Nutritional strategies
to improve intestinal health
and so reduce the use of antibiotics

AFMA, Sun City, RSA
Loek de Lange
Mar-2016
Ingredients

- GIT-tract and its microbes
- Mode of action of AGP’s
- Nutritional means:
  - Carbohydrates / fiber
  - Protein
  - Fat
  - Additives
  - Feed processing technology

Summary

Take Home Messages
Gut function

Grenier and Applegate, 2013

Between the cells

Through the cell

Mannitol

Glysar

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Intestinal disorders

Nature Reviews | Gastroenterology & Hepatology 2015
Effect of citrus pectin on intestinal permeability

Figure 6. The paracellular (mannitol) and transcellular (glysar) permeability in broilers fed a corn/soybean meal diet with and without 3% highly methylated citrus (HMC) pectin (Van der Klis en Versantvoort, 1999).
Composition of the bacterial community of the ilea and ceca of broiler chickens as determined by sequencing of 1,230 clones from a 16S rDNA community DNA library (Lu et al, 2003).
Microbial composition (T-RFLP) in the ileum and caeca of broilers at day 27 on good and moderate farms (de Lange and Wijten, 2008)

On day 27 the micro biota in the crop and ileum is little divers, and in the caeca much more divers.
Effect of pectin and bacterial activity on fat digestibility

Source: Langhout et al. (2000)
Mode of action AGP’s
(Gaskins, 2002; Dibner, 2005; Page, 2006 cited by Niewold, 2007)

- Inhibit endemic subclinical infections, and thus reduce metabolic costs of the (innate) immune system
- Reduce growth-depressing metabolites such as ammonia and bile degradation products produced by microbes
- Reduce microbial use of nutrients
- Enhance the uptake and use of nutrients, because the intestinal wall in AGP-fed animals is thinner
Loss of net energy by fermentation

- **Glucose** → 2 * Lactic acid
- **C6H12O6** → 2 * C3H6O3
- **NE:** 12.4 => 11.6 MJ/kg; loss **6.5%**

- **Glucose** → 1 * Lactic ac. + 1 * Acetic ac. + H2O + CO2
- **C6H12O6 + O2** → 1 * C3H6O3 + 1 * C2H4O2 + H2O + CO2
- **NE:** 12.4 => 5.8 + 3.23 = 9.03 MJ/kg; loss **27.2%**
Effect AGP on relative quantity of L. Acidophilus

(de Lange, 2007)
Consequences of microbes in the GIT

Advantages
- Stimulates development immune system
- Competitive exclusion
- Helps to digest NSP’s

Disadvantages
- Competes with host for nutrients
- Potential pathogenic
- Deconjugates bile salts
- Production of toxic compounds
- Stimulation of the immune system has a price (protein)
- Less secretion of brush border enzymes

It is all about a balance between host and microbes!!!
Nutritional interventions

- Carbohydrates / fiber
- Protein
- Fat
- Additives
- Feed processing technology
Carbohydrates: cereals

Effect of [barley + wheat]/maize ratio (BWM - - -) and the occurrence of NE (incidence —)
Carbohydrates / viscosity

<table>
<thead>
<tr>
<th>CMC in diet (g/kg)</th>
<th>0</th>
<th>5</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCR</td>
<td>1.91</td>
<td>1.99</td>
<td>2.45</td>
</tr>
<tr>
<td>Water/Feed</td>
<td>1.35</td>
<td>1.60</td>
<td>2.45</td>
</tr>
<tr>
<td>Viscosity crop (mPa.s)</td>
<td>1.5</td>
<td>5.7</td>
<td>20.0</td>
</tr>
<tr>
<td>Viscosity duodenum (mPa.s)</td>
<td>1.4</td>
<td>3.5</td>
<td>7.6</td>
</tr>
<tr>
<td>Viscosity lower jejenum (mPa.s)</td>
<td>1.2</td>
<td>5.0</td>
<td>9.9</td>
</tr>
<tr>
<td>Viscosity lower ileum (mPa.s)</td>
<td>17.3</td>
<td>23.7</td>
<td></td>
</tr>
</tbody>
</table>

Increasing intestinal viscosity stimulates bacterial activity in the small intestine, initiating dysbacteriosis, inflammation and wet litter

