How Alternatives to Antimicrobials Function in the Gut

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What will we talk about?

Where are we with antibiotic reduction

- What should be though about with antibiotic reduction
 - What are examples of alternatives being used?

How to build a program



Pillars of an in-feed preventative drug program

Anticoccidial



Ionophore

- May kill parasites in the gut in the short-term and decrease parasite development in the gut in long-term; leaky
- Can get resistance, more difficult but not impossible
- Chemical coccidiostat
 - Stops parasite development in the gut (can continue if drug taken away); kills parasite in the gut
 - Easy to get resistance
- EU has kept this

Antibiotics

- Most preventative programs
 - Prevention of gram positive bacteria (e.g. Clostridium perfringens)
 - Treatments for either gram negative (e.g. *E. coli*) or gram positive bacteria (e.g. *Clostridum perfringens*)
- Treatment still remains (EU, USA, Canada)





US and Canadian Direction

US

Veterinary Feed Directive → 2017 due date

- Judicious antibiotic use veterinary oversight
- Treatment still allowed
- Allow ionophores, chemicals, BMD
- Never ever 3 → NO antibiotics, NO growth promotants, NO animal byproducts

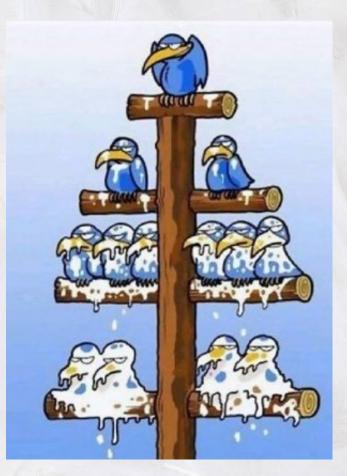
Canada

Veterinary Drug Directive → 2018 due date

- Judicious antibiotic use veterinary oversight
- As producer only able to access through vet prescription and purchase through commercial feed mill, vet, pharmacy
- Treatment still allowed
- CFC/TFC position will allow ionophores, chemicals
- Raised Without Antibiotics → NO antibiotics, NO ionophores, YES chemicals, YES live coccidiosis vaccines, YES animal byproducts
- Treatment still remains (EU, USA, Canada)

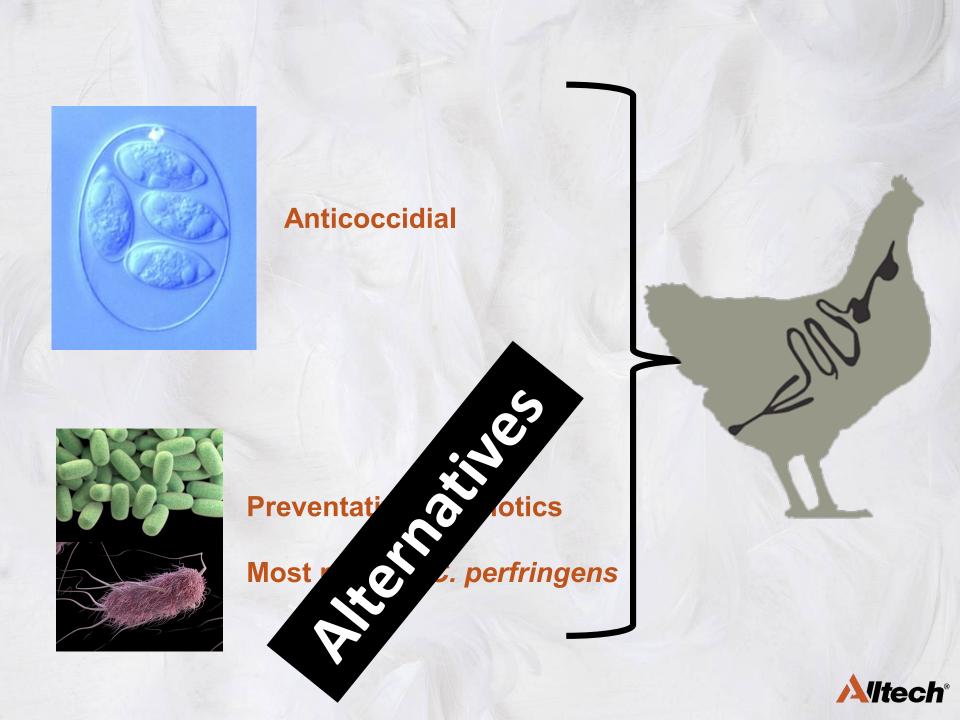


Let's be the leader of the pack



Whether you agree or don't agree, let's at least be the leader of the pack





The gut is an ecosystem

Microbes

Villi and microvilli

Gut health is balance

www.behance.net/gallery/12469903/Inside-the-Body-Health-Diseas



A program approach needed

No silver bullet

- ✓ Feed management
- ✓ Water management
- ✓ Management on farm
- ✓ Additive program



