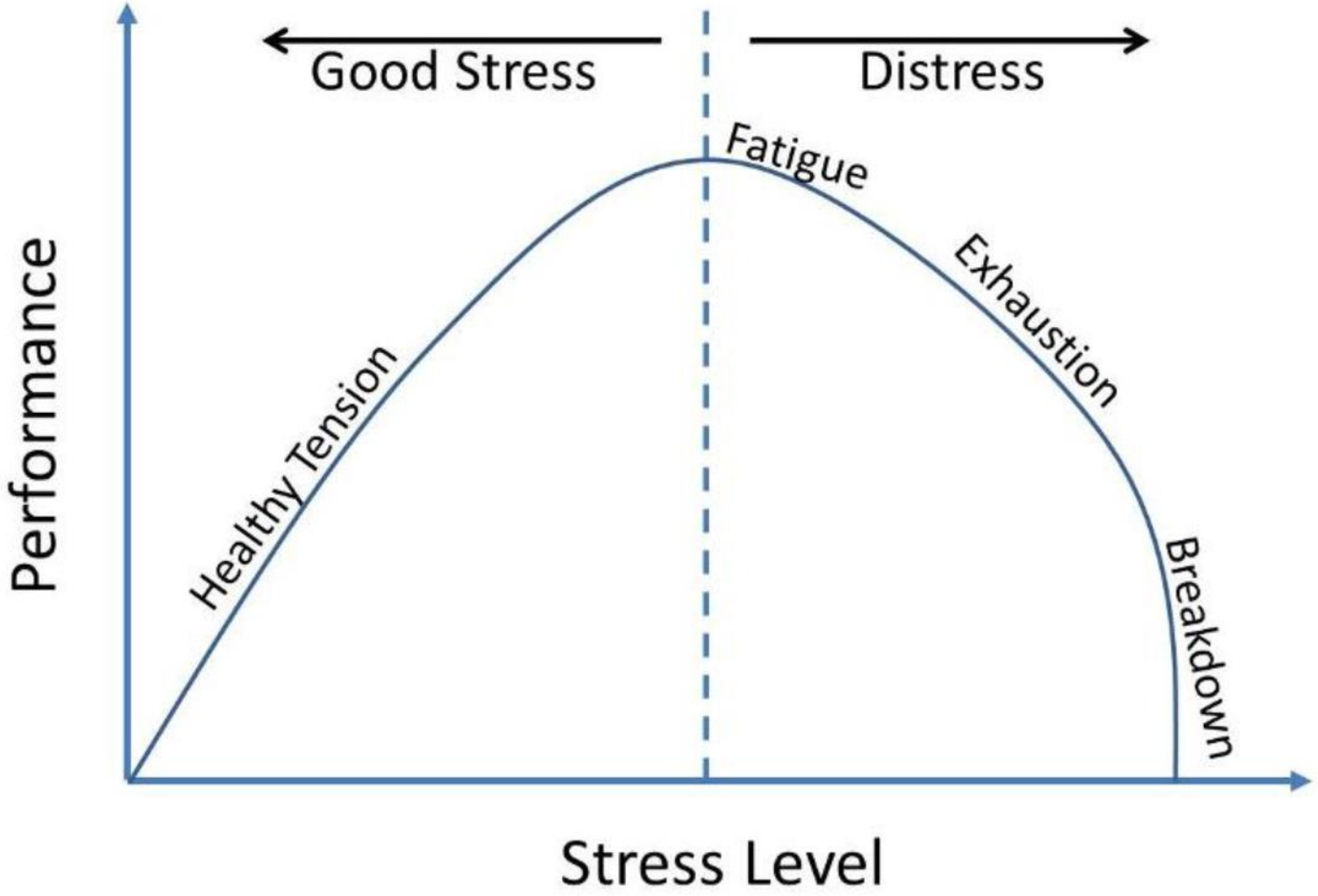
Stress

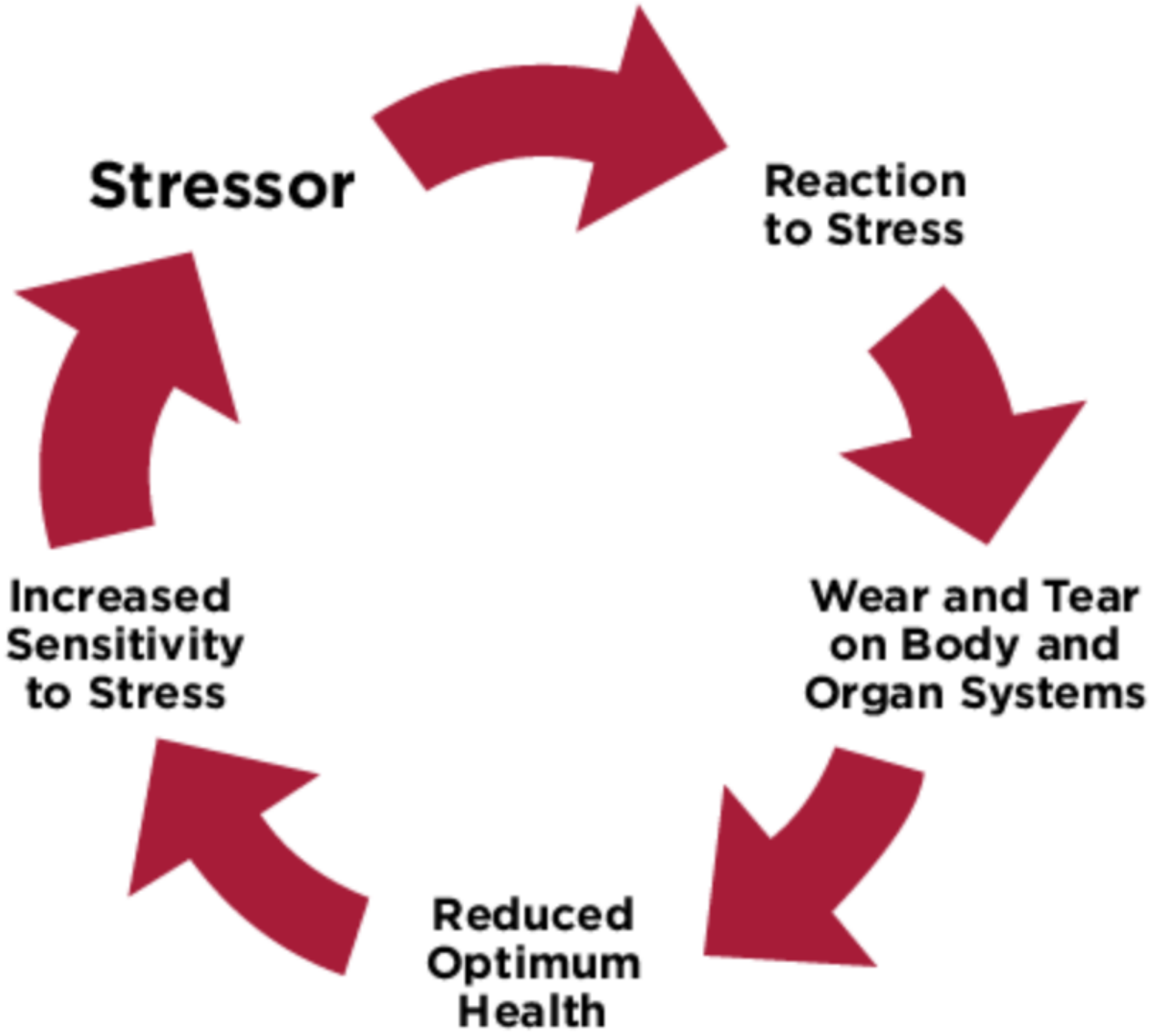
A Primer for Gut Health Management and Impact on Animal Performance

PREVENT – PROTECT – RESILIANCE

Definition of stress

- A state of mental, emotional, environmental or physical strain or tension resulting from adverse or very demanding circumstances
- Can be a singular dramatic stressor or a result of cumulative minor events


Good Stress
Distress
Performance
Fatigue
Healthy Tension
Exhaustion
Breakdown
Stress Level


Stressor
Reaction to Stress
Wear and Tear on Body and Organ Systems
Reduced Optimum Health
Increased Sensitivity to Stress

What are known stressors in animal production systems that result in poor performance and health?

