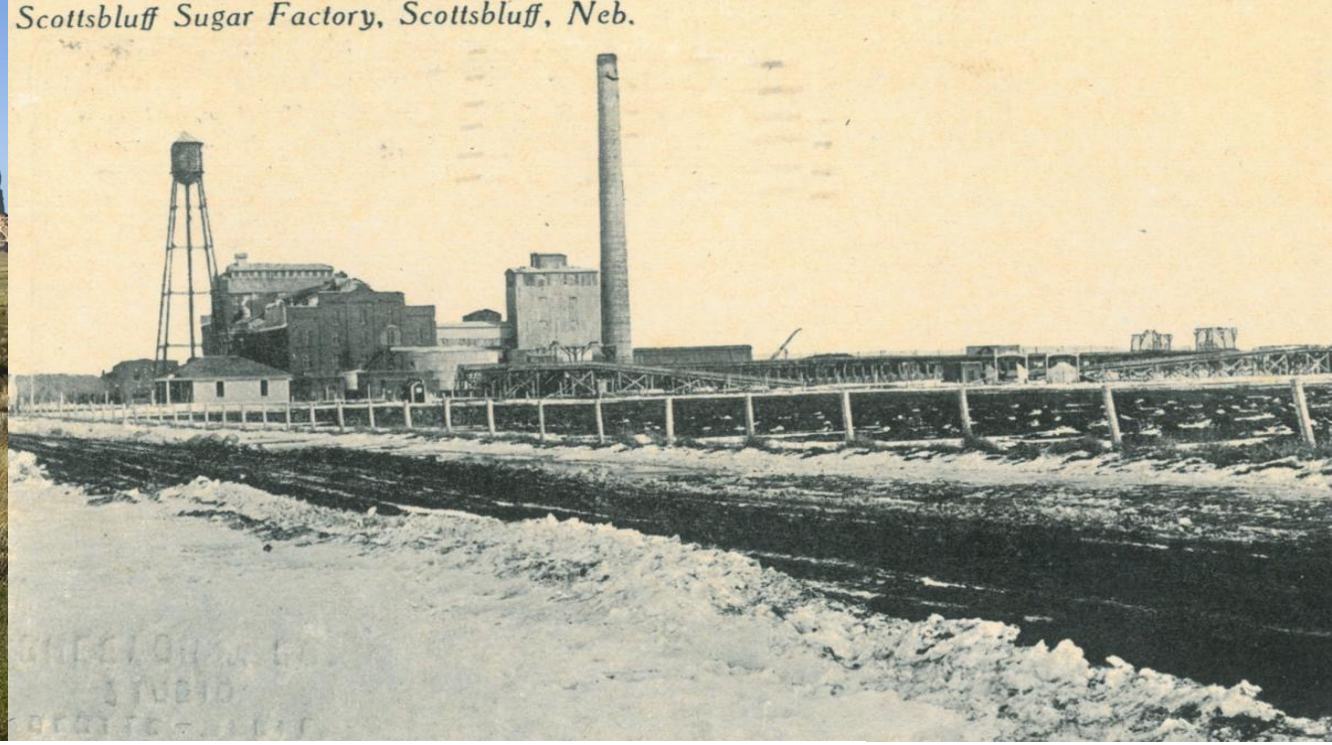
FEEDING QUALITY FORUM

Exploring New Control Methods for Liver Abscesses

Jeff Heldt, PhD PAS

Beef Technical Lead, Micronutrients USA LLC



In 1906, the Great Western Sugar Co. purchased land in Scottsbluff for a new plant that was constructed with equipment moved from the just-closed Ames plant and additional new machinery. Gus Heldt moved to the Scottsbluff facility and became the agricultural superintendent. During one of its first years in production, the Scottsbluff factory was working with the capacity of over 1,000 tons of beets per day.