A Program Approach: Feed

 Nutrition Goal
 Optimal nutrient digestibility
 Optimal performance
 Minimal Digestive upsets
 Optimal return

Your nutritionist helps you...

Ingredient selection & levels Ingredient quality Digestibility Amino acid balance Fatty acid levels and ratios Vitamins Minerals Avoid mycotoxin contamination



Poultry Industry Council

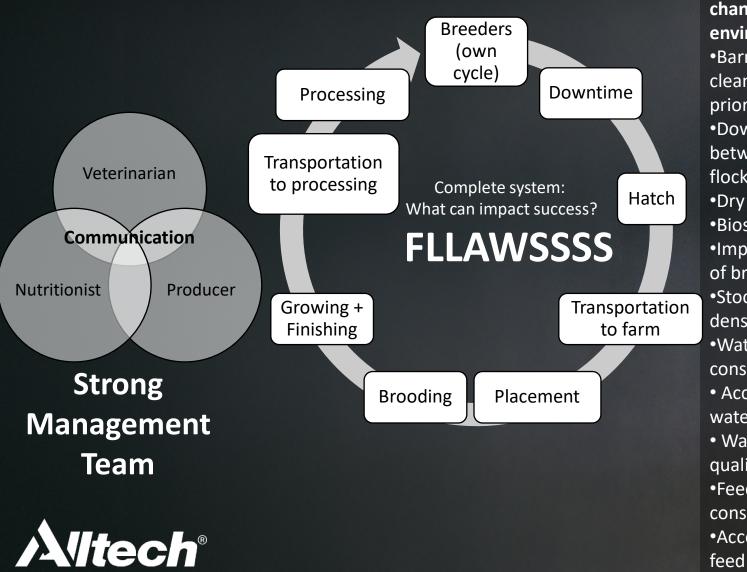
A Program Approach: Water

- Water is the forgotten nutrient
- Poultry ingest ~2X more water than feed
- Bad quality water → negatively impacts production
- Also have to look at:
 - Water management
 - Water equipment

Organism	Minimum pH	Optimum pH	Maximum pH	
Bacillus acidocaldarius	2.0	4.0	6.0	Good bacteria
Lactobacillus acidophilus	4.0-4.6	5.8-6.6	6.8	
Escherichia coli	4.4	6.0-7.0	9.0	1
Pseudomonas aeruginosa	5.6	6.6-7.0	8.0	Potentially bad & bad
Clostridium perfringens		6.0-7.6	8.5	bacteria



Operational Excellence



•Birds more •Supplement sensitive to al feed & changes in water during environment brooding •Barn •Litter quality cleanliness •Litter prior to flock moisture •Down time •Lighting between intensity flocks •Lighting •Dry clean? schedule Biosecurity •Barn Importance temperature of brooding •Barn •Stocking humidity density Ventilation •Water •Etc... consumption Access to water • Water quality •Feed consumption Access to

A Program Approach: Additives

No silver bullet

Antibiotic reduction & elimination

→ Need a combination of additives

Different uses for different additives







What is already in the feed?