- Heat
- Overcrowding
- Pen movements
- Handling
- Transportation
- Ventilation
- Sanitation/hygiene
- Feed/water availability and consistency
- Transition/parturition

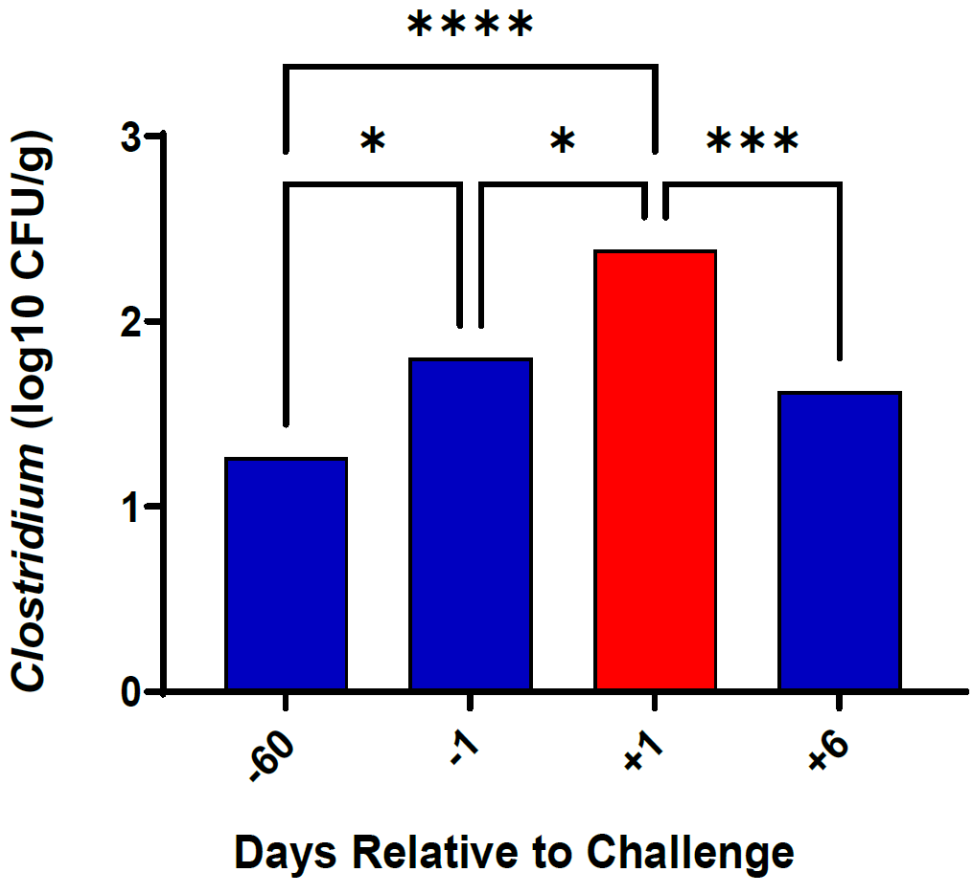
Keep in mind

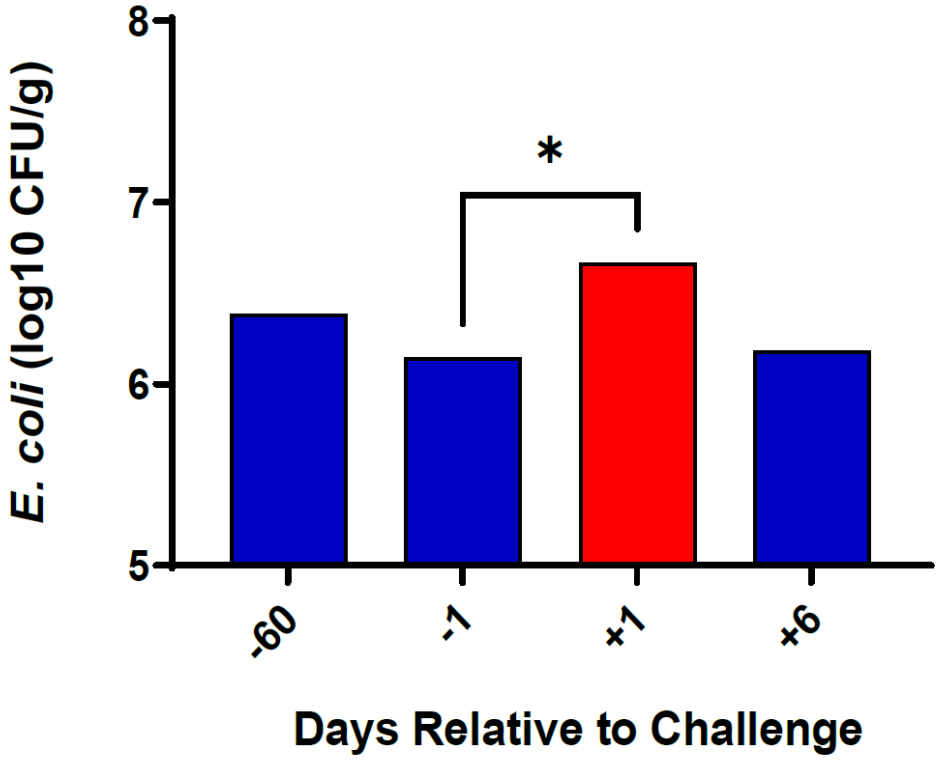
- Stressors are cumulative and can result in:
  - poor performance
  - increased pathogen shedding or infections
  - leaky gut/compromised gut integrity
  - immunosuppression

How to separate out the “stress discussion”?

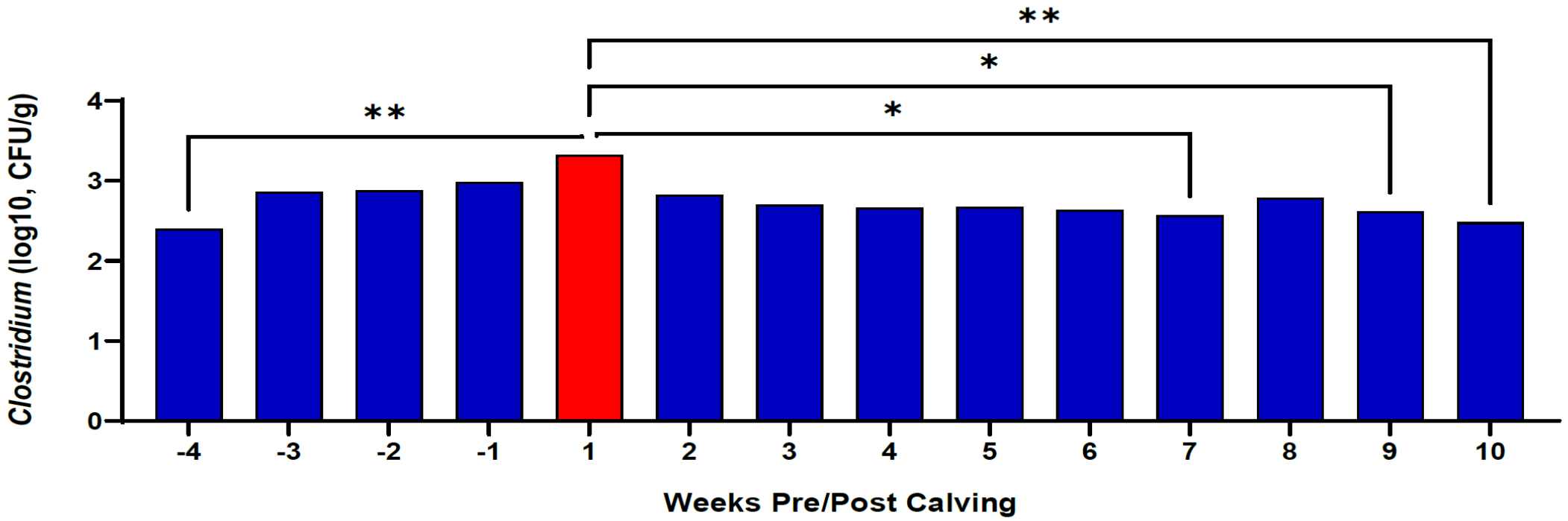
- Management, housing, good husbandry practices:
  - these will mitigate or reduce the effects of stressors, but many stressors cannot be prevented
  - parturition, transportation, environmental, etc., stress will always happen. We can mitigate the effects but not eliminate them.
- Feed supplements can:
  - **prevent** – binding mycotoxins, reducing pathogen load
  - **protect** – strengthening intestinal cells against damage by toxins and pathogens; alerting the immune system to be ready for anything
  - increase **resiliency** – moderating hyper-inflammation to speed recovery