Van der Klis et al, 1993
Viscosity

- Bacterial activity
  - Nutrients for bacteria
  - Digestibility
    - Intestinal damage
    - Permeability
      - Immune system
  - Viscosity
    - Viscosity
Carbohydrates / fiber

- Fiber can be inert and indigestible (oat hulls), or partly soluble and fermentable (soybean hulls or sugar beet pulp)
- Coarse, inert fiber stimulates gut motility and re-absorption of water
- Fermentable fiber has a high water holding capacity
## Carbohydrates / inert fiber

<table>
<thead>
<tr>
<th></th>
<th>BWG (g)</th>
<th>Feed intake (g/day)</th>
<th>Water intake (ml/day)</th>
<th>FCR</th>
<th>Water to feed ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>798 (^a)</td>
<td>51.2 (^bc)</td>
<td>152(^bc)</td>
<td>1.350(^ab)</td>
<td>1.82 (^b)</td>
</tr>
<tr>
<td>+5% oat hulls(^1)</td>
<td>764 (^b)</td>
<td>48.0 (^e)</td>
<td>139 (^a)</td>
<td>1.321 (^a)</td>
<td>1.76 (^a)</td>
</tr>
<tr>
<td>+5% oat hulls(^2)</td>
<td>775(^{ab})</td>
<td>50.2 (^{cd})</td>
<td>155 (^c)</td>
<td>1.366 (^b)</td>
<td>1.75 (^a)</td>
</tr>
<tr>
<td>Coarse ground corn(^3)</td>
<td>792 (^a)</td>
<td>50.5 (^{cd})</td>
<td>145(^{ab})</td>
<td>1.329 (^a)</td>
<td>1.89 (^c)</td>
</tr>
<tr>
<td>Control + citrus pectine</td>
<td>598 (^d)</td>
<td>50.8(^{bcd})</td>
<td>191 (^d)</td>
<td>1.783 (^d)</td>
<td>2.41 (^e)</td>
</tr>
<tr>
<td>+5% oat hulls(^1)</td>
<td>635 (^c)</td>
<td>48.8 (^{de})</td>
<td>182 (^d)</td>
<td>1.616 (^c)</td>
<td>2.33 (^d)</td>
</tr>
<tr>
<td>+5% oat hulls(^2)</td>
<td>644 (^c)</td>
<td>53.5 (^a)</td>
<td>204 (^e)</td>
<td>1.626 (^c)</td>
<td>2.28 (^d)</td>
</tr>
<tr>
<td>Coarse ground corn(^3)</td>
<td>675 (^c)</td>
<td>49.8(^{cde})</td>
<td>182 (^d)</td>
<td>1.664 (^d)</td>
<td>2.41 (^e)</td>
</tr>
</tbody>
</table>

\(^1\) Oat hulls were added on isocaloric basis; \(^2\) Oat hulls were added on top (diet dilution); \(^3\) Corn was ground by hammer mill over 8 mm instead of 3 mm sieve (D50: 940 \(\mu\)m and 610 \(\mu\)m respectively)

- Inert fiber reduces water/feed ratio especially at diets with increased viscosity

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Van der Klis et al, 1999
Carbohydrates / fermentable fiber (SBP: sugar beet pulp)

- With fiber from sugar beet pulp water/feed ratio goes up
- Interaction between cereal and fiber from sugar beet pulp on FCR

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Wheat</th>
<th>Corn</th>
<th>SBP</th>
<th>CF</th>
<th>Gain d5-18</th>
<th>FCR d5-18</th>
<th>W/F</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>45</td>
<td>0.0</td>
<td>25</td>
<td>25</td>
<td>517</td>
<td>1.473</td>
<td>1.72</td>
</tr>
<tr>
<td>II</td>
<td>45</td>
<td>2.5</td>
<td>28</td>
<td>28</td>
<td>514</td>
<td>1.411</td>
<td>1.79</td>
</tr>
<tr>
<td>III</td>
<td>45</td>
<td>5.0</td>
<td>31</td>
<td>31</td>
<td>502</td>
<td>1.388</td>
<td>1.92</td>
</tr>
<tr>
<td>VII</td>
<td>45</td>
<td>0.0</td>
<td>0.0</td>
<td>25</td>
<td>526</td>
<td>1.368</td>
<td>1.75</td>
</tr>
<tr>
<td>VIII</td>
<td>45</td>
<td>2.5</td>
<td>28</td>
<td>28</td>
<td>517</td>
<td>1.356</td>
<td>1.84</td>
</tr>
<tr>
<td>IX</td>
<td>45</td>
<td>5.0</td>
<td>31</td>
<td>31</td>
<td>507</td>
<td>1.364</td>
<td>1.92</td>
</tr>
</tbody>
</table>