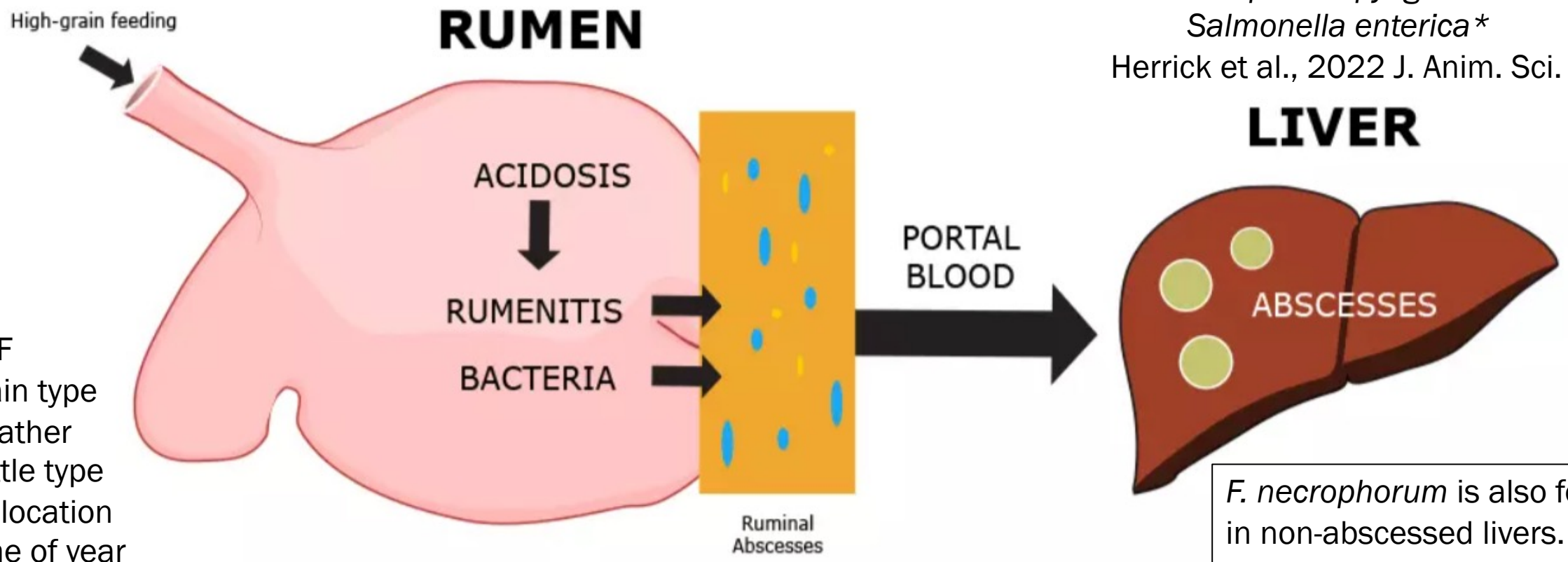
Micronutrients

a Nutreco company

Topics

- Liver Abscess
  - What is it?
  - What is the damage?
- Current Situation
- New Findings
- New Interventions
- Diagnostics
- Take-Home Message

Fusobacterium necrophorum
Fusobacterium fundiliforme
Trueperella pyogenes
*Salmonella enterica**
Herrick et al., 2022 J. Anim. Sci.



Pathogenesis of liver abscesses in cattle fed a high grain diet.

Adapted from Nagaraja, T.G. and M. M. Chengappa, 1998

DOF
Grain type
Weather
Cattle type
US location
Time of year
Roughage Level
Bunk management
Inadequate control measures
Others……

F. necrophorum is also found in non-abscessed livers.
Stotz et al., 2021. J. Anim. Sci.

"We have discovered that multiple bacterial species found in the abscesses of livers are also prevalent in the soil organic matter of animal pens. The prevalence of these bacterial species in the pens not only differs among different regions of the US, but also differs among pens of Holstein cattle and beef breeds."

Smith et al., 2020. J. Anim. Sci. abstract

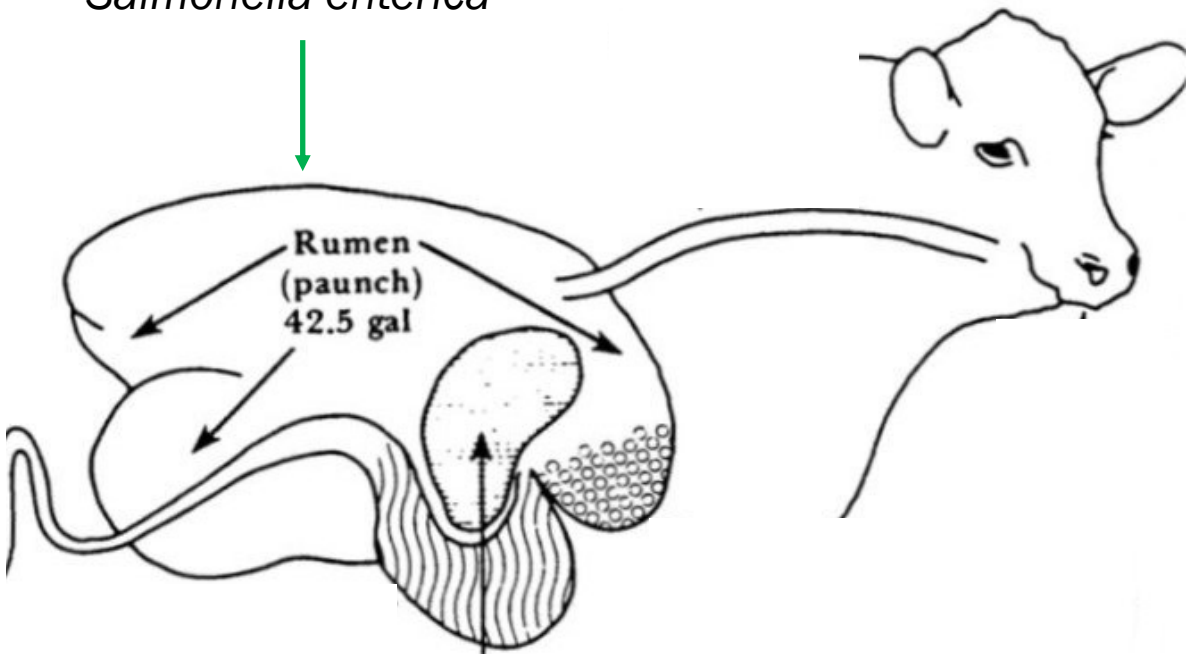
Liver Abscesses

- Concern of the Beef industry for 75+ yrs
  - 1944 research report on ulcerative rumen lesions
- Major reason for liver condemnation
- Costs Packing phase $60M+ annually
- Costs Production phase ??? Annually
  - ↓ DMI, FE, ADG, LW, HCW, DP,
  - ↑ Carcass trim
- Liver Abscesses = 46% of condemnations in 1991 NBQA but increased to 66% (Herrick, 2018)

- Research efforts continue: Universities & Corporate

Current Dogma

Fusobacterium necrophorum
Fusobacterium fundiliforme
Trueperella pyogenes
*Salmonella enterica**



Current Approved Control and Prevention Methods

- Feed-grade antibiotics
  - Chlortetracycline
  - Oxytetracycline
  - Tylosin*
  - Virginiamycin
- Vaccines
  - Inconsistent

Figure 7. Frequency distributions for specific liver condemnations from all carcasses sampled in NBQA Market Cow and Bull 2007 and 2016

