Beyond Antibiotics: Challenges and Opportunities of Managing Broilers without Medicated Feed

Rob Renema, PhD, FICN

broiler QC
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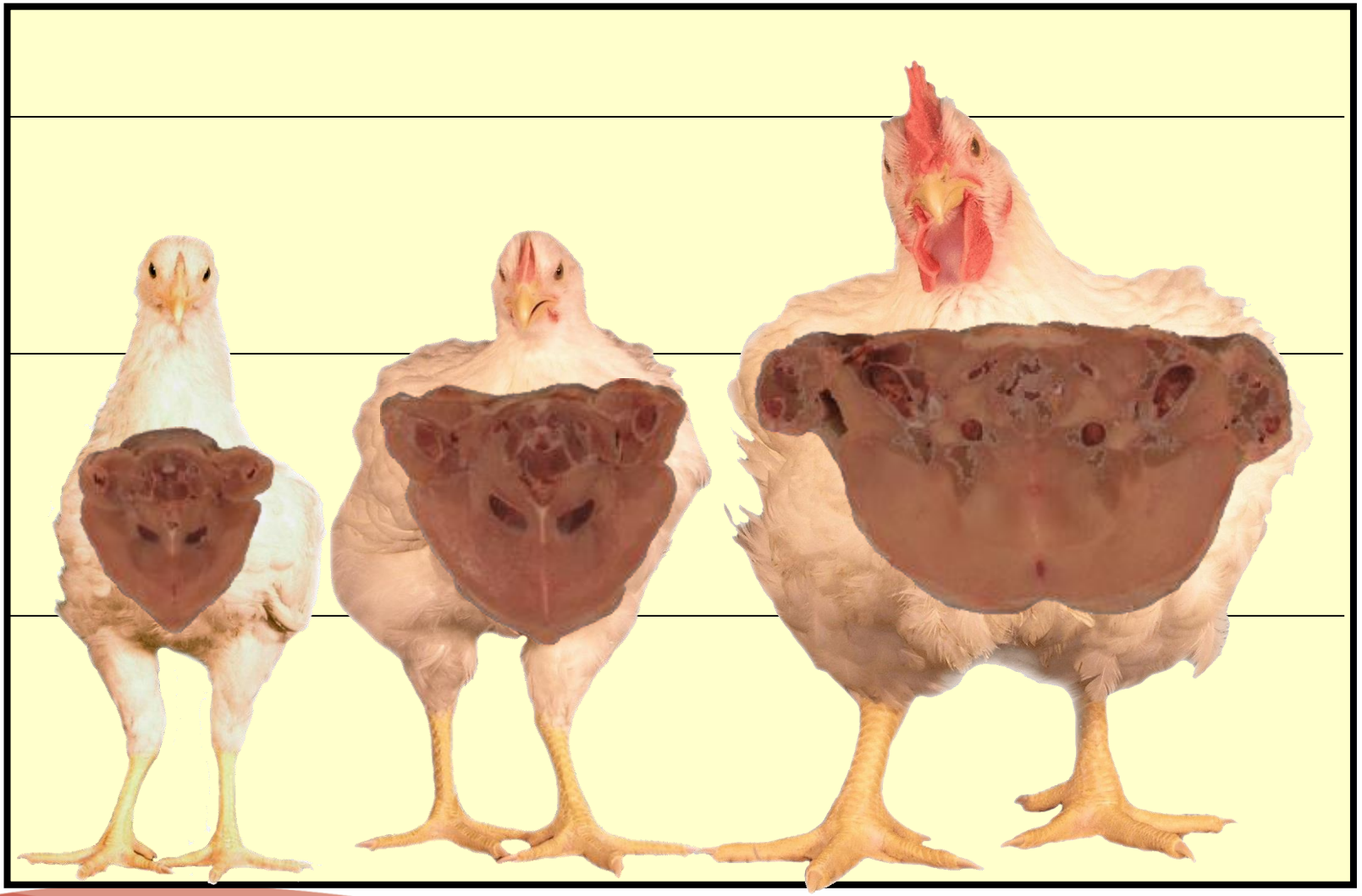
Beyond Antibiotic Growth Promoters: Finding our Way Together

SUMMARY

- No single solution that works as well or as consistently as Antibiotic Growth Promoters (AGPs) have worked.
- Need to explore mix of AGP replacements and enhanced bird health (via feed additives and management)
- Best results when flock management conditions also considered
  - Brooding management
  - Environmental management
  - Water system management
  - Flock Health

Broiler Growth to 6 weeks of Age



Broiler 50 years ago Broiler 30 years ago Today's Broiler

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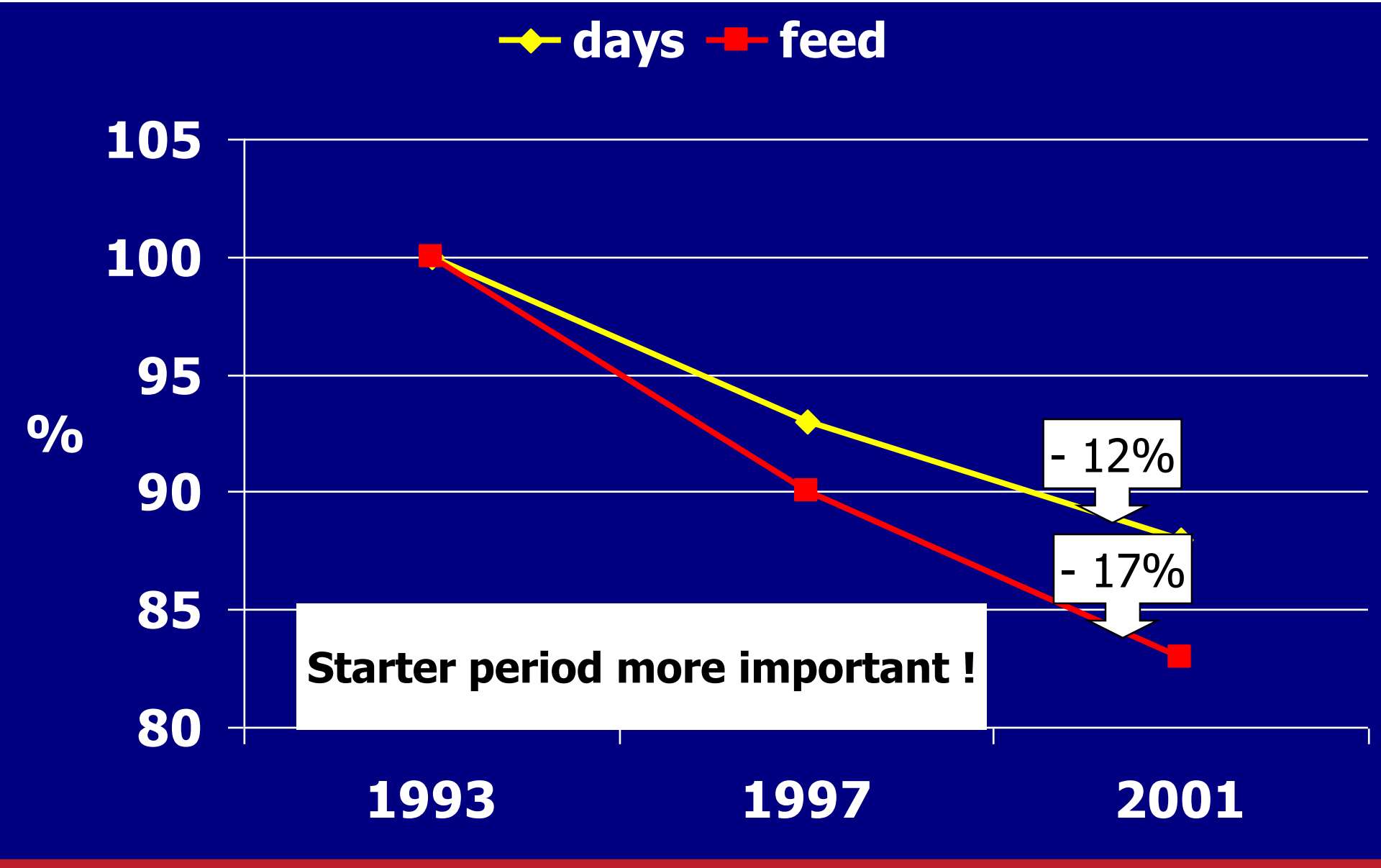
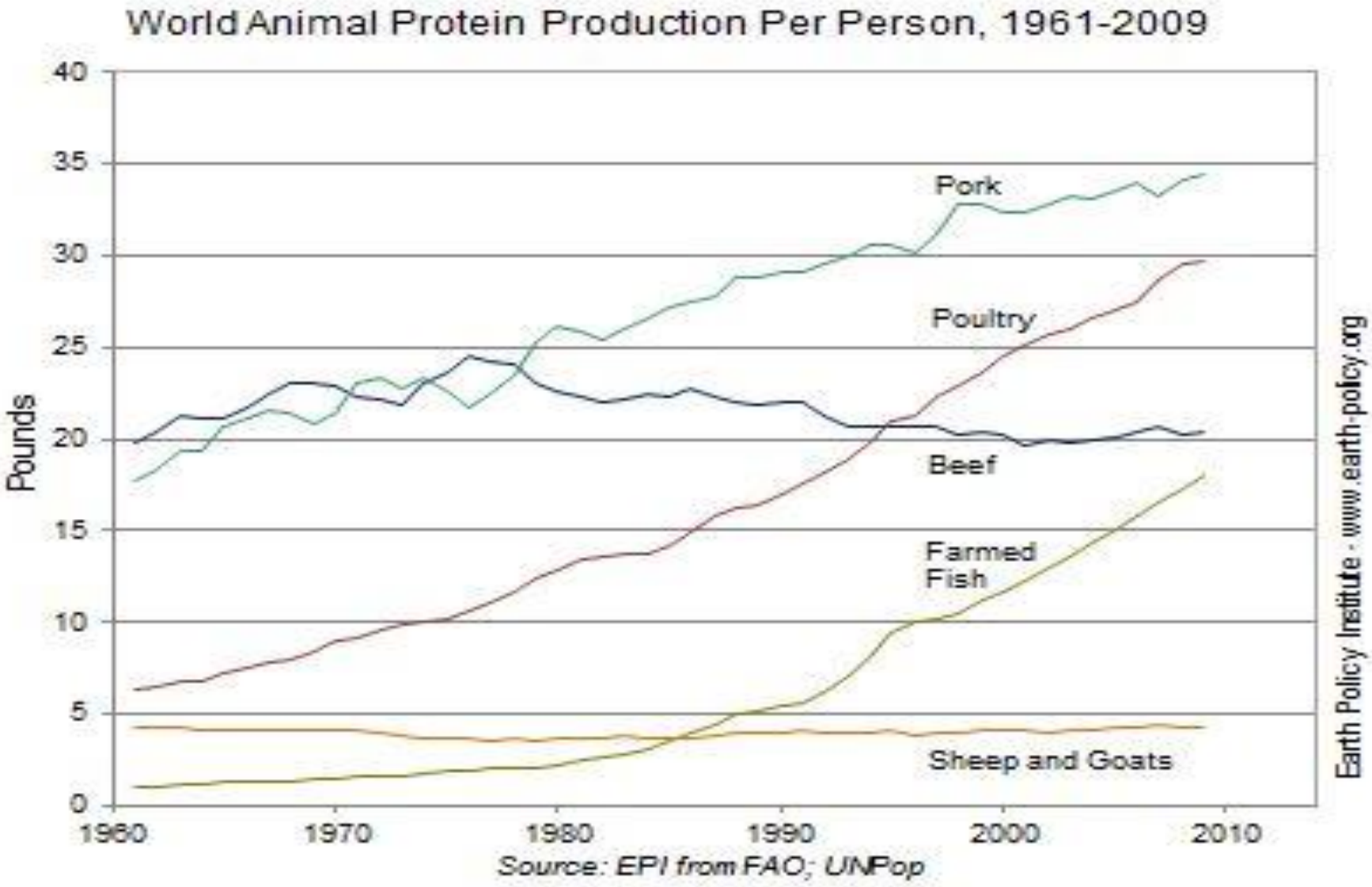
Age & Feed to Produce a 2040 g Broiler



Are AGPs a Solution for Poor Quality Management Conditions?

- AGP research in 1950s demonstrated overall response to AGPs inversely-proportional to well-being of experimental animals
- Impact of AGPs reduced when housing, hygiene, nutrition and health optimized
- Are AGPs a crutch for those not willing or able to focus on management conditions?
  - Hatchery injection of antibiotics
  - Bird density
  - Health challenges due to poor brooding, culling, environmental conditions etc.


