Antimicrobial Stewardship/Treatment Optimization – Humans

John Conly CM MD CCFP FRCPC FCAHS FAMMI FACP FIDSA FSHEA
Professor of Medicine, Microbiology, Immunology & Infectious Diseases
Medical Director IPC and Antimicrobial Stewardship, Calgary and Area
University of Calgary and Alberta Health Services, Calgary, Canada

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AMR: A One Health Approach Graduate Online Course
I acknowledge the traditional territories of the Blackfoot and Treaty 7 peoples including the Siksika, Piikuni, Kainai, Tsuut’ina, and Stoney Nakoda First Nations. Calgary is also home to the Metis Nation of Alberta, Region III.

Source: https://www.ucalgary.ca/indigenous
Faculty/Presenter Disclosure/Acknowledgements

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  - Honoraria: None
  - Speakers' Bureaux, advisory boards: Received funding to attend a meeting on HAI from the CDC and bioMerieux
  - Grants/Clinical Trials: Local PI for the STRIVE S. aureus vaccine trial spinal surgery (Pfizer) and holds grants from CIHR, AI-HS, PHAC, AH, AHS, EDT.
  - Patents, royalties: None
  - Investments in health organizations: None
  - Other influential affiliations: Member of committees with PHAC, WHO and CIHR
Objectives

- Outline the frequency and impact of antibiotic use
- Review the general background on antibiotic stewardship
- Describe the evidence base to support stewardship as a means to improve patient safety and quality of care
- Provide the Canadian context for stewardship and give examples of stewardship in Canada

Note: Primary learning outcome relates to limiting antimicrobial misuse in various contexts
True or False or…. Not sure?

- Multidrug resistant (MDR) microbes are resistant to 3 or > antimicrobial classes
- In the last 2 decades only 5 new antibiotics were under development by Pharma vs 4 drugs to treat erectile dysfunction
- Antimicrobial stewardship results in more costly drugs being used appropriately to save costs
- A 3 prong approach of infection control, antimicrobial stewardship, and environmental decontamination has been advocated to overcome antimicrobial resistance
True or False or…. Not sure?

- **TRUE:** Multidrug resistant (MDR) microbes are resistant to 3 or > antimicrobial classes
- **TRUE:** In the last 2 decades only 5 new antibiotics were under development by Pharma vs 4 drugs to treat erectile dysfunction
- **FALSE:** Antimicrobial stewardship results in more costly drugs being used appropriately to save costs
- **TRUE:** A 3 prong approach of infection control, antimicrobial stewardship, and environmental decontamination has been advocated to overcome antimicrobial resistance
Antimicrobial Use

- Therapeutic
  - Life threatening situations
  - Potentially life threatening

- Prophylaxis
  - Non-life threatening – easier to alter physician prescribing behaviour
  - Accounts for up to 30% of antibiotic use

- Other
  - Anti-inflammatory, prokinetic, fatigue of chronic lyme
Frequency of Use of Antimicrobials

- Antimicrobials are among the most commonly used class of drugs in Canadian hospitals.
- Pharmacy expenditures – represent a significant proportion of an institution’s total budget.
- 55.7% of patients discharged from 323 hospitals in US in 2010 received antibiotics during their hospitalization.
- Recent point prevalence survey Calgary hospitals: 30% of patients on antimicrobials on any given day.

Fridkin et al. Vital Signs: Improving antibiotic use among hospitalized patients. MMWR March 7, 2014 / 63(09);194-200
5 Principles of Antibiotic Resistance

1. Given sufficient time and drug use, antibiotic resistance will emerge – resistance has arisen to every antibiotic.

2. Resistance is progressive – evolving from low levels through intermediate to high levels.

3. Organisms resistant to one drug are likely to become resistant to others.

4. Once resistance appears it is likely to decline slowly if at all.

5. The use of antibiotics by one person affects others in the immediate and extended environments.

Levy SB NEJM 1998;338:1376-1378
Antimicrobial Stewardship - Definition

“The optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance.”

