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FEED ADDITIVES AS ALTERNATIVES TO ZINC OXIDE TO REDUCE POST WEANING DIARRHOEA



ZERO ZINC SUMMIT 2019
Copenhagen, 17-18. June

› Medical ZnO:

- › Approved in Denmark as a medicinal drug:
- › Can - upon veterinary prescription - be used up to a level of **3,000 ppm** for **treating piglet diarrhea during** the first 14 days post-weaning
- › Also in organic pig production

› **Feed additives:**

- › applied to improve the performance of *healthy* animals or to cover the animals' physiological requirements
- › not considered as alternatives to medical ZnO
- › Zinc is a feed additive (max. 150 ppm for piglets) including ZnO.

Lowering the level of dietary crude protein (from around 21-23% to 18%) is probably the most clearly documented *feeding strategy** to reduce the incidence of PWD in piglets**

- Not because other dietary strategies do not work, but there is a general lack of in vivo studies investigating the impact of feed additives using PWD as the primary outcome!

*Other strategies: weaning age and weaning environment.

**Source: 'A critical review on alternatives to antibiotics and pharmacological zinc for prevention of diarrhoea in pigs post-weaning' (Lauridsen, Højberg, Kongsted and Canibe, 2017)

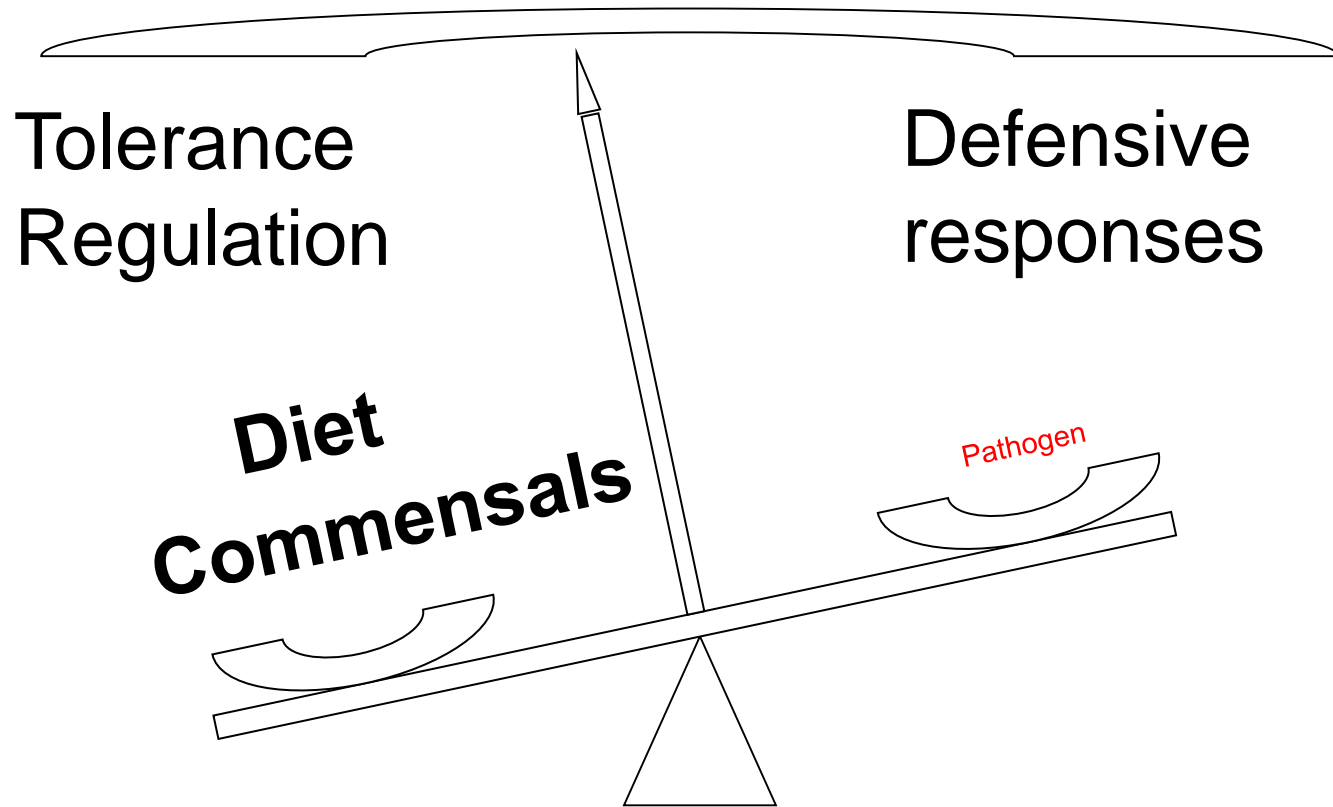
HOW TO CONSIDER FEED ADDITIVES?