Example of transport stress on *Clostridia* and *E.coli* shedding (in "healthy" animals)

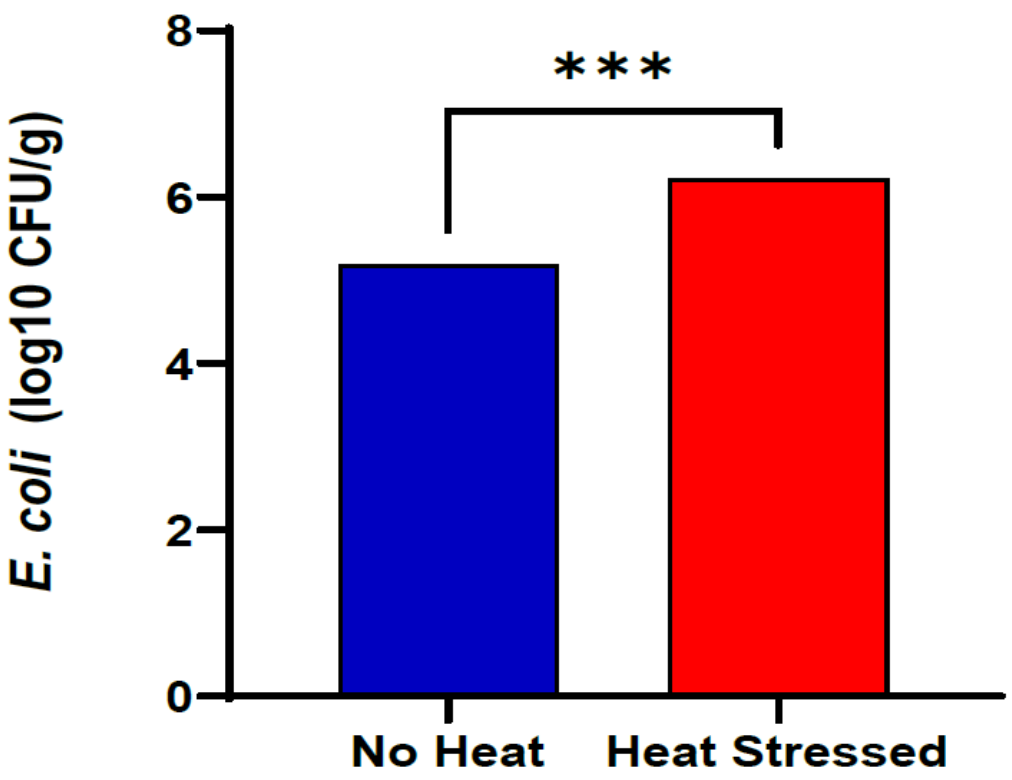


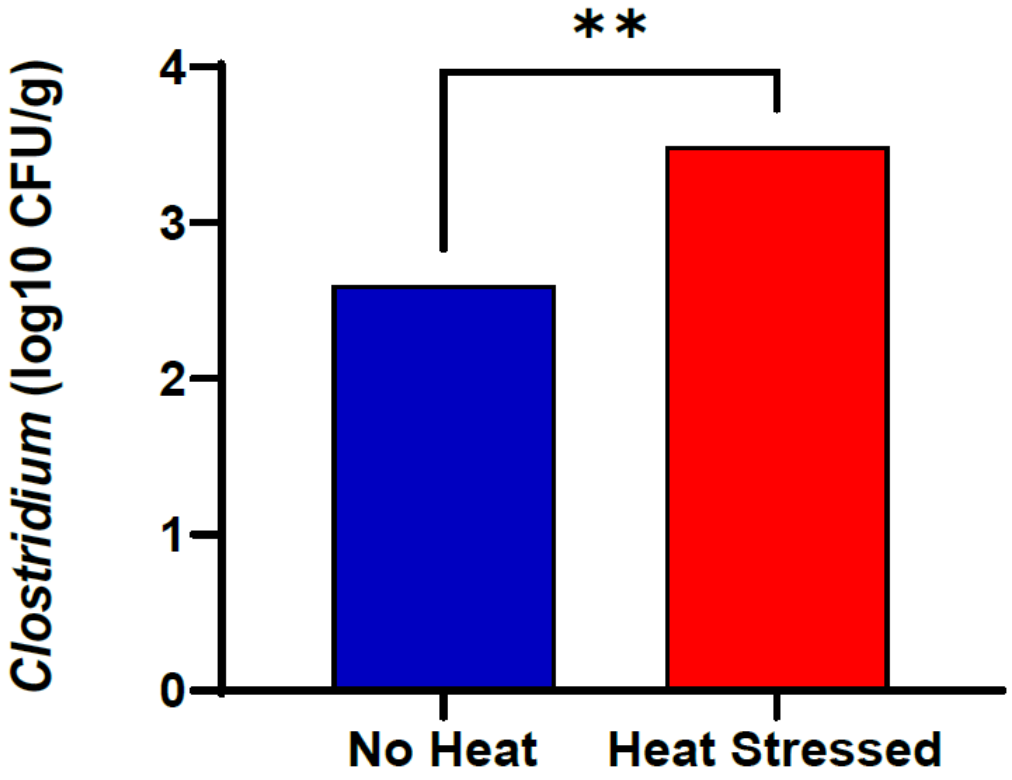


Example of calving stress on *Clostridia* shedding (in “healthy” animals)



Example of heat stress on *Clostridia* and *E.coli* shedding (in "healthy" animals)





