, 2014

“India’s dreadful sanitation, uncontrolled use of antibiotics and overcrowding coupled with a complete lack of monitoring the problem has created a tsunami of antibiotic resistance that is reaching just about every country in the world,” said Dr. Timothy R. Walsh, a professor of microbiology at Cardiff University.
“Each year in the United States, at least 2 million people become infected with bacteria that are resistant to antibiotics and at least 23,000 people die each year as a direct result of these infections. Many more people die from other conditions that were complicated by an antibiotic-resistant infection.

The total economic cost of antibiotic resistance to the U.S. economy has been difficult to calculate. Estimates vary but have ranged as high as $20 billion in excess direct healthcare costs, with additional costs to society for lost productivity as high as $35 billion a year (2008 dollars).”
"... 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 1945
Antibiotic Stewardship

- Process of improving antibiotic use by using coordinated actions
- Recognizes importance of antibiotics
  - Needed in human and animal health
  - Shared resource
- Focused on optimizing use, not withholding antibiotics
- Goal is to optimize:
  - Drug. Choosing the right antibiotic for the infection and patient
  - Dose. Giving the right amount of antibiotic
  - Duration. Giving the antibiotic for the right amount of time
The Stewardship Balancing Act

Unintended consequences

- Toxicity, adverse drug effects
- Risk of developing severe infection, e.g., *C. difficile*
- Emergence of resistance
- Financial costs

Unintended consequences

- Untreated, more severe infection
- Disease spread in population
- Diagnostic uncertainty
- Negative patient/client relationships
- Potential litigation
Leadership Commitment: Dedicating resources

Accountability: Single leader

Drug Expertise: Single pharmacist leader

Action: Implementing at least one recommended action
  - Systematic evaluation of ongoing treatment need after 48hr (“antibiotic time out”)
  - Pharmacy-driven interventions (e.g., authorization, automatic dose adjustment)
  - Infection-specific interventions (e.g., community-acquired pneumonia, UTI)

Tracking: Monitoring antibiotic prescribing and resistance patterns

Reporting: Regular reporting on antibiotic use and resistance
  - For doctors, nurses, relevant staff

Education: Informing clinicians about resistance, optimal prescribing
Examples of Antibiotic Stewardship Actions in Human Healthcare

• Pharmacy-level interventions
  • Antibiotic formulary use
  • Required pharmacist consultation, approval for last-resort drugs
  • Audit process for restricted antibiotics

• Processes to optimize prescribing
  • Antibiotic review within 48–72 hours (“time-out”)
  • Antibiogram use
  • Audit of bug-drug mismatches
  • Identify opportunities for parenteral to enteral conversion and de-escalation

• Focus on protocols for clinical syndromes
  • Algorithm use (e.g., criteria for initiation of antibiotics)
  • Order set application
  • Audit of evidence-based practice guidelines
One Health is the integrative effort of multiple disciplines working locally, nationally and globally to obtain optimal health for people, animals and the environment. Together, the three make up the One Health triad, and the health of each is inextricably connected to the others in the triad. Understanding and addressing the health issues created at this intersection is the foundation for the concept of One Health.

- American Veterinary Medical Association

https://www.avma.org/KB/Resources/Reference/Pages/One-Health.aspx
Why a One Health Approach for Antibiotic Stewardship?

In order to fully understand and approach antibiotic resistance and antibiotic stewardship effectively in Minnesota we need a multi-disciplinary approach.
History of Antibiotic Stewardship in Minnesota Healthcare

Minnesota Department of Health (MDH) and partners

- Minnesota Antibiotic Resistance Collaborative (early 2000s)
  - Guidance for outpatient and long-term care
  - Cough and cold kits
- Antibiotic stewardship conferences (2012-14)
- MDH guidance and tools (2012-2014)
  - Acute care stewardship toolkit
  - Long-term care stewardship toolkit
History of Antibiotic Stewardship in Animal Health

- Quality assurance programs
  - Residue prevention
- USDA Veterinary accreditation modules
- Judicious antibiotic usage guidelines developed by AVMA, allied veterinary organizations
- AVMA Task Force for Antimicrobial Stewardship in Companion Animal Practice
What About the Environment?