- › feed additives should be considered as a strategy to enhance **gut health**, hence preventing pigs from developing diarrhea
- › **Focus of this presentation will be modes of action to prevent ETEC* infection** (because this is the major cause of diarrhea during the first 14 days post weaning).

› *Enterotoxigenic E. Coli



When mucosal barrier is intact: Primary role of the local immune system is to keep harmful antigens within the intestinal lumen. Peristalsis and mucus flow clear potentially harmful antigens via faeces



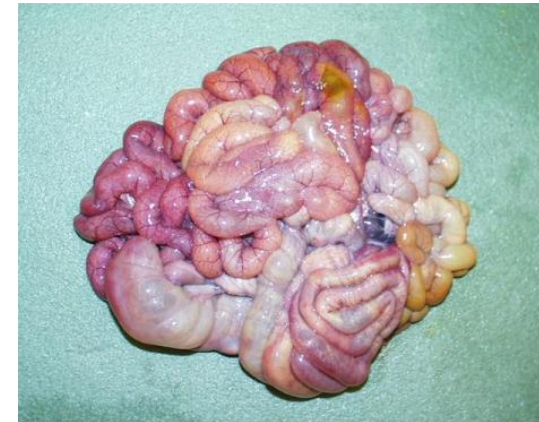
When the mucosal barrier is broken: inflammatory processes are activated to eliminate potentially harmful antigens. Acute responses are demanded, however harmful if chronic

