Using Antimicrobials Like We Want to Keep Them

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Kansas State University
Regulations

- Animal Medicinal Drug Use Clarification Act (AMDUCA)
  - Regulations published in 1996
- Concurrent feeding of feed additives not cleared to be fed together
  - No ELDU in feed
  - Topdressing is the same as feeding
FDA Activity

- Regulation of GMO animals
- Guidance 209
- Guidances 152 and 159
- CPG for compounding
  - 5th circuit court of appeals decision, July 18, 2008
- Comments solicited relative to VFDs (3-29-10)
- Proposed milk sampling plan for residues at dairies with repeated cull cow residue violations. (2011) Why?
Legislation

- PAMTA
- California
- New York
Where do we overlap with the MDs?

- We will talk about use of antimicrobials that are the same or in the same group.
- If there are linked genes in a resistant cassette, then co-selection for resistance is not dependant on mechanism of action.
Januray 20, 2010

VITAL SIGNS

Regimens: Tailor Medicine Levels to Size and Weight, Doctors Say

By RONI CARYN RABIN

When pediatricians prescribe medicine for children, they take the child’s size and weight into account and adjust the dose accordingly. But with few exceptions, medical practitioners take a one-size-fits-all approach when prescribing drugs to adults, whether the patient is petite or extra large.

That is a mistake, according to two doctors writing recently in the medical journal The Lancet. They argue that dosages of antibiotics should be based on a patient’s size, with higher doses for heavier patients.

Dr. Matthew E. Falagas, director of the Alfa Institute of Biomedical Sciences in Athens, Greece, and a professor of medicine at Tufts University, School of Medicine in Boston, is one of the authors. Dr. Falagas used himself, 6-foot-2 and 198 pounds, and a female student who worked with him, 120 pounds and barely five feet tall, as an example.

“If we go with the same diagnosis of pneumonia or bronchitis to a New York hospital today,” he said, “we will be given the same dose of antibiotics. I should receive almost twice the dose compared with her.”

Though doses of many cancer drugs are calculated based on body weight because of their toxicity, Dr. Falagas said, there are no guidelines stipulating that doctors should
Where do we overlap with the MDs?

- **Fluoroquinolones**
  - Originally ciprofloxacin (Cipro)
    - Multiple new human fluoroquinolones in the last few years
  - Very important in human therapy
    - Anaerobic and Gram (+) spectrum has been expanding.
  - Oral and injectable therapy in humans
  - In cattle, we use
    - Enrofloxacin (Baytril) - injectable
    - Danofloxacin (A-180) - injectable
Where do we overlap with the MDs?

- **Macrolides for humans**
  - Erythromycin, azithromycin (Zithromax), clarithromycin (Biaxin), Telithromycin (Ketek)

- **Macrolides for cattle**
  - Tylosin (Tylan) – injectable, feed
  - Erythromycin (Gallimycin) – injectable, hard to find or not available anymore
  - Tilmicosin (Micotil) – injectable (oral in swine)
  - Tulathromycin (Draxxin) – injectable
Where do we overlap with the MDs?

- **Cephalosporins**
  - Humans use 1\(^{\text{st}}\) through 4\(^{\text{th}}\) generations
    - 3\(^{\text{rd}}\) generation examples: Cefpodoxime (human [Vantin], and companion animal veterinary [Simplicef] labels), ceftriaxone (Rocephin)
    - 4\(^{\text{th}}\) generation extended-spectrum: Cefepime (Maxipime)
  - In cattle
    - Ceftiofur (Naxcel, Excenel, Excede) – 3\(^{\text{rd}}\) generation, injectable only
Where do we overlap with the MDs?

- **Tetracyclines**
  - Humans use a much broader range of compounds
    - “first generation” – tetracycline
    - “second generation” – doxycycline, minocycline, demeclocycline
    - “third generation” – glycylcyclines (tigecycline)
  - In cattle
    - Oxytetracycline, chlortetracycline, tetracycline
U. S. CTC, TC and OTC Cattle Approval Examples

- **Feed efficiency/Rate of gain**
  - CTC: 10 mg/lb BW for up to 5 days
  - CTC: 400 g/ton to provide 10 mg/lb per day in calves up to 250 lbs
  - TC: 22 mg/kg for 3-5 days in calves

- **Prevention/Control**
  - CTC: 0.5 mg/lb per day in beef cattle over 700 lbs
  - OTC: 0.5 to 2.0 g/hd per day
  - CTC: 350 mg/hd per day in beef cattle under 700 lbs
  - CTC: 350 mg/hd per day in beef cattle
  - CTC: 70 mg/hd per day in growing cattle over 400 lbs
  - CTC: 25 - 70 mg/hd per day in calves 250 – 400 lbs
  - CTC: 0.1 mg/hd per day in calves up to 250 lbs

- **Treatment**
  - CTC: 350 mg/hd per day in beef cattle

These are not all of the CTC, TC, and OTC indications, but are selected to illustrate the regimen range.
Where do we overlap with the MDs?

- **Phenicols**
  - Chloramphenicol in humans
  - Florfenicol (nuflor), a 2nd generation derivative, used in cattle

- **Aminoglycosides**
  - Gentamicin, Amikacin, others in humans
  - Oral neomycin (Biosol) in cattle

- **Sulfas**
  - Humans – primarily potentiated sulfas
  - Cattle – sulfadimethoxine (Albon), sulfamethazine, Sulfachlopyridazine (Vetisulid)
Where do we overlap with the MDs?