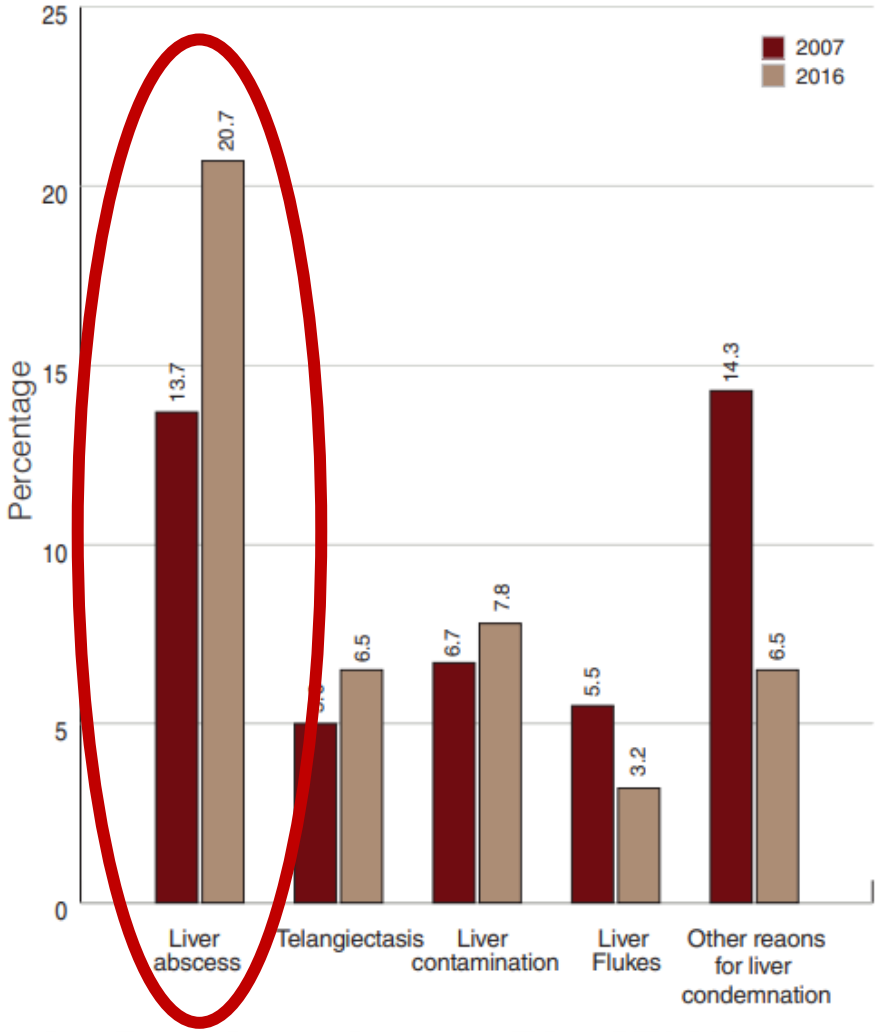
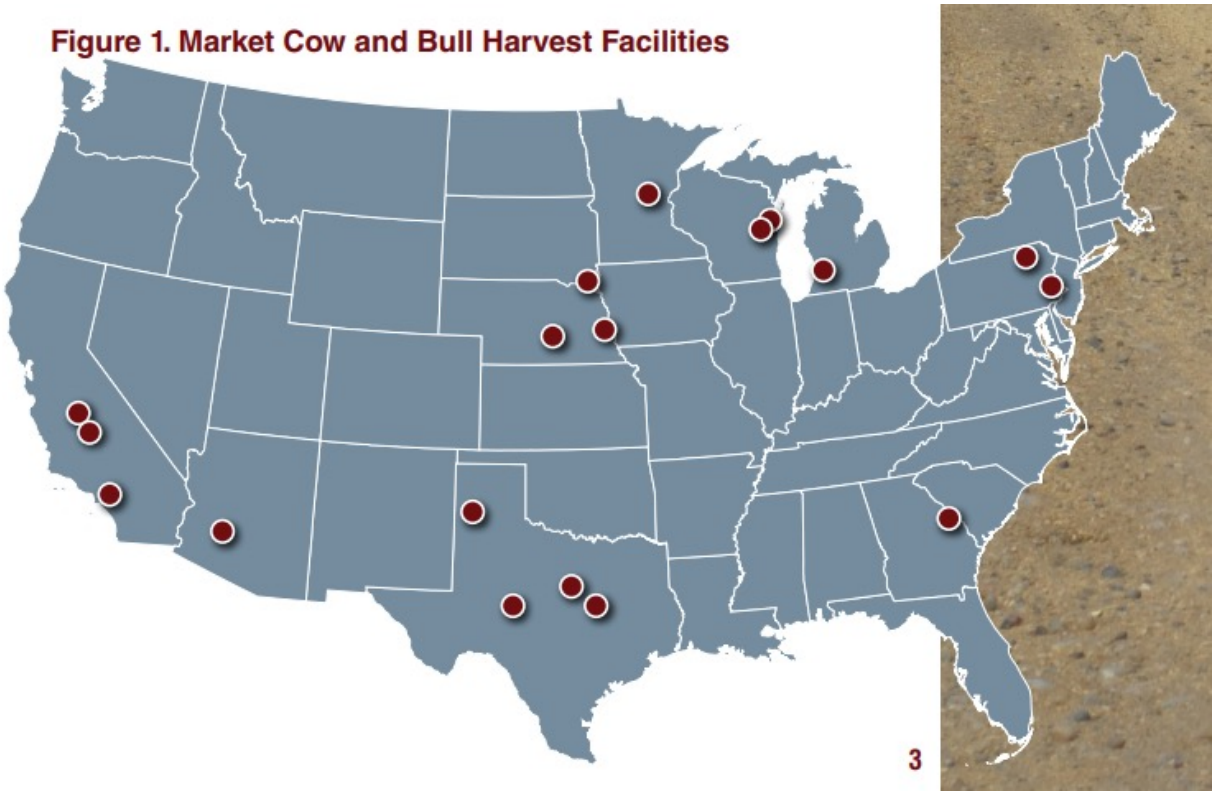