✓ Enzymes✓ Minerals

Often "inorganic" – salt form of mineral

✓ Vitamins





Enzymes help to break down nutrient components so more accessible to bird Promote intestinal health → most of digestion done by end of upper intestine and help to feed beneficial bacteria of upper intestine

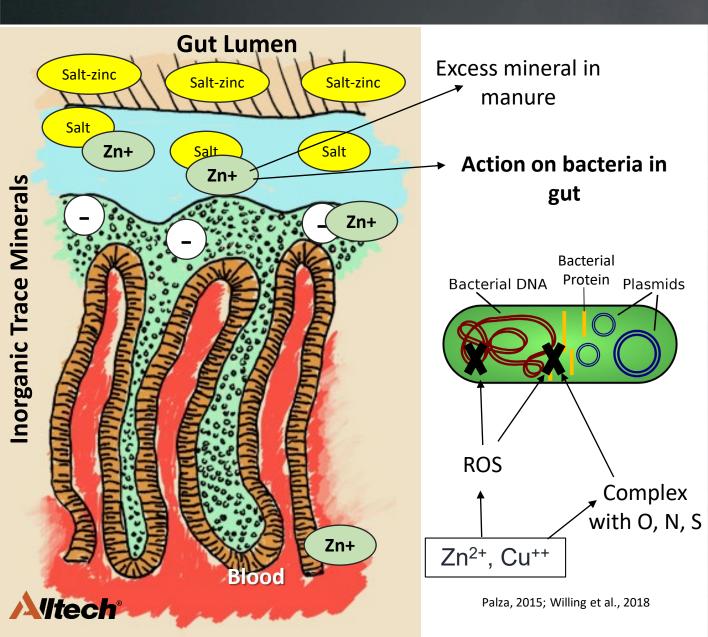


Bubbles in ceca or cecal droppings bacteria fermentation





Inorganic Zinc and Copper

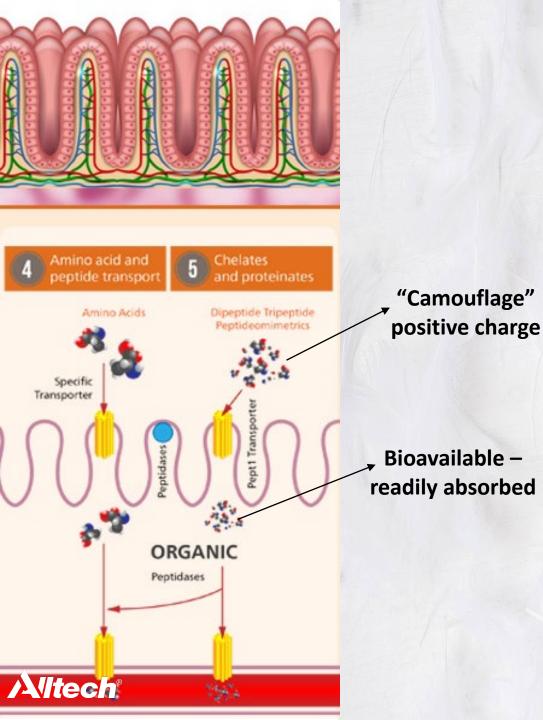


Willing et al., 2018

- Used at high levels in the feed or sometimes water
 - Above what is required
- Copper sulfate mouth lesions when levels too high

Resistance issues

- Plasmids
- Transferred
- Suggested ↑ resistance to antibiotics



Presenting Minerals in Different Forms

- Replicate plant material forms in a manufacturing process
- Make the plant take up more mineral



Phytogenics

Plant derived compound from broad range of plant materials - Use of the actual plant (e.g. powder), use of extract (natural or synthetic), use of essential oil (e.g. hydrocarbons, oxygenated compounds, nonvolatile residues)

- Potential for variation
- What is the dose?

Various suggested mode of action depending on chemical compound used

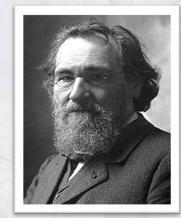
Applegate et al., 2010; Becerril et al., 2012; Muthamilselvan et al., 2016; Willing et al., 2018



Historical Research with Alternatives: Probiotics



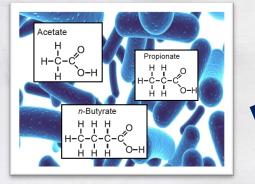
~4000 BCE



1907 - Elie Metchnikoff



1973 – Nurmi & Rantala



Bacteria metabolites

1965-2003+ – Redefining definitions of probiotics,
1989 USDA use "direct-fed microbials"





Chow, 2002; Nava et al., 2005; Hume, 2011; Perumalla et al., 2012

Probiotics

"Viable microorganisms that when ingested have a beneficial effect in the prevention & treatment of specific pathologic conditions"

Competitive exclusion

Selection criteria



Does it colonize the gut permanently (e.g. Bacillus vs. Lactobacillus)?

