
# Feed alternatives for antibiotics in production animals

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## Animal production

Why is proper nutrition important?

- Profit
- Environment
- Health



## Animal production

Profit

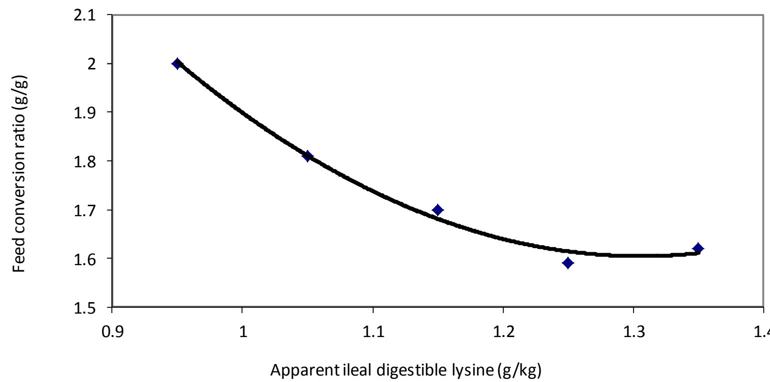
**Feed conversion ratio**

| Feed price (€/ton) | 2.30 | 2.40 | 2.50 | 2.60 | 2.70 | 2.80 | 2.90 | 3.00 |
|---|---|---|---|---|---|---|---|---|
| 200 | 41.4 | 43.2 | 45.0 | 46.8 | 48.6 | 50.4 | 52.2 | 54.0 |
| 210 | 43.5 | 45.4 | 47.3 | 49.1 | 51.0 | 52.9 | 54.8 | 56.7 |
| 220 | 45.5 | 47.5 | 49.5 | 51.5 | 53.5 | 55.4 | 57.4 | 59.4 |
| 230 | 47.6 | 49.7 | 51.8 | 53.8 | 55.9 | 58.0 | 60.0 | 62.1 |
| 240 | 49.7 | 51.8 | 54.0 | 56.2 | 58.3 | 60.5 | 62.6 | 64.8 |
| 250 | 51.8 | 54.0 | 56.3 | 58.5 | 60.8 | 63.0 | 65.3 | 67.5 |
| 260 | 53.8 | 56.2 | 58.5 | 60.8 | 63.2 | 65.5 | 67.9 | 70.2 |
| 270 | 55.9 | 58.3 | 60.8 | 63.2 | 65.6 | 68.0 | 70.5 | 72.9 |
| 280 | 58.0 | 60.5 | 63.0 | 65.5 | 68.0 | 70.6 | 73.1 | 75.6 |
| 290 | 60.0 | 62.6 | 65.3 | 67.9 | 70.5 | 73.1 | 75.7 | 78.3 |
| 300 | 62.1 | 64.8 | 67.5 | 70.2 | 72.9 | 75.6 | 78.3 | 81.0 |



## Animal production

Profit



## Animal production

Environment

- Crude protein content
- Mineral content (P, Cu, Zn)



## Animal production

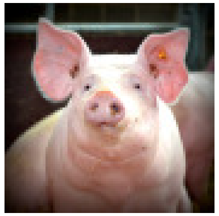
Health

- Replacement of antibiotics



## The use of antibiotics in pigs

Why are they used?





## The use of antibiotics in pigs

Why?

- To improve performance results
- To prevent/treat disease

## The use of antibiotics in pigs

To improve performances: AGP

- Forbidden in Europe since 2006
- The quest for alternatives
  - Organic acids
  - Pro-/pre-/synbiotics
  - Enzymes
  - Essential oils
  - Minerals



## The use of antibiotics in pigs

To treat or prevent disease

- Can we lower the amount of therapeutically used antibiotics by properly feeding our animals?



## Proper feeding

To prevent or treat disease

- Four cases
  - ***E. Coli (ETEC, colibacillosis)***
  - *Streptococcus suis*
  - *Salmonella enterica*
  - *Brachyspira hyodysenteriae*



## *E. Coli*

- When does it cause disease?
- Why?