• Antibiotic residues found in groundwater and surface waters
  • Complex mixtures of antibiotics and metabolites
  • Urban and agricultural pathways to contamination

• Outstanding questions
  • How do antibiotics in environment influence overall resistance?
  • How does antibiotic exposure impact ecology and human health?
  • How can we mitigate impact on environment?
One Health Antibiotic Stewardship Collaborative

- Multi-partner initiative to address antibiotic use
- Inter-agency approach by government
  - MDH, MN Board of Animal Health, MN Ag, MN Pollution Control Agency
- Stakeholders from academia, human and veterinary clinical practice, professional and industry associations, healthcare systems, producer organizations
Fall 2015

- Steering Committee prepares summit materials
- Prepare participants with homework

January 19, 2016

- Summit
- Develop consensus on strategic plan framework

Winter/Spring 2016

- Disseminate Summit outcomes
- Form technical workgroup
- Refine strategic plan and assess resources

Summer 2016

- Launch strategic plan
- Actively seek out resources
- Begin to implement
Mission

• Provide a collaborative environment to promote judicious antibiotic use and reduce the impact of antibiotic-resistant pathogens of human, animal, and environmental health importance

Vision

• Minnesota leaders in human, animal, and environment health will work together to raise awareness and change behaviors to preserve antibiotics and treat infections effectively
## Common Wants and Fears Around Stewardship and Resistance

<table>
<thead>
<tr>
<th><strong>WANTS</strong></th>
<th><strong>FEARS</strong></th>
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<tbody>
<tr>
<td>Collaboration, common goals, recognize alignment &amp; differences</td>
<td>Ineffective antibiotics, untreatable infections, death, adverse effects</td>
</tr>
<tr>
<td>Decisions made on unbiased data, not politics or public perception</td>
<td>Reactionary decisions without sound science, incorrect assumptions</td>
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<tr>
<td>Community understanding and informed participation</td>
<td>Overregulation replacing careful medical assessment</td>
</tr>
<tr>
<td>Minimize environmental contamination for safe food and water supply</td>
<td>Negative impact on environment and ecosystem</td>
</tr>
</tbody>
</table>
Minnesota Health Commissioner Dr. Ed Ehlinger announces Friday, July 1, 2016, that four state agencies are working together on the problem of overuse of antibiotics. 

(Forum News Service photo by Don Davis)
Strategic Plan Goals

• Promote understanding of one health antibiotic stewardship
  • Share resources through online platform
  • Support public engagement on antibiotic use
  • Hold exchanges among practitioners in different fields

• Improve human antibiotic stewardship
  • Make tools available to track antibiotic use across continuum of care
  • Set state human health antibiotic goals
  • Develop honor roll recognition system for health care facilities
Strategic Plan Goals (cont.)

- Improve animal antibiotic stewardship
  - Communicate national antibiotic goals for animal stewardship
  - Promote animal agriculture best practices
  - Increase access to stewardship resources for companion animal medicine
  - Facilitate public engagement on animal stewardship
- Develop “antibiotic footprint” tools
  - Understand impact of antibiotics in the environment
  - Help prescribers make choices to decrease their own antibiotic footprint
One Health Antibiotic Stewardship
Director:
Together, we keep antibiotics working in Minnesota

Amanda Beaudoin, DVM, PhD
Director of One Health Antibiotic Stewardship,
Minnesota Department of Health
Amanda.Beaudoin@state.mn.us
One Health Antibiotic Stewardship Collaborative: Structure

Four technical work groups

• One Health Workgroup: To promote understanding of One Health antibiotic stewardship across disciplines
  • Experience sharing and exchanges among practitioners in human, animal, and environmental health, public outreach