Tolerance
Regulation

Defensive
responses

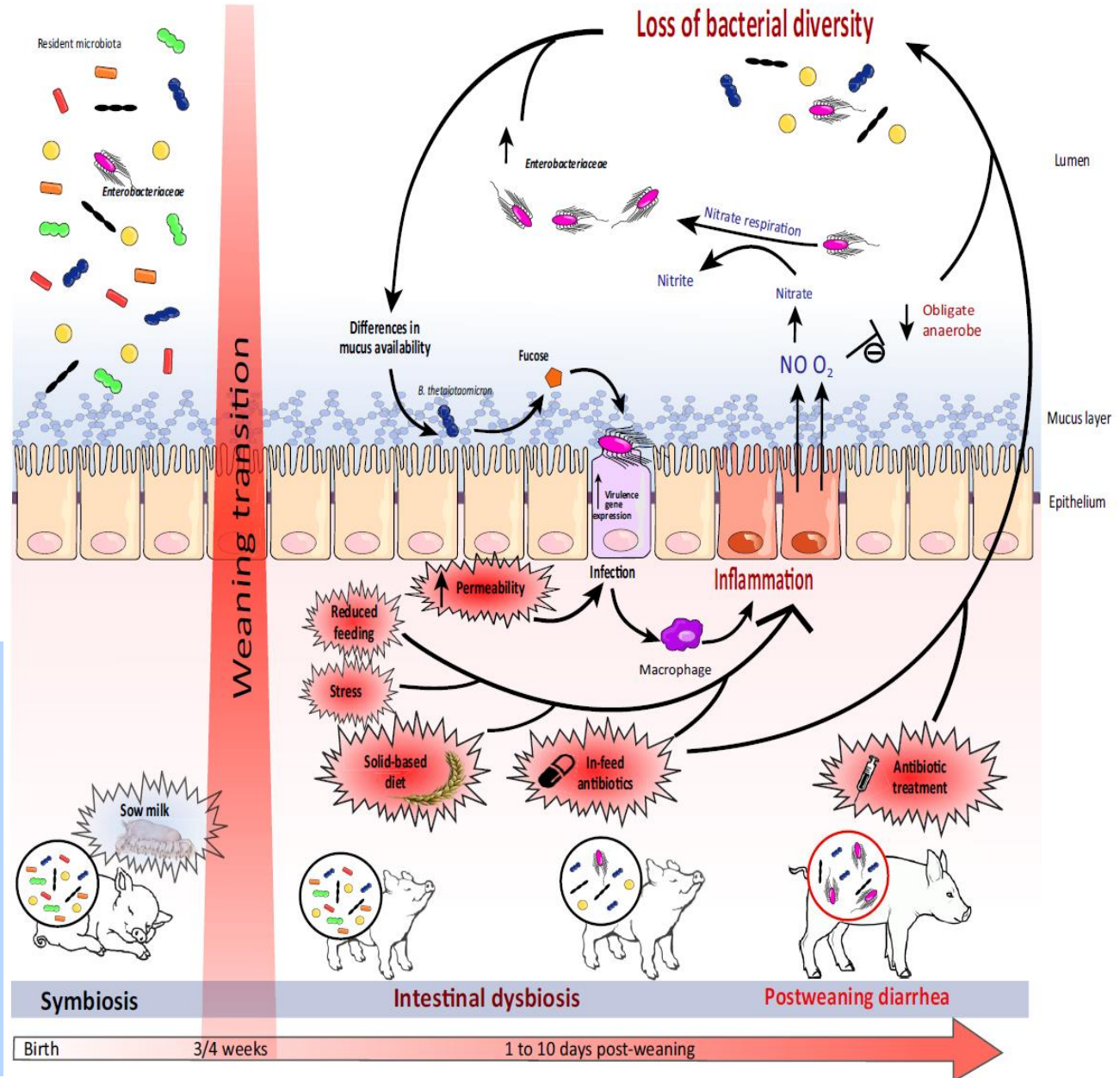
Diet
Commensals

Pathogen



Weaning stress can lead to dysbiosis and enhance risk of ETEC Infection.

Many parameters can be measured to study the gastrointestinal ecology – and to assess gut health.



Disease level progression

Progression of ETEC infection

Growth of ETEC

Adhesion & colonisation

Disruption of commensals

Stimulation of immune responses; loss of epithelial barrier function

Microbiota

How can feed additives prevent the progression of ETEC infection?



Host

Progression of ETEC infection

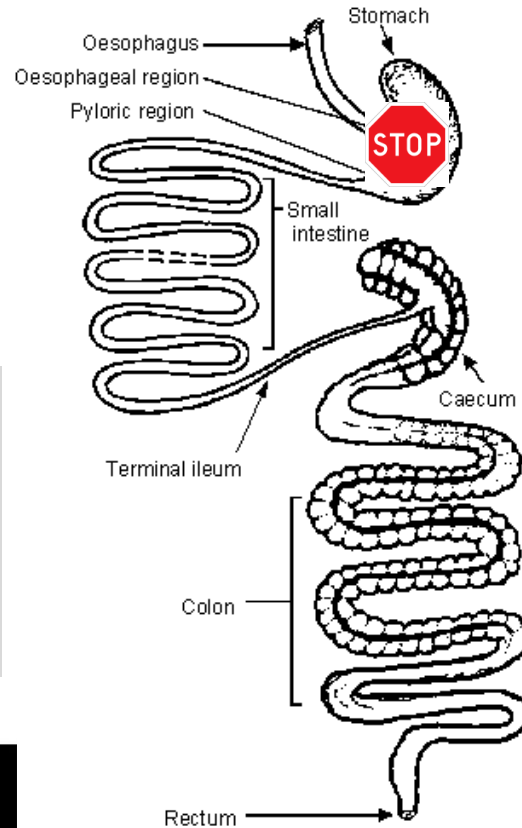
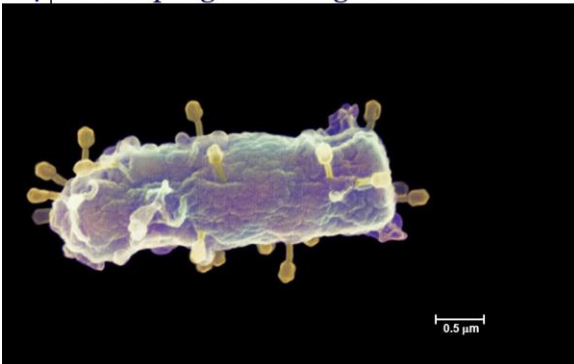


Growth of ETEC

Prevention by:

- Lowering pH
- Antibacterial activity

T4 bacteriophage infecting an *E. coli* cell



Examples of feed additives:

- Organic acids, acidifiers
- Lysozymes, bacteriophages
- Antimicrobial peptides
- Antmicrobial lipids