Take away

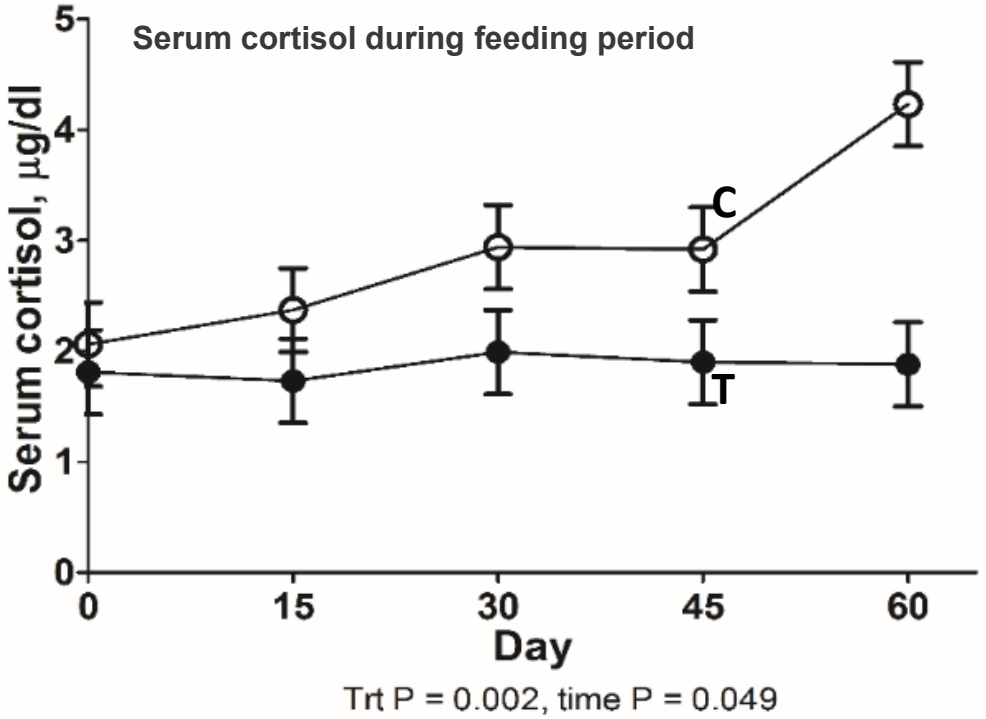
- 3 different stressors
  - shipping
  - calving
  - heat
- All three resulted in reduced intestinal ability to fight pathogens (*Clostridium* and *E.coli*)
- Keep in mind:
  - **over 70% of any animal's immunity/disease resistance is in the gastrointestinal tract**