World Animal Protein Production Per Person, 1961-2009
Pounds
40
35
30
25
20
15
10
5
0
1960
1970
1980
1990
2000
2010
Pork
Poultry
Beef
Farmed Fish
Sheep and Goats
Source: EPI from FAO; UNPop
Earth Policy Institute - www.earth-policy.org

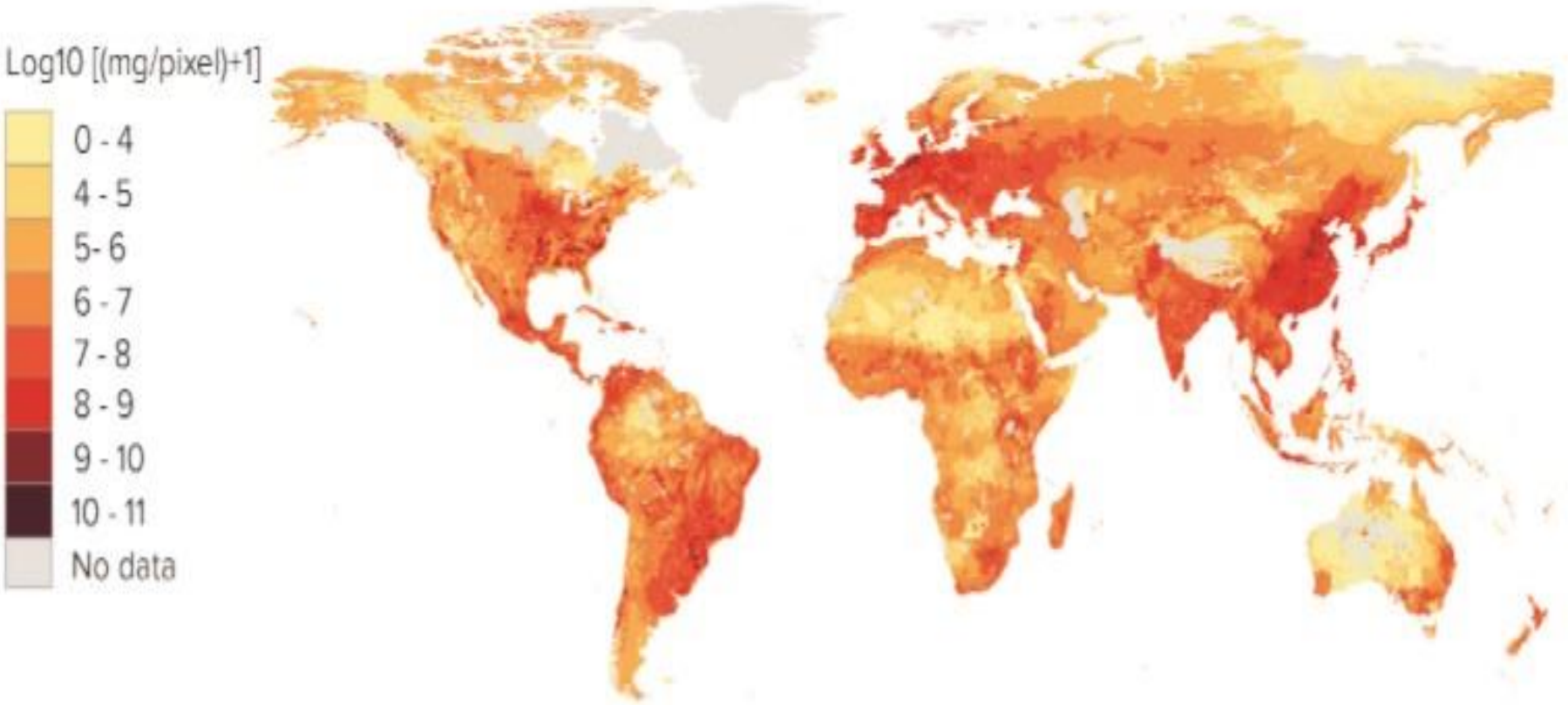


FIGURE 3-1: Global antibiotic consumption in livestock (milligrams per 10 km² pixels) 2010

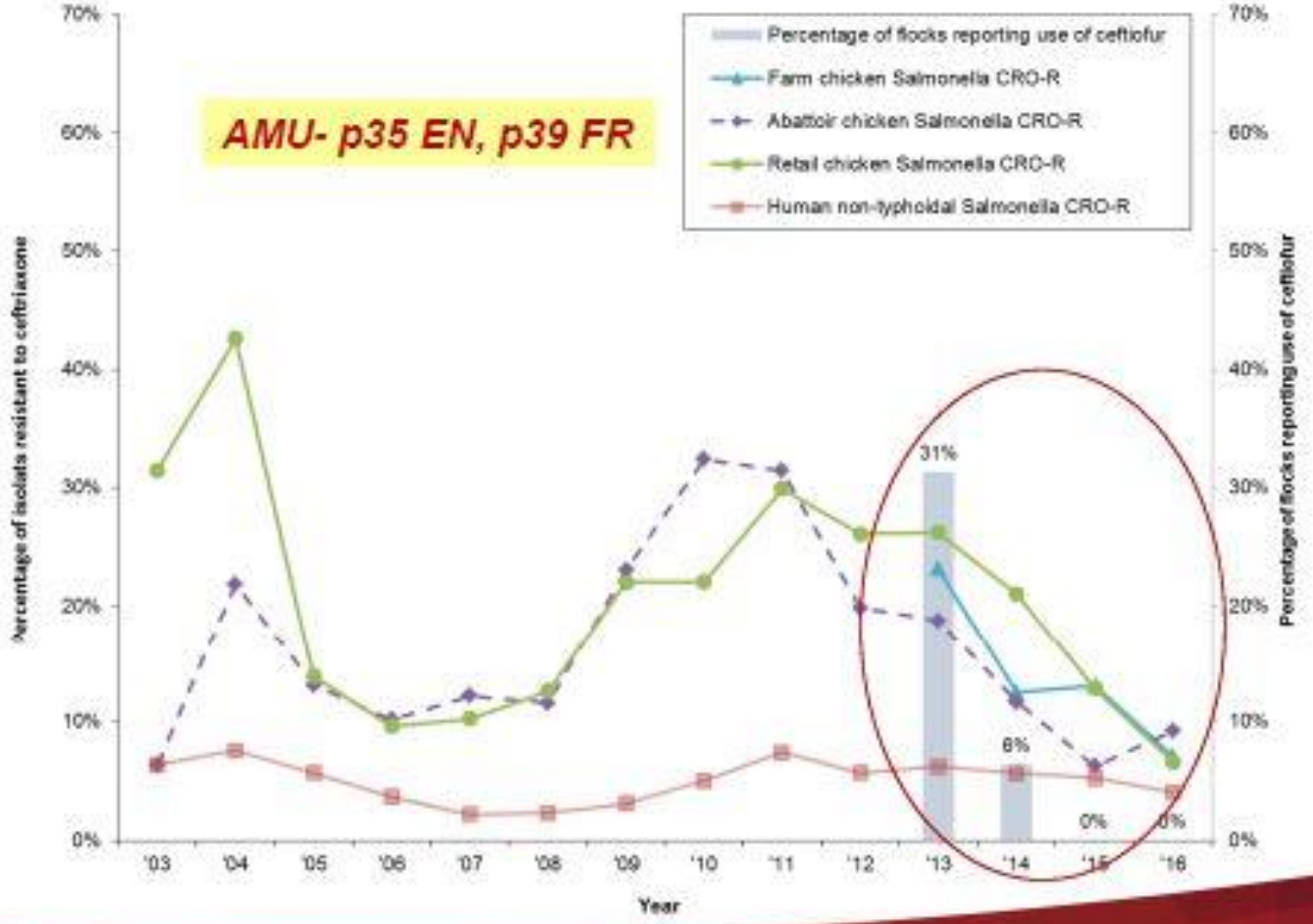
Source: Van Boeckel et al. 2015

Antibiotics Impacted by Voluntary Canadian Bans in 2018 (Cat. 2) and 2021 (Cat. 3)

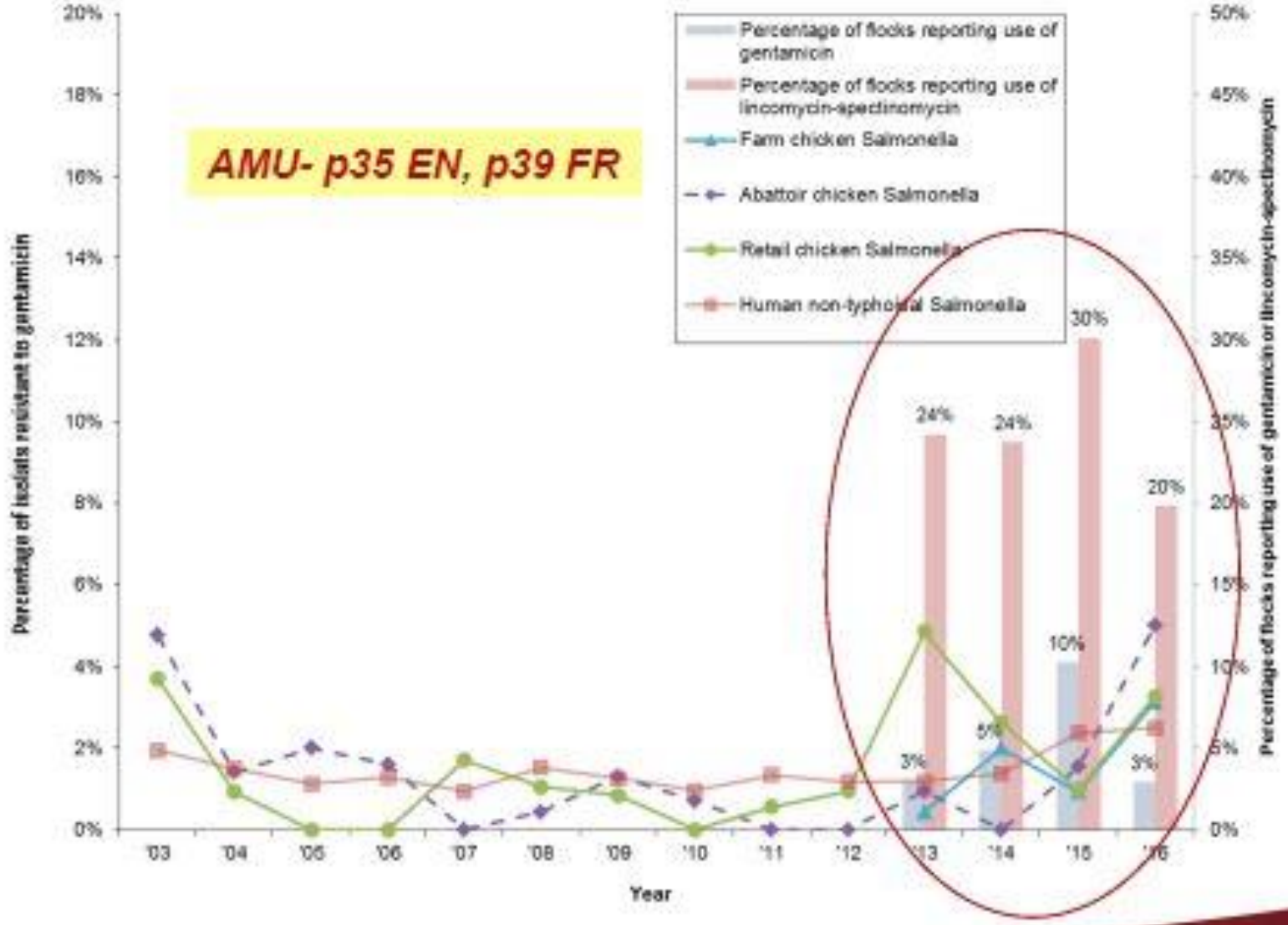
* Not an exhaustive list, but those most used in a preventive fashion:

	Drug Family/Name	Brand Name
Antibiotic Use at the Hatchery		
Category II	Lincomycin+Spectinomycin	Linco-Spectin
	Gentamcyin	Gentocin
Antibiotic Use in the Feed		
Category II	Virginiamycin	Stafac, Virginiamycin
	Lincomycin HCL	Lincomix
	Tylosin	Tylan
	Penicillin G Procaine	Pen-P, Penicillin G Procaine
Category III	Bacitracin	BMD, Albac, Zinc Bacitracin
Antibiotic Use in the Water		
Category II	Penicillin+Spectinomycin	Vibiomed Booster, Medivit, Super Booster

Data integration: resistance of *Salmonella* to ceftriaxone from chickens and humans and farm-level antimicrobial use data



Data integration: resistance of *Salmonella* to gentamicin from chickens and humans and farm-level antimicrobial use



Environmental Incidence of Antibiotic-resistant Bacteria

- Mehdi et al, 2018: Even though low levels used in feed, the additive effect of all production is tonnes of antibiotics being released into environment
  - Risk for biotransformation and bioaccumulation
  - Resistant bacteria found in fields months after spreading
  - Antibiotics interact with soil differently
    - Some travel further down than others
    - Affected by soil type (silty or clay)

- Furtula (2013) reported 58% of *Enterococcus spp*. Isolates in surface water and 100% of isolates in groundwater were resistant to more than one antibiotic

Where is the Biggest Impact of Removing AGPs from Animal Production?

- Growth response to AGPs appears to be small in optimised production systems
- Suggests loss of income minimal in high-income industrialized countries
  - US: Production benefit of AGP not covered by cost to add to feed
- Loss of income higher in lower income countries with less developed hygiene and production practices

Where is the Biggest Impact of Removing AGPs from Animal Production?

Table 6. Species-specific relative average daily growth difference between animals raised with and without antibiotics as growth promoters.