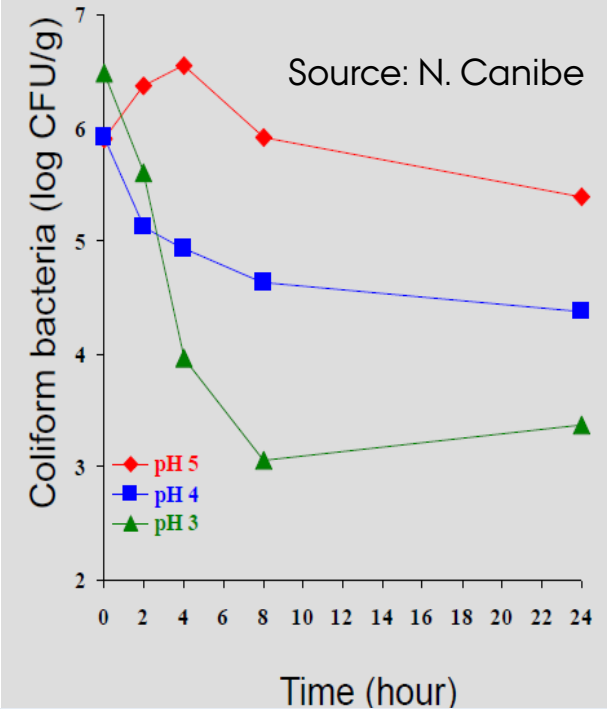
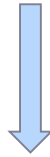


Figure: Change of population density of coliform bacteria in stomach content incubated at various pH

Progression of ETEC infection



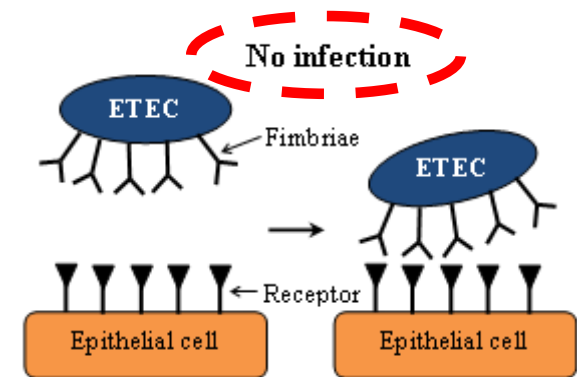
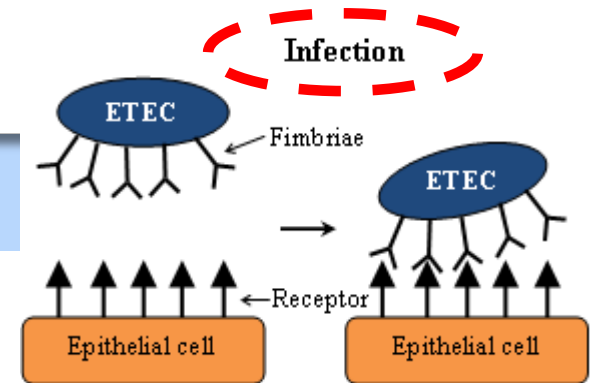
Adhesion & colonization

Prevention by:

- Reduction in sensitivity of fimbria
- Blocking the fimbria of the ETEC

Examples of feed additives:

- Specific immunoglobulins
- Bacteriophages
- Yeast derivatives



Progression of ETEC infection



Symbiosis

Disruption of
commensal;
dysbiosis

Prevention by:

- Maintaining a balanced commensal microbiota

Probiotics: 'live microorganisms that, when administered in adequate amounts, confer health benefits to the host'

Prebiotics: 'fermentable components, that induce specific changes in composition and/or activity of the gastrointestinal microbiota and conferring host well-being and health benefits'

Examples of feed additives:

- Pre- and probiotics
- Medium-chained fatty acids (C8-C12)
- Others with probiotic-like characteristics