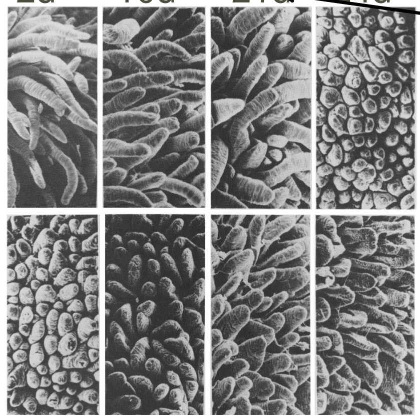
## *E. Coli*

- Weaning
  - Stress
  - Immunity gap
  - Change of feed



## *E. Coli*

2d 10d 21d 24d



Weaning

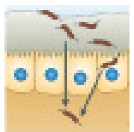
28d 35d 42d 49d

From: Cera et al., 1988



## *E. Coli*

Epithelial layer damage → ↑
trans- and paracellular permeability
attachment and invasion


www.nature.com

Smith *et al.*, 2010



## *E. Coli*

→ How can feeding management prevent disease?

# *E. Coli*

## How can feeding management prevent disease?

- Lower the amount of bacteria
- Increase resistance
  - Intestinal integrity
  - Immune system



# *E. Coli*

## Lowering the amount of bacteria

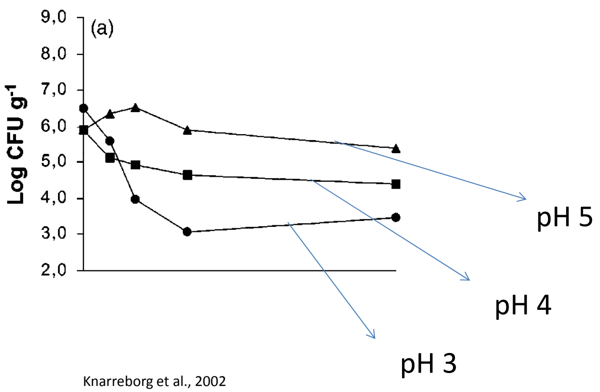
- Dietary protein concentration
- Organic acids
- Antibodies



# *E. Coli*

## Lowering the amount of bacteria

- pH




Knarreborg et al., 2002



# *E. Coli*

## Lowering the amount of bacteria

Table 3
Specific bacterial growth or death rate in response to various organic acids in stomach content at pH 4.5

| Acid (100 mM) | Coliform bacteria ($h^{-1}$) | Lactic acid bacteria ($h^{-1}$) |
|---|---|---|
| Control | −0.25 | 0.63 |
| Propionic acid | −0.19 | 0.53 |
| Formic acid | −0.69 | 0.24 |
| Butyric acid | −1.16 | 0.28 |
| Lactic acid | −1.39 | 0.53 |
| Fumaric acid | −2.31 | −0.69 |
| Benzoic acid | <−7.00 | −2.31 |

Knarreborg et al., 2002

# *E. Coli*

## Lowering the amount of bacteria

- Antibodies
  - Spray dried plasma/egg yolk antibodies
  - In seed produced antibodies



# *E. Coli*

## Spray dried plasma

Table 1.

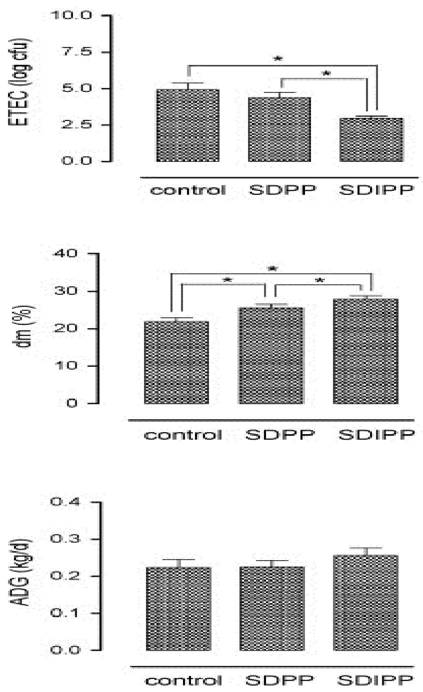
Effect of dietary SDPP on bacteria ($\log_{10}$ cfu/g intestinal contents) in the gastro-intestinal tract of piglets.