	1980s literature (%)	2000s literature (%)
Cattle	7	3
Chickens	4	0.7
Pigs	9	1

- Growth response to AGPs appears to be small in optimised production systems
- Loss of income higher in lower income countries with less developed hygiene and production practices

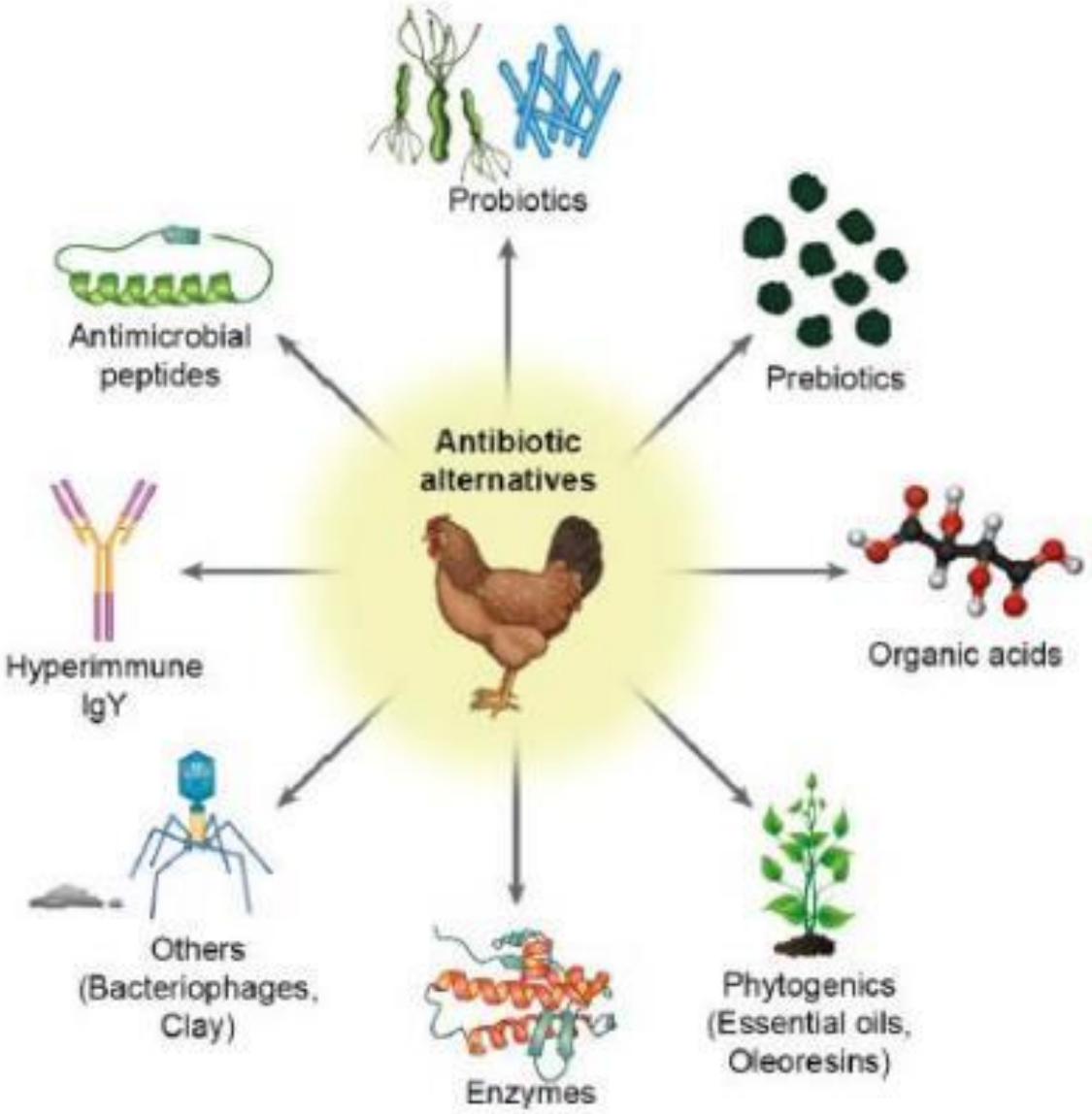


Fig. 1. Various classes of antibiotic alternatives that are available for use in poultry production.

Gadde et al., An. Health. Res. Rev. 2017

Survey of Botanical Alteratives to Antibiotics

Diaz-Sanchez et al., 2015. Poult. Sci 94:1419-1430

Table 2. *Continued.*

Feed additive	Inclusion Rate	Performance effect	Reference
Cinnamon	200ppm	Improve BW and FCR	(Al-Kassie, 2009)
Grape Seed Extract (GSE)	0.6g kg^{-1} 1.8g kg^{-1} 3.6g kg^{-1}	No effects on growth performance	(Brenes and Roura, 2010)
Moringa oleifeira leaf	5% 10%	Performance decrease at inclusion levels above 5%	(Olugbemi et al., 2010)
Biomin P.E.P 125 poultry	125g/tn	BW improvement 2210 ± 253 gr	(Perić et al., 2010)
Thymol (Thy) Cinnamaldehyde (Cn)	15gr/tn (thy) 5 gr/tn (cn)	Increase BW by 4 to 5%	(Tiihonen et al., 2010)
Green Tea extract	0.1g/kg 0.2g/kg	Increase BW and FE	(Erener et al., 2011)
Ginger	250 g/100kg 500g/100kg 750g/100kg	No effects on performance	(Mohammed and Yusuf, 2011)
Grape Pomace Con (GPC) Grape Seed Extract (GSE)	60g/kg 7.2g/kg	GSE decreased weight gain	(Viveros et al., 2011)
Rosemary leaf Rosemary EOs	5.7; 8.6; 11.5g/kg 100; 150; 200mg/kg	Rosemary EOs improve LWG and FE	(Yesilbag et al., 2011)
Thyme extract	0.2% 0.4% 0.6%	No significant effect on BW/FCR	(Pourmahmoud et al., 2013)
Enviva EO 101	100 g/tn	Improve BW by 1,924 gr Improve FCR by 1.90	(Amerah et al., 2012)

Table 2. *Continued.*

Feed additive	Inclusion Rate	Performance effect	Reference
Moringa oleifera leaf	25% 50% 75% 100%	Improve feed intake At higher inclusion levels decrease final weight/WG	(Gadzirarayi et al., 2012)
Rosemary EO Oregano EO EO mixture	50 to 100mg/kg 50 to 100 mg/kg 1,000 mg/kg	Improved BW and FE	(Mathlouthi et al., 2012)
Copaiba EO	0.30 mL kg^{-1} 0.45 mL kg^{-1} 0.60 mL kg^{-1}	Decrease on performance at high inclusion levels	(Aguilar et al., 2013)
Grape Seed Extract (GSE)	0.025g/kg 0.25g/kg 2.5g/kg 5g/kg	Reduction in BW gain up to 2.5g/kg	(Chamorro et al., 2013)
Thymol+Carvacrol	60 mg/kg 100 mg/kg 200 mg/kg	Increase ADG (g) by 71.4% Increase G:F (g/Kg) by 601	(Hashemipour et al., 2013)
Tecnaroma Herbal Mix PL	100 g/tn 200 g/tn 300 g/tn 400 g/tn 500 g/tn	Improve BW by 3.418 to 3.427 Kg Improve F:G ratio by 1.64 to 1.68	(Khattack et al., 2014)
Marjoram leaf	0.5% 1.0% 1.5%	Improve LBW, BWG, FCR, and FI	(Ali, 2014)

Alternatives to AGPs

- Experiments have shown products that do mimic AGP action in the gut, but not always with growth promotion
  - Only want to pursue solutions that also have a growth promoting aspect?
  - Could be part of a larger solution of enhanced gut/bird health?
  - Don’t underestimate the impact of Immunological Stress
    - Can increase BMR, decrease feed intake, and decrease BW gain

Alternatives to AGPs that Retain Growth Effects

Table 4
Proposed alternatives to antimicrobial growth promoters.

Alternative	Host effects	Bacteria effects	Growth effects	Species
Plant extract (*Macleaya cordata*)	↓ Inflammation	Not reported	Enhanced growth	Poultry
Mushroom polysaccharide extracts (*Lentinus edodes*)	Not reported	Not reported	Enhanced growth	Poultry
Direct-fed microbial (*Bacillus amyloliquefaciens*)	↑ Villus crypt height	↑ *Lactobacillus* spp.	Enhanced growth	Poultry
Probiotics (*Lactobacillus reuteri* and *L. reuteri*, *Bacillus subtilis* + *Saccharomyces cerevisiae* combination)	Stimulates intestinal immunity	↓ *Escherichia coli*	Enhanced growth	Poultry
Chinese herbal medicine	Not reported	Not reported	Enhanced growth and efficiency	Poultry
Antimicrobial peptide (AMP-P5)	Not reported	↓ Caecal and ileal coliforms	Enhanced growth	Swine
Catechins (epigallocatechin gallate)	Not reported	Not reported	Enhanced growth	Swine
Plant extract (*Scrophularia striata* and *Ferulago angulata*)	↓ Heterophil/lymphocyte ratio, ↓ plasma triglyceride	↑ Caecal *Lactobacillus* spp., ↓ caecal and ileal coliforms	Enhanced growth	Poultry

- Products consisted of plant extracts or direct-fed microbials
  - This is the starting point for proven products that enhance growth and likely have some host or bacterial AGP replacement function
- Proven health or growth affect from other commercial and non-commercial products could still be part of a larger solution. Need mix of AGP replacements and enhanced bird health (via feed additives and management).

Brown et al., 2016

2019 Poultry Nutrition & Feed Survey

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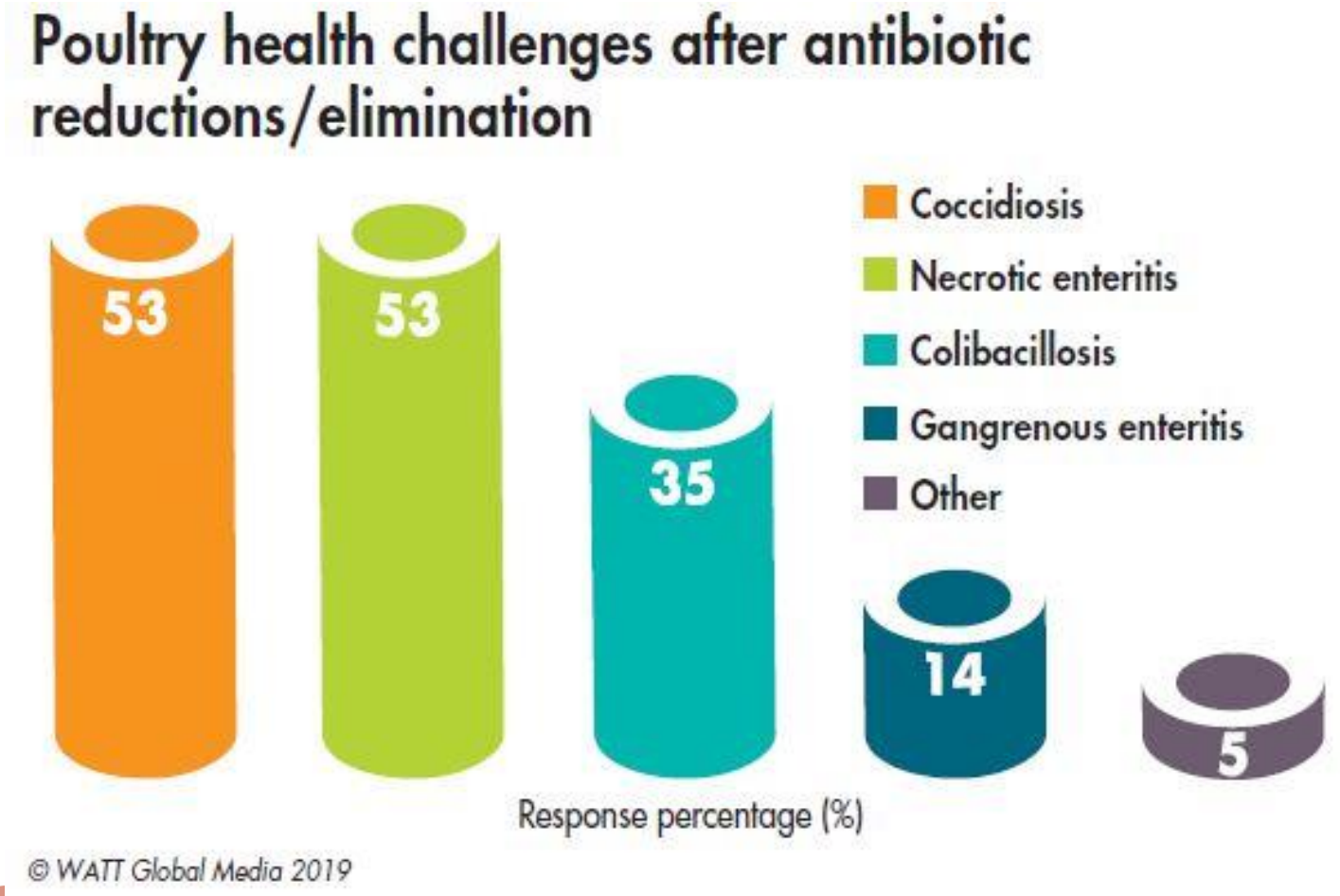
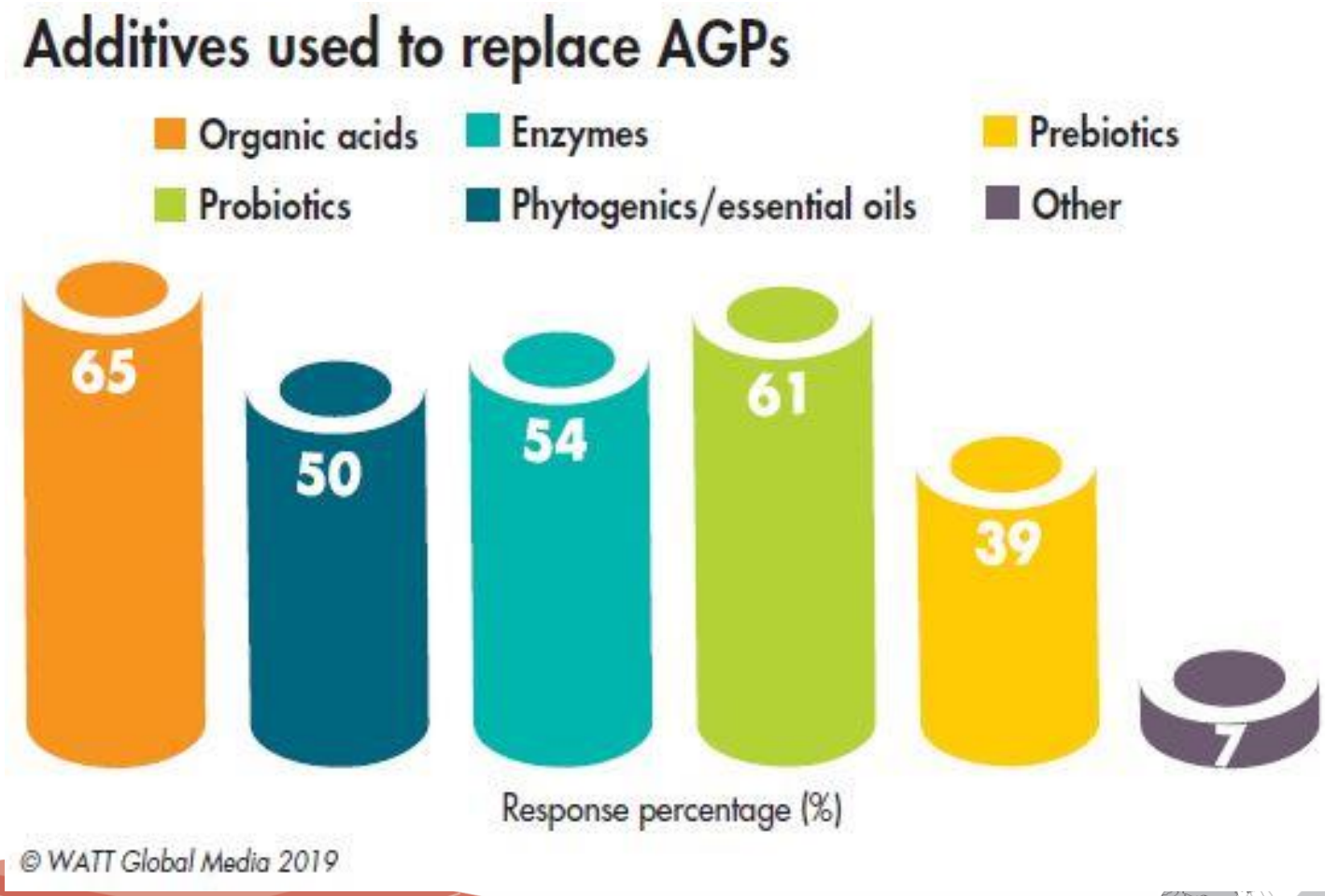
Poultry USA, April 2019