Kempen et al, 1994
### Effect of fiber on microbes

<table>
<thead>
<tr>
<th>Fibre source</th>
<th>Crop</th>
<th></th>
<th>Ceca</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0%$^3$</td>
<td>5% OH</td>
<td>5% SBP</td>
<td></td>
</tr>
<tr>
<td>Crop</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Lactobacilli</em></td>
<td>7.9$^b$</td>
<td>7.1$^b$</td>
<td>8.4$^a$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceca</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Lactobacilli</em></td>
<td>9.8</td>
<td>8.6</td>
<td>10.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Clostridium perfr.</em></td>
<td>5.9$^a$</td>
<td>1.2$^b$</td>
<td>6.2$^a$</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Enterobacterias</em></td>
<td>8.4$^a$</td>
<td>5.9$^b$</td>
<td>8.4$^a$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Log10 cfu/g
2 Reared in floor pens
3 Contained 3.9% NDF

Mateos *et al.*, 2012
Nutritional interventions

- Carbohydrates / fiber
- Protein
- Fat
- Additives
- Feed processing technology
Protein digestion

Intestinal lumen

Protein

Pancreatic protease

Amino acids

Bacteria

Toxic metabolites: ammonia, biogenic amines, skatol, phenol

Blood
## Trial with interaction between protein and Virginiamycin

<table>
<thead>
<tr>
<th>Virginiamycin</th>
<th>20 ppm</th>
<th>0 ppm</th>
<th>20 ppm</th>
<th>0 ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Und. Crude Protein</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>BWG (g)</td>
<td>2156</td>
<td>2065</td>
<td>2151</td>
<td>1989</td>
</tr>
<tr>
<td>FCR</td>
<td>1.756</td>
<td>1.767</td>
<td>1.772</td>
<td>1.811</td>
</tr>
<tr>
<td>Biogenic amines</td>
<td>86</td>
<td>91</td>
<td>&lt;10</td>
<td>250</td>
</tr>
</tbody>
</table>

Smulders (SFR), 1999
Effect AGP on FCR at high and low Undigestible CP

Feed Conversion Rate

High UCP

Low UCP

Control Virginam.

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Effect of Undigestible Crude Protein on FCR

At constant EAA, extra UCP worsens FCR

De Lange et al, 2003
Nutritional interventions

- Carbohydrates / fiber
- Protein
- Fat
- Additives
- Feed processing technology
Fat digestion

Lipase → enzyme for fat degradation

Bile acids → emulsification of fat → formation of micelles → surface increase → improvement of fat digestibility

Bacteria in the intestine can deconjugate bile salts and so reduce digestion of fat.
Effect of fat (7.8%) in broiler feed; infected with E. Ac. at day 18

<table>
<thead>
<tr>
<th></th>
<th>ADG d18-23</th>
<th>FCR d18-23</th>
<th>Dig.fat d16</th>
<th>Dig.fat d23</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>g/d</td>
<td>g/g</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Control An. fat</td>
<td>48.4</td>
<td>1.752</td>
<td>81</td>
<td>87</td>
</tr>
<tr>
<td>Inf. An. fat</td>
<td>36.8</td>
<td>2.054</td>
<td>83</td>
<td>8</td>
</tr>
<tr>
<td>Inf. Coc. oil</td>
<td>43.0</td>
<td>1.850</td>
<td>89</td>
<td>49</td>
</tr>
<tr>
<td>Inf. Soy oil</td>
<td>38.6</td>
<td>2.037</td>
<td>89</td>
<td>16</td>
</tr>
</tbody>
</table>