| | Control diet | SDPP diet | SEM |
|---|---|---|---|
| Stomach | | | |
| Enterococci | 3.92 | 3.71 | 0.43 |
| Enterobacteriaceae | 1.79 | 0.89 * | 0.30 |
| Sulphate reducing Clostridia | 1.68 | 2.09 * | 0.12 |
| Lactobacilli | 7.19 | 7.89 | 0.49 |
| Jejunum | | | |
| Enterococci | 4.72 | 4.59 | 0.44 |
| Enterobacteriaceae | 4.93 | 5.75 | 0.66 |
| Sulphate reducing Clostridia | 0.90 | 1.19 | 0.23 |
| Lactobacilli | 7.06 | 8.25 | 0.69 |
| Caecum | | | |
| Enterococci | 5.62 | 5.30 | 0.33 |
| Enterobacteriaceae | 6.62 | 6.16 | 0.40 |
| Sulphate reducing Clostridia | 3.39 | 3.36 | 0.23 |
| Lactobacilli | 7.78 | 8.48 | 0.41 |

* Significant difference versus control group ($P < 0.05$).

Van Dijk et al., 2001






Niewold et al., 2007

# *E. Coli*

## Immunised egg powder

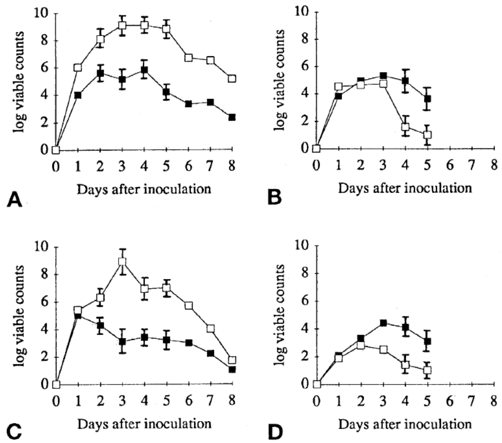



Fig. 1. Means (±S.E.M.) of the faecal viable counts of inoculated bacteria beginning with the first day of inoculation (day 0) with *E. coli* F18ab (experiment 1: A,B) and *E. coli* F18ac (experiment 2: C,D). Two treatments each with five or six pigs per treatment are shown: egg powder with homologous antibody high (closed squares) and control without egg (open squares). Challenge and viable counts were done during egg powder treatment (A,C), and 14 days later after termination of the treatment (B,D).