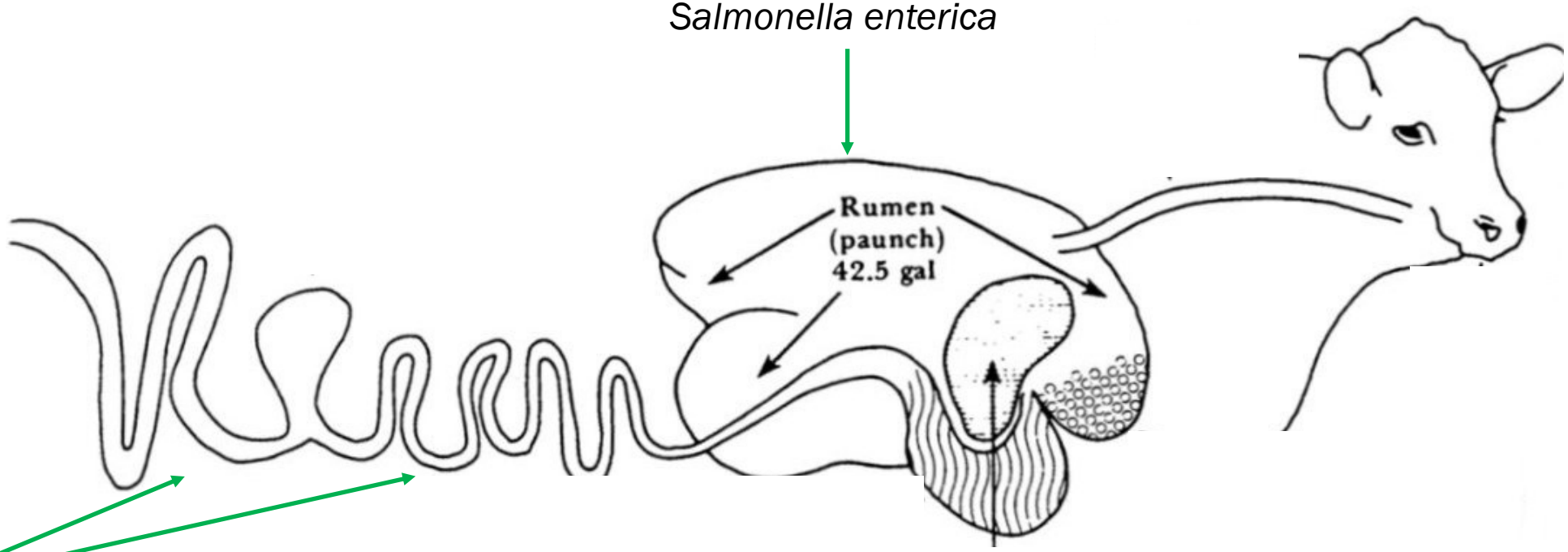
Figure 1. Market Cow and Bull Harvest Facilities



2016 National Beef Quality Audit

New Findings

Fusobacterium necrophorum
Fusobacterium fundiliforme
Trueperella pyogenes
Salmonella enterica