Adams, SFR (1993)
Effect of feed ingredients on intestinal health

➢ Treatments:
   1. Control
   2. MCT
   3. MCFA
   4. Slowly degradable starch
   5. MCT + slowly degradable starch
   6. Lactose

➢ Broilers were challenged with Clostridium perfringens and Campylobacter jejuni

   Jansman et al, 2006
### Mortality (%) day 6 - 35

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control</td>
<td>12.2</td>
</tr>
<tr>
<td>II</td>
<td>MCT</td>
<td>11.5</td>
</tr>
<tr>
<td>III</td>
<td>MCFA C10/C12</td>
<td>2.6</td>
</tr>
<tr>
<td>IV</td>
<td>Slowly degradable starch</td>
<td>11.5</td>
</tr>
<tr>
<td>V</td>
<td>MCT and slowly degr. starch</td>
<td>12.2</td>
</tr>
<tr>
<td>VI</td>
<td>Lactose</td>
<td>10.9</td>
</tr>
</tbody>
</table>

*Jansman et al, 2006*
### Clostridium perfringens ($^{10}\log \text{cfu/g}$)

<table>
<thead>
<tr>
<th></th>
<th>Jejunum</th>
<th></th>
<th>Ileum</th>
<th></th>
<th>Caeca</th>
<th></th>
<th>Caeca</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dag 15</td>
<td>Dag 17</td>
<td>Dag 17</td>
<td>Dag 17</td>
<td></td>
<td>Dag 24</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Control</td>
<td>8,58&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8,21&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5,73&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;6,15&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>MCT</td>
<td>8,22&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8,27&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5,47&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;6,15&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>MCFA</td>
<td>6,87&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6,89&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5,58&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;6,15&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Starch</td>
<td>9,28&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8,61&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6,68&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;6,15&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>MCT + Starch</td>
<td>8,88&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8,13&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6,08&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>Lactose</td>
<td>8,85&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8,76&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5,83&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup>Onderste detectielimiet

Jansman, 2006
Feed Conversion Ratio day 0 - 35

Jansman et al, 2006
### Digestibility fat and fatty acids in jejunum

<table>
<thead>
<tr>
<th></th>
<th>Control (I)</th>
<th>MCT (II)</th>
<th>MCFA (III)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat</td>
<td>45</td>
<td>63</td>
<td>62</td>
</tr>
<tr>
<td>C10</td>
<td>-</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td>C12</td>
<td>-</td>
<td>91</td>
<td>93</td>
</tr>
<tr>
<td>C16:0</td>
<td>32</td>
<td>47</td>
<td>61</td>
</tr>
</tbody>
</table>

*Jansman et al, 2006*
Conclusions experiment with feed ingredients

- Feed ingredients can have a big effect on NE and animal performance after a challenge with Clostridium Perfringens and Campylobacter jejuni
- MCFA improve intestinal health and FCR
- MCT improve FCR
Medium Chain Fatty Acids

- Free fatty acids with of 6 – 12 C-atoms:
  - C6:0 caproic acid
  - C8:0 caprylic acid
  - C10:0 capric acid
  - C12:0 lauric acid

- Have a hydrophilic carboxyl group and a hydrophobic methyl group, which make them have emulsifying and detergent properties

- Anti-bacterial mostly against Gram-positive bacteria (Galbraith et al, 1971; Kabara et al, 1972; Feldlaufer et al, 1993), but also against Gram-negative (Bergsson et al, 1998), with C10 and C12 having the highest activity

- Sources: coconut oil and palm kernel fat
Fig. 3

Disruption of electron transport chain by:
- direct binding to electron carriers.
- insertion between carriers preventing their interaction.
- complete displacement of carriers from the membrane.
- preventing carrier interactions by reducing fluidity of the membrane.

Interference with oxidative phosphorylation by:
- preventing correct functioning of ATP synthase by direct binding or complete displacement from the membrane.
- reducing proton gradient/membrane potential by increasing membrane permeability to protons or FFAs dissociating a proton inside the cell and then returning to the extracellular space.