- **Penicillins**
  - **Humans**
    - Penicillin G and Penicillin V
    - Oxacillin
    - Ampicillin
    - Extended spectrum – Ticarcillin, Piperacillin
    - Potentiated – ticarcillin-clavulanic acid (Timentin), ampicillin-sulbactam (Unasyn), Piperacillin-tazobactam (Zosyn)
  - **In cattle**
    - Procaine Pen G, Procaine/Benzathine Pen G
    - Ampicillin (Polyflex)
    - Hetacillin (Hetacin K) – converted to ampicillin
No use of the same class

- Carbapenems
  - Imipenem
  - Meropenem
- Glycopeptides
  - Vancomycin
- Streptogramins
  - “Synercid”
  - Virginiamycin (Vmax, labeled for cattle and swine, but limited use)
- Oxazolidinones
  - Linezolid
- Ionophores
  - In cattle but no similar class in humans, no genetic co-resistance demonstrated.
- Bambermycins
  - As for the ionophores
Human Resistance Problems

What resistance problems are affecting human therapeutics?

*Streptococcus pneumoniae*

*Staphylococcus aureus* (MRSA, VRSA)

*Salmonella*

*Shigella dysenteria*

*E. coli*
More Human Resistance

*Enterococcus faecalis, faecium (VRE)*
*Pseudomonas aeruginosa*
*Mycobacterium tuberculosis*
*Neisseria gonorrhea*
*Clostridium difficile*
*Campylobacter*
The Basics of Therapy

- Characterization of a disease challenge
- Case definitions
- Regimen design
- Consistent application of protocols
- Outcome evaluation
Treatment Protocols

Before you even start deciding which antibiotic…

- First treatment criteria
- Treatment success/failure criteria
- When to apply success/failure criteria
- Managing single-injection therapy in the home pen
- When do you STOP?
Case Definitions
Case Definition Examples

- These BRD examples need to be characterized as important or misleading criteria.
- Depression
- Nasal discharge
- Ocular discharge
- Rumen fill/appetite
- Rectal temperature
- Lung sounds
### Lot 8099

#### Temp vs. First treat, Failure, Dead, First treat success, Case fatality

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<th>Temp</th>
<th>First treat</th>
<th>Failure</th>
<th>Dead</th>
<th>First treat success</th>
<th>Case fatality</th>
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**Days to death:** 13, 7, 2, 80

#### Temp vs. First treat, Failure, Dead, First treat success, Case fatality

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Applying Protocols

- Plan your work and work your plan
- Deviating from consistent protocol application makes evaluation of outcomes a useless waste of time
- Understanding your antibiotic use and outcomes of treatment are critical
Respiratory Treatment Program

Getting distracted in the treatment shack…

- One antibiotic at a time
- Things that don’t help
  - Routine use of an anti-inflammatory or steroid
  - Antihistamines
  - Revacc at treatment
  - Probiotics
  - Vitamins
Treatment Records

Inadequate Treatment Records
## A Basic Treatment Record

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<th>Trt</th>
<th>Date</th>
<th>Initials</th>
<th>Diagnosis</th>
<th>Temp</th>
<th>Drug and total dose</th>
<th>Comments</th>
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Respiratory Protocols

- Low risk
- High risk
- Heavy cattle
- Acute Interstitial Pneumonia (AIP)
- Tracheal edema (Honkers)
- Diphtheria
General

- Environmental control for vaccines/drugs?
- Needles
- Injection systems
- Is everyone trained in product administration?
Injection Systems

- Disinfectants will inactivate MLV vaccines
- Drug residues can interact with other drugs
- Only enter bottles with sterile needles
Realistic Health Expectations

- **High Risk**
  - $\geq 10\%$ morbidity
  - Case fatality rate 5-10\% (or higher)
  - 1\textsuperscript{st} treatment success 50-60\%

- **Low Risk**
  - $< 10\%$ morbidity
  - CF 1-2\%
  - 1\textsuperscript{st} trt success 80-90\%
So, just how much difference do we make with antibiotics, anyway?
Number Needed to Treat by Disease

All FOI studies except pinkeye (all papers) and one paper in footrot
Antibiotics at Processing

- Treatment for control of respiratory disease?
  - Injectable vs. Feed
- Pick your groups for treatment carefully
Increasing morbidity

Number of Lots

MassMed Economics

Negative  Neutral  Positive

Increasing morbidity →
Musculoskeletal Disease

An example where diagnosis makes a big difference in what works and what doesn’t

- Footrot
- Toe and Sole Abscesses
- Undifferentiated lameness
- Hairy Heel Wart
- Infectious arthritis
Typical stance of affected cattle
Typical stance of affected cattle
Biopsy positive for Treponema
Biopsy positive for Treponema
Classic “Strawberry” Hairy Heel Wart lesion, 9-12-05
Erosion extended to front of foot in an advanced case
Using Antibiotics Like We Want to Keep Them

1. Carefully select the animals that will get antibiotics
2. Plan your regimens based on evidence
3. Stick to your plan
4. Evaluate your outcomes with reasonable expectations
5. It’s not just about potential problems in humans, it is about preserving the ability to treat diseases in the animals under our care.