Fusobacterium necrophorum
Meredith et al., 2017. J. Anim. Sci. abstract

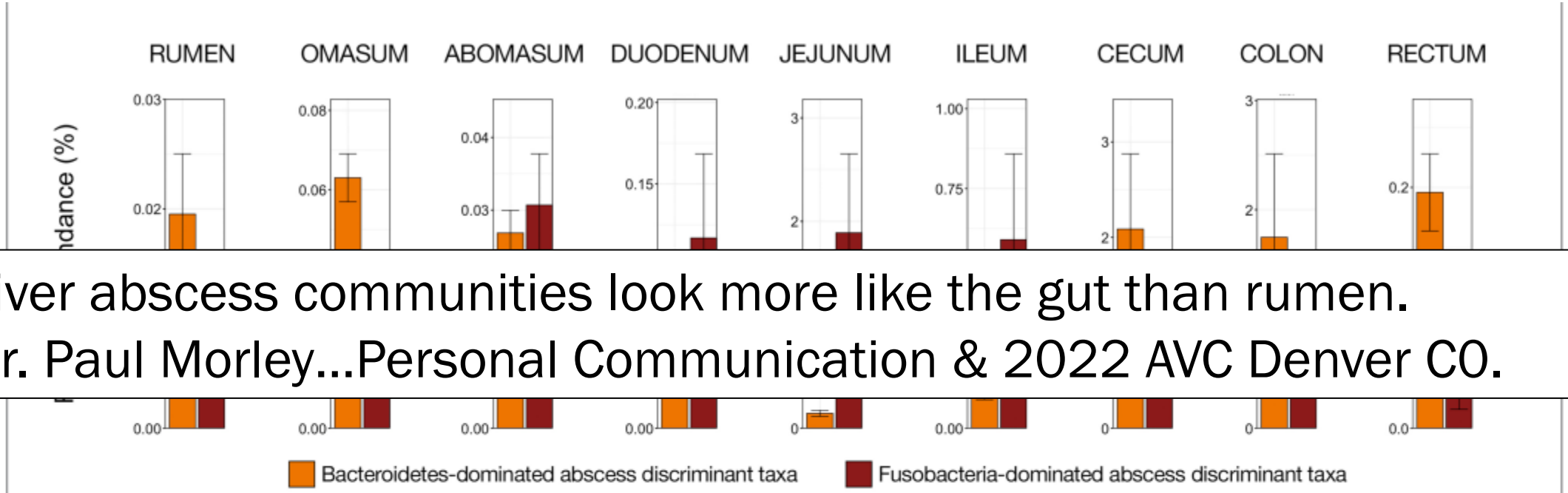
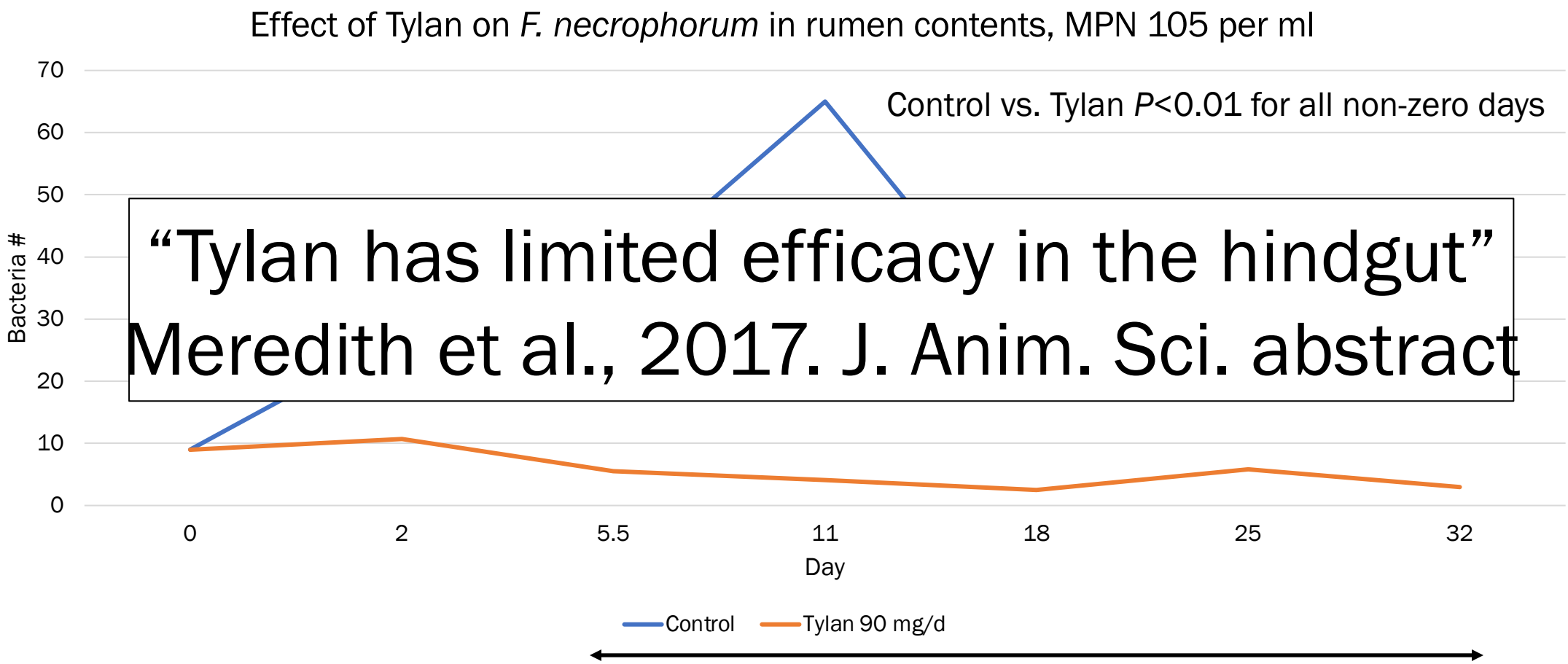


FIGURE 6 | Bar plots demonstrating the relative abundances of all genera discriminant of LA microbial communities classified as high Bacteroidetes (left; shades of orange) and high Fusobacteria (right; shades of red) with nine locations of the bovine gastrointestinal tract (GIT). All genera detected are listed in the legends. Error bars represent the SEM. Significant differences between GIT locations are noted by an asterisk for the aggregate relative abundance of discriminant genera of high Bacteroidetes communities (Pairwise Wilcoxon rank-sum with Benjamini–Hochberg correction, $p < 0.05$, $n = 34–56$) and high Fusobacteria communities (Pairwise Wilcoxon rank-sum with Benjamini–Hochberg correction, $p < 0.05$, $n = 34–56$). Bar plot demonstrating the aggregate abundance of genera discriminant of high Bacteroidetes or high Fusobacteria LA communities at each of the nine GIT locations investigated sorted from left (proximal GIT) to right (distal GIT). Error bars represent the SEM.

Liver abscess communities look more like the gut than rumen.
Dr. Paul Morley…Personal Communication & 2022 AVC Denver C0.

Pinnell, et al., 2022. Front. Microbiol.

Tylan effectiveness in the rumen



"Tylan has limited efficacy in the hindgut"
Meredith et al., 2017. J. Anim. Sci. abstract

Nagaraja et al., 1999. Am. J. Vet. Res.