Antimicrobial Stewardship - Definition

- In Canada antimicrobial stewardship is considered to be the responsible planning and management of resources in order to prevent and moderate the development of antimicrobial resistance.

- May consider from multiple perspectives – clinical, public health, systems, governance
  - human and animal settings.
Antimicrobial Stewardship Programs

- **Quality improvement and patient safety**
  - Improve quality of medical care
  - Reduce adverse events and allergies

- **Collateral damage reduction**
  - Prevention of resistance by selection for drug-resistant organisms [ESBLs, MRSA, VRE]
  - *C. difficile*; AAD; unwanted colonization with MDROs)

- **Cost containment**
  - Reduction in antimicrobial costs
  - Clinical and economic burden of antibiotic resistance

### Table 3: Incidence of hospital-acquired CDAD per 1000 patient-days of use of various classes of antibiotics among all inpatients at the Centre hospitalier universitaire de Sherbrooke

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th>Period; incidence per 1000 patient-days of antibiotic use*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrow-spectrum penicillins</td>
<td>1.4 (28/19908)</td>
</tr>
<tr>
<td>β-lactam/β-lactamase inhibitors</td>
<td>1.0 (7/7267)</td>
</tr>
<tr>
<td><strong>Cephalosporins</strong></td>
<td></td>
</tr>
<tr>
<td>First-generation</td>
<td>2.3 (30/12779)</td>
</tr>
<tr>
<td>Second-generation</td>
<td>3.9 (55/13984)</td>
</tr>
<tr>
<td>Third-generation</td>
<td>2.7 (18/6786)</td>
</tr>
<tr>
<td><strong>Carbapenems</strong></td>
<td></td>
</tr>
<tr>
<td>First-generation</td>
<td>2.7 (7/2553)</td>
</tr>
<tr>
<td>Second-generation</td>
<td>2.4 (21/8673)</td>
</tr>
<tr>
<td><strong>Aminoglycosides</strong></td>
<td></td>
</tr>
<tr>
<td>First-generation</td>
<td>1.6 (48/29693)</td>
</tr>
<tr>
<td>Second-generation</td>
<td>4.9 (19/3861)</td>
</tr>
<tr>
<td>Macrolides</td>
<td>1.9 (5/2625)</td>
</tr>
<tr>
<td><strong>Quinolones</strong></td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>2.0 (20/10092)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>2.5 (9/3658)</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>0.2 (8/1706)</td>
</tr>
</tbody>
</table>

*Calculated from numbers in parentheses: the numerator represents the number of patients with hospital-acquired CDAD who received a given class of antibiotic during the 2 months before diagnosis, and the denominator represents the total number of patient-days that this class of antibiotic was used among all inpatients.

Pepin J et al. CMAJ 2004;171:466-472
Failure of Infection Control Measures - Reduction in CDAD with Targeted Antibiotic Consumption Intervention

Economic Impact of Inadequate Antimicrobial Stewardship

- Increased morbidity, mortality and LOS and attendant costs

- Toxicity of last line therapies is high
  - Colistin; tigecycline

- Increased costs
  - patients
  - hospitals and payers

Conly J. Can Med Assoc J 2002;167(8):885-890;
Antimicrobial Stewardship Policies

Persuasive

- Education for prescribers
  - Conferences
- Peer Review
  - Utilization review with feedback
- Tailoring or de-escalation of therapy
- Academic detailing
  - Face to face presentations
- Therapeutic guidelines
  - National, regional, local
- Sequential antimicrobial therapy (IV to oral conversion)
- Computer assisted decision support

Antimicrobial Stewardship Policies

Restrictive

- Cascade susceptibility reporting
- Controlled formulary
- Automatic stop orders
  - IV vs. oral
- Automatic therapeutic interchange
- Restricted antimicrobial agents
  - Approval necessary a priori vs. concurrent review and feedback
- Antibiotic order forms
- Infectious Diseases consultations