2019 Poultry Nutrition & Feed Survey



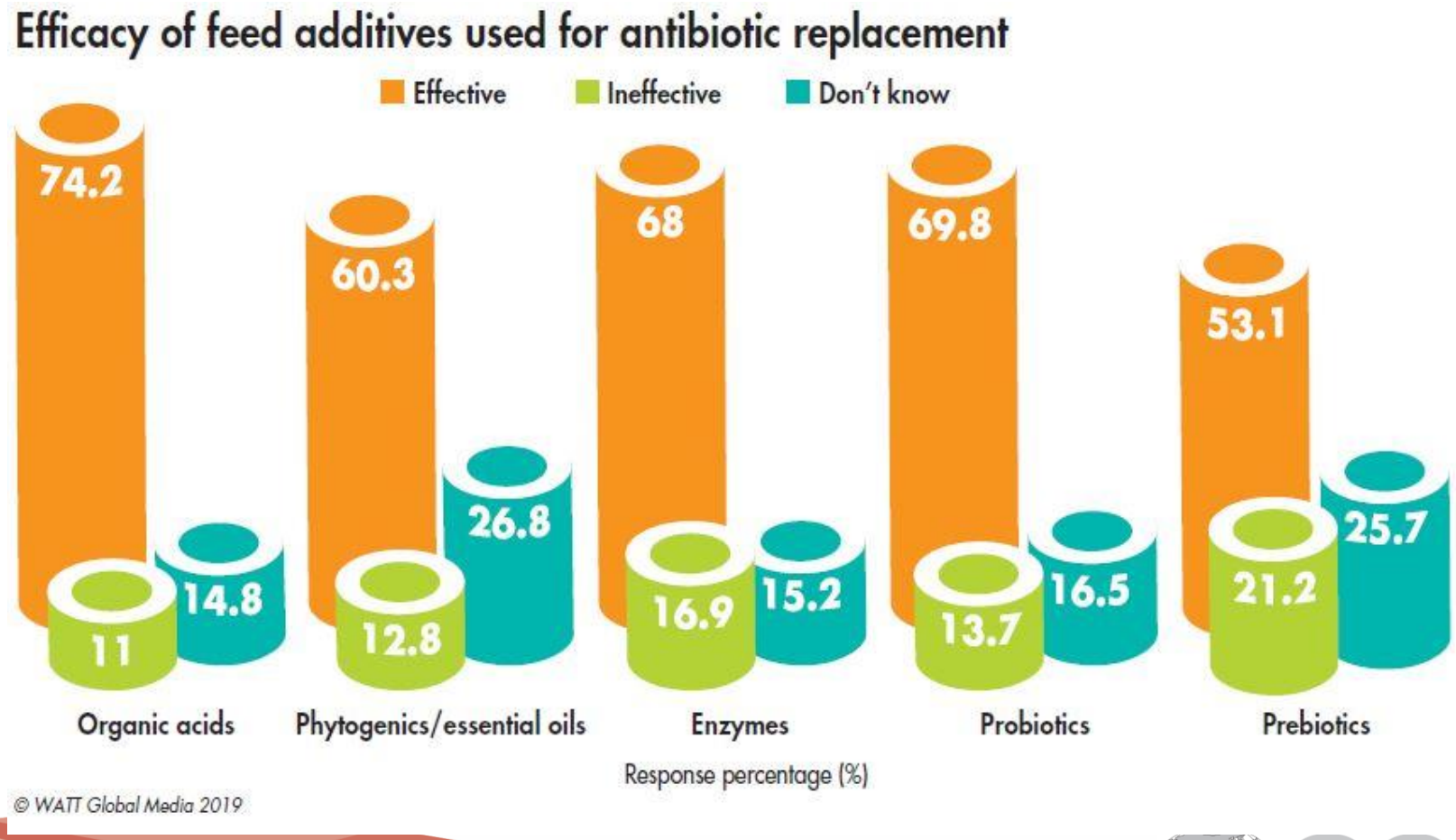
Poultry USA, April 2019

2019 Poultry Nutrition & Feed Survey



Poultry USA, April 2019

2019 Poultry Nutrition & Feed Survey



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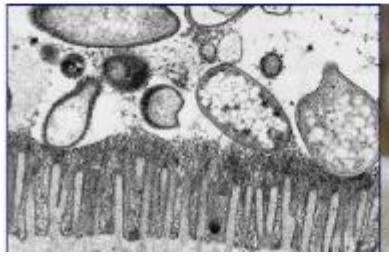
Poultry USA, April 2019

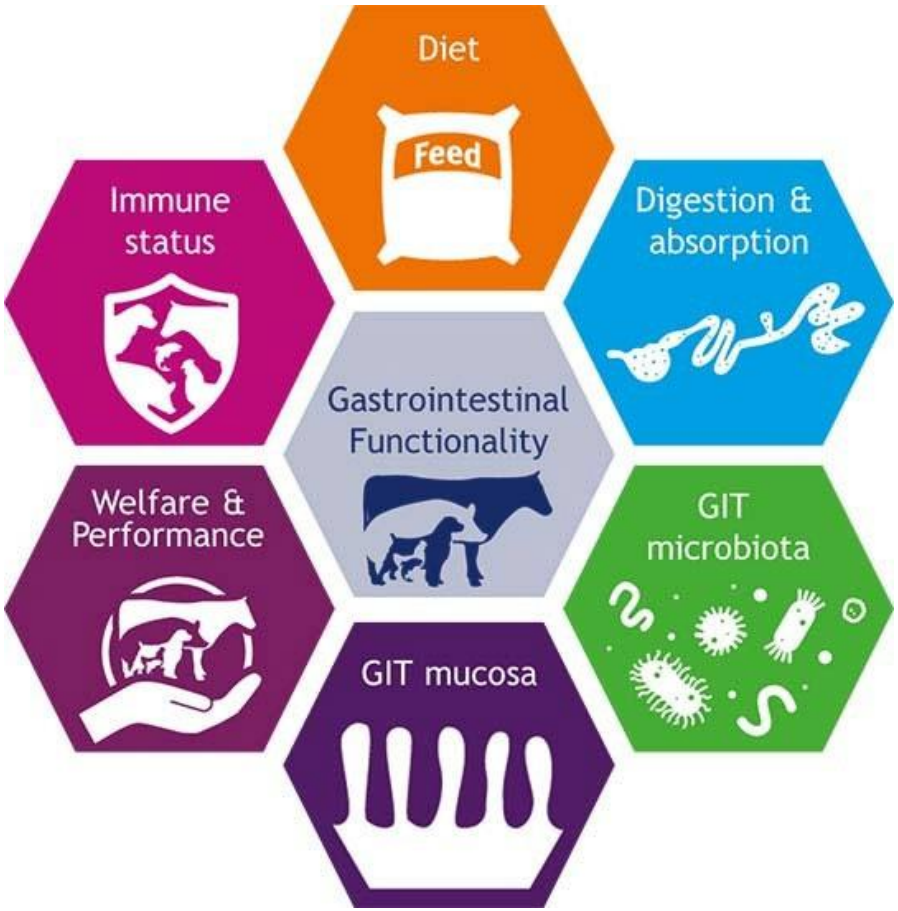
Gastro-Intestinal Tract (GIT) Maintenance

- GIT consumes approximately 20% of dietary energy
- Protein turn-over rate of 50 to 75% per day (Cant et al., 1996)
- ~25% of daily protein synthesis can be secreted into the gut (Simon et al., 1983)
- Contains > 70% of all immune cells found in the body (Kagnoff, 1993)



Source: Todd Applegate DSM webinar 2020

What is Gut Health?



* Gastrointestinal functionality = “steady state where microbiome and the intestinal tract exist in symbiotic equilibrium and where welfare and performance of the animal is not constrained by intestinal dysfunction” (Celi et al., 2017).
* Combination of gut physiology, endocrinology, microbiology, immunology and nutrition.

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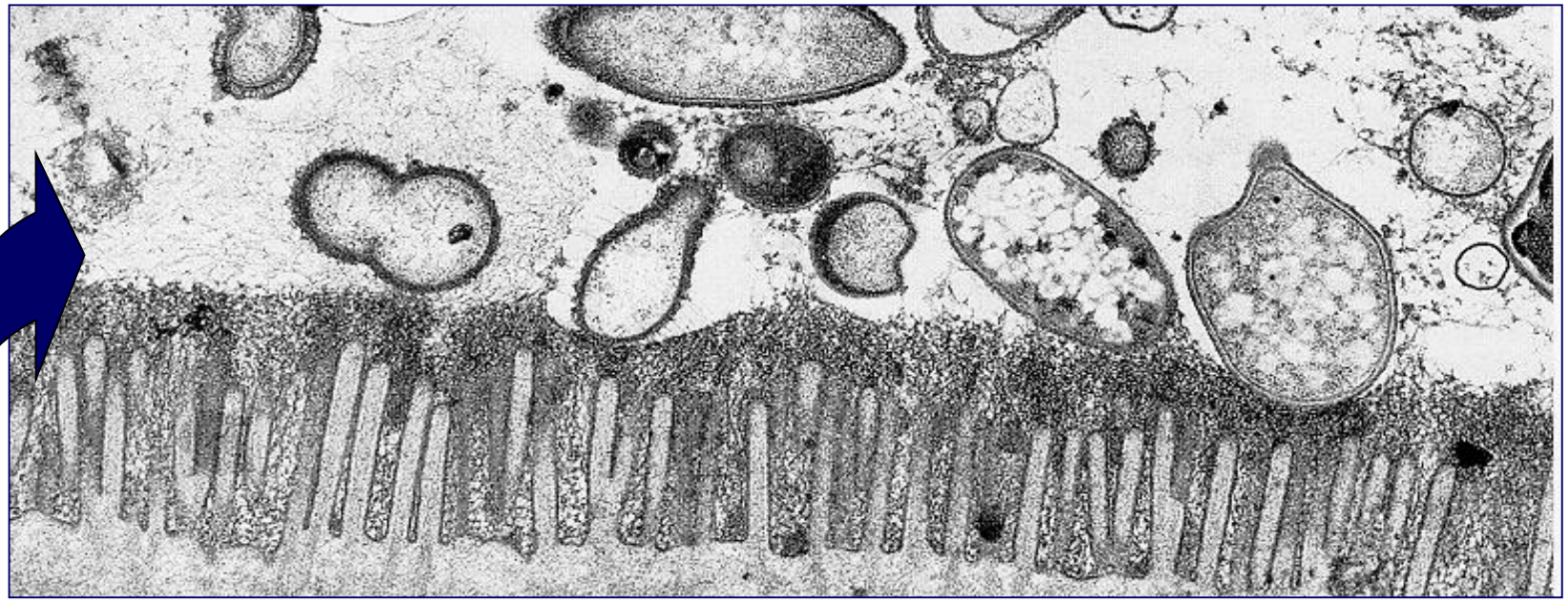
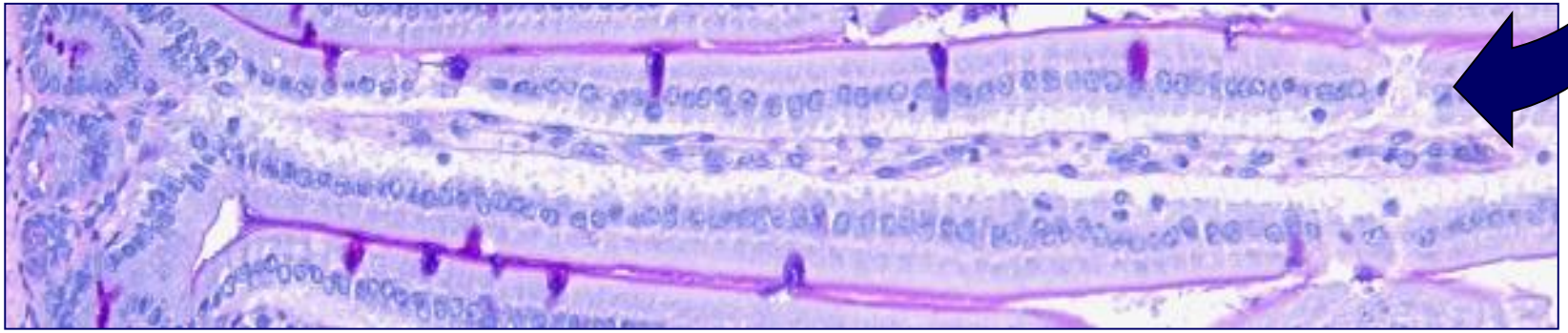
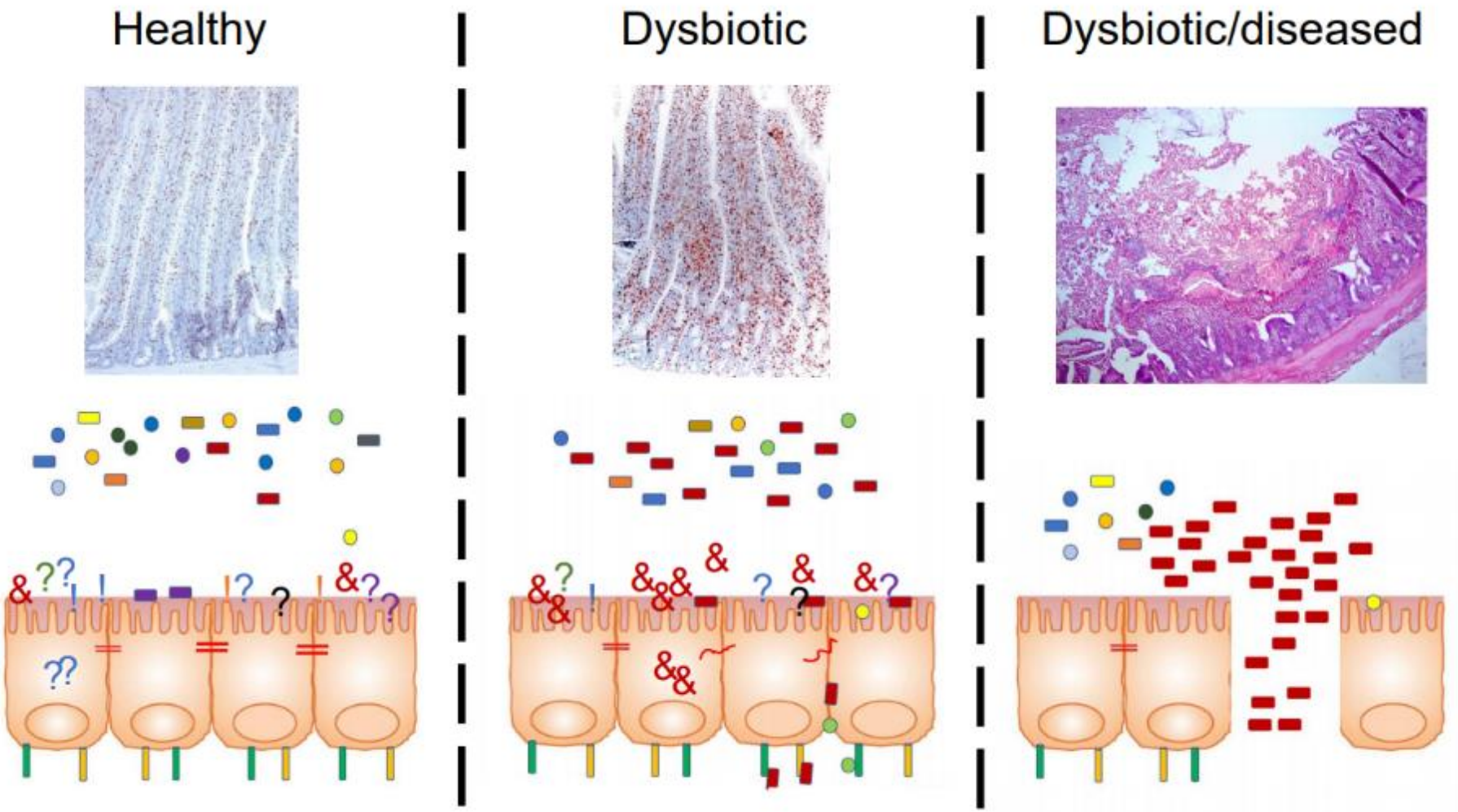
Based on Pietro Celi, 2019



