Gut health and broiler performance
Maarten De Gussem, DVM
Merial Avian Forum
July 13th 2016, Tokyo
Overview

- Importance of gut health in 2016 poultry production
- Interaction of microbiota, immunity and performance: key messages
- Negative gut health drivers
- Bacterial enteritis vicious circle
- How to drive good gut health in 2016?
Gain in FCR and BW 2016?

- Typically said ‘mainly from genetics’ but what does it mean?
  - Lines with high feed intake behaviour: shortens life span, less nutrients for maintenance!
    - Issues with capability of digestion and absorption of this intake
    - As soon something goes wrong, bacterial enteritis vicious circle is instigated
    - Lot of focus on controlling bacterial element of the bacterial enteritis (AGP, probiotics, acids,....)
  
- But indications of changing (innate) immune system e.g. Enterococcus problems: normal inhabitant, able to slip through (innate immunity) gut barrier
Overview

- Importance of gut health in 2016 poultry production
- Interaction of microbiota, immunity and performance: key messages
- Negative gut health drivers
- Bacterial enteritis vicious circle
- How to drive good gut health in 2016?
Intestinal morphology

- Lumen of small intestine
- Intestinal mucosa
- Villi
- Columnar epithelial cells
- Microvilli (brush border)
- Connective tissue core
- Lymphatic lacteal
- Capillary network
Intestinal mucosa

Figure 1.

Enterocytes
Goblet cells
Ileal Lumen
Microvilli
Brush border

adapted from Austgen et al
Intestinal health and integrity

- **Structural integrity**
  - Long and wide villi: greater surface for absorption
  - Small crypts: lower tissue turnover, less energy and protein required for recovery
  - Goblet cells: produce protective mucins
  - Strong tight junctions:
    - Prevent bacteria and toxic substances to enter the cells and the blood, and cause inflammation and ‘leaky gut’

- **Physiologic activity:**
  - Greater particle size promotes peristalsis and reverse peristalsis: better mixture with enzymes and digestion
Intestinal morphology

- Enormous surface area!

Human:
- Skin: 2 m²
- Lung: 100 m²
- Intestine: 300 m²

In direct contact with the outer environment
Host defense mechanism: gut barrier function
- Maximize the protective innate immunity
- Prevent inflammatory response, keep a state of oral tolerance

Complex regulation of the microbial ecosystem:
- Suppress invasion of pathogens (Salmonella, E. coli)
- Increase diversity in de microflora (AGP vs non AGP!)
- Inhibit overgrowth (Clostridium perfringens – Clostridiaceae)
Intestine – most important immune organ

A large percentage of vaccinations goes through drinking water!
GALT gut associated lymphoid tissue

- Peyer’s patches
- Caecal tonsils
- Meckel’s diverticle
- Oesophageal and pyloric tonsils
- 50% of avian immune system!
What if you stimulate GALT?

- Over stimulation of the immune system
  - Some products can potentially harm the performance
  - When this happens, immune response (adaptive and immunity) will further improve, but ADG will stagnate and FCR will increase (Humphrey and Klasing, 2004)
Mucosa-associated microbial community

- Link between immune system and microbiota!

Vandenabeele et al., FEMS Microbiol Rev 2009
Development of the gut microbiota

After Van Immerseel-Arrieta et al., Front Immunol 2014
A complex biochemical network …

The adult gut ecosystem:

More than $10^{14}$ bacteria

More than 100-fold number of genes compared to host

Huge number of metabolites/proteins, …
Diversity and Succession of the Intestinal Bacterial Community of the Maturing Broiler Chicken
Jiangrang Lu,1 Umelaalim Idris,1 Barry Harmon,2 Charles Hofacre,1 John J. Maurer,1,3 and Margie D. Lee1,3*
Department of Avian Medicine1 and Department of Pathology,2 College of Veterinary Medicine, The University of Georgia, Athens, Georgia 30602, and Center for Food Safety, The University of Georgia, Griffin, Georgia 302233

