Antibiotics in Milk Replacers

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R. M. Thornsberry, D.V.M., M.B.A.

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Compliments of:
Thomas Coletti, DVM
Surgical Resident
Veterinary Specialty Service
St. Louis Missouri

Definition of an Antibiotic

- A substance, such as penicillin or streptomycin, produced by or derived from certain fungi, bacteria, and other organisms, that can destroy or inhibit the growth of other microorganisms.
- Antibiotics are utilized in the prevention and treatment of infectious diseases.
- Antibiotics are utilized parenterally, orally, and topically.

Discovery of Antibiotics

- Fleming recounted that the date of his discovery of penicillin was on the morning of Friday, September 28, 1928. It was a fortuitous accident. Fleming noticed a petri dish containing *Staphylococcus* plate culture he had mistakenly left open, which was contaminated by blue-green mold, which had formed a visible growth. There was a halo of inhibited bacterial growth around the mold.

Penicillin was a Miracle Drug

- By June 1942, there was just enough U.S. penicillin available to treat ten patients
- A moldy cantaloupe in a Peoria, Illinois market in 1943 was found to contain the best and highest-quality penicillin after a worldwide search.
- During World War II, penicillin made a major difference in the number of deaths and amputations caused by infected wounds among Allied forces, saving an estimated 12%–15% of these wounded veterans from death or amputations

Methicillin—Not used in veterinary medicine

Resistant—Used to classify Staph

Staphylococcus—Gram Positive Cocci ubiquitous in nature

Aureus—Species of Staph

MRSA Timeline

- 1942-1944: Introduction of Penicillin
- 1947: First report of penicillin resistance
- 1959: Introduction of Methicillin
- 1961: First MRSA in Humans (in the UK)
- 1972: First MRSA in a cow with mastitis
- 1981: First MRSA in the U.S. (the press designated it the "Super Bug")
- 1996: First VRSA (Vancomycin Resistant)

MRSA

- **Three Types of MRSA**
  - Hospital associated
    - Most common type
    - Responsible for most cases
    - Responsible for most severe cases
  - Community associated
    - Second most common type
    - Mainly skin pustule type expression
  - Zoonotic—animal to man transmission questionable?
    - Incidental—Can discover pig strains on hog worker's skin, but it is cleared within a few weeks and does not cause disease in humans
    - If even documented?

MRSA—CDC Statistics

- In 2005 -The estimated number of people developing a serious MRSA infection (i.e., invasive) was about 94,360
- In 2005- Approximately 18,650 persons died during a hospital stay related to these serious MRSA infections
- 85% of MRSA infections are hospital associated
- 12-14 % of MRSA infections are community associated

MRSA

Reverse Zoonosis

- **Most common is Reverse Zoonosis**
  - Spills over from humans to animals
  - Humans transmit MRSA to domestic animals
    - Post surgery infections in canines and horses from MRSA colonized surgeon

Antibiotics Since the Dawn of Time

- Antibiotics have been produced in nature since the dawn of time by bacteria, fungi, and protozoa
- Utilized to prevent growth of competitive organisms
- Resistance to antibiotics
  - Mechanism by bacteria to resist the negative effect of antibiotic on growth and development
  - In core samples of perma frost, identified in bacteria thousands of years old and frozen in the ice
  - Resistance to multiple antibiotics identified in these ancient bacteria—May mean nothing other than chemical signals

Antibiotics are not new to nature, just a new discovery for man!!!

Antibiotic Resistance

- Horizontal Gene Transfer—R Factor sharing—Can occur in Gram Negative intestinal bacteria
- Unlinked point mutations—Not common, if actually identified in a population of bacteria.
- Environmental population pressure—Resulting in bacteria that are naturally resistant becoming an ever increasing percentage of a given population of bacteria due to improper antibiotic usage over time.
- In other words, the naturally resistant bacteria are the only ones left to reproduce and become an ever increasing percentage of a given bacterial population in response to improper antibiotic use.

Antibiotic Resistance-Per Wikipedia

- Antibiotics are used in animals that are used as human food, such as cows, pigs, chickens, fish, etc., and these drugs can affect the safety of the meat, milk, and eggs produced from those animals and can be the source of superbugs. For example, farm animals, particularly pigs, are believed to be able to infect people with MRSA. The resistant bacteria in animals due to antibiotic exposure can be transmitted to humans via three pathways, those being through the consumption of meat, from close or direct contact with animals, or through the environment. **(Misleading information!!!)**

Antibiotic Resistance—The Truth

- H. Scott Hurd, D.V.M., Ph.D., College of Veterinary Medicine, Iowa State University, Ames, Iowa
- Former Deputy Undersecretary of Food Safety, USDA
- Director WHO Collaborating Center for Risk Assessment and Hazard Identification in Foods of Animal Origin
- Response to CBS News Segments on Antibiotics – February 9 and 10, 2010 www.drovers.com

Antibiotic resistance is real, but do not blame animal agriculture.