Zuniga et al., 1997

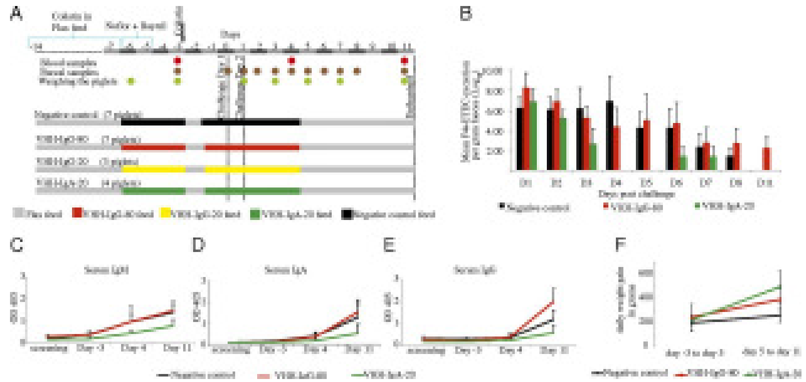
# *E. Coli*

## Lowering the amount of bacteria

- In seed produced antibodies



### VHH-IgA feed reduces F4+ETEC infection in challenged piglets.

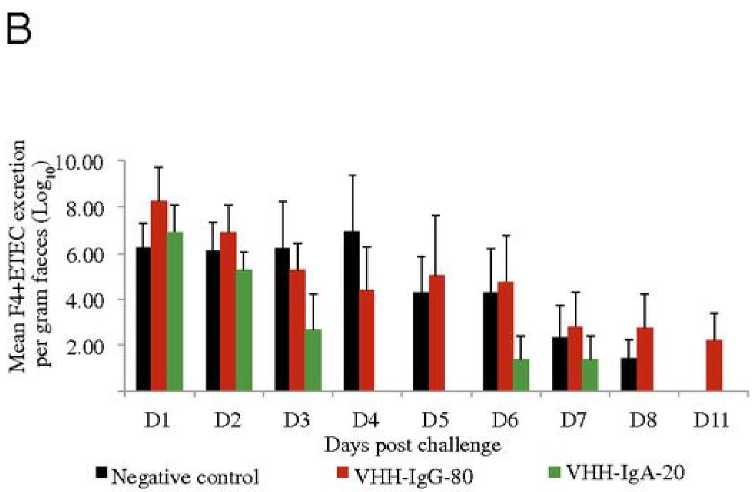



Virdi V et al. PNAS 2013;110:11809-11814



PNAS

### VHH-IgA feed reduces F4+ETEC infection in challenged piglets.

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PNAS

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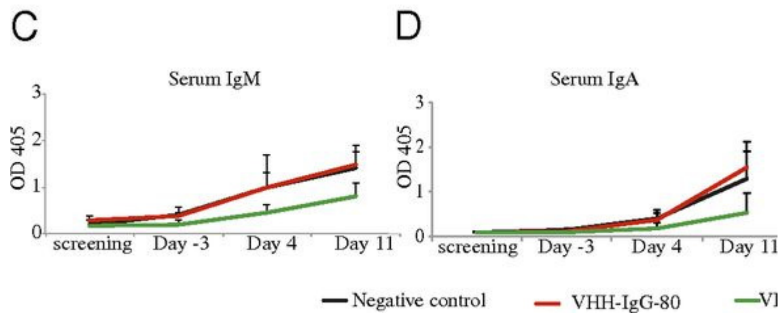



Virdi V et al. PNAS 2013;110:11809-11814



PNAS

## *E. Coli*

How can feeding management prevent disease?

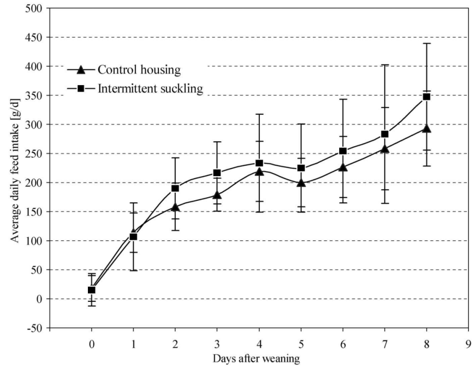
- Lower the amount of bacteria
- Increase resistance
  - Intestinal integrity
  - Immune system



## *E. Coli*

Maintaining intestinal integrity

- Feed intake!




Millet et al., 2008



## *E. Coli*

Maintaining intestinal integrity

- Feed intake!
  - Liquid feeding
  - Flavours?
  - Amino acids
  - Optimal creep feed consumption

  - Water intake!
- Minerals: ZnO



## *E. Coli*

Increasing feed intake

- Liquid feeding
  - Nutrient density!

## *E. Coli*

### Increasing feed intake

- Flavours?
  - If they have the choice…

But

Masking the quality?