Mainly Gram-positives
An example: Firmicutes
Polysaccharides

Oligosaccharides

Firmicutes, lactobacilli, bifidobacteria, Clostridium cluster IX
Propionate

Lactate, acetate

Monosaccharides

H₂SO₄⁻ → H₂, H₂S

Butyrate

Methanogenic bacteria (Archaebacteria)

Van Immerseel

Sulphate reducers (SRB), e.g. Desulfovibrio

Also Enterobacteraceae (SALMONELLA !)
Mucosa-associated microbial community

- Butyrate producing bacteria
- Mucin-degrading bacteria
- Enterobacteriaceae, Clostridia

Butyrate production in proximity of epithelial cells and in close association with invading and histotoxic pathogens
Overview

- Importance of gut health in 2016 poultry production
- Interaction of microbiota, immunity and performance: key messages
- Negative gut health drivers
- Bacterial enteritis vicious circle
- How to drive good gut health in 2016?
Gut Health: main negative drivers 2016

- **Infectious causes**
  - **Bacterial**: mainly
    - *Clostridium perfringens* (Necrotic Enteritis)
    - Clostridiaceae (Bacterial Enteritis, BE) and other undefined overgrowth – This is ‘new’ – emerging since 2000
  - **Parasitological**: mainly protozoal *Eimeria* spp. causing subclinical damages - This is old – since 1900
  - **Viral**: broilers ‘black box’ for the moment: rota-, corona-, entero-, adeno-, astro- and reoviruses

- **Feed Quality and Management**
  - **Anti-Nutritional Compounds**
    - Non starch Polysaccharides
    - Mycotoxins
  - **Poor physical texture / Form of Feed**
    - Structure in feed helps developing the gut physiology and improving gut health
  - **Poor feed management with 2016 “high-intake” broiler lines**
According to own assessments and from veterinary diagnostics labs, 60% to 80% of the indications for AB treatments in broilers in EU are due to gut health issues – gut health issues main problem of broiler health in 2015.

Respiratory and other issues (IBDV, NDV, IBV, ORT, colibacillosis,…) still important but progress in vaccination options has made gut health issues much more important than 10 years ago.
Vaccination for gut health issues far behind

- Lack of focus vaccine producing companies? Not really
  - REO vaccine, coccidiosis vaccines, Clostridium vaccine…. But none of them are products used in standard ways versus NDV, IBV, IBDV vaccinations….

- Indicating the complexity gut microbiotic environment and interactions with complex immune system in the gut!

- The gut lumen is considered ‘outside body’, but with high permeability in order to allow absorption of nutrients (coming from outside the bird!)

- A similar protective level is needed as e.g. skin but for much larger surface, and with need for exchange of digestive components versus nutrients
Coccidiosis

- **Parasitic** disease, **protozoa** (unicellular) of genus **Eimeria**
- In **chickens** - 7 species,
- **Broilers** (till +/- 6 weeks):
  - *E. acervulina*
  - *E. maxima*
  - *E. tenella*
  - *E. praecox*
  - *E. mitis*
- For **older chickens** also important 2 species
  - *E. necatrix*
  - *E. brunetti*

Lesion scoring
Intestinal damage: subclinical coccidiosis

Ileum, **uninfected** turkey poult, 3 weeks old (650X)

Ileum, turkey poult with **subclinical** coccidiosis, 3 weeks old (650X)
Intestinal damage: *E. tenella*
Intestinal damage: *E. necatrix*
# Real life example gut health scoring