Antibiotic Resistance—The Truth

- Antibiotics utilized in animal feed have not been associated with a major health risk to human health
- MRSA associated with livestock is strain 398
- Strain 398 has not been identified in human disease surveillance for MRSA
- Antibiotic use in modern livestock facilities are not associated with the development of MRSA
- Methicillin has never been used in animals in the United States
- There is no supportive data suggesting that feed grade antibiotic use has led to unsafe food.

Antibiotic Resistance—The Truth

- **Results of banning feed use antibiotics in European countries:**
  - Must wait until pigs are sick to use an antibiotic
  - Resulted in an increase in diarrhea in pigs and a 25% increase in death loss
  - Resistance rates in human Salmonella cases increased and MRSA cases dramatically increased
  - Increased cost of production.
  - Reduced efficiency of production.
  - Compromised animal welfare.

Antibiotic Resistance—The Truth

- **Results of banning antibiotic use in animal feed:**
  - Dramatic reduction in the number of farms--from 25,000 to 10,000 as a result of banning the use of feed grade antibiotics to prevent disease
  - Because the government only allows use of antibiotics once an animal becomes infected, antibiotic use to treat sick pigs increased by 100% and especially so for certain classes of antibiotics commonly utilized for human medicine

Antibiotics in Milk Replacer

- Since the 1950's
- Neomycin and Oxytetracycline approved by the FDA
- Historically utilized at a 2 to 1 ratio as prevention
- 200:100, 400:200, 666:333, 800:400
- As of October 2, 2010: Therapeutic level only!!!
  - 1 to 1 ratio of neomycin and oxytetracycline
  - 2000 grams of neomycin and oxytetracycline per ton
    - 8 ounces of milk replacer powder per 100 pounds per feeding
  - 1600 grams of neomycin and oxytetracycline per ton
    - 10 ounces of milk replacer powder per 100 pounds per feeding

Antibiotics in Milk Replacer

- **Approved label for neomycin and oxytetracycline**
  - 10 mg of each antibiotic per pound of body weight per day
  - 1 gram of each antibiotic per 100 pound calf per day
  - Feed continuously for 7-14 days in the sole ration; in feed or milk replacers.
  - If symptoms persist after using 2 or 3 days, consult a veterinarian.
  - Treatment should continue 24 to 48 hours beyond remission of disease symptoms.
  - Daily intake is based on body weight of calf fed.

Antibiotics in Milk Replacer

- **Label Directions**
  - Over the counter label.
  - Livestock producer is responsible for following label, keeping records of intake, dates treated, and dates treatment ended.
  - Livestock producer is responsible for feeding the medicated milk replacer according to label directions.
  - Technically, the antibiotic containing feed can be fed at any point in the production period up to 20 months of age.
  - Technically, the antibiotic is to be fed continuously for only 14 days, as needed to treat specific disease conditions.

Antibiotics in Milk Replacer

- For treatment of bacterial enteritis caused by *Escherichia coli a*nd bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida* susceptible to oxytetracycline
- Treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin
- Limited to:
  - Calves
  - Beef and non-lactating dairy cattle

Antibiotics in Milk Replacer

- **Residue Warning:**
  - Withdraw 5 days before slaughter in 10mg/lb dosage.
  - Use of more than one product containing neomycin or failure to follow withdrawal times may result in illegal drug residues.
  - A withdrawal period has not been established for use in preruminating calves (any calf under 300 pounds)
  - Do not use in calves to be processed for veal.
  - A milk discard time has not been established for use in lactating dairy cattle.
  - Do not use in female dairy cattle 20 months of age or older.

Antibiotics in Milk Replacer

- **2008 there were 406 identified drug residues in bob veal or veal calves**
  - Bob veal—any calf from birth to several weeks of age and under 200 pounds to be harvested for human consumption
  - Veal—any calf from birth to 550 pounds raised on a liquid diet for a specific veal market
- **Of the 406 identified drug residues in veal calves,**
  - 178 were neomycin residues—single greatest culprit!!!
  - 12 were oxytetracycline residues
  - 42 were Banamine, 34 were penicillin
  - 55 were sulfa drugs (SMZ tablets, Albon, sulfamethazine)

Antibiotics in Milk Replacer

- **Neomycin**
  - Does not normally pass the intestinal blood barrier, except
    - Within the first 48 hours following birth, and
    - If a necrotizing enteritis occurs that disrupts the intestinal blood barrier, such as occurs with Salmonellosis and coccidiosis.
  - **Do Not, Under Any Circumstances, Ever**
    - Feed a neomycin or oxytetracycline containing milk replacer to any calf expected to enter the bob veal or veal market.

Antibiotics in Milk Replacer

- **Neomycin—If it is not absorbed, why use it?**
  - Works in the lumen of the intestinal tract.
  - Reduces bacterial shedding, both for *Salmonella spp.* and *Escherichia coli*.
  - Inexpensive at therapeutic dose of 1600 grams per ton.
  - If absorbed, neomycin will bind to the distal tubules and collecting ducts of the kidneys.
  - This chemically bound neomycin can be detected up to 180 days after dosage.
  - No aminoglycocide antibiotic, neomycin, streptomycin, or gentamicin can be administered parenterally in food animals because of potential kidney residues.