Complex cellular communities





Source: Filip van Immerseel DSM webinar 2020

Alternatives to AGPs: Confusion over Expectations vs. Advancement

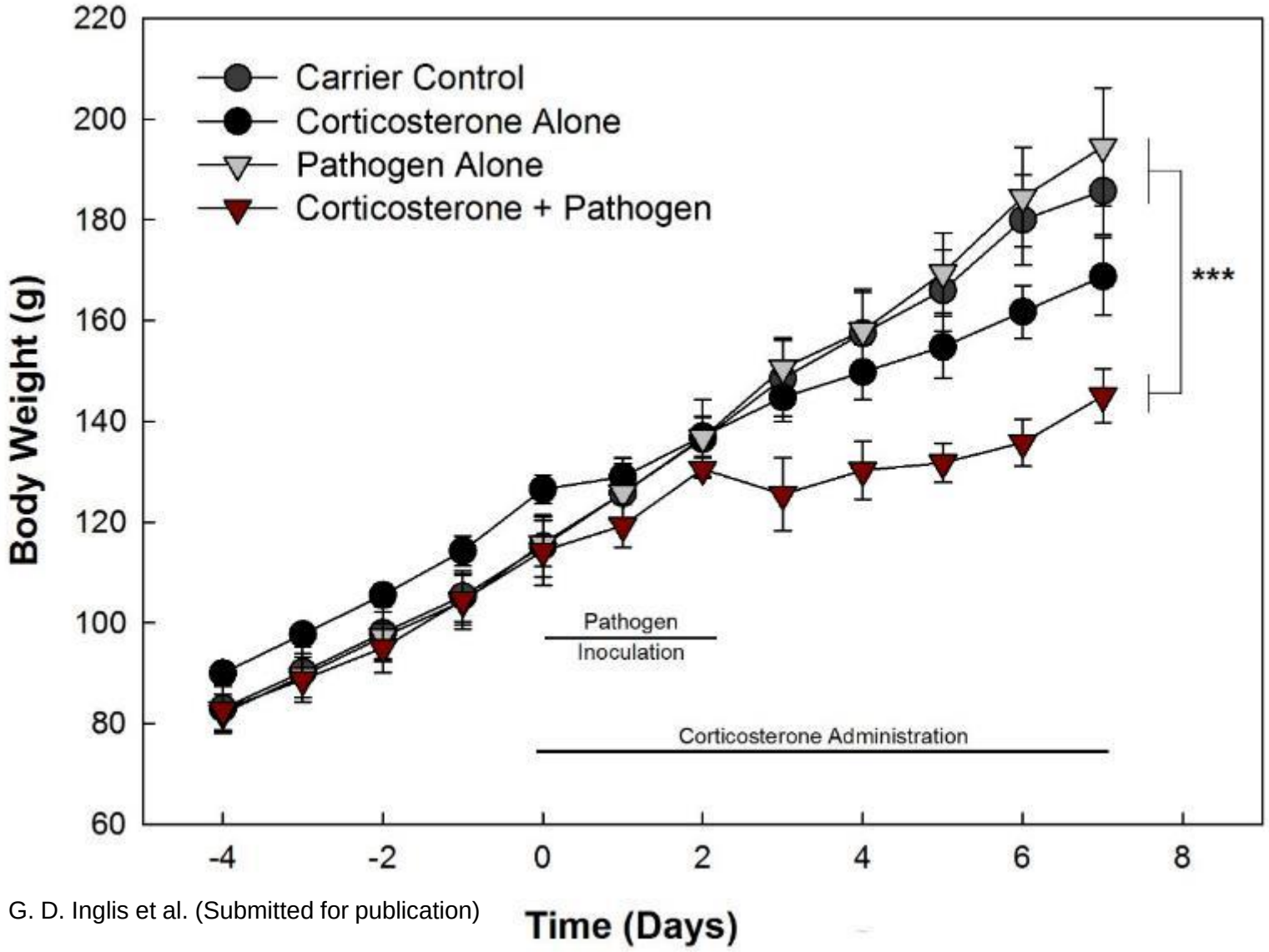
- Feed additives vs. other reasons?
  - Progress through better genetics, husbandry, health practices, and biosecurity.
  - Not through nutritional feed additives alone.

- Opportunity for alternative to AGP technologies to continue to improve to meet ongoing challenges of the transition away from antibiotics
  - Clear that understanding of host-microbiome interactions is a necessary part of this future

Identify Mechanisms of AGPs and Use This to Identify / Design AGP Replacements

- Observational empirical methods that have led to variable results for many products that have the potential to work
  - “feed them and weight them” studies
- More recently see more work studying mechanisms involved in AGP function and working to identify alternatives that mimic physiological response to AGPs
  - Do they impact the gut flora, action of the gut, or both?
  - How + Why they work (or don’t!)
- Animal environment (density, stress, activity level, diet, feed form) will influence both gut microbiota and the host.

Impact of Bacterial Pathogens and Stress on Broiler Growth (AAFC, Lethbridge, AB)

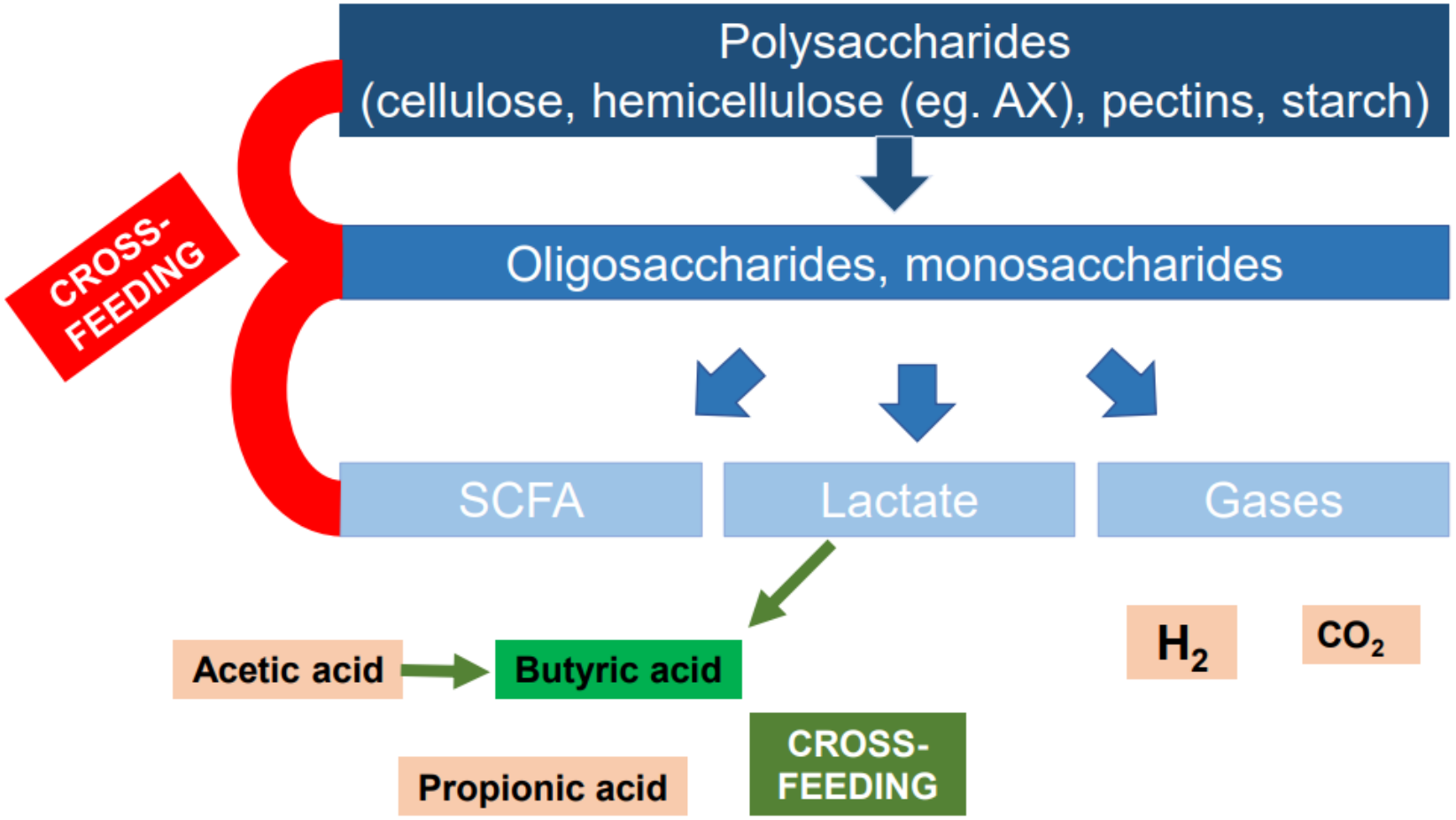


G. D. Inglis et al. (Submitted for publication)

Things to Think About when Planning Farm Strategies without Access to AGPs

- Optimal combinations of antibiotic replacement products provided in combination with good management practices and appropriate vaccination program is needed to ensure consistent success
  - Can create competitive advantage with a ‘product suite’ that promotes gut health and uniform growth
- Complementary products (ex: SCFA and MCFA)
- Good flock health plan (ex: bioshuttle programs, timing of vaccination vs. feed additives)

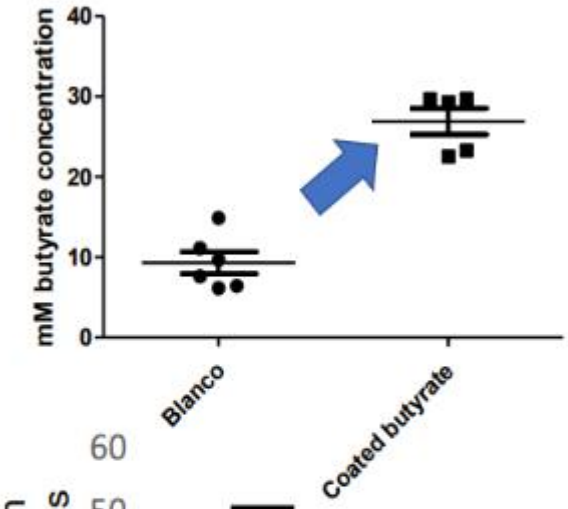
Microbial carbohydrate fermentation and short-chain fatty acids

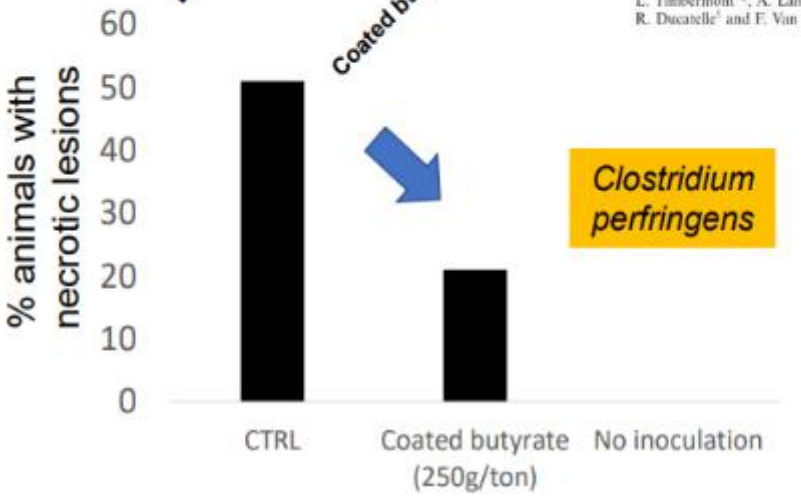


Butyric acid produced in ceca. Needed to help replace gut epithelial cells

Source: Filip van Immerseel DSM webinar 2020

Butyrate can affect pathogen behavior: *Clostridium perfringens* and *Salmonella*