<table>
<thead>
<tr>
<th>Birds</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days)</td>
<td>14</td>
<td>17</td>
<td>18</td>
<td>20</td>
<td>20</td>
<td>21</td>
<td>24</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td><em>E. acervulina</em></td>
<td>0.67</td>
<td>0.50</td>
<td>1.33</td>
<td>2.67</td>
<td>1.50</td>
<td>2.00</td>
<td>0.00</td>
<td>0.67</td>
<td>0.67</td>
<td>0.17</td>
</tr>
<tr>
<td><em>E. maxima</em></td>
<td>0.33</td>
<td>0.00</td>
<td>0.50</td>
<td>0.33</td>
<td>0.50</td>
<td>0.83</td>
<td>0.50</td>
<td>1.00</td>
<td>0.67</td>
<td>0.67</td>
</tr>
<tr>
<td><em>E. tenella</em></td>
<td>0.00</td>
<td>0.00</td>
<td>0.17</td>
<td>0.00</td>
<td>0.00</td>
<td>0.17</td>
<td>0.00</td>
<td>0.00</td>
<td>0.33</td>
<td>0.17</td>
</tr>
<tr>
<td>TMLS*</td>
<td>1.00</td>
<td>0.50</td>
<td>2.00</td>
<td>3.00</td>
<td>2.00</td>
<td>3.00</td>
<td>0.50</td>
<td>1.67</td>
<td>1.67</td>
<td>1.01</td>
</tr>
<tr>
<td>Dysbacteriosis</td>
<td>0.67</td>
<td>1.33</td>
<td>1.33</td>
<td>1.5</td>
<td>1</td>
<td>2.17</td>
<td>1.67</td>
<td>2</td>
<td>1.67</td>
<td>1.5</td>
</tr>
<tr>
<td>Feet</td>
<td>0.00</td>
<td>0.00</td>
<td>1.17</td>
<td>0.00</td>
<td>0.33</td>
<td>2.33</td>
<td>2.00</td>
<td>0.50</td>
<td>2.00</td>
<td>1.17</td>
</tr>
<tr>
<td>Hocks</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.17</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Legs</td>
<td>0.17</td>
<td>0.17</td>
<td>0.5</td>
<td>0.33</td>
<td>0.67</td>
<td>0</td>
<td>0.67</td>
<td>0.67</td>
<td>0.33</td>
<td>0.17</td>
</tr>
</tbody>
</table>

## Farm

<table>
<thead>
<tr>
<th>Birds</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>6</th>
<th>72</th>
<th>120</th>
<th>48</th>
<th>84</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days)</td>
<td>28</td>
<td>31</td>
<td>34</td>
<td>34</td>
<td>34</td>
<td>34</td>
<td>22</td>
<td>30</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td><em>E. acervulina</em></td>
<td>0.33</td>
<td>0.17</td>
<td>0.33</td>
<td>0.00</td>
<td>0.00</td>
<td>0.68</td>
<td>0.63</td>
<td>0.48</td>
<td>0.45</td>
<td>0.53</td>
</tr>
<tr>
<td><em>E. maxima</em></td>
<td>0.50</td>
<td>0.67</td>
<td>0.50</td>
<td>0.67</td>
<td>0.33</td>
<td>0.53</td>
<td>0.46</td>
<td>0.50</td>
<td>0.45</td>
<td>0.34</td>
</tr>
<tr>
<td><em>E. tenella</em></td>
<td>0.67</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.17</td>
<td>0.12</td>
<td>0.11</td>
<td>0.15</td>
<td>0.02</td>
<td>0.23</td>
</tr>
<tr>
<td>TMLS*</td>
<td>1.50</td>
<td>0.84</td>
<td>0.83</td>
<td>0.67</td>
<td>0.50</td>
<td>1.32</td>
<td>1.03</td>
<td>1.13</td>
<td>0.93</td>
<td>1.1</td>
</tr>
<tr>
<td>Dysbacteriosis</td>
<td>1.5</td>
<td>2.67</td>
<td>1.33</td>
<td>1.33</td>
<td>1.83</td>
<td>1.61</td>
<td>1.43</td>
<td>0.48</td>
<td>1.05</td>
<td>1.13</td>
</tr>
<tr>
<td>Feet</td>
<td>0.00</td>
<td>0.33</td>
<td>0.83</td>
<td>0.83</td>
<td>0.00</td>
<td>0.69</td>
<td>0.69</td>
<td>0.69</td>
<td>0.69</td>
<td>0.69</td>
</tr>
<tr>
<td>Hocks</td>
<td>0.17</td>
<td>0.33</td>
<td>0.50</td>
<td>0.00</td>
<td>0.00</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Legs</td>
<td>0</td>
<td>0.17</td>
<td>1</td>
<td>0.17</td>
<td>0.67</td>
<td>0.37</td>
<td>0.41</td>
<td>0.31</td>
<td>0.45</td>
<td>0.45</td>
</tr>
</tbody>
</table>
Necrotic Enteritis (NE)