## *E. Coli*

### Increasing feed intake

- Way of providing the feed

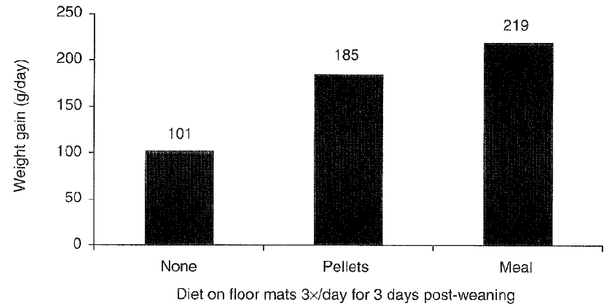



**Fig. 4.7.** Mat-feeding improves growth performance in weaned pigs. (From Mavromichalis and Baker, 2000.)



## *E. Coli*

### Increasing feed intake

- Amino acids
  - Valine
  - Tryptophan



## *E. Coli*

### Increasing feed intake

**Table 1.** Influence of valine and tryptophan concentration on performances of the piglets [1,2].

| | Low Valine | | High Valine | | | P | | |
|---|---|---|---|---|---|---|---|---|
| | Low Tryptophan | High Tryptophan | Low Tryptophan | High Tryptophan | SEM | SID VAL | SID TRP | SID VAL x SID TRP |
| Bodyweight, kg | | | | | | | | |
| 5 weeks of age | 9.45 | 9.48 | 9.40 | 9.44 | 0.04 | 0.514 | 0.616 | 0.993 |
| 7 weeks of age | 14.09 | 14.41 | 15.29 | 15.35 | 0.12 | <0.001 | 0.185 | 0.374 |
| 9 weeks of age | 20.88 | 21.47 | 23.51 | 23.58 | 0.21 | <0.001 | 0.157 | 0.267 |
| Daily feed intake, g | | | | | | | | |
| 5-7 weeks | 565 | 571 | 648 | 636 | 9 | <0.001 | 0.776 | 0.430 |
| 7-9 weeks | 897 | 899 | 1004 | 1008 | 13 | <0.001 | 0.871 | 0.952 |
| 5-9 weeks | 731 | 735 | 826 | 822 | 11 | <0.001 | 0.871 | 0.952 |
| Daily weight gain, g | | | | | | | | |
| 5-7 weeks | 332 | 352 | 421 | 423 | 60 | <0.001 | 0.194 | 0.287 |
| 7-9 weeks | 485 | 504 | 587 | 588 | 8 | <0.001 | 0.326 | 0.382 |
| 5-9 weeks | 408 | 428 | 504 | 505 | 7 | <0.001 | 0.136 | 0.215 |
| Feed efficiency, g/g | | | | | | | | |
| 5-7 weeks | 0.587 | 0.619 | 0.652 | 0.665 | 0.007 | <0.001 | 0.034 | 0.377 |
| 7-9 weeks | 0.544 | 0.563 | 0.585 | 0.584 | 0.005 | 0.001 | 0.313 | 0.266 |
| 5-9 weeks | 0.560 | 0.585 | 0.610 | 0.616 | 0.004 | <0.001 | 0.031 | 0.159 |

[1]Data are means of 16 pens per treatment

[2]SID = standardized ileal digestible, VAL= valine, TRP = tryptopan

Millet, 2012

# *E. Coli*

## Maintaining intestinal integrity

- ZnO

**Table 3**
Effects of feeding diets containing either no ZnO (control), 3000 mg/kg ZnO (ZnO) or 100 mg/kg microencapsulated ZnO (M
lenge with enterotoxigenic *E. coli* (ETEC) on the expression of post-weaning colibacillosis and plasma and faecal zinc conce
data).[a]

| | No ETEC challenge | | | ETEC challenge | | | SEM[f] |
|---|---|---|---|---|---|---|---|
| | Control | ZnO | ME-ZnO[b] | Control | ZnO | ME-ZnO | |
| *n*[c] | 12 | 12 | 12 | 12 | 12 | 12 | |
| Diarrhoea index[e] | 13.1 | 0.0 | 6.0 | 16.1 | 5.4 | 3.4 | 4.8 |
| Days with therapeutic antibiotic treatment[f] | 1.8 | 0.0 | 0.8 | 2.3 | 0.7 | 0.5 | 0.41 |
| Plasma zinc, mg/L[g] | 0.73 | 2.48 | 0.65 | 0.64 | 2.28 | 0.83 | 0.146 |
| Faecal zinc, g/kg[g] | 1687 | 13961 | 2694 | 1787 | 14329 | 2209 | 412.0 |

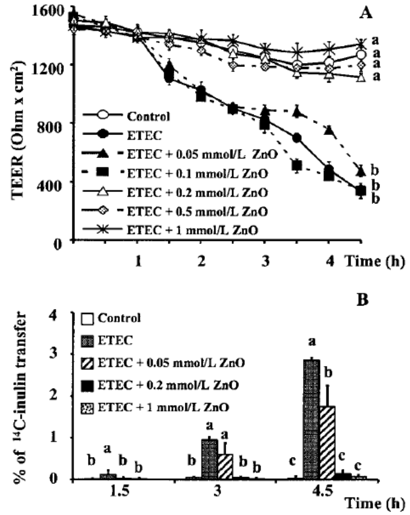
Kim et al., 2012



# *E. Coli*

## Maintaining intestinal integrity

- ZnO




Roselli et al., 2003



# *E. Coli*

## How can feeding management prevent disease?

- Lower the amount of bacteria
- Increase resistance
  - Intestinal integrity
  - Immune system