Establishing an Antimicrobial Stewardship Program

- Multiple guidelines exist in the literature
  - IDSA guidelines for developing an institutional program to enhance antimicrobial stewardship
    *Clin Infect Dis 2007;44: 159–177*
  - Policy statement on antimicrobial stewardship
    *Infect Control Hosp Epidemiol. 2012;33:322-7*
  - Guidance for the knowledge and skills required for antimicrobial stewardship leaders
    *Infect Control Hosp Epidemiol. 2014 35(12):1444-51*
  - Implementing an antibiotic stewardship program:
    *IDSA evidence based guideline
Components of an Antimicrobial Stewardship Program

Minimum Requirements
- Core multidisciplinary team formation
- Formulary with restrictions
- Guidelines relevant to the facility and preauthorization for certain agents
- Measure and monitor antimicrobial use
- Provision of local antibiograms

Core and Supplemental Strategies
- Core: Formulary restrictions and prospective audit and feedback
- Supplemental: education, pathways, de-escalation, iv to oral stepdown, others
Tailoring or De-Escalating Antimicrobials

- Based on natural history of clinical phases of illness
- Acute → Subacute → Convalecent phase
- Empiric antibiotics in acute phase
- Entry to subacute phase about 72-96 hours
- Susceptibilities arrive 48-72 hours
- Timing at Day 3 ideal as process measure to tailor or de-escalate

Clinical Benefits of Sequential Antibiotic Therapy

- Earlier discontinuation of IV
  - Increased patient comfort
  - Decreased risk of complications
- Enhanced mobilization
- Reduced risk of nosocomial infection
- Earlier discharge from hospital
- Improved quality of life
Evidence Base to Support Antimicrobial Stewardship

- Reduction in antimicrobial resistance
  - Finland’s consumption of macrolide antibiotics decreased from 2.40 defined daily doses/1000 inhabitants/day in 1991 → 1.38/1000 inhabitants/day in 1992 (p=0.007) and continued to 1996 due to national guidelines.
  - With decrease in consumption - ↓ in erythromycin resistance of Gr. A streptococci from throat swabs – 16.5% (1992) → 8.6% (1996)

Seppala H et al. N Engl J Med 1997;337:441-446
Evidence Base to Support Antimicrobial Stewardship

Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis

Emelie C Schuts, Marlies E J L Hulscher, Johan W Mouton, Cees M Verduin, James W T Cohen Stuart, Hans W P M Overdijk, Paul D van der Linden, Stephanie Natsch, Cees M P M Hartogh, Tom F W Wolfs, Jeroen A Schouten, Bart Jan Kullberg, Jan M Prins

Summary
Background Antimicrobial stewardship is advocated to improve the quality of antimicrobial use. We did a systematic review and meta-analysis to assess whether antimicrobial stewardship objectives had any effects in hospitals and long-term care facilities on four predefined patients’ outcomes: clinical outcomes, adverse events, costs, and bacterial resistance rates.

Methods We identified 14 stewardship objectives and did a separate systematic search for articles relating to each one in Embase, Ovid MEDLINE, and PubMed. Studies were included if they reported data on any of the four predefined outcomes in patients in whom the specific antimicrobial stewardship objective was assessed and compared the findings in patients in whom the objective was or was not met. We used a random-effects model to calculate relative risk reductions with relative risks and 95% CIs.

Findings We identified 145 unique studies with data on nine stewardship objectives. Overall, the quality of evidence was generally low and heterogeneity between studies was mostly moderate to high. For the objectives empirical therapy according to guidelines, de-escalation of therapy, switch from intravenous to oral treatment, therapeutic drug monitoring, use of a list of restricted antibiotics, and bedside consultation the overall evidence showed significant benefits for one or more of the four outcomes. Guideline-adherent empirical therapy was associated with a relative risk reduction for mortality of 35% (relative risk 0.65, 95% CI 0.54–0.80, p<0.0001) and for de-escalation of 66% (0.44, 0.30–0.66, p<0.0001). Evidence of effects was less clear for adjusting therapy according to renal function, discontinuing therapy based on lack of clinical or microbiological evidence of infection, and having a local antibiotic guide. We found no reports for the remaining five stewardship objectives or for long-term care facilities.

Interpretation Our findings of beneficial effects on outcomes with nine antimicrobial stewardship objectives suggest they can guide stewardship teams in their efforts to improve the quality of antibiotic use in hospitals.