- Acute or chronic enterotoxaemia
  - Mortality +/- 10% (5-50%)
  - Some strains of *Clostridium perfringens*
  - **NetB producing strains only?!**
  - Alpha toxin less important
  - Layers and breeders often when production almost at peak production

- Rather rare in broilers
- Acute clinical disease
- Pathognomonic lesions: necrosis intestinal wall, haemorrhage
- Same contributory factors as Bacterial Enteritis!!
- But… less in non-AGP then in AGP countries?
  - Less variation in microbiota
  - Immunomodulation AGP?
Vicious circle of BE – example coccidiosis

0. Normal gut with well developed villi

1. Coccidia infecting gut mucosa, causing villus atrophy

2. Damaged gut reacts by: villus fusion, increase of mucus production Goblet cells and immune reaction causing inflammation

3. Immune reaction and damage causes plasma protein leakage/intestinal function decreased, more nutrients in gut

4. Clostridiaceae (rods) grow on available nutrients, mucus and plasma proteins and attach to gut lining, causing further reaction of immune system and gut defences (mucus,…)
Histologic/microscopic signs BE

- Normal lining and/or tight junctions are damaged
- More villus fusion as natural reaction on breach of gut barrier
- More inflammatory cells in the gut mucosa
  - Higher number of T-Lymphocytes and heterophils infiltrated
  - Try to stop invading bacteria
- More mucus-producing Goblet cells
  - Try to replace the physical gut barrier
  - But good feeding source for Clostridiaceae
- Decreased villus length
- Decreased villus/crypt ratio
  - Larger crypt as turnaround of intestinal cells is increased and villi are shorter
- All together signs of poorer gut health
Inflammation
Goblet cells, heterophile infiltration
Villi: fusion, length
Crypt hyperplasia
Vicious cycle of pathogenesis of BE

1. Presence of nutritional factors that favour some bacterial groups and disfavour others causing disbalance
2. Inflammation and oxidative stress caused by interference of microbiota with mucosa
3. Morphological and functional alterations in the gut
4. Less functional gut

High feed intake, high NSP levels, coccidiosis, mycotoxines, viruses
Solutions to Vicious circle of BE

Reduce feed intake, limit NSP levels, avoid coccidiosis, avoid viral infections, mycotoxins

Suppress bacterial proliferation (antibiotics, acids, probiotics, AGP ....)

Presence of nutritional factors that favour some bacterial groups and disfavour others causing disbalance

Inflammation and oxidative stress caused by interference of microbiota with mucosa

Less functional gut

Use exogenous enzymes, use better digestible feed

Add beta glucan, butyric acid or other products for faster restoration gut morphology, reduce inflammation and oxidative stress
Solutions to Vicious circle of BE

High feed intake, high NSP levels, coccidiosis

Reduce feed intake, limit NSP levels, avoid coccidiosis, avoid viral infections, mycotoxins

Suppress bacterial proliferation (AGP, antibiotics, acids, probiotics, EO, …)

Presence of nutritional factors that favour some bacterial groups

Opportunity for poultry industry: we can do better than only using antimicrobial agents!