• Human Antibiotic Stewardship Workgroup
  • Develop goals, roadmap, incentives (honor roll) for stewardship programs in healthcare facilities
• Animal Antibiotic Stewardship Workgroup
  • Support stewardship efforts and agricultural best practices, producer quality assurance programs, data on actual on-farm use, companion animal stewardship resources

• Antibiotic Footprint Workgroup: to develop an antibiotic footprint tool and improve understanding of environmental considerations
  • Tool to describe antibiotic use and environmental impacts; advocacy for environmentally friendly antibiotic disposal
Antibiotic Stewardship: How We Talk About It

- Stewardship is the process of improving antibiotic use
- Recognizes importance of antibiotics
  - Essential to human healthcare and veterinary medicine
  - Shared resource; optimizing use benefits everyone
- All antibiotic use leads to resistance
  - There is some contribution from every sector using antibiotics
  - Focused on optimizing use, not eliminating antibiotics
• Human, animal, and environmental health are inseparable
• Lack of “proof” of harm is not an argument for irresponsible use
• Greater abuse in other disciplines is not an argument for injudicious use in yours
• Acknowledgement that there are unreasonable critics!
  • Exaggerate harms
  • Fail to acknowledge real benefits
• Behavior change is key
Antibiotic Stewardship: How We Talk About It (cont.)

- 5 D’s of judicious usage common to all fields:
  - Diagnosis. Using an antibiotic only when clinically indicated
  - Drug. Choosing the right antibiotic for the infection and patient
  - Dose. Giving the right amount of antibiotic
  - Duration. Giving the antibiotic for the right amount of time
  - De-escalation. Switching drug or route to better target treatment
Challenges to Stewardship in All Fields

• Competing priorities
  • Good of the whole vs. individual patients, animals?
  • Definition of “optimal”, “judicious”, “appropriate”

• What are the “low-hanging fruit” for stewardship in each field?

• How can we set goals and identify progress without data?

• How can we get data on antibiotic use?

• How can we design meaningful research?

• Communication across fields and with the public
Statewide Assets

• Excellent working relationship among state agencies
• Academic excellence in antibiotic resistance research
• Large and progressive livestock industries
• Advanced and engaged healthcare industry and quality organizations
• Academic Health Center with medicine, veterinary medicine, dentistry, pharmacy, public health
• Representation on Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PAC-CARB)

One Health collaborative approach
Antibiotic Resistance and Stewardship for Minnesota’s Dental Professionals

Room for Improvement in Dental Antibiotic Prescribing

- Dentists prescribe approximately 10% of all antibiotics in U.S. outpatient settings.
- Dentists most commonly prescribe penicillins. This is consistent with dental prescribing guidelines. However, dentists also prescribe a large amount of broad-spectrum antibiotics, including macrolides (e.g. azithromycin) and quinolones (e.g. ciprofloxacin).

- A 2015 study conducted in Minnesota revealed that dentists prescribe in more situations than recommended by professional practice guidelines.

Other Consequences of Antibiotic Use

- Antibiotics have an effect on healthy gastrointestinal bacteria that can last after patients have finished the prescription. This leaves patients at risk for Clostridium difficile disease, a cause of antibiotic-related diarrhea. C. difficile is a difficult to eradicate pathogen.
- Antibiotics cause a risk of side effects, including allergies and organ damage.
- Because of increasing resistance, some of the only antibiotics available to treat infections caused by resistant bacteria must be given intravenously and have a risk of toxic effects.

The Truth About: MILK AND ANTIBIOTICS

- Truth: It is against the law to sell milk with antibiotics.
- Milk cannot be tested positive in less than 2 out of every 10,000 tanks in the U.S. (National Milk Drug Residue Database). Milk that has antibiotics is discarded.
- When a cow is treated with antibiotics, farmers follow federal guidelines on how long they must discard the milk in order to prevent drug residues in milk.
- If a drug label does not say how long to discard milk, the farmer must work with a veterinarian to determine the proper time.
- All sources of milk undergo testing by the Minnesota Department of Agriculture to ensure it meets antibiotic safety standards.
- Samples are tested every 30 days. In the event of a positive test, the milk is discarded.
- Scientists and government officials review and approve the tests used to detect antibiotics in milk. These experts make sure the tests are able to detect even very low levels of milk.
- Just like people, cows get infections that need to be treated with antibiotics.
- When a cow is treated with antibiotics, the farmer must dispose of that cow’s milk until tests show there is no evidence of antibiotics in the milk.
- Federal guidelines mandate the minimum amount of time that a cow’s milk must be discarded after the cow receives the last antibiotic treatment.