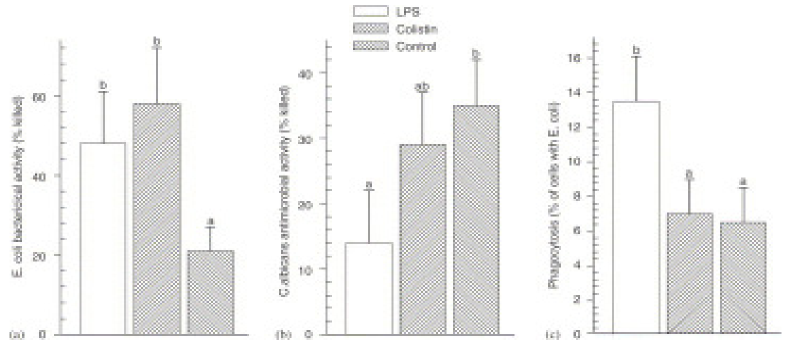



Fig. 4 (a) Effect of LPS or colistin (polymyxin E) injection on the bactericidal activity against E. coli (ATCC # 51813 of whole blood from chicks ( n =average of three pens). (b) Effect of LPS or colistin injection on the antimicrobial activity against ...

Sam Millet , Jennie Bennett , Kelly A. Lee , Michaela Hau , Kirk C. Klasing

**Quantifying and comparing constitutive immunity across avian species**

Developmental & Comparative Immunology Volume 31, Issue 2 2007 188 - 201

http://dx.doi.org/10.1016/j.dci.2006.05.013

# *E. Coli*

## The cost of immunity

| | Developmental time | Developmental cost | Maintenance cost | Nutritional cost | Effectiveness | | Pathological cost of use |
|---|---|---|---|---|---|---|---|
| | | | | | Novel chalenge | Repeated challenge | |
| Non-specific immunity including acute phase response | short | low | medium | very high | good | good | very high |
| Specific lymphocyte-mediated immunity | long | very high | low | low | poor | excellent | variable |

After: Klasing, 2007



# *E. Coli*

## "Immunomodulation"

- Reduce inflammation → growth promotion
- Fight disease/increase resistance?



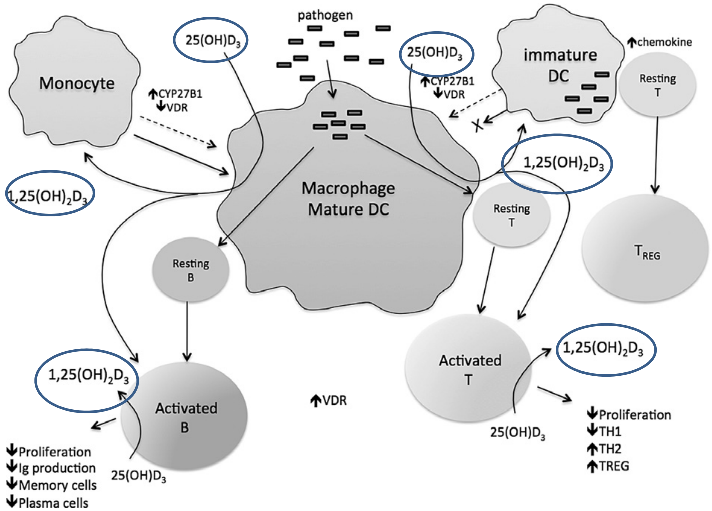
# *E. Coli*

## "Immunomodulation"

- Glucans
- Mannans
- Essential oils
- Spray dried plasma
- Lactoferrin
- Vitamin D



# Vitamin D and the immune system




O'Brien and Jackson, 2012

# Proper feeding

To prevent or treat disease

- Four cases
  - *E. Coli (ETEC, colibacillosis)*
  - ***Streptococcus suis***
  - *Salmonella enterica*
  - *Brachyspira hyodysenteriae*



# *S. suis*

Can feeding management prevent disease?

CASE REPORT

Drum SD, Hoffman LJ. Unusual *Streptococcus suis* type 2 disease on two farms feeding incorrectly formulated nursery feed. *Swine Health and Production*. 1998;6(5):217–218.

**Unusual *Streptococcus suis* type 2 disease on two farms feeding incorrectly formulated nursery feed**

**Steven D. Drum, DVM, MS; Lorraine J. Hoffman, MS, PhD**



# *S. suis*

How can feeding management prevent disease?