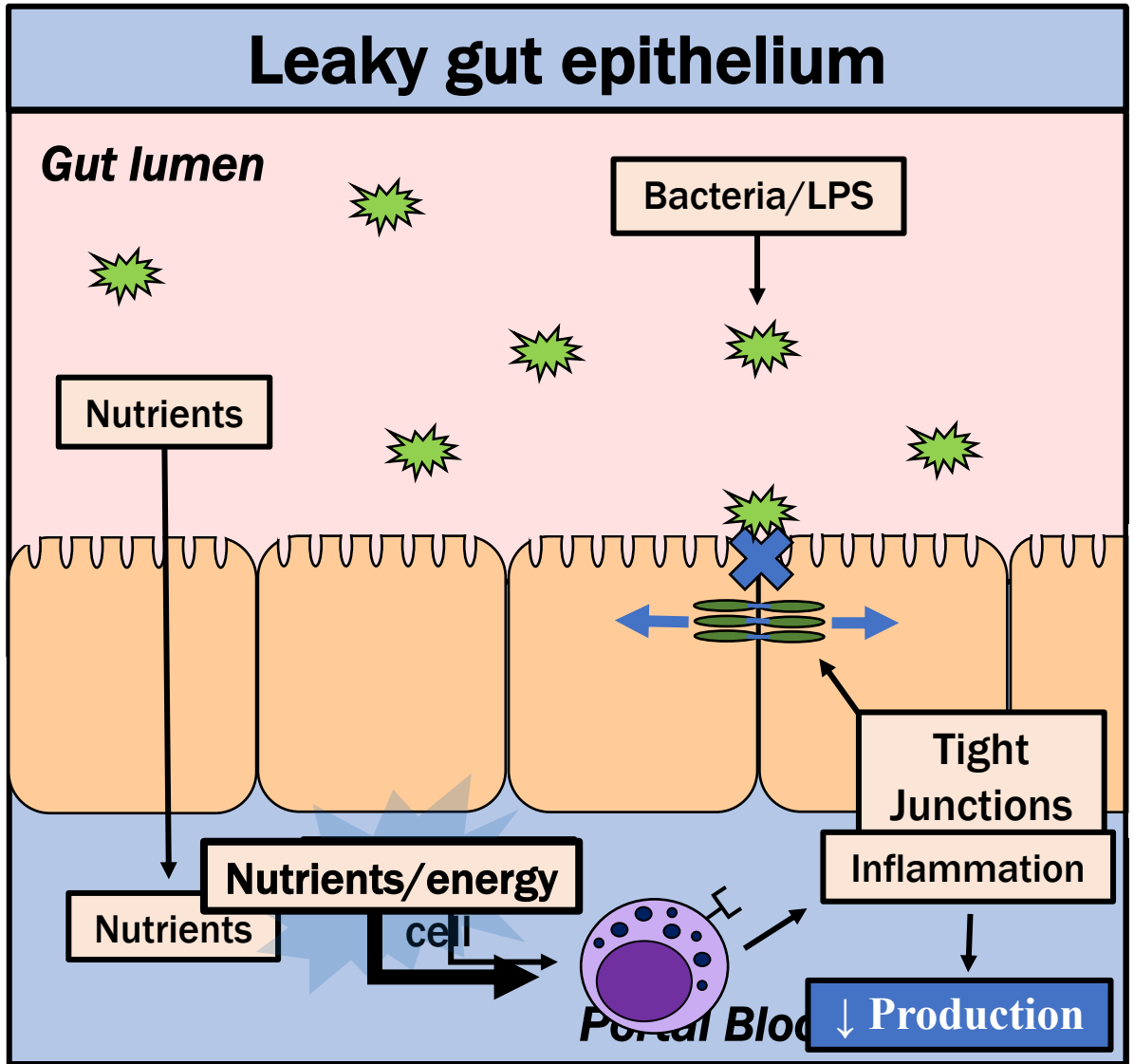
Leaky Gut

- Inflammation is nutrient and energetically expensive
  - Likely contributes to periparturient metabolic disease (Horst et al., 2021)
- Many potential sources of inflammation:
  - Lung
  - Uterus
  - Mammary gland
  - Gastrointestinal tract

- Psychological stress
- Heat stress
- Feed restriction
- Rumen acidosis

STRESS

Rumen? Hindgut? Both? Neither?



Causal vs. Correlated….

Does *Fusobacterium* cause liver abscess or does some other condition allow *Fusobacterium* to be opportunistic???

Because of this new information….do we need new interventions or combinations of interventions???

Potential Control and Prevention Methods

- Probiotics/Prebiotics
  - Probiotics: beneficial living microorganisms
  - Prebiotics: substrates that are selectively used by host organisms
    - Serve as substrates for healthy/beneficial microorganisms
- Yeast/Yeast products (live yeast are technically a Probiotic)
- Immunoglobulins
  - Antibodies to stimulate the immune system
- Bacteriophages
  - A virus that infects and replicates within bacteria and archaea

Potential Control and Prevention Methods

- Trace Minerals/Zinc
- Phytogenics (Plant-based bioactive compounds)
  - Ex.: essential oils
- Proprietary products
  - Multiple ingredients with varying MOA

Current State of Interventions

- Probiotics/Prebiotics
  - Adair et al., 2021. J. Anim. Sci. abstract (60 hd)
    - Control (nothing) vs. DFM
    - No difference in LA rate (*P*-value not reported)
      - 13.7% vs. 10.3%

Current State of Interventions

- Yeast/Yeast Products
  - Scott et al., 2017. Prof. Anim. Sci. (1,495 hd)
    - Control (Mon/Tylan/Bovamine) vs. *Saccharomyces cervisiae* fermentation product prototype
    - No difference in LA rate ($P \geq 0.23$)
      - 20.9% vs. 16.3%
  - Huebner et al., 2019. Sci. Rep. (4,689 hd)
    - Control (nothing) vs. *Saccharomyces cervisiae* fermentation product
    - No difference in LA rate ($P = 0.79$)
      - 38.9% vs. 38.1%

Current State of Interventions

- Immunoglobulins
  - IGY: humoral immunity of egg-laying species
    - Harvested from egg yolks from hyper-immunized hens using a predetermined antigen
      - Customized to *F. necrophorum*
  - Stotz et al., 2021. Trans. Anim. Sci. (64 hd Holsteins)
    - Tylan vs. IGY
    - No difference in LA rate and severity (*P*=0.213)
      - 65.4% vs. 48.2%

Current State of Interventions

- Bacteriophages
- Bacteriophages were first discovered in 1915 by William Twort, and in 1917 by Felix d'Herelle realized that they had the potential to kill bacteria
- They are ubiquitous in the environment and are recognized as the most abundant biological agent on earth
- Can be used to kill bad bacteria in a way that is similar to the way we use antibiotics.
  - Advantages compared to antibiotics….antibiotics usually kill different types (species) of bacteria, while bacteriophages generally attack only one kind of bacteria.
    - Do not affect beneficial bacteria, and most of the time we do not want to exterminate all the bacteria, only the “bad guys”.