Effects on Mortality of Stewardship Components

De-escalation (Forest Plot)

Prescribing empiric therapy based on guidelines (Forest plot)

Guideline-adherent empirical therapy  RRR for mortality of 35% (relative risk 0.65, 95% CI 0.54–0.80, p<0.0001) and for de-escalation of 56% (0.44, 0.30–0.66, p<0.0001)
De-escalation in ICU

- Cohort study on the safety and impact on in hospital and 90-day mortality of antibiotic de-escalation in patients admitted to the ICU with severe sepsis or shock (n=628)
- Defined as antibiotic D/C or change of antibiotic to one with a narrower spectrum once culture results available
- Outcomes: De-escalation in 219 patients; MV analysis, independent RF associated with in-hospital mortality were septic shock, SOFA score the day of culture, inadequate empirical antimicrobial therapy
- **De-escalation was a protective factor [OR 0.58; 95 % CI 0.36–0.93]**
- Why? Less toxicity; NI; collateral damage

Effectiveness of Antimicrobial Stewardship Policies

- Based on evidence most effective interventions appear to be restrictive administrative methods including formulary control applied at the institution or provincial level.

- Enablement and restriction were independently associated with a larger effect size (high-certainty evidence).

Antimicrobial Stewardship
Canadian Setting

- Historic issues
- Accreditation Canada
- Public Health Agency of Canada initiatives
- Provincial initiatives
- Local Initiatives
Stewardship in the Canadian Setting

Historic overview

1997 Canadian Consensus Conference “Controlling antimicrobial resistance. An integrated action plan for Canadians” recommendations
- establish antibiotic stewardship and antibiotic use teams in all Canadian hospitals by:
  a. incorporating them into accreditation standards;
  b. obtaining support from administrative leadership
- establish antimicrobial use, monitoring, and intervention programs

- obtain, analyze and disseminate data/information on antibiotic use in humans and animals in a timely manner and present it in standard formats e.g. Defined Daily Dose

Stewardship in the Canadian Setting

Historic overview

- 2009 Pan-Canadian Stakeholder Consultations on Antimicrobial Resistance
  - develop a universally agreed to definition of antimicrobial stewardship ….
  - develop a coordinated integrated inter-disciplinary Pan-Canadian approach….
  - develop and promote public and professional awareness of antimicrobial stewardship responsibilities and concerns
- 2014 Senate Briefings; NCCID Report of Antimicrobial Resistance and Antimicrobial Utilization in Canada; Accreditation Canada ROP; Federal Framework for Action
- 2015 Auditor General Report AMR in Canada

A New Accreditation Standard

- Accreditation Canada developed a “Required Organizational Practice” (ROP) under Medication Use on Antimicrobial Stewardship in 2013
  - “The organization has a program for antimicrobial stewardship to optimize antimicrobial use”
  - Applies to all acute care organizations
  - Applicable as of May 2014
  - Organizations should use a tailored approach consistent with their size, service environment and patient population

Source: Accreditation Canada
1. The organization implements an antimicrobial stewardship program
2. The program includes lines of accountability for implementation
3. The program is inter-disciplinary
4. The program includes interventions to optimize antimicrobial use that may include:
   - audit and feedback
   - a formulary with approved indications
   - guidelines and clinical pathways for antimicrobial utilization
   - strategies for streamlining or de-escalation of therapy
   - parenteral to oral conversion of antimicrobials
   - education
   - dose optimization
Antimicrobial Stewardship Progress Report: Central Zone

Issue 1: April 2016

Antimicrobial Stewardship Initiatives in Central Zone

The Central Zone Antimicrobial Stewardship Working Group develops and implements targeted initiatives that assist physicians, pharmacists, nurses and other healthcare professionals in practicing good antibiotic stewardship. Contact the Central Zone Antimicrobial Stewardship Working Group if you would like more information. There are several sites in need of an antimicrobial stewardship champion, contact us if are interested in representing your site or program.