Immune support in unchallenged ruminant trials (normal day-to-day stress)

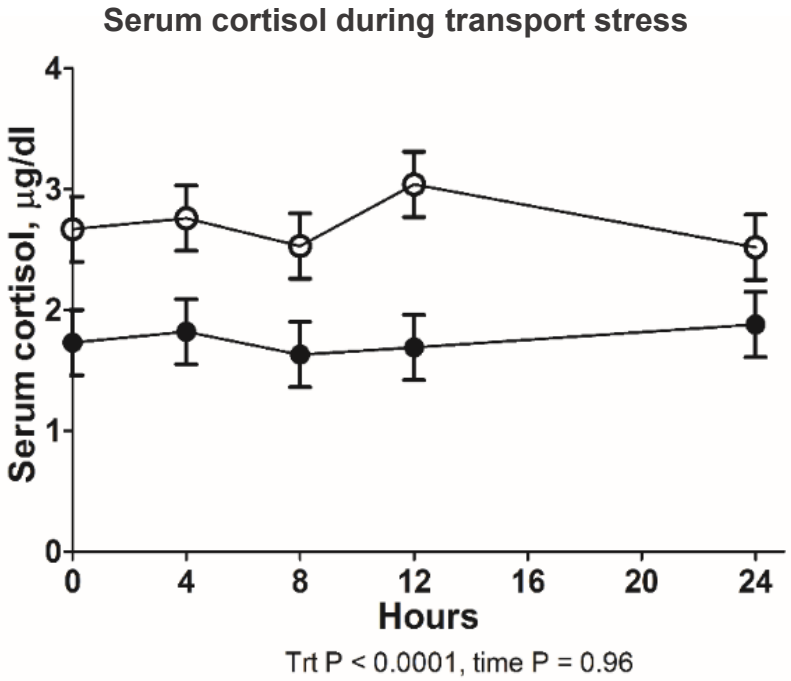
Parameter measured	CEL-MAX effect compared to control	Stage of animal	Publication
Interferon gamma	lower (P<0.05)	receiving beef heifers	Dom. Ani. Endocrinology
Haptoglobin	lower (P<0.05)	receiving beef heifers	Domestic Ani. Endocrinology
IL-8	lower (P<0.05)	receiving beef heifers	Domestic Ani. Endocrinology
Serum cortisol	lower (P<0.05)	receiving beef heifers	Domestic Ani. Endocrinology
Heterophil phagocytosis of E. coli	increase at all time points tested (p=0.1)	transition cows	JDS
IL-6	lower (P<0.05)	transition cows	JDS

Take away: there are interventions (treatments and managerial) that can improve the animal's ability to resist the effects of stress and improve performance