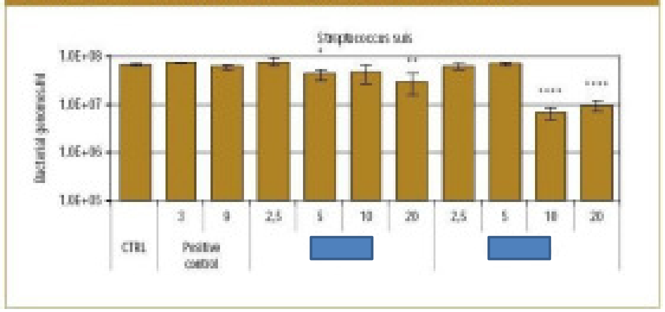
- Lower the amount of bacteria
  - Route of infection?
- Increase resistance
  - Intestinal integrity?
  - Immune system



# *S. suis*

Lower the amount of bacteria

Figure 2 - Effect of SCFA and MCFA mix ( ) on number of S suis bacteria.
* p<0.05; ** p<0.01; **** p<0.0001 significantly different compared to the negative control group.




- But: is it an important route of infection?

# *S. suis*

Table 4. Quantitative real-time PCR analysis of total bacteria, lactoba
stomach, jejunum and ileum

| | Stomach | |
|---|---|---|
| Species | Day 21 | Day 24 |
| Bacteria | 5.40 ± 0.07 | 7.95 ± 0.61* |
| Lactobacilli | 4.55 ± 0.13 | 6.04 ± 0.54* |
| Lactobacilli/bacteria (%) | 14.13 | 1.23 |
| *L. sobrius* | 4.14 ± 0.25 | 5.64 ± 0.15* |
| *L. sobrius*/bacteria (%) | 5.50 | 0.49 |
| *S. suis* | < 4 | 7.36 ± .06* |
| *S. suis*/bacteria (%) | < 3.98 | 25.70 |

*Significant differences between day 21 and day 24 compared at P < (
Three samples were quantified for each age and counts are expressed a

FEMS Microbiol Ecol 66 (2008) 546–555

Su et al., 2008



# *S. suis*

How can feeding management prevent disease?

- Increase resistance
  - Intestinal integrity?
  - Immune system

**Influence of dietary beta-glucan on growth performance, nonspecific immunity, and resistance to Streptococcus suis infection in weanling pigs.**
S S Dritz, J Shi, T L Kielian, R D Goodband, J L Nelssen, M D Tokach, M M Chengappa, J E Smith and F Blecha

*J ANIM SCI* 1995, 73:3341-3350.

Pigs fed b-glucan had decreased ( *P* < .10) plasma haptoglobin on d 14, 21, and 28 after weaning. However, Fisher's Exact test revealed that more (*P* <.04) pigs fed a diet containing .025% b-glucan died by d 12 after challenge with *S. suis*.



# Proper feeding

To prevent or treat disease

- Four cases
  - *E. Coli (ETEC, colibacillosis)*
  - *Streptococcus suis*
  - ***Salmonella enterica***
  - *Brachyspira hyodysenteriae*



# *Salmonella enterica*

How can feeding management prevent disease?

- Lower the amount of bacteria
- Increase resistance
  - Intestinal integrity?
  - Immune system

## *Salmonella enterica*

### How can feeding management prevent disease?

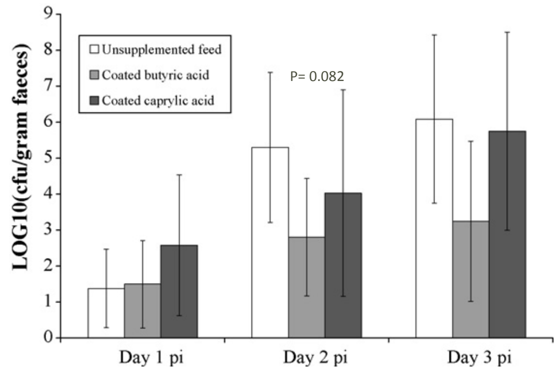
- Lower the amount of bacteria
  - Pelleting
    - + feed contamination
    - - protection in the animal
    - →non-pelleted, coarsely ground meal
      - →Increased fermentation in stomach
  - Fermented liquid feed
  - Organic acids?



## *Salmonella enterica*

### How can feeding management prevent disease?

- Organic acids for Salmonella control?