MINNESOTA

One Health Resource Library: for Animal Healthcare and Agriculture

Antibiotic stewardship is important to animal health and the safety of food produced. Although antibiotics remain a necessary tool to manage infectious disease in animals and livestock, using antibiotics responsibly is essential to reducing antibiotic-resistant bacteria and protecting the health and wellbeing of animals and humans. Use of best animal management practices such as vaccine use, parasite control, stress reduction, environmental management, and proper nutrition management can also reduce the need for antibiotics. To promote the effective implementation of antibiotic stewardship, the Minnesota Department of Agriculture compiled a list of resources for veterinarians, producers, and animal health care and agriculture according to companion animal or beef, dairy, or poultry.
Minnesota State Fair
Eco-Experience Building,
2017
Exchanges: One Health Workgroup Field Trip - Antibiotic Stewardship Rounds, Infectious Disease Pharmacy, Acute Care Hospital
Exchanges: One Health
Workgroup Field Trip - Dairy Farm
Exchanges: One Health Workgroup Field Trip - Wastewater Treatment Plant (December 2017)
Minnesota One Health Antibiotic Stewardship Collaborative

What is One Health Antibiotic Stewardship?

Antibiotics are powerful tools for fighting and preventing infections. However, widespread use of antibiotics has resulted in an alarming increase in antibiotic-resistant infections. Antibiotic stewardship consists of coordinated interventions that promote judicious antibiotic use and reduce the impact of antibiotic-resistant pathogens. A One Health approach recognizes that human, agricultural, and companion animal, and environmental health are interconnected, and issues such as antibiotic stewardship require a collaborative effort across multiple disciplines. We believe that a One Health approach will create an informed public and professionals that can communicate, and practice a more holistic approach to antibiotic stewardship.
Minnesota One Health Partners

• Abbott Northwestern Hospital

• Allergan
  Allina Health
  Association for Professionals in Infection Control and Epidemiology – Minnesota
  Blue Cross Blue Shield
  Children’s Hospitals and Clinics of Minnesota
  Emergency Physicians Professional Association - Minnesota
  HealthEast
  HealthPartners
  Hennepin County Medical Center

• Hormel Foods
  Land O’Lakes
  Leading Age Minnesota
  M Health
  Mayo Clinic
  Merck Research Labs
  Metropolitan Council
  Minnesota Association of Physician Assistants
  Minnesota Beef Council
  Minnesota Board of Animal Health
  Minnesota Board of Medical Practice
  Minnesota Board of Veterinary Medicine
  Minnesota Department of Agriculture
  Minnesota Department of Health

• Minnesota Department of Natural Resources

• Minnesota Farm Bureau
  Minnesota Farmers Union
  Minnesota Hospital Association
  Minnesota Medical Association
  Minnesota Milk Producers Association
  Minnesota Nurse Practitioners
  Minnesota Pollution Control Agency
  Minnesota Pork Board
  Minnesota State Cattlemen’s Association
  Minnesota Turkey Growers Association
  North Dakota State University
  Park Nicollet

• Pipestone Veterinary Services

• Rock Veterinary Clinic
  Regions Hospital
  Sanford Health
  St. Paul Infectious Disease Associates, Ltd.
  Stratis Health
  University of Minnesota
  University of St. Thomas
  US Geological Survey
  Veterans Affairs Healthcare System
  Zoetis Animal Health
Parting Thoughts

“It is not in the stars to hold our destiny but in ourselves”

William Shakespeare

One Health, One World let’s keep it intact!!