Gutiérrez, et al., 2016 Frontiers; Clokie et al., 2011. Bacteriophage

Current State of Interventions

- Bacteriophages cont.
- Potential uses
  - Bacteriophages can be used to clean hospitals or industrial surfaces, since they can destroy undesirable bacteria like disinfectants do.
  - It is also possible include bacteriophages in foods, which will work similar to chemical preservatives. Bacteriophages will wait in the food until some bad bacteria contaminate it and, like playing hide-and-seek, when the bacteriophages find their bacterial targets, they will catch them.

Gutiérrez, et al., 2016 Frontiers; Clokie et al., 2011. Bacteriophage

Current State of Interventions

- Trace Minerals
  - Wagner et al., 2008. Prof. Anim. Sci. (189 hd)
    - Cu, Zn, and Mn Sulfate vs. 50% level from OTM
    - No difference in LA rate (*P*=0.77)
      - 11.6% vs. 12.9%
  - Sexson et al., 2010. Prof. Anim. Sci. (288 hd)
    - Cu, Zn, and Mn Source (Sulfate & Combo)
    - No difference in LA rate (*P*≥0. 38)
      - 5.5-11.4% incidence rate
  - Berrett et al., 2015. Prof. Anim. Sci. (4,689 hd)
    - No TM, Cu, Zn, and Mn source (Sulfate & Combo), and TM level evaluated
    - No difference in LA rate (*P*=0.23)
      - 10.0%-16.7% incidence rate

Current State of Interventions

- Trace Minerals
  - Caldera et al., 2016. Prof. Anim. Sci. (400 hd)
    - Cu, Zn, and Mn Source (Sulfate & Hydroxy) and TM level
    - No difference in LA rate
      - 0-7% incidence rate
  - Heldt and Davis., 2019. Appl. Anim. Sci. (1,707 hd)
    - Cu, Zn, and Mn Source (Combo & Hydroxy)
    - No difference in LA rate or severity ($P \geq 0.38$)
      - 32.0% vs. 33.6% incidence rate
  - Heldt et al., 2020. J. Anim. Sci. abstract (2,758 hd)
    - Cu, Zn, and Mn Source (Combo & Hydroxy)
    - No difference in LA rate or severity ($P \geq 0.22$)
      - 19.7% vs. 19.4% incidence rate

Current State of Interventions

- Zinc
  - Wagner et al., 2008. Prof. Anim. Sci. (199 hd)
    - Zn Source (Sulfate and Combo)
    - No difference in LA rate (*P*=0.96)
      - 15.8% vs. 16.2%
  - Wagner et al., 2016. Prof. Anim. Sci. abstract (288 hd)
    - Zn Source (Sulfate, Combo, and Hydroxy) and level
    - No difference in LA rate (*P*=0.88)
      - 34.3%-44.4% incidence rate
  - Wagner et al., 2019. J. Anim. Sci. abstract (432 hd)
    - Zn Source (Sulfate, Combo, and Hydroxy)
    - No difference in LA rate (*P*=0.79)

Current State of Interventions

- Zinc
  - Ashworth et al., 2019. Am. Assoc. Bov. Pract.
    - Exp. 1 (42 hd)
      - Acidosis challenged steers (50% of previous 7 d DMI for two days)
      - 90 ppm supplemental Zinc Amino Acid complex tended (*P*=0.12) to reduce LA rate in steers that did not receive any supplemental zinc (6% vs. 24%)
    - Exp. 2 (>10,000 hd)
      - Retrospective analysis of feedlot studies
      - Supplemental Zinc Amino Acid complex reduced (*P*<0.03) LA rate compared to not feeding Zinc Amino Acid complex (8.5% vs. 10.5%)
      - Supplemental Zinc Amino Acid complex reduced (*P*<0.01) A+ LA rate compared to not feeding Zinc Amino Acid complex (2.4% vs. 3.4%)

Current State of Interventions

- Phytogenics – Promote Health (Make the Host Healthier)

phytochemical

The term 'phyto' originated from a Greek word meaning plant. Phytonutrients are certain organic components of plants, and these components are thought to promote human health. Fruits, vegetables, grains, legumes, nuts and teas are rich sources of phytonutrients. Unlike the traditional nutrients (protein, fat, vitamins, minerals), phytonutrients are not 'essential' for life, so some people prefer the term 'phytochemical'. (USDA Agricultural Research Service)

www.cancer.gov

Interesting compounds, yet the Animal Nutrition Industry is obsessed with the *antimicrobial* aspects of phytochemicals.