Antibiotics in Milk Replacer

- **Oxytetracycline**
  - Is absorbed to some degree from the intestinal tract into the bloodstream.
  - A broad spectrum antibiotic.
  - Has antiprotozoal activity as well as antibacterial activity.
    - Anaplasmosis and Q Fever
  - Quick withdrawal period of 5 days prior to slaughter.
  - At therapeutic levels exhibits some positive benefits for treating pneumonia caused by *Pasteurella multocida*.
  - May have some benefit in reducing the impact of *Mycoplasma bovis* infection.
  - Inexpensive at therapeutic dose of 1600 grams per ton.

Antibiotics in Milk Replacer

- **What can you expect from therapeutic levels?**
  - Reduced scour days by 50 percent
  - Reduced death loss.
  - Increased starter feed intake.
  - Increased average daily gain.
- **Why?**
  - Calves that are not sick continue to eat.
  - Calves that do not scour consume more starter feed.
  - Healthy calves gain more weight.
  - Healthy calves make safe food.

Antibiotics in Milk Replacer

- **Are there any negatives?**
  - No!!!
- Don't calves on therapeutic levels of neomycin and oxytetracycline have a sterile intestine?
  - Some do.
- Doesn't feeding this new high level of antibiotics in milk replacer wipe out all the good bacteria in the digestive tract?
  - In some calves, but it does not matter.

Antibiotics in Milk Replacers

- How can you make such statements?
  - **Because I have conducted the research!!!**
- Calves started on 1600 grams per ton of neomycin and oxytetracycline at the first sign of infectious diarrhea, vs. an equal number of calves on non-med
  - Ate twice as much starter--49.1 pounds vs. 26.7 pounds in 42 days on milk.
  - Gained 1.40 pounds per day vs. 0.95 pounds per day.
  - Had 36 scour days vs. 72 scour days--a 50% reduction
  - Had a zero death loss vs. a 16% death loss
  - Weaned at 42 days with 53.4 pounds gain vs. 30 pounds

Antibiotics in Milk Replacer

- Scouring calves were cultured by taking a rectal culture utilizing a sterile cotton swab.
- Bacterial isolation and antibiotic sensitivity testing, as well as PCR testing for virus and protozoan causes of diarrhea were conducted at Iowa Veterinary Medical Diagnostic Laboratory.
- *Salmonella spp.* and *Escherichia coli* were identified.
- Cryptosporidiosis was identified.
- Rota (Rio) virus was identified.

Antibiotics in Milk Replacer

- Two calves were discovered to have a sterile rectal culture with no bacterial isolation of any kind.
- These calves were carefully observed throughout the 42 day milk replacer feeding trial.
- These two calves exhibited no deleterious impacts associated with having a sterile rectal culture.
- These two calves were unremarkable when compared to their trial mates at weaning.
- These two calves were unremarkable when compared to their trial mates at 9 weeks of age.

Antibiotics in Milk Replacer

- While it is true that some calves will have a reduced bacterial population in the digestive tract while consuming a therapeutic level of neomycin and oxytetracycline in milk replacer,
  - It did not generate negative impacts.
  - Calves apparently picked up intestinal bacterial populations upon cessation of antibiotic therapy from pen mates, feed, forage, and their environment.
  - No pharmaceutically induced diarrhea was noted.
  - No observable negative symptoms were noted.
  - Performance was not negatively impacted.

Antibiotics in Milk Replacer

- Make full utilization of the available therapeutic antibiotic regime in milk replacer feeding.
- Take full advantage during the first 2 weeks of milk replacer feeding, the time when most infectious enteritis will be diagnosed.
- Do not be alarmed by warnings that feeding therapeutic levels of antibiotics in milk replacer sterilizes the intestine.
- Do not be misled into thinking the proper therapeutic utilization of antibiotics in milk replacer produces antibiotic resistance.

Antibiotics in Milk Replacer

- **What more could you ask for from modern science?**
  - Inexpensive compared to individual animal dosing.
  - Reduced scour days.
  - Reduced death loss.
  - Increased starter feed intake.
  - Improved average daily gain.
  - Reduced fecal shedding of pathological bacteria into your calf raising facilities.
  - Healthy fast growing dairy replacement heifers or dairy beef calves are the end result of this management tool.

Antibiotics in Milk Replacer

- **One other approved level**--for improved feed efficiency and daily rate of gain in cattle
  - 16 grams of Neomycin and 16 grams of Oxytetracycline per ton if feeding 10 ounces powder twice daily
  - 20 grams of Neomycin and 20 grams of Oxytetracycline per ton if feeding 8 ounces of powder twice daily
  - Approved for continuous feeding in milk replacers and starter feeds
  - Label requirements and withdrawal times apply
  - Do not, under any circumstances, feed this level in milk replacer or feed to bob veal or veal calves.

Thank You!!!

R. M. Thornsberry, D.V.M., M.B.A.