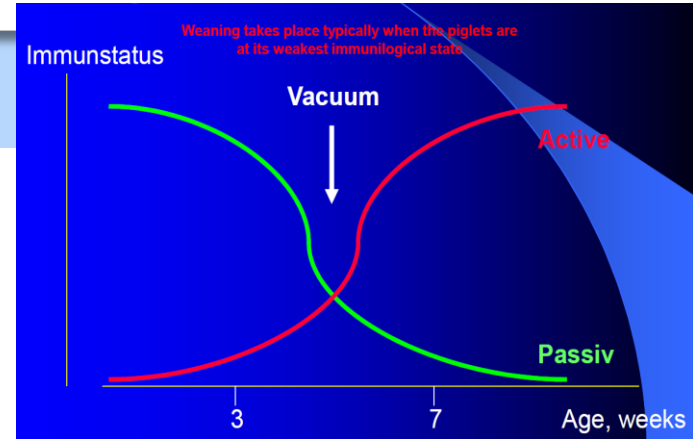
Progression of ETEC infection

Prevention by:

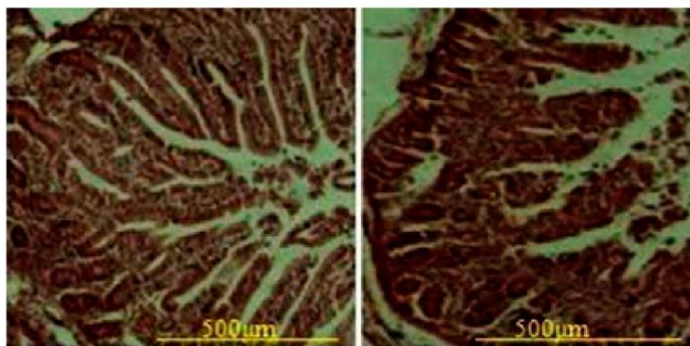
- Improving the pigs' own immune function
- Enhance mucosal integrity and/or morphology of epithelium in small intestine

Examples of feed additives:

- Immunoglobulins
- Fatty acids, vitamins, trace elements

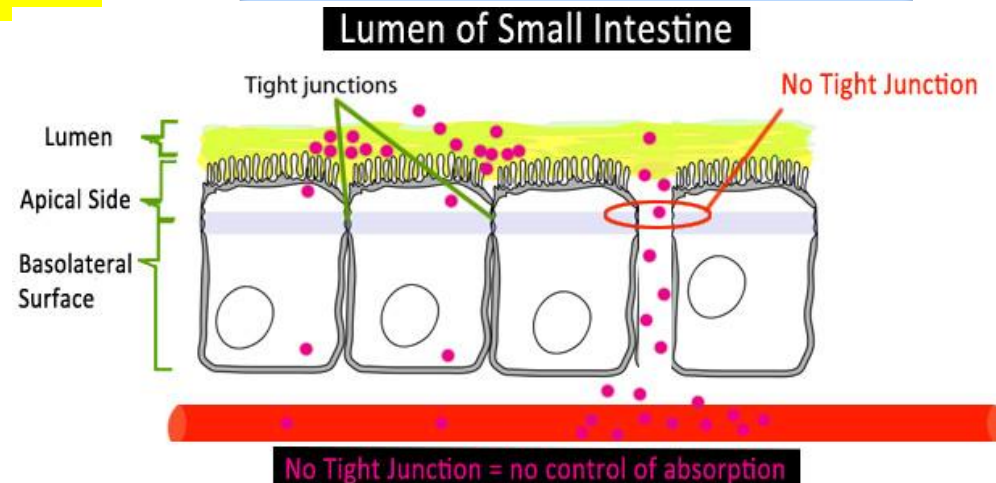


Stimulation of immune responses; loss of epithelial barrier function



Control

Weaning



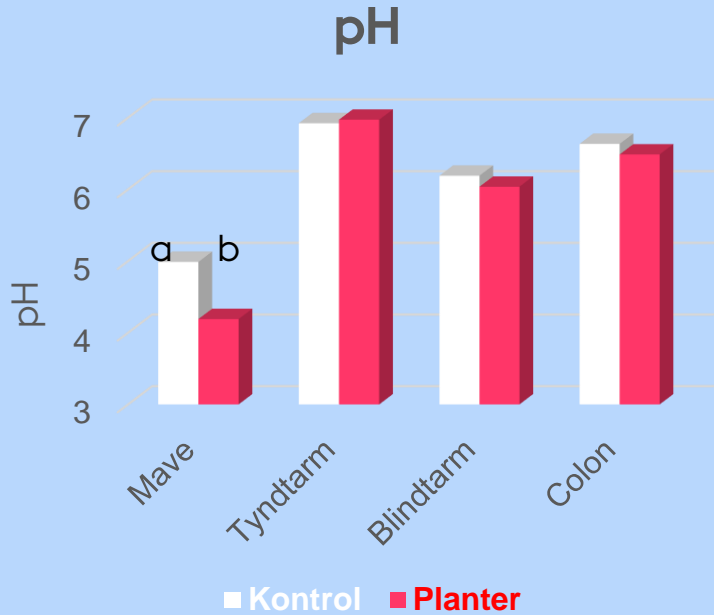
BLENDS OR COCKTAILS?