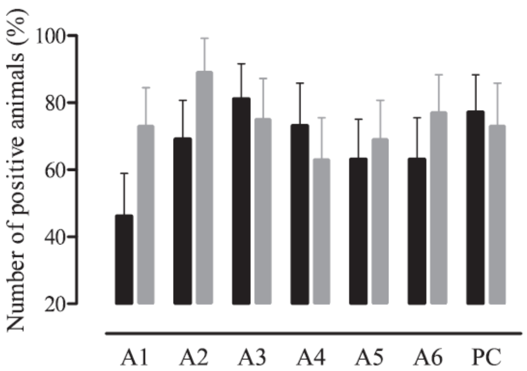

Boyen et al., 2008



## *Salmonella enterica*

### How can feeding management prevent disease?

- Organic acids for Salmonella control?




Michiels et al., 2012



## *Salmonella enterica*

### How can feeding management prevent disease?

- Organic acids for Salmonella control?

Two additives, both containing SCFA and one of them benzoic acid as well and the other one also containing essential oils, and supplemented at more than 2.7 g of active ingredients per kg of feed, showed evidence of reducing *Salmonella* shedding and colonization in young piglets. Additives containing butyric acid and MCFA failed to inhibit *Salmonella* contamination in the current experimental setup; however, this was likely because of the low inclusion rate. The limited overall effect of the tested organic acids urges for a multitarget approach for *Salmonella* control.

Michiels et al., 2012

## Proper feeding

To prevent or treat disease

- Four cases
  - *E. Coli (ETEC, colibacillosis)*
  - *Streptococcus suis*
  - *Salmonella enterica*
  - ***Brachyspira hyodysenteriae***



## *Brachyspira hyodysenteriae*

How can feeding management prevent disease?

***Nutrient Requirements and Interactions***

**The Incidence of Swine Dysentery in Pigs Can Be Reduced by Feeding Diets That Limit the Amount of Fermentable Substrate Entering the Large Intestine[1,2,3]**

*JOHN R. PLUSKE,[4] PETER M. SIBA, DAVID W. PETHICK, ZORICA DURMIC, BRUCE P. MULLAN* AND DAVID J. HAMPSON[5]*

*School of Veterinary Studies, Murdoch University, Murdoch WA 6150 Australia and *Agriculture Western Australia, South Perth WA 6151, Australia*



## *Brachyspira hyodysenteriae*

How can feeding management prevent disease?

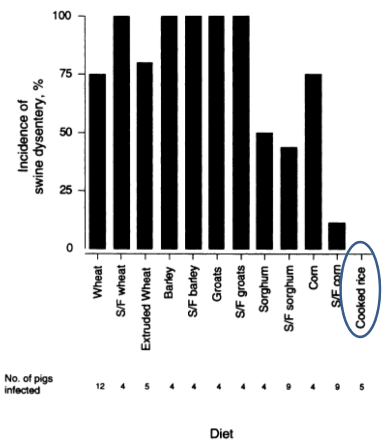



*FIGURE 2* The incidence of swine dysentery (%) in pigs fed different diets (pooled results from Experiments 1 and 2).



## *Brachyspira hyodysenteriae*

How can feeding management prevent disease?

**Diets containing inulin but not lupins help to prevent swine dysentery in experimentally challenged pigs**

C. F. Hansen, N. D. Phillips, T. La, A. Hernandez, J. Mansfield, J. C. Kim, B. P. Mullan, D. J. Hampson and J. R. Pluske

*J ANIM SCI* 2010, 88:3327-3336.
doi: 10.2527/jas.2009-2719 originally published online June 4, 2010

Diets supplemented with highly fermentable carbohydrates from inulin may protect pigs against developing swine dysentery by modifying the normal microbiota in the gastrointestinal tract.

# CONCLUSION

Can we lower the amount of therapeutically used antibiotics by properly feeding our animals?

- YES, but…
- No magic solution
- A lot needs to be done still



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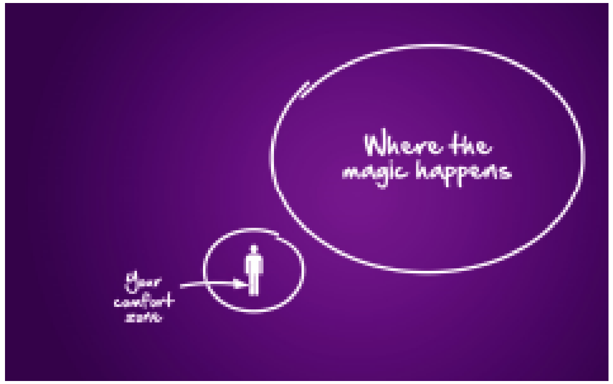
# Questions?

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