Beneficial bacteria function? Altering communities? Metabolites working?

Large proportion of use in neonatal animals

Chow, 2002; Nava et al., 2005; Applegate et al., 2010; Hume, 2011; Perumalla et al., 2012



More than just the microbes there

Each bacteria can release signal molecules

Each bacteria release metabolites

Ricke, 2003; Gauthier, 2008; Kim and Kim 2015; Bedford and Gong, 2018; Deepa et al., 2018;

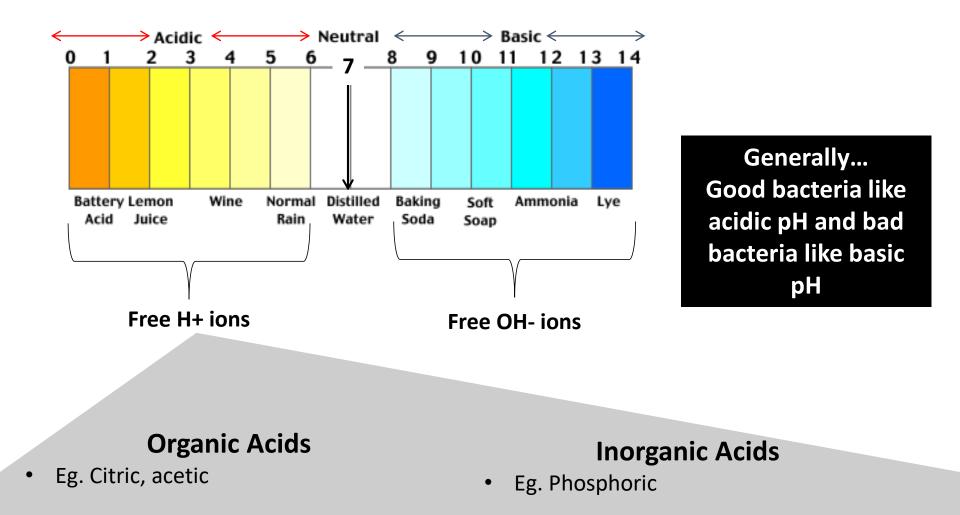
https://mhrussel.wordpress.com/2013/07/18/new-meaning-to-the-term-gut-feeling-gut-bacteria-and-the-brain/

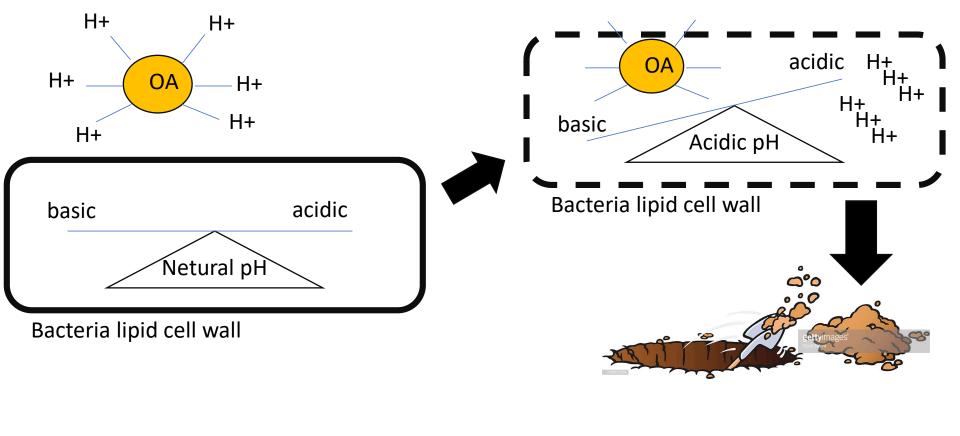
Bacteria can:

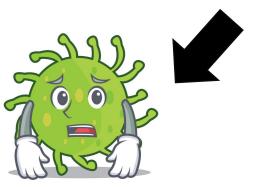
- ✓ Make own environment
- ✓ Make use of environment
- ✓ Communicate
- Bacterial metabolites impact the intestinal tract
 - Fermentation of carbohydrates
 - Butyric acid, acetic acid, proprionic acid, gas
- Diversity of bacteria

 diversity
 of metabolites







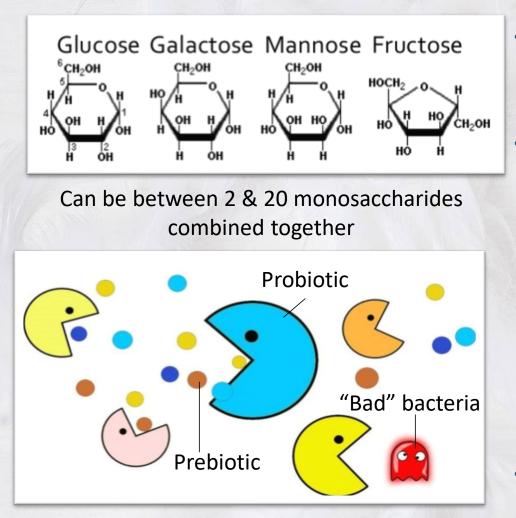




Bearson et al., 1997; Ricke, 2003

Prebiotics

"Non-digestible food ingredients with selective effects on GIT microbiota"



Gibson and Roberfoid, 1995; Macfarlane et al., 2006; Hume, 2011

1995 – Gibson & Roberfoid

 Initial definition & gained attention from medical community

Qualifiers

- Not broken down or absorbed in upper GIT
- Selective substance for one or limited beneficial commensal bacteria & stimulate them to grow &/or be activated
- Alter GIT flora for healthier composition
- (Induce luminal/systemic effects beneficial to host health)
- Eg. FOS, Inulin, Galato.., MOS is different



Different uses?



Yeast

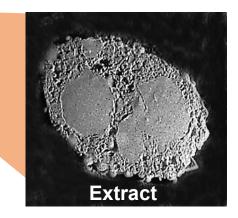
Saccromyces cervesia (Brewer's yeast)

Whole yeast

15-90% mannose (w/w)

Outer (mannanoligosaccharide)

Inner (glucomannan)



• N- and Oglycosylations anchored to amino acids

- α-side chains mostly
- Agglutinate, antigenic, immunogenic

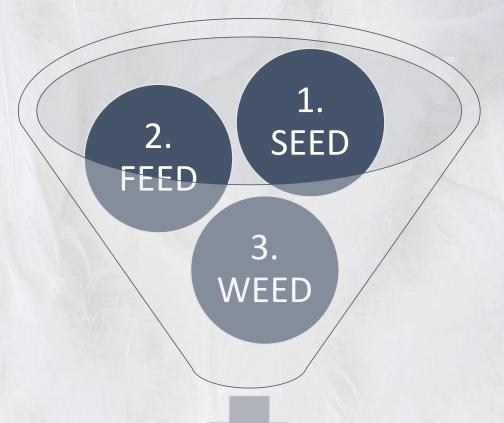
- ß-glucans
- Porous structure
- "Sticky"+Stacking effect – Hydrogen bonds, van der Waals

 Highly digestible proteins



Putting Programs together 3 steps as described by Dr. Steve Collett

Holistic approach: A "start to finish" management system



Support for intestinal tract and optimum conditions for digestion



New alternatives are popping up everyday

Be vigilant on the research & background information of the technology

Key Criteria for the Selection of an Alternative

- 1. Consumer acceptance?
- 2. Safety?
- 3. Pellet stability?
- 4. Mode of action?
- 5. Consistency?

Zinc oxide Copper sulfate Essential oils Herbs Organic acids Enzymes Probiotic: Bacillus Probiotic: Lactic acid bacteria Metabolites of probiotics Prebiotic: FOS Mannan Rich Fraction

. . .

Choosing the Right Combination or Program

- 1. What is your goal?
- 2. What is your challenge?
- 3. What can you fix/improve?
- 4. Product mode of action?
- 5. What should you use?



4

Take home message

- 1. Alternatives to antibiotics appear to be "new norm" in developed world
 - a) Varied harvesting & manufacturing
 - b) Varied mode of action
- 2. Combination of alternatives is key
 - a) Based on mode of action
 - b) Remember, no silver bullet
 - c) Avoid "a rose by any other name"
- 3. Ask the question of your goal for an alternative programa) Goal? Challenge? To be fixed? Mode of action? To be used?



Thank You

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