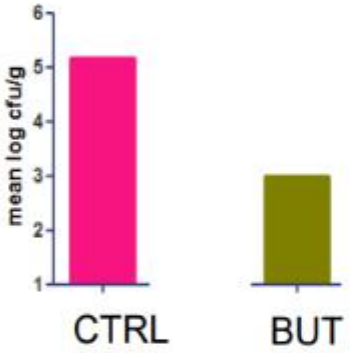


Butyrate Specifically Down-Regulates *Salmonella* Pathogenicity Island 1 Gene Expression

I. Gantois,[1]* R. Ducatelle,[1] F. Pasmans,[1] F. Haesebrouck,[1] I. Hautefort,[2] A. Thompson,[2] J. C. Hinton,[2] and F. Van Immerseel[1]

Control of *Clostridium perfringens*-induced necrotic enteritis in broilers by target-released butyric acid, fatty acids and essential oils

L. Timbermont[1]*, A. Lanckriet[1], J. Dewulf[2], N. Nollet[3], K. Schwarzer[3], F. Haesebrouck[1], R. Ducatelle[1] and F. Van Immerseel[1]



VETERINARY RESEARCH

RESEARCH ARTICLE Open Access

Effect of in feed administration of different butyrate formulations on *Salmonella* Enteritidis colonization and cecal microbiota in broilers

Butyrate must be provided in coated form to survive in the gut until the ceca

Immune modulation, growth performance, and nutrient retention in broiler chickens fed a blend of phytogenic feed additives

V. Pirgozliev,[*,†,1] S. C. Mansbridge,[†] S. P. Rose,[†] H. S. Lillehoj,[‡] and D. Bravo[§]

- Commercial blend: 5% carvacrol, 3% cinamaldehyde, 2% capsicum oleoresin
  - Normal growth conditions (no disease challenge)
- Increased feed intake + growth while reducing FCR
  - Reduced inflammatory response = lower energy requirement for gut maintenance
  - Increased energy utilization, lower heat production
  - Stronger immune modulation in corn vs. wheat diets.

2019 Poultry Science 98:3443–3449

Mexican oregano essential oils given in drinking water on performance, carcass traits, and meat quality of broilers

Ana Cecilia Hernández-Coronado,* Ramón Silva-Vázquez,† Zayd Eliud Rangel-Nava,* Carlos Alberto Hernández-Martínez,* Jorge R. Kawas-Garza,* Michael E. Hume,‡ and Gerardo Méndez-Zamora *,1

* 2019 Poultry Science 98:3050–3058
* *Poliomintha longiflora* Gray (**PLG**) and *Lippia berlandieri* Schauer (**LBS**), in drinking water (**DWt**) on the performance, slaughter variables, and meat quality of broilers over a 40 D period of growth.
* No impact on growth. Meat quality traits for LBS worse than control. Sensory attributes best for PLG group. Promising that can provide source of oregano oil that also affects other key attributes.

* Bottom Line: Not all oregano oils work the same!

Glutamine aids gut health in broilers raised without antibiotics

- Glutamine is “conditionally essential” in times of stress and challenge. Important for highly prolific cells such as intestinal epithelial cells, T cells, B cells and macrophages
  - Approximately 30% of dietary glutamine used in the gut
  - Precursor in the citric acid cycle and precursor to glutathione, an important antioxidant.
- During a coccidiosis infection, birds have to build more intestinal epithelial cells
  - Glutamine supporting role in cellular reproduction

J. Oxford (U of Georgia) Poultry Health Today interview July, 2019

Digesting Peptidoglycan(PGN) Remnants to Disrupt Interference with Digestion

- PGN is a cell wall structural component stabilizes internal osmotic pressure and is essential for cell survival.
  - During microbiome replication and death, PGN fragments are released into the gut.
  - PGN fragments make up 30-90% of the dry weight of Gram+ and 10% of Gram- bacteria.
- Degradation of PGN from cell wall fragments by a novel microbial glycosyl hydrolytic muramidase originating from fungus (Cohn et al., 2018), increased broiler body weight gain by 5.0% and reduce FCR by 2.5% (Yegani et al., 2018)
  - Catalyzes degradation of PGN remnants only. Disrupts PGN interference with digestive processes?

Use of *Bacillus Subtilis* PB6 as a potential antibiotic growth promoter replacement in improving performance of broiler birds

Sathishkumar Jayaraman,*,[1] Partha Pratim Das,* Prakash Chandra Saini,* Barun Roy,† and Paresh Nath Chatterjee†

Table 1. Treatment Groups used in the trial.

Treatment groups	Description	Dosage (g/ton of feed)
Control	Corn – Soya broiler diet	NIL
Treatment 1	Control Diet + *B. subtilis* PB6	500 g /ton
Treatment 2	Control Diet + BMD	350 g /ton
Treatment 3	Control Diet + AVL	80 g /ton

Spores of *B. subtilis* PB6 contained 5×10^{11} cfu/kg.
AVL – Avilamycin; BMD - bacitracin methylene disalicylate.
BMD was obtained from Zoetis Inc. and avilamycin was obtained from Elanco. Dosage of BMD and avilamycin were based on manufacturer's recommendations.

- Growth and feed conversion efficiency of experimental diet as good or better than diets containing BMD or Avilamycin

Poultry Sci. 2017: 96: 2614-2622

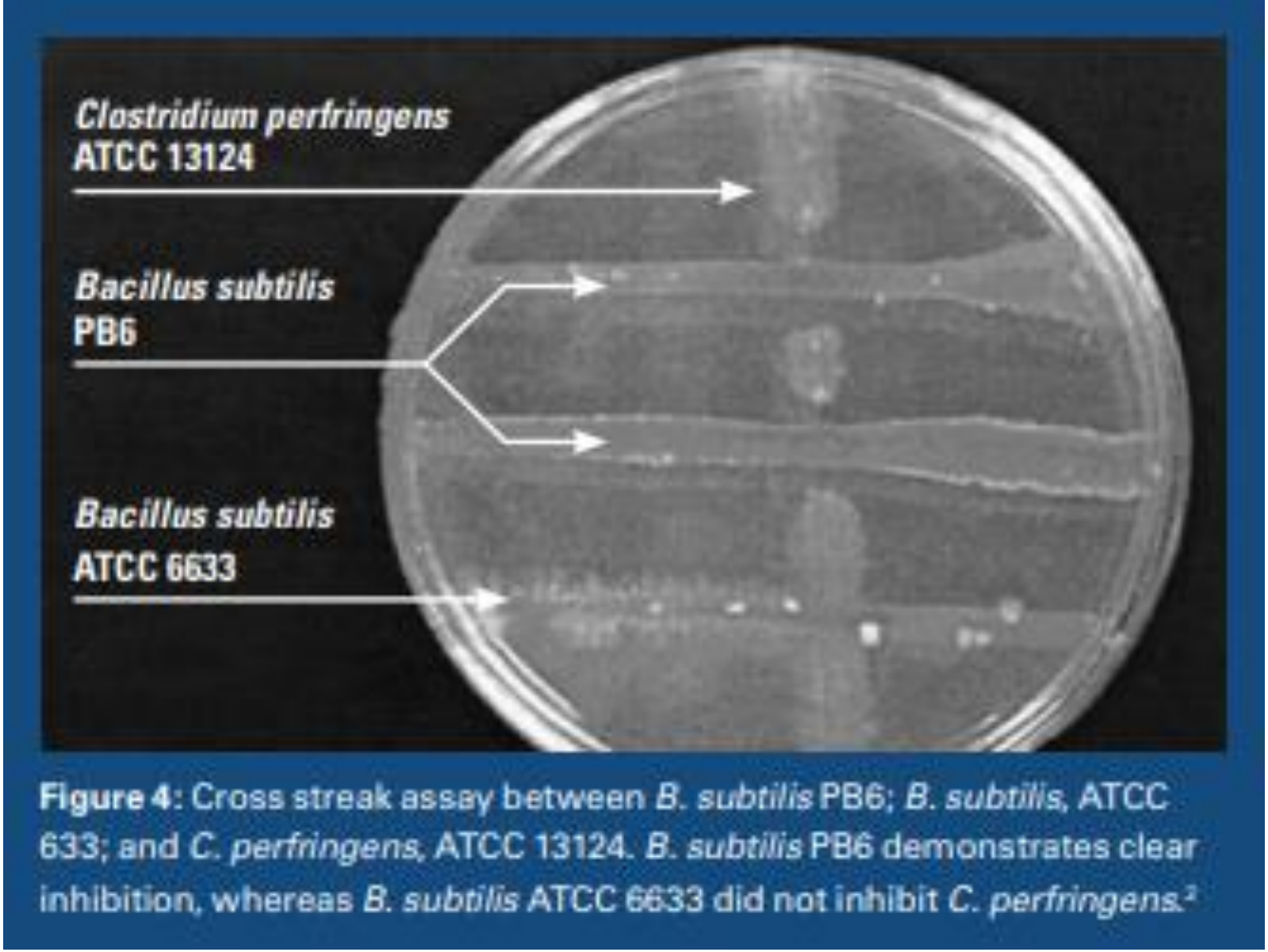


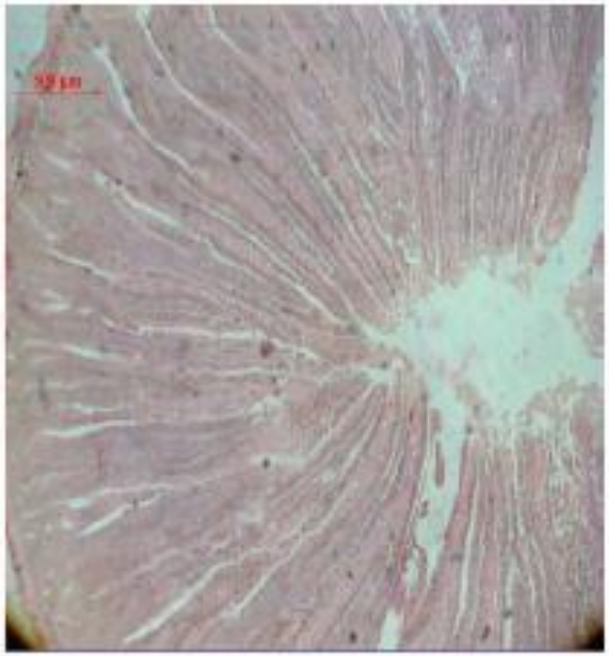
Figure 4: Cross streak assay between *B. subtilis* PB6; *B. subtilis*, ATCC 633; and *C. perfringens*, ATCC 13124. *B. subtilis* PB6 demonstrates clear inhibition, whereas *B. subtilis* ATCC 6633 did not inhibit *C. perfringens*.[2]

MODE OF ACTION

The *B. subtilis* PB6 in CLOSTAT has been found to secrete one or more biocidal proteins that are inhibitory towards certain strains of pathogenic bacteria, such as *Clostridium* spp. These proteins disrupt the membrane of bacteria, causing leakage of the cell contents and ultimately killing the pathogenic bacteria without harming the beneficial gut microflora.

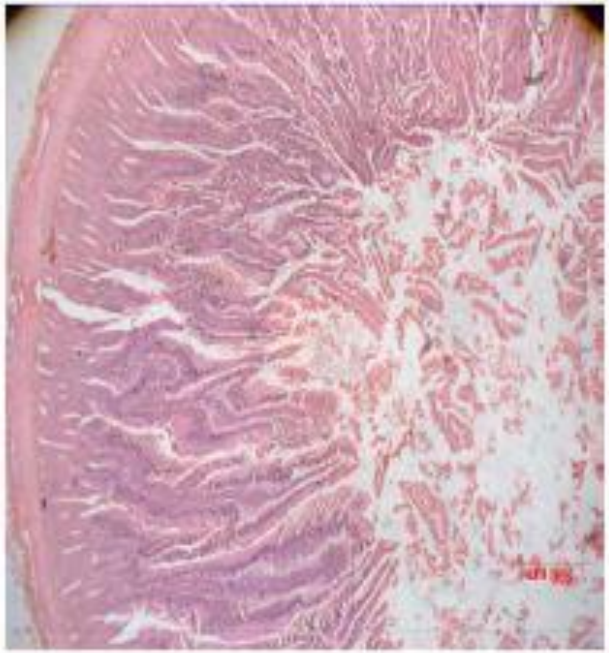
Figure 1: PB6 surfactants impact on *Clostridium perfringens* cell wall structure