Antimicrobials Highly Associated with CDI

The AHS Antimicrobial Stewardship Committee monitors 14 antimicrobials highly associated with *Clostridium difficile* infection (CDI) at select sites in each zone. Information collected from these sites may give us an indication of the effectiveness of zone antimicrobial stewardship strategies.

Total Number of Antimicrobial Resistant Organisms (AROs) and *Clostridium difficile* Infections (CDI)

Each quarter, the Infection Prevention & Control Provincial Surveillance team releases details on a number of AROs and CDI rates within each zone. For October—December 2015, Central Zone reported 16 hospital-acquired CDI cases, a rate of 1.5 cases per 10,000 patient days.

Access your IP&C Report Here

More Details on Zone Stewardship

Shrink YOUR antibiotic footprint by practicing stewardship everyday!

This past November, AHS celebrated Antibiotic Awareness Week with the launch of the ‘Reduce Your Antibiotic Footprint’ campaign.

Newsletter Spotlight

To remove your name from the mailing list, please click here.

Questions or comments? E-mail us at AHS.AntimicrobialStewardship@AHS.ca
The power to make a difference in stewardship is in your hands.
Question for Discussion

- Does the ‘Tackling Antimicrobial Resistance and Antimicrobial Use: A Pan-Canadian Framework for Action (GC, 2017) go far enough in its recommendations on stewardship?
- What else could be done?
Antimicrobial stewardship in veterinary medicine

J Scott Weese DVM DVSc DipACVIM
Disclosures

Employee: University of Guelph

Grants/Research contracts:
- Canadian Institutes of Health Research (CIHR)
- Canadian Foundation for Innovation
- National Science and Engineering Research Council (NSERC)
- JPI-AMR
- Equine Guelph
- Ontario Veterinary College Pet Trust
- American Kennel Club Canine Health Foundation

Speaking engagements
Vetoquinol, Merck, Hill’s Pet Nutrition, Royal Canin Canada, Brief Media, Trupanion

Other
Editor-in-Chief, Clinician’s Brief (Brief Media)
<table>
<thead>
<tr>
<th>Result</th>
<th>Staphylococcus aureus/peptidoglycan</th>
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<tbody>
<tr>
<td>Level</td>
<td>Y</td>
</tr>
<tr>
<td>Amoxicillin Cla霉素</td>
<td>R</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>R</td>
</tr>
<tr>
<td>Cefuroxim</td>
<td>R</td>
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<tr>
<td>Cefoxitin</td>
<td>R</td>
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<td>Cephaloridin</td>
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<tr>
<td>Cilastatin</td>
<td>R</td>
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<tr>
<td>Erythromycin</td>
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<tr>
<td>Gentamicin</td>
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<tr>
<td>Metronidazol</td>
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<td>Orifloxacin</td>
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<tr>
<td>Tetracyclin</td>
<td>R</td>
</tr>
<tr>
<td>Trimethopin/Sulf</td>
<td>R</td>
</tr>
</tbody>
</table>
What is antimicrobial stewardship in a veterinary context?

“Use of practical measures to optimize the use of antimicrobials, understand the use of antimicrobials, maximize the beneficial impacts on animal health, welfare and production, and minimize the risk of antimicrobial resistance affecting humans, animals and the environment”
Should we be talking about Antibiotic use or stewardship in ‘animals’?
<table>
<thead>
<tr>
<th>Patient:</th>
<th>SPECK SCARIDILLO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td>4Y</td>
</tr>
<tr>
<td>Sex:</td>
<td>F Neutered: U</td>
</tr>
<tr>
<td>Species:</td>
<td>Avian</td>
</tr>
</tbody>
</table>

**Accession:**

**Hosp. ID#:**

**PRELIMINARY**

*REPEAT CBC. ON LINEZOLID, METRONIDAZOLE, PIPERACILLIN AND MARBOFLOXACIN.*
**Educate**

Prescribers/dispensers

**Empower**

**Facilitate**

**Measure**

**Motivate**

**Restrict**

**Users**
Diarrheic Calf Treatment Algorithm

Calf with Diarrhea

- Bright, alert Drunk well
  - Monitor demeanor and milk intake.