Formation of peroxidation or auto-oxidation products
- FFAs
- Hydroperoxides
- Free radical species
- Aldehydes
- Oxylipins

Inhibition of nutrient uptake

Cell lysis
Induction of autolysis

Inhibition of FA biosynthesis

Enzyme inhibition

Desbois and Smith, 2009
**Experiment with C10 + 12**

<table>
<thead>
<tr>
<th>Grower diet (g/kg)</th>
<th>Control</th>
<th>MCFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheat</td>
<td>458</td>
<td>464</td>
</tr>
<tr>
<td>Rye</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Animal fat</td>
<td>44</td>
<td>18</td>
</tr>
<tr>
<td>Soybean oil</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Capric acid</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Lauric acid</td>
<td></td>
<td>27</td>
</tr>
<tr>
<td>BW day 35 (g)</td>
<td>1804</td>
<td>1929</td>
</tr>
<tr>
<td>FCR-1.8-3</td>
<td>1.520</td>
<td>1.404</td>
</tr>
</tbody>
</table>

MCFA suppressed many species: Firmicutes including Lactobacilli, Micrococcaceae en Enterococcaceae in the ileum, but promoted Enterobacteriaceae and some specific Lactobacilli

Van der Hoeven-Hangoor et al, 2013
## Experiment with C6, C8 and C10 (Hejdysz, 2012)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>BWG</th>
<th>FCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neg. Control</td>
<td>2243</td>
<td>1.541</td>
</tr>
<tr>
<td>Pos. Control</td>
<td>2287</td>
<td>1.505</td>
</tr>
<tr>
<td>Caproic acid (C6:0)</td>
<td>2294</td>
<td>1.536</td>
</tr>
<tr>
<td>Caprylic acid (C8:0)</td>
<td>2270</td>
<td>1.511</td>
</tr>
<tr>
<td>Capric acid (C10:0)</td>
<td>2215</td>
<td>1.506</td>
</tr>
<tr>
<td>Mix C6, 8 and 10</td>
<td>2230</td>
<td>1.500</td>
</tr>
</tbody>
</table>

- Positive control: + 70 ppm Salinomycine
- 0.85% MCFA in diet
Nutritional interventions

- Carbohydrates / fiber
- Protein
- Fat
- Additives
- Feed processing technology
Additives: to be discussed

- Probiotics
- Prebiotics
- Essential oils
- Enzymes
- Immune modulators
- Phytogenic products
- And so on: antimicrobial peptides, lactylates, resins, clay minerals and ……
Effect AGP on FCR +/- enzyme

Schutte, 1997
Nutritional interventions

- Carbohydrates / fiber
- Protein
- Fat
- Additives
- Feed processing technology
Effect of processing temperatures on broiler performance and viscosity of feed, 0 – 21 days

<table>
<thead>
<tr>
<th>Temp. (°C)</th>
<th>Weight gain (g)</th>
<th>FCR (g/g)</th>
<th>Viscosity feed (cPs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>639</td>
<td>1.53</td>
<td>6.5</td>
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<tr>
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<td>1.52</td>
<td>7.0</td>
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<tr>
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<td>95</td>
<td>643</td>
<td>1.54</td>
<td>9.3</td>
</tr>
<tr>
<td>105</td>
<td>628</td>
<td>1.58</td>
<td>15.2</td>
</tr>
</tbody>
</table>

Wheat based diets extruded with conditioning for 60 seconds at different temperatures

- Processing temperatures of 95 and 105 °C tend to depress animal performance, presumably caused by increased viscosity, due to xylan solubilisation, starch gelatinisation and ……!? 

Creswell and Bedford, 2006
Summary

- Feed can have a big effect on intestinal health
- Especially a high dietary viscosity and fermentation of protein in the hind gut have a negative effect
- MCFAs are effective at improving intestinal health and feed utilization
Take Home Messages

- Use a concept to replace AGP’s in feed, instead of just taking out one additive and putting in another one.
- Use coarsely grinded, non viscous grains and reduce viscosity by using xylanases and by keeping pelleting temperatures low.
- Use highly digestible and well balanced protein.
- Use well tested antibacterial fats / additives as MCFA’s.
- Use occasionally some coarse inert fiber (occasions: low crude fiber in diet, finely ground feed, viscous grains, high infectious pressure, young age).

Thank you for your attention!