Control



B. subtilis PB6

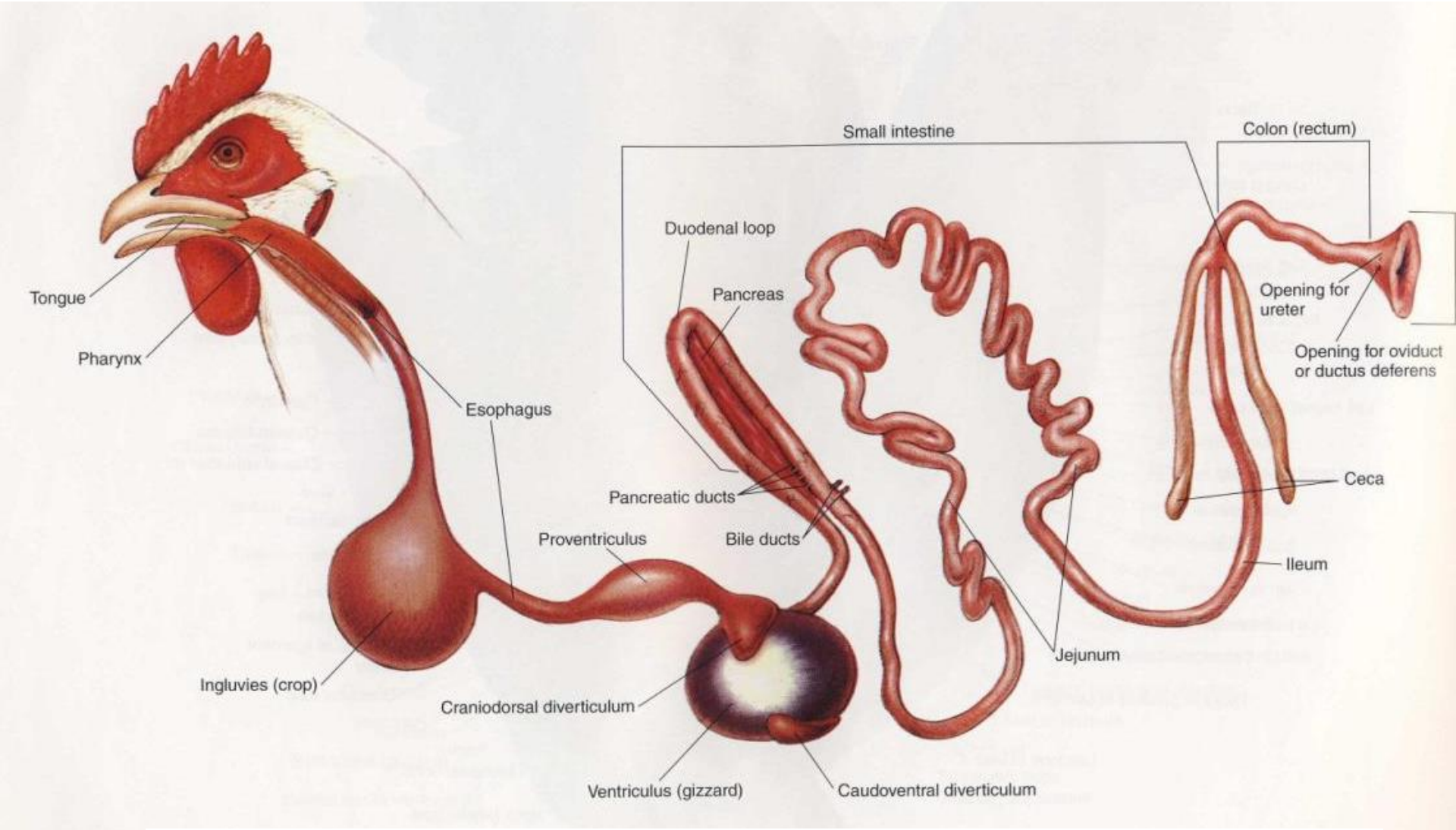
BMD



AVL

Bacillus Subtilis PB6 changed villi structure (elongated, parallel., higher density)

Jayaraman et. al., 2017



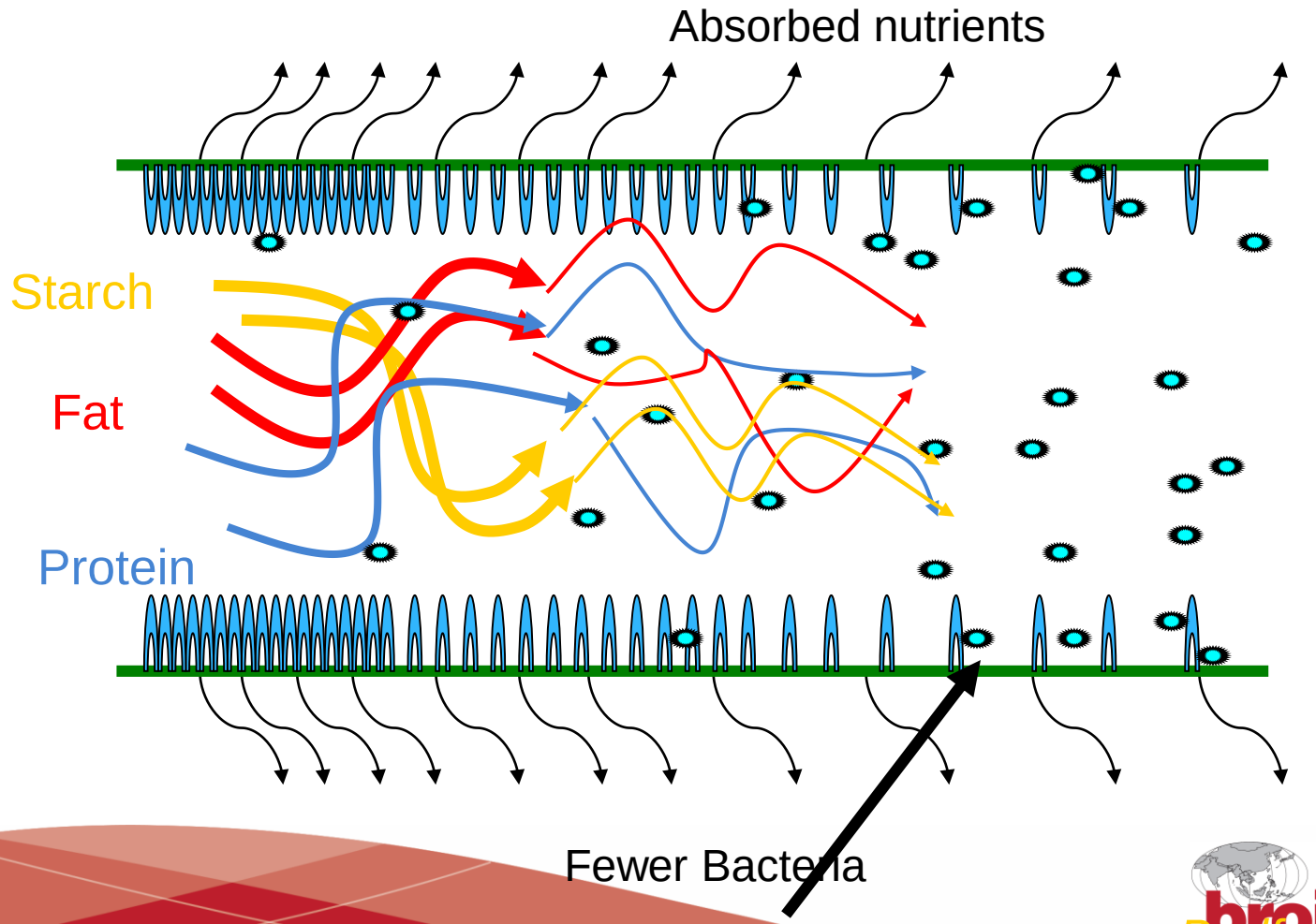
Healthy gut = better FCR.

- Mimic nature with whole/rolled wheat and/or acidifiers

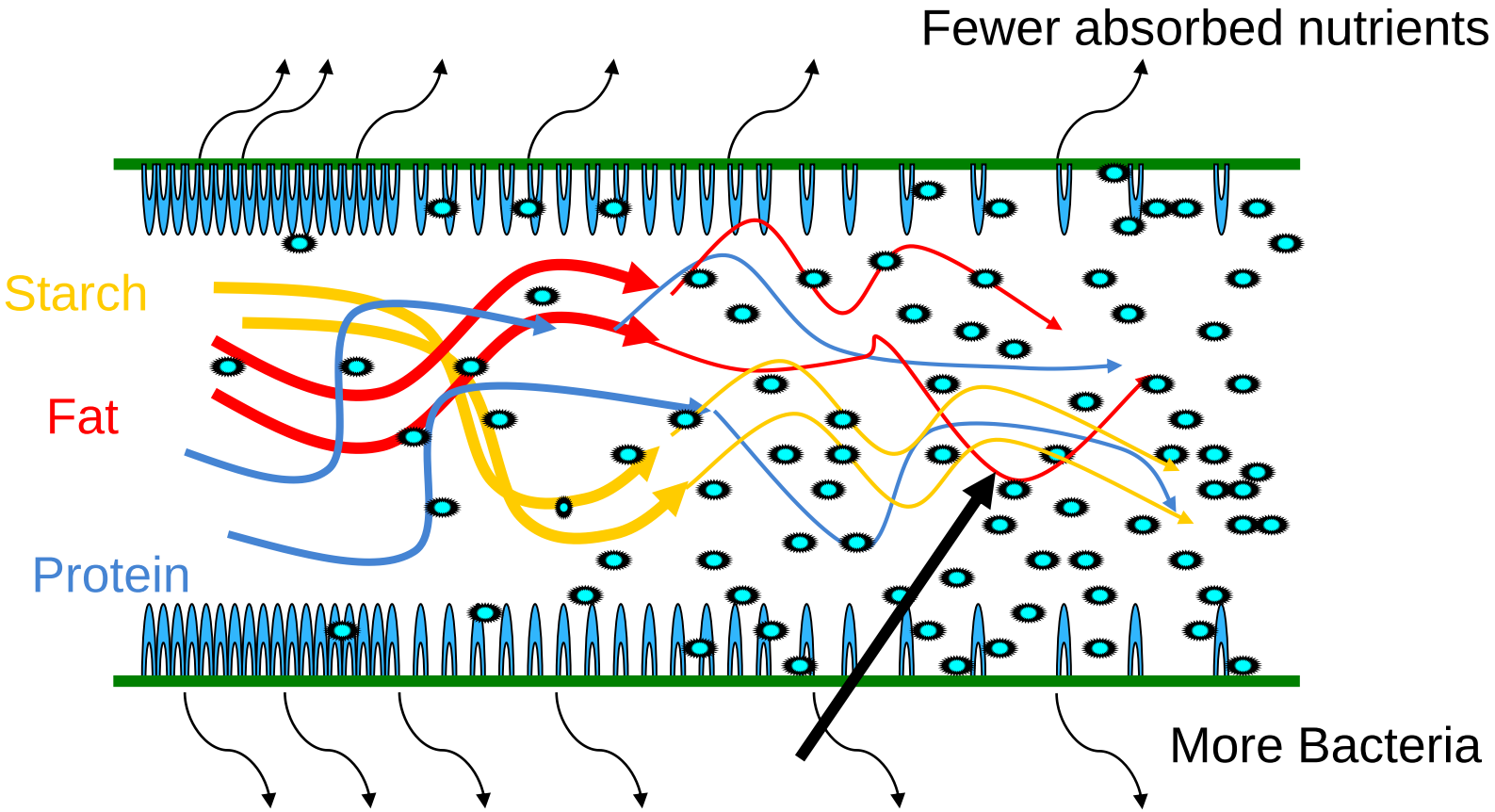
Focus on Gut Function and Flock Health

- Know antibiotics respond better when supplemented to poor quality diets (Corn > Wheat > Barley)
  - Does the same apply to alternatives to AGPs?
- Enzymes improve digestibility of wheat and barley, depending upon qualitative differences.
  - Enzymes have similar growth & FCR benefits to AGPs (Rosen, 2001)
- Undigested protein: Source of animo acids for pathogens such as *C. perfringens* fermented to biogenic amines and keto acids

Optimal rate of digestion results in little substrate for bacteria



Poor digestion by the bird leads to more substrate for bacteria



Response is to produce more enzymes and grow a larger intestine. Costly in energy terms.

Bedford (2002)

Feed-based Solutions

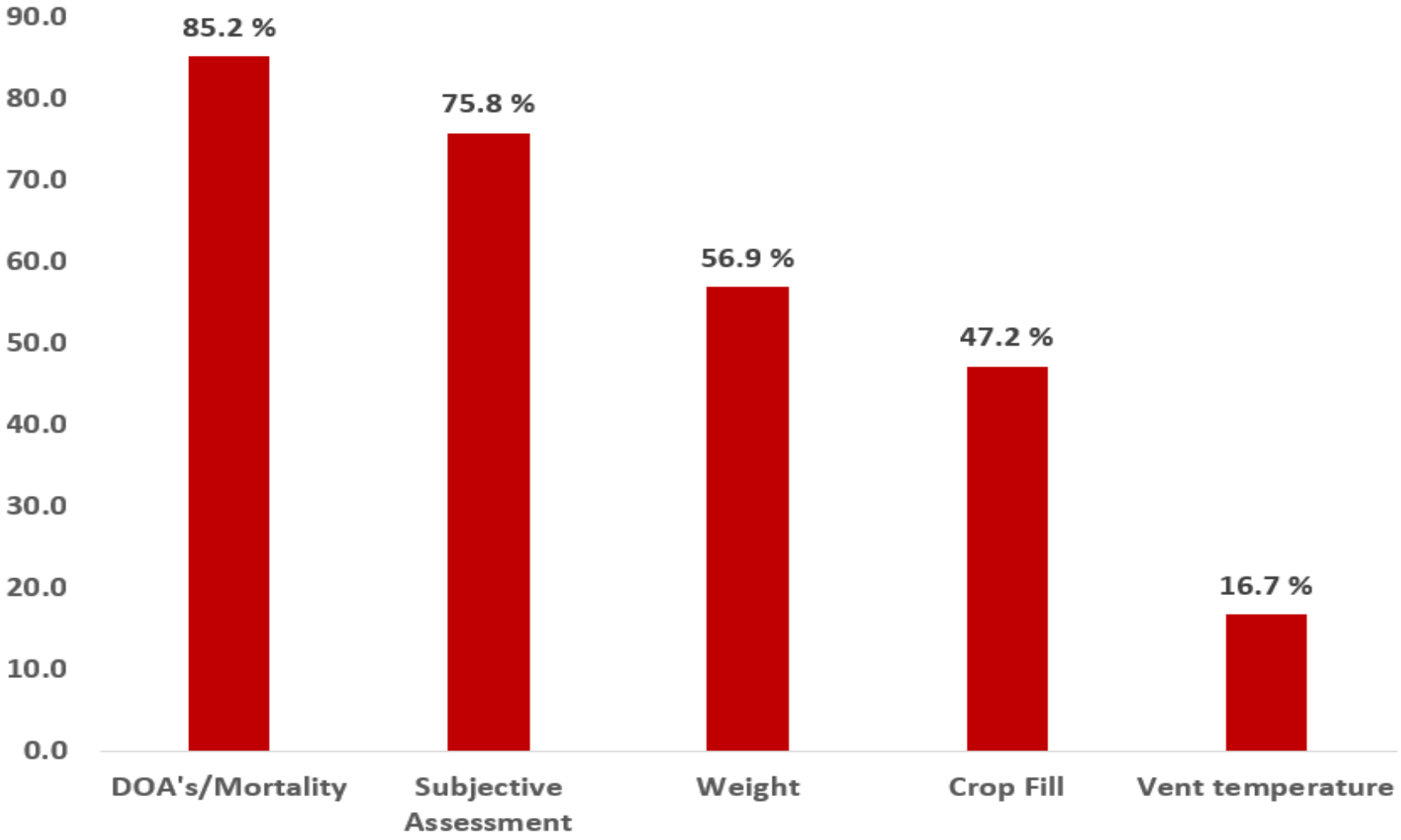
- Be careful where you source your feed additives: not all are created equal
- Commercial products usually based on proven results
  - Must recognize that nothing does as much as antibiotics could do on their own
  - Blends or use of multiple products to target specific aspects of your overall goals may be needed

MULTINAT PRO GREEN™	GALLINAT+™	GALLINAT™	POULTRYGROW 250™
Fermentation Product for Poultry Feeds	Blend of organic acids and essential oils for poultry feed	Blend of essential oils for poultry feed	Fermentation product for poultry feeds

Where can I Make a Difference?