- Dull, drinking slowly or less than normal intake
  - FEVER
    - NO: Oral electrolytes, NSAIDS*. Monitor attitude and temperature. Evaluate response over 24 to 48 h.
    - YES: Oral electrolytes, NSAIDS, Antibiotics**. Monitor attitude and temperature at least twice daily.

- Very depressed, drinking <30% of normal intake
  - FEVER
    - NO: Oral electrolytes, NSAIDS, Antibiotics. Monitor attitude and temperature over 24 to 48 h.
    - YES: Oral electrolytes +/- IV fluids, NSAIDS, Antibiotics. Evaluate response over 24 to 48 h.

- Bloody diarrhea
  - Oral electrolytes +/- IV fluids NSAIDS Antibiotics

* NSAIDS: Non-steroidal antiinflammatories such as meloxicam (Metacam™).
** The routine antibiotic that is used should be determined in conjunction with the farm veterinarian. Example: Trimethoprim sulfa.
Figure 5.2: Antimicrobial treatment rates in 10 dairy farms before (BP) and after (AP) implementation of an algorithm for treatment of diarrheic calves.
Barriers

- Education of users and vets
- Confidence in not recommending/administering antimicrobials
- Farm culture

- Defensive medicine

- Bad outcomes are very evident (and ascribed to no AMU), good ones are not evident
Research Article
Antimicrobial Use Guidelines for Treatment of Urinary Tract Disease in Dogs and Cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases

J. Scott Weese,1 Joseph M. Blondeau,2 Dawn Boothe,3 Edward B. Breitschwerdt,4 Luca Guardabassi,5 Andrew Hillier,6 David H. Lloyd,7 Mark G. Papich,8 Shelley C. Rankin,9 John D. Turnidge,10,11 and Jane E. Sykes11

Guideline and Recommendation
J Vet Intern Med 2017;31:279-294

Antimicrobial use Guidelines for Treatment of Respiratory Tract Disease in Dogs and Cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases

De-escalation

“I took over a case this morning and it’s on ampicillin, clindamycin, enrofloxacin, doxycycline and metronidazole. Do we need all those drugs?”
Barriers to de-escalation

- Thinking about it
- Confidence in narrowing spectrum
- Submission of cultures
- Decision-making support (e.g. pharmacists)
- Limited availability of good quality guidelines
- Defensive medicine
Think about numbers….

- 1000 dogs treated for cystitis
Think about numbers....

- 1000 dogs treated for cystitis

- Pre-intervention
  - 220 kg of antibiotic

- Post-intervention
  - 25 kg of antibiotic
Think about numbers….

- 1000 dogs treated for cystitis

- Pre-intervention
  - Amoxicillin, CIA
  - 22 mg/kg PO q12h for 5d

- Post-intervention
  - Marbofloxacin, HP-CIA
  - 5 mg/kg PO q24h for 5d
Think about numbers….

- 1000 dogs treated for cystitis

- Pre-intervention
  - Amoxicillin, CIA
  - 22 mg/kg PO q12h for 5d

- Post-intervention
  - Marbofloxacin, HP-CIA
  - 5 mg/kg PO q24h for 5d
### Antimicrobial class

#### CRITICALLY IMPORTANT ANTIMICROBIALS

*Highest Priority Critically Important Antimicrobials*
- Cephalosporins (3rd, 4th and 5th generation)
- Glycopeptides
- Macrolides and ketolides
- Polymyxins
- Quinolones

*High Priority Critically Important Antimicrobials*
- Aminoglycosides
- Ansamycins
- Carbapenems and other penems
- Glycylcyclines
- Lipopeptides
- Monobactams
- Oxazolidinones
- Penicillins (natural, aminopenicillin antipseudomonal)
- Phosphonic acid derivatives
- Drugs used solely to treat tuberculosis other mycobacterial diseases

#### HIGHLY IMPORTANT ANTIMICROBIALS
- Amidopenicillins
- Amphenics
- Cephalosporins (1st and 2nd generation) and cephamycins
- Lincosamides
- Penicillins (anti-staphylococcal)
- Pseudomonic acids
- Riminofenazines
- Steroid antibacterials
- Streptogramins
- Sulfonamides, dihydrofolate reductase inhibitors and combinations
- Sulphones
- Tetracyclines