- › not a single molecule can influence at all steps of ETEC infection!
- › Potential for investigating blends of feed additives (such as MCFA and organic acids), or cocktails (probiotic strains), or,.....
- › **Plant extracts, fruits/berries, algae have gained interests**
- › These ‘natural’ foods may encompass both antibacterial and immunomodulatory properties
- › Factors such as dose, time of provision, stability in feed, bioactive components should be researched!

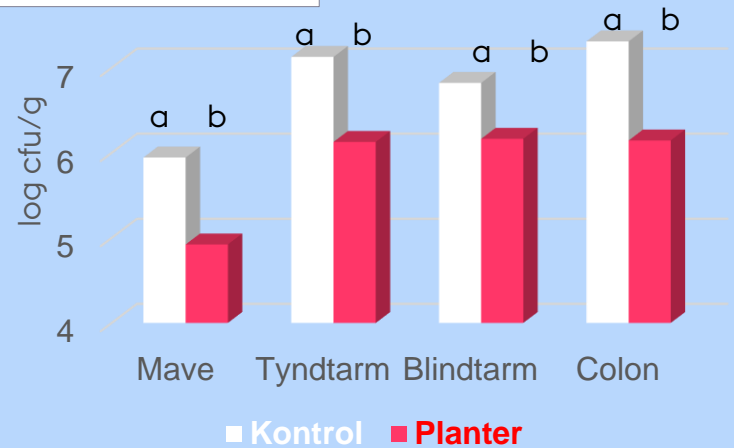
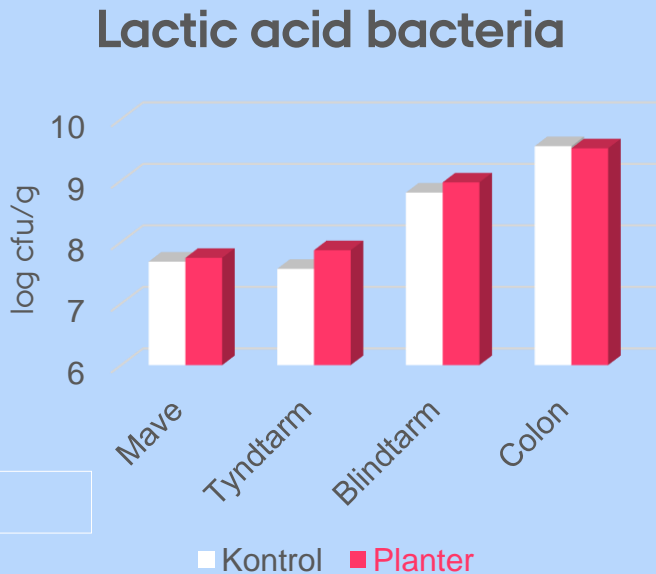
Effect of adding 3% ramsoms and 3% lingonberries to piglets post weaning

Ongoing (organic) research project with focus on PWD (E. coli challenge trials) and bioactive component(s) (allicin & derivatives)
 Source: Højberg & Canibe

Plant powder



lactic acid bacteria



ZERO ZINC BEFORE 2022 ?

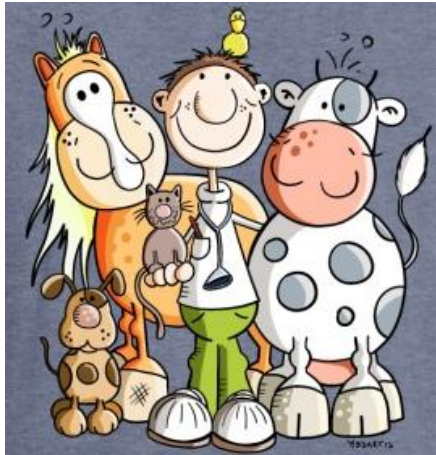


Farmer:
I will manage
after a
'cold turkey'

Nutritionists:
We (all-ready) have
solutions/concepts



www.alamy.com - C8WFX7



Veterinarian:
More antibiotic
Treatment?