- Brooding
- Water system management
- Environmental management
- Flock Health

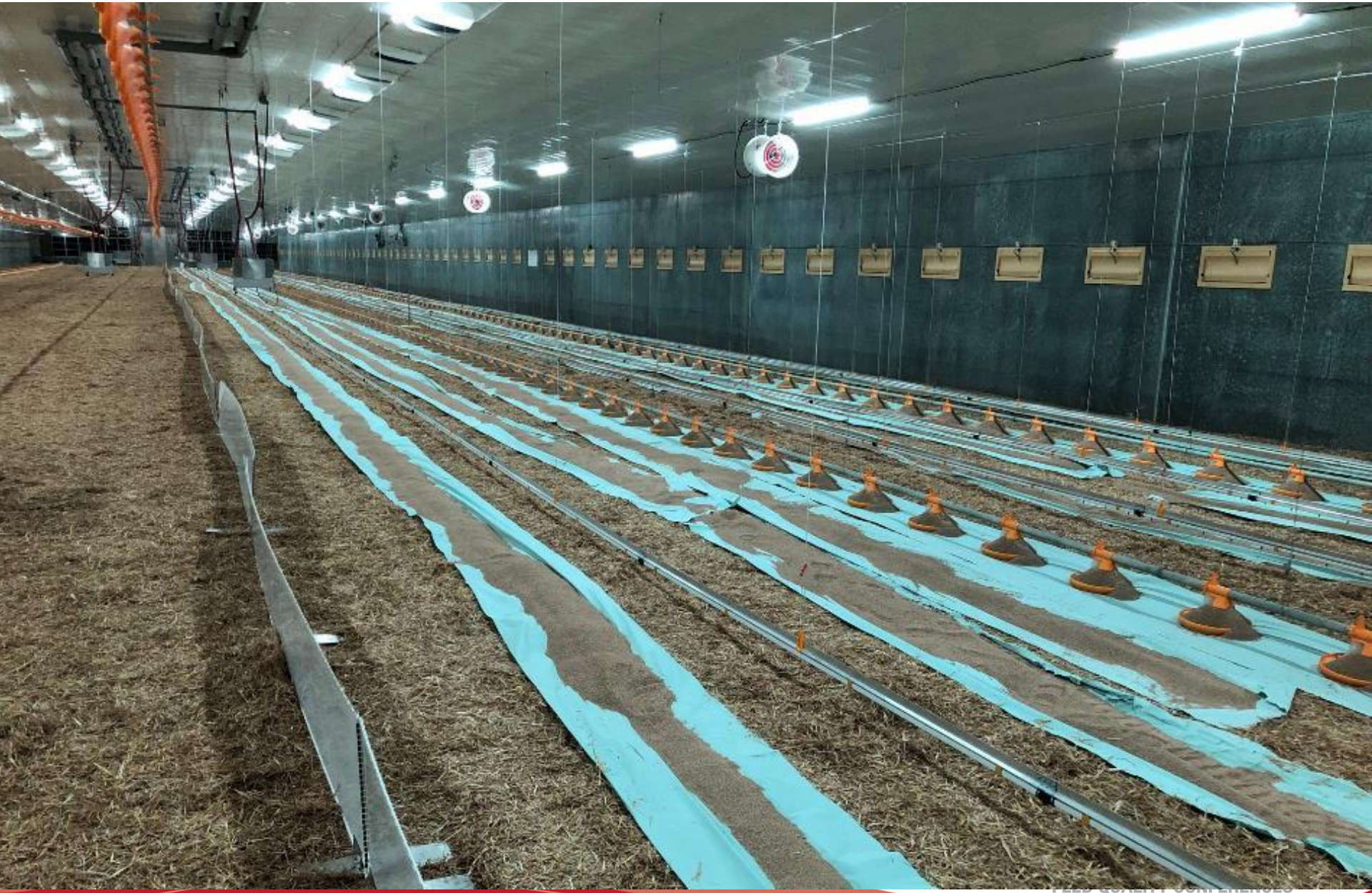
What Measures Should We Take During Brooding?



Is There a Way to Brood Broilers to Optimize Environment, Feed and Water Management, and Flock Health?

- Raised Without Antibiotics (RWA) programs driving management change
- Focus on optimizing flock health and quality brooding to ensure continued bird health and disease resistance
  - Good maternal and broiler vaccination programs in place
  - Focus on quality incubation (single stage when possible)
- Moving away from whole-house brooding to half-house brooding
- By considering applying these methods to our operations, we can be prepared for the loss of AGPs in our production systems

Half-house Brooding



Chick Quality Essential: Keeping your broiler production value chain clean

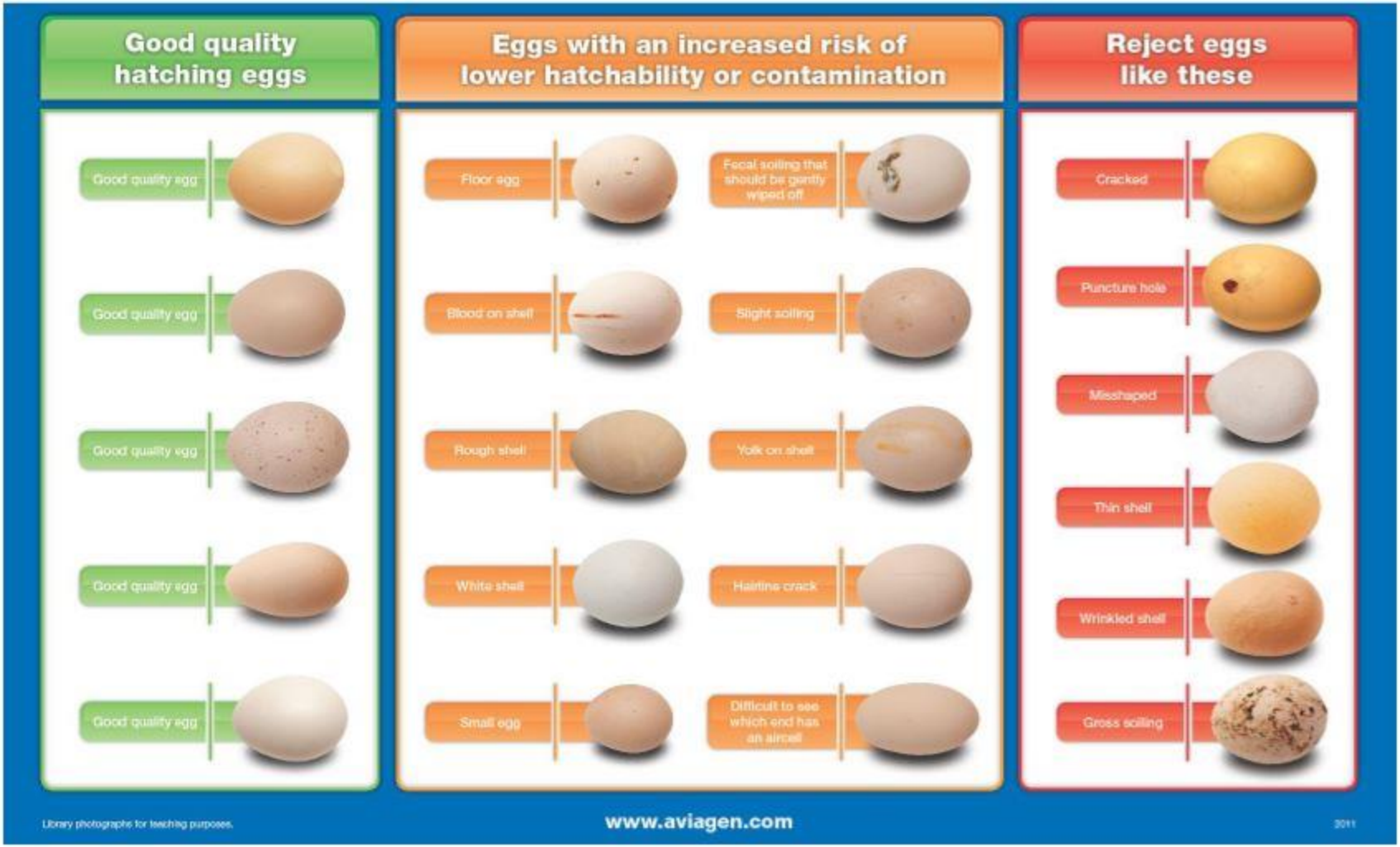
Egg shell contamination and 14 day mortality

Egg condition	Total bacteria	Coliforms	14 day mortality
Clean	600	123	0.9
Soiled	20,000	904	2.3
Dirty	80,000	1,307	4.1

(J. M. Mauldin)

Contaminated eggs increase broiler disease and mortality

What is a good quality hatching egg?



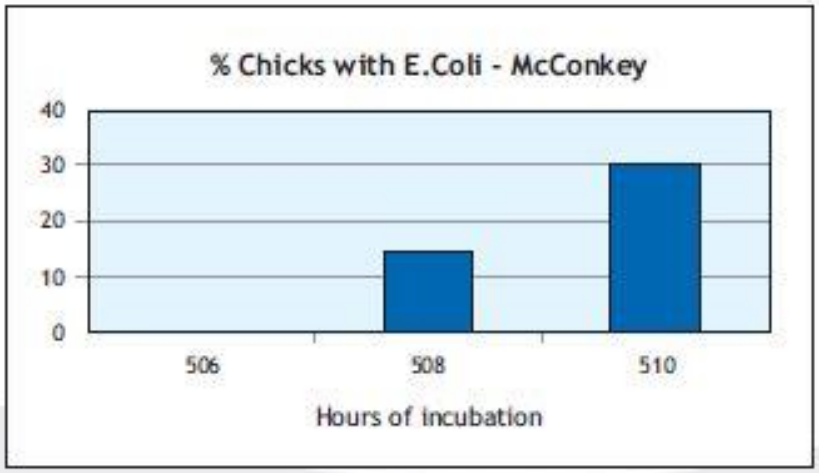
1. Hatchery

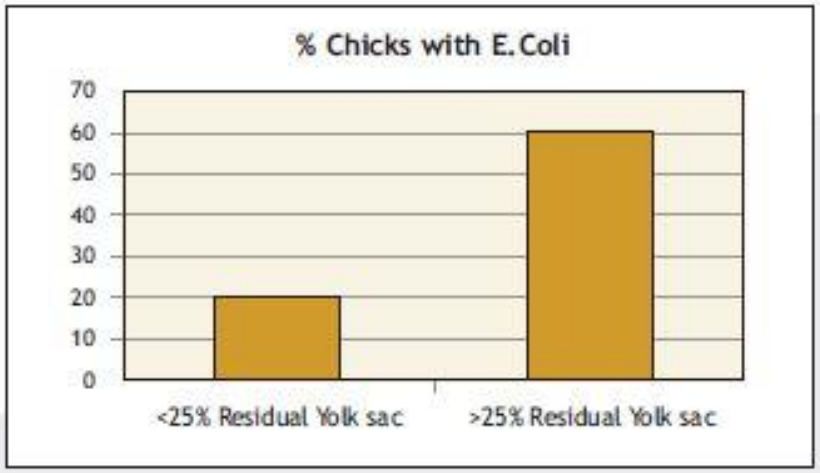
1.24. How to establish good chick quality? - Colibacillosis control

Consequences of overheating embryos
E. Coli susceptibility *(Trial Cobb Spain, 2011)*

It is not clear if overheated embryos are more sensitive because they spend longer in the hatchers (hatch early), but the % of E.Coli isolations seem to increase with:

- Hours of incubation
- Bigger yolk sacs





Salmonella and Campylobactor Control

- More of a food safety issue than a flock health issue.
- *Salmonella* and *Campylobacter* are difficult to manage because chickens are a reservoir host.
- Both pathogens have genes enabling them to evade the chicken's immune system, survive the gut environment and utilize host resources for energy production — all factors that help them colonize the gut in high numbers.

Salmonella and Campylobactor Control

- Farm management factors contributing to the prevalence of *Salmonella* and *Campylobacter* during live production
  - Stress due to overcrowding, insufficient biosecurity and contaminated litter or feed.
- For Salmonella, broilers (and breeders) can be successfully vaccinated with a modified live vaccine
- Programs with probiotics and prebiotics reduce their growth

- What you may be doing to improve gut health without antibiotics is also contributing to food safety

A Chain Is Only As Strong As It's Weakest Link

Every Flock Is A Load Test On The Performance Chain

Beyond Antibiotic Growth Promoters: Finding our Way Together

SUMMARY

- No single solution that works as well or as consistently as Antibiotic Growth Promoters (AGPs) have worked.
- Need to explore mix of AGP replacements and enhanced bird health (via feed additives and management)
- Best results when flock management conditions also considered
  - Brooding management
  - Environmental management
  - Water system management
  - Flock Health