#### IMPORTANT ANTIMICROBIALS
- Aminocyclitols
- Cyclic polypeptides
- Nitrofurantoinns
- Nitroimidazoles
- Pleuromutilins
Traffic Light System: Drugs
### Categorization of Antimicrobial Drugs Based on Importance in Human Medicine

(Version - April, 2009)

<table>
<thead>
<tr>
<th>Antimicrobial class</th>
<th>Examples</th>
</tr>
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<tr>
<td>Aminoglycosides</td>
<td>Streptomycins</td>
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<tr>
<td>Ansamycins</td>
<td>Sulfonamides, dihydrofolate reductase inhibitors and combinations</td>
</tr>
<tr>
<td>Carbapenems and other penems</td>
<td>Sulfones</td>
</tr>
<tr>
<td>Glycylcyclines</td>
<td>Tetracyclines</td>
</tr>
<tr>
<td>Lipopeptides</td>
<td></td>
</tr>
<tr>
<td>Other mycobacterial diseases</td>
<td>Nitrofurans, Nitroimidazoles, Pleuromutilins</td>
</tr>
</tbody>
</table>

**Critically Important Antimicrobials for Human Medicine**

5th Revision 2016
Ranking of medically important antimicrobials for risk management of antimicrobial resistance due to non-human use.

**EMA**

Categorisation of antibiotics for use in animals for prudent and responsible use.
Does restriction of antimicrobials in animals have an impact on resistance?
Yes..but....

- Some conflicting data
  - Between bacteria
  - Between drugs
  - Between studies

- Focused on single bug/drug combinations
Ceftiofur Resistance in *Salmonella enterica* Serovar Heidelberg from Chicken Meat and Humans, Canada

Lucie Dutil, Rebecca Irwin, Rita Finley, Lai King Ng, Brent Avery, Patrick Goerlin, Anne-Marie Bourgault, Linda Cole, Danielle Daigle, Andrea Delakas-Kal, Walter Demoulin, Linda Hoang, Greg S. Homman, Johanne Israël, Françoise Janelle, Anne Mali, Ana Pacagnella, and Dylan R. Hoiar
Antibiotic use selects for resistance…

So…

Antibiotic-free farms should have less resistance
Zinc resistance of *Staphylococcus aureus* of animal origin is strongly associated with methicillin resistance

Lina M. Cavaco 1,*, Henrik Hasman 1, Frank M. Aarestrup 1

Research Group for Antimicrobial Resistance and Molecular Epidemiology, National Food Institute, Technical University of Denmark, Copenhagen, Denmark

Zooonoses and Public Health

**Zinc Oxide Therapy Increases Prevalence and Persistence of Methicillin-Resistant *Staphylococcus aureus* in Pigs: A Randomized Controlled Trial**

M. J. Silfierz 1, R. Friendship 2 and J. S. Weese 1

Short communication

**Effects of tetracycline and zinc on selection of methicillin-resistant *Staphylococcus aureus* (MRSA) sequence type 398 in pigs**

Arshnee Moodley a,*, Søren Saxmose Nielsen b, Luca Guardabassi a

a Department of Veterinary Disease Biology, Faculty of Life Sciences, University of Copenhagen, Frederiksberg C, 1870, Denmark
b Department of Large Animal Sciences, Faculty of Life Sciences, University of Copenhagen, Frederiksberg C, 1870, Denmark
It’s not only ‘antibiotics’ that drive antibiotic resistance

“It makes sense” isn’t evidence.
What is the net impact of stopping prophylactic tetracycline use in food animals if...

- Disease rates increase
- More important drug classes are used for treatment

Is it ethical to use antibiotics as a ‘crutch’ to enable suboptimal practices?
WHAT DO WE WANT?
EVIDENCE-BASED CHANGE
WHEN DO WE WANT IT?
AFTER PEER REVIEW
Infection prevention Rocks!!!