Current lens in animal nutrition

The Targets

E. coli O157

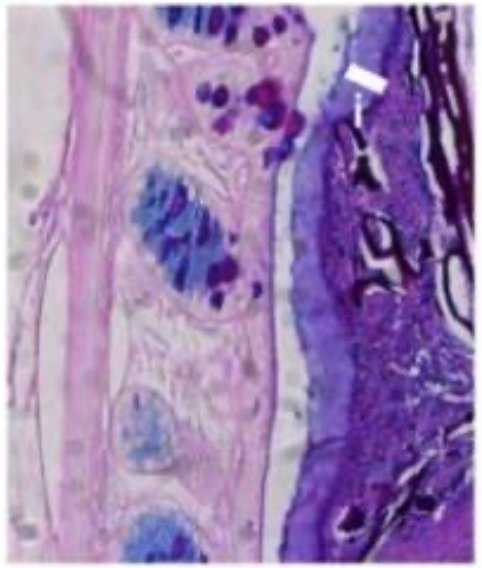
Phytotechnology

- Use plants with antimicrobial properties
- Always the same actives
- Replace antibiotics in feed
- Kill target pathogens
- Prevent & treat disease
- Silver bullet solutions
- One size fits all

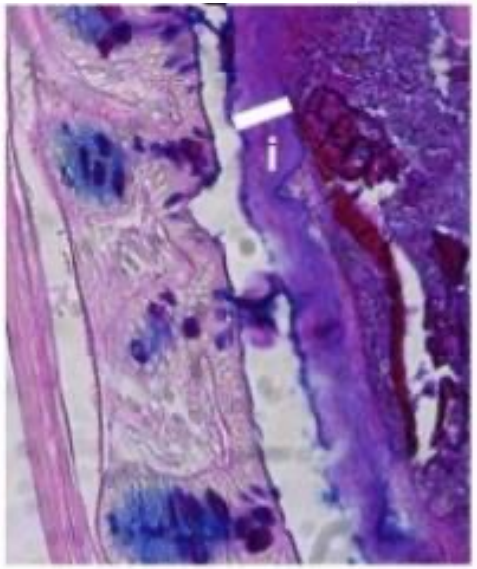
Clarified lens for animal nutrition

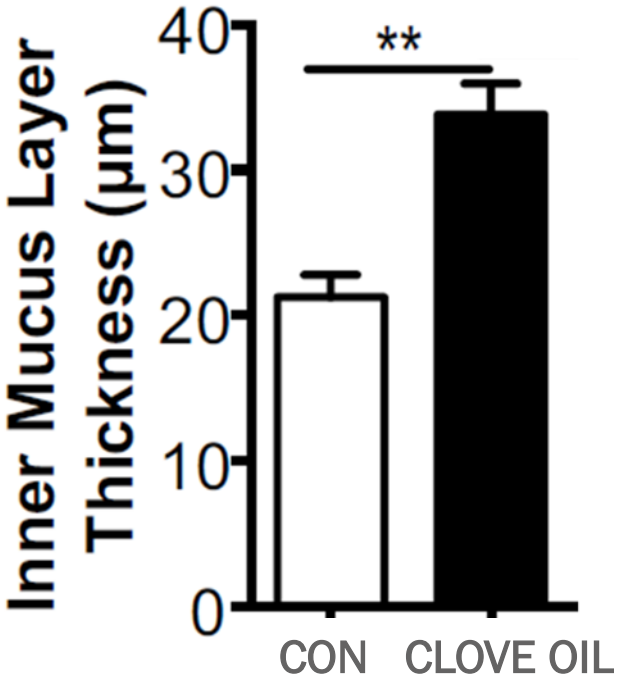
Help the Host

CONTROL



CLOVE OIL





Clove oil improves intestinal structure

...but does not kill the bacteria.

Wlodarska et al., 2015 Sci. Rep.

Current State of Interventions

- Phytogenics – Antimicrobial Activity
  - Meyer et al., 2009. J. Anim. Sci. (468 hd)
    - Control (Tylan) vs. EO
    - Tylan was better than EO in LA rate or severity ($P \leq 0.04$)
  - Samii et al., 2016. J. Anim. Sci.
    - Limonene is an organic compound in lemons, oranges, and grapefruit that has known activity against gram – bacteria
    - Limonene supplementation deceased ruminal concentration of *F. necrophorum* ($P=0.03$)
      - May decrease LA
  - Araujo et al., 2018. Prof. Anim. Sci. (656 hd)
    - Control (Mon/Tylan) vs. EO
    - No difference in LA rate or severity ($P \geq 0.23$)
  - Roubicek et al., 2021. J. Anim. Sci. abstract
    - Phytophenols from green tea, grape seed, and rosemary inhibited *T. pyogenes*
  - Salih et al., 2021. J. Anim. Sci. abstract
    - Phytophenols from black and sumac sorghum inhibited *F. necrophorum, F. fundiliforme, T. pyogenes, and S. enterica*

Diagnostics

- Animal Measurements
  - Macdonald et al., 2017. Vet. Tec.
    - Albumin and cholesterol are established indicators of hepatic function and are consistently related to the presence of LA
  - Bair et al., 2020. Appl. Anim. Sci. (363 hd)
    - Infrared thermography (*P*=0.55), hair cortisol (*P*=0.96), and serum cortisol (*P*=0.21) showed no effect on LA scores
      - Measurements taken 2 days pre-harvest
  - Herrick et al., 2020. Appl. Anim. Sci. (153 hd)
    - Whole blood and serum can be used to detect differences in cattle with and without LA
      - Platelets, hemoglobin, hematocrit, globulin, albumin
      - Blood taken at harvest

Take-Home Messages

- The multi-factorial causes of liver abscesses will likely avert **Absolute** prevention or control
- Liver abscesses are poly-microbial with bacterial communities from both rumen and lower GIT

- Potential Opportunities
  - Improved Zinc sources (Host)
  - IGY (Host)
  - Bacteriophages (Antimicrobial)
  - Phytogenics (Host)
- New control measures should target:
  - Bacterial control both ruminally and post-ruminally
  - GIT strength/integrity (Avoid Leaky Gut Concept)

Questions

Jeff Heldt
Jeff.heldt@micro.net