Use exogenous enzymes, use better digestible feed

After De Gussem, 2010
Macroscopic signs of BE: 0-10

http://www.vetworks.eu/gut-health/
Overview

- Importance of gut health in 2016 poultry production
- Interaction of microbiota, immunity and performance: key messages
- Negative gut health drivers
- Bacterial enteritis vicious circle
- How to drive good gut health in 2016?
Prevention for gut health issues in 2016

- Anticoccidials in all countries registered and used

- Antimicrobial Growth Promotors (AGP) : banned in some countries (EU, and EU-like)

- “Alternative Gut Health Products” : replacing AGP in EU markets, but also in other….
Pressure on AB, AGP, …

- In some areas, high income mainly, ABF production is gaining ground
- ABF?
  - No growth promotors
  - No growth promotors or preventive antimicrobials
  - No growth promotors, preventive or metaphylactic use
  - No growth promotors, preventive, metaphylactic or therapeutic use of (human) critical AMB except if documented no alternative
  - No growth promotors, preventive, metaphylactic, therapeutic use of (human) critical AMB at all
  - No AMB at all, except ionophores
  - No AMB, including ionophores
  - …
Good veterinary practices

2.A Veterinarians and Animals

- Veterinarians shall endeavour to ensure the welfare and health of the animals under their care in whichever section of the veterinary profession they work.
- Veterinarians shall always take into account the five freedoms² for assessing animal welfare.
- When aware of violations to animal welfare legislation, veterinarians shall immediately bring this to the attention of the owner of the animal(s) and do everything within their reach to solve the problem.
- Veterinarians shall treat all animals in their care with respect.

FIVE FREEDOMS

1. Freedom from Hunger and Thirst - by ready access to fresh water and a diet to maintain full health and vigour.
2. Freedom from Discomfort - by providing an appropriate environment including shelter and a comfortable resting area.
3. Freedom from Pain, Injury or Disease - by prevention or rapid diagnosis and treatment.
4. Freedom to Express Normal Behaviour - by providing sufficient space, proper facilities and company of the animal's own kind.
5. Freedom from Fear and Distress - by ensuring conditions and treatment which avoid mental suffering.
Split of AB use in poultry EU (2016)

AB –type (est.)

- Broad (G+/G-)
- Narrow (G-)
- Narrow (G+)

Copyright 2016 VETWORKS
Split of AB use in poultry EU (2016)

**Indication** (est., own data)

- **Gut health (G+)**
- **Respiratory (G-)**
- **Systemic (G+/G-)**
- **Other (G+/G-)**
Diagnose better!

- Very often, when wet litter occurs, Bacterial enteritis treatment is started without proper diagnosis
- No isolation possible, no antibiogram, only macroscopic possible in field conditions. Need for veterinarian = cost.
- Improve/standardise diagnostics through scoring system (0 low - 10 high)
  - Set thresholds for AB treatment - example
    - 0 – 2 no treatment needed
    - 3 - 5 only non-AB alternative treatments allowed
    - 6 - 10 AB allowed, only narrow spectrum G+
  - Document scoring for each treatment !!
- **Audit procedures : check threshold levels**
Alternatives to enhance gut health

- Pre- & probiotics (VC2)
- Phytotherapeutics (herbs and etheric oils) (VC1, VC2, VC3, VC4)
- Enzymes (VC4), beta-glucans (VC2, VC3)
- Others: Bacteriophages (VC2), Antimicrobial peptides (VC2), Toll-like receptor agonists (VC3)
- Organic Acids (VC2 & VC3)
Conclusion

- Gut health is the key to successful poultry production for the future as we need high feed intake broilers to be sustainable.
- Gut immune system, and interaction with microbiota better understood by the year.
- Several negative drivers regarding gut health, but all triggering the same vicious circle of bacterial enteritis.
- Understanding this BE vicious circle helps understanding why AGP worked, and why we can do better today even.
Conclusion

- There is a real threat of reducing welfare when ABF is applied blindly and bluntly.
- Alternatives don’t only work against bacteria, but mostly also have other features that support gut health (as did AGP!)
- Alternatives, depending on the type, improve gut developmental physiology, modulate immune response of GALT, reduce oxidative stress, prevent initial damage, improve digestibility,...
- Reductions of antibiotic use has led to paradigm shift in thinking about gut health and its relation with performance in poultry industry.
- Therefore antibiotic reduction is not a liability, but an opportunity.
- Yesterdays “alternatives” are today “standard” – chose the right ones and you are ready for Tomorrow!
Thank you for your attention

Questions:
maarten.degussem@vetworks.eu
+32473999379