Scientists:
We research
to provide
solutions



ONGOING RESEARCH: LIQUID FEED/FERMENTED LIQUID FEED (CANIBE, 2018-, VETFORLIGIII)

In Denmark, liquid feed (with varying degrees of fermentation) is frequently used.

Why fermentation?

Reduces coliform bacteria and other pathogens in the GI-tract (also salmonella!)



Mode of action:

- ❖ Low pH
- ❖ High concentration of organic acid

Running time

- ❖ Fermented liquid feed
- ❖ Added a probiotic (a way of giving up to 10^9 bacteria/g feed)

Starting in the suckling period

ONGOING RESEARCH: PROBIOTICS

- MANY MECHANISMS – AND THEREFORE OPPORTUNITIES
- COMBINATION OF STRAINS ? DOSE? WHEN TO APPLY? SOW/PIGLET?

RobustPig: Early inoculation of probiotics to newborn piglets



RESEARCH ARTICLE

Impact of *Bacillus* spp. spores and gentamicin on the gastrointestinal microbiota of suckling and newly weaned piglets

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Immunomodulating effects of probiotics for microbiota modulation, gut health and disease resistance in pigs

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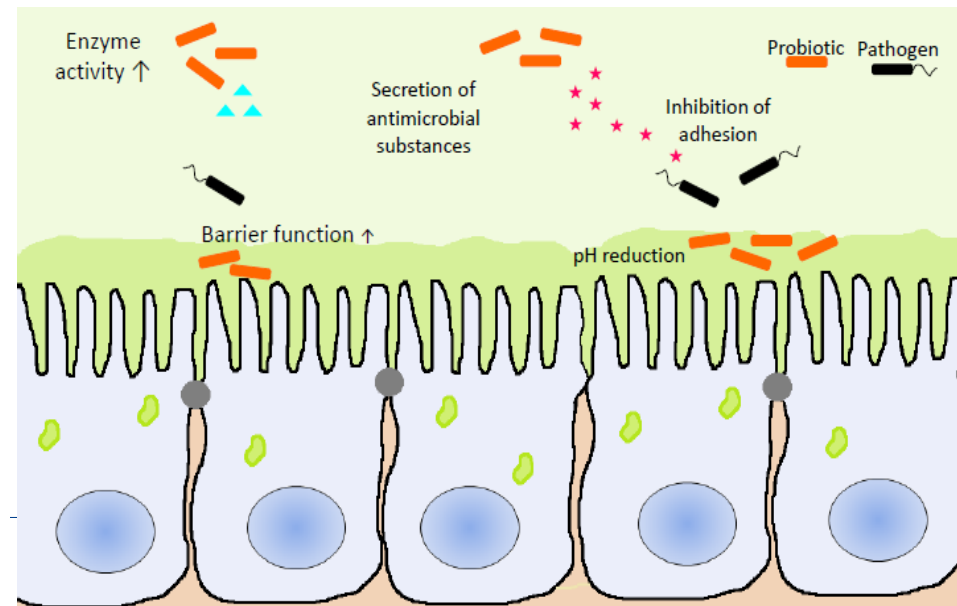
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Source: Lea Hübertz Birch Hansen (Chr. Hansen+AU)

ONGOING RESEARCH: NUTRITIONAL IMMUNOMODULATION



- › Fatty acids, vitamins and trace elements are essential for immune development and responses
- › Micronutrient deficiencies are linked to increased risk of enteric infectious disease and diarrhoea in human
- › Transient deficiency during weaning?
- › Lack of research in pigs: vitamins, fatty acids and health

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- › The influence of selenium and selenoproteins on immune responses of poultry and pigs

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Transfer of fatty acids, vitamins and trace elements to piglets to enhance gut health and robustness: via sow nutrition and/or milk formular?

CONCLUSION AND PERSPECTIVES

- › There is probably not a single feed additive, which can exchange ZnO
- Many feed additives share several of the mode of actions by which ZnO can prevent diarrhoea
- The ideal feed additive for enhancing gut health is probably a combination or cocktail of agents with antibacterial and immunomodulatory effects targeting the specific challenges as ETEC infection progresses
- **Starting nutritional interventions already during the suckling period may be necessary in order to efficiently influence the interaction between the microbiota and the host!**

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-AU-Foulum
-Department of Animal Science