CEL-MAX receiving trial: transport stress (example of RESILIENCY)



Trt P = 0.002, time P = 0.049

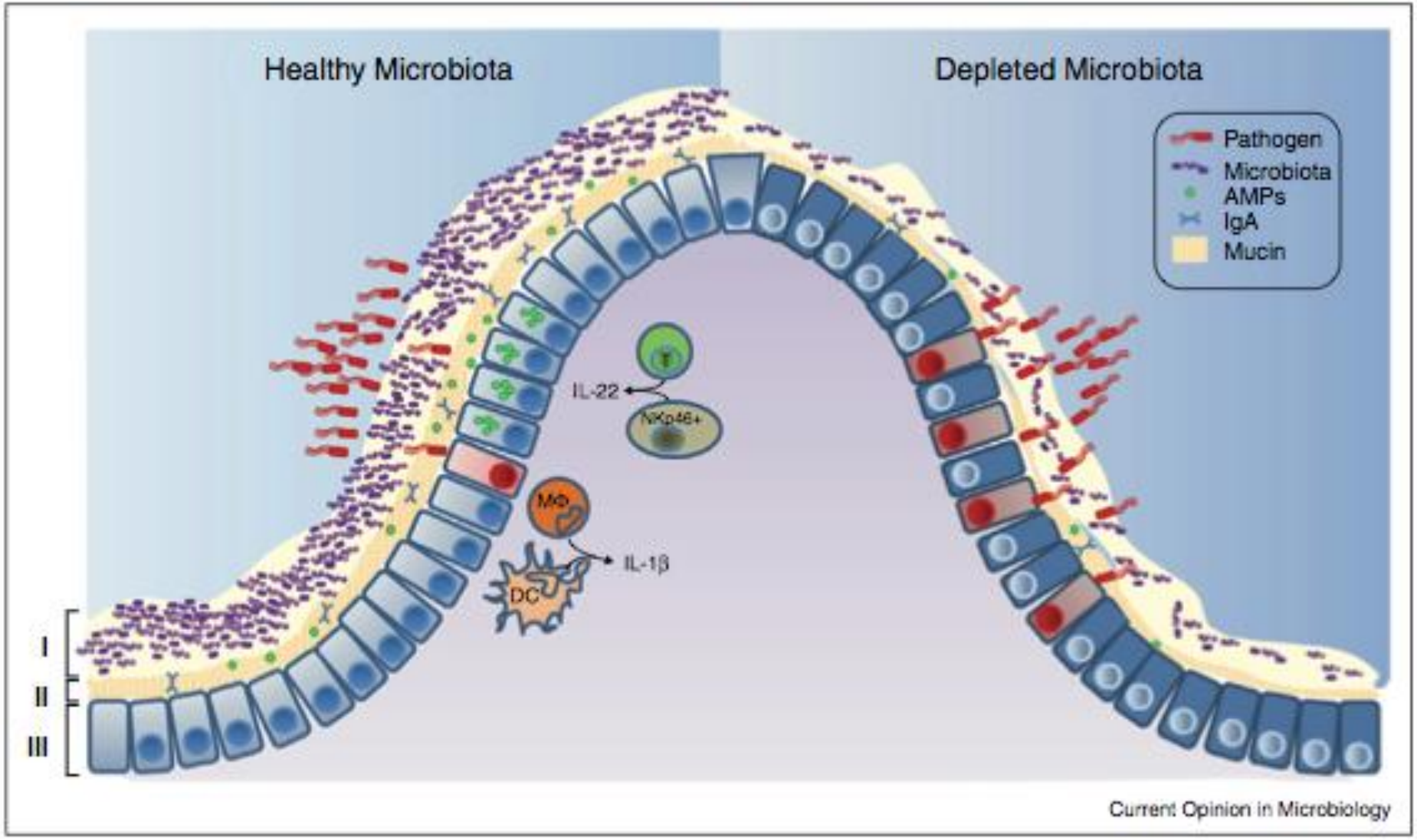


Trt P < 0.0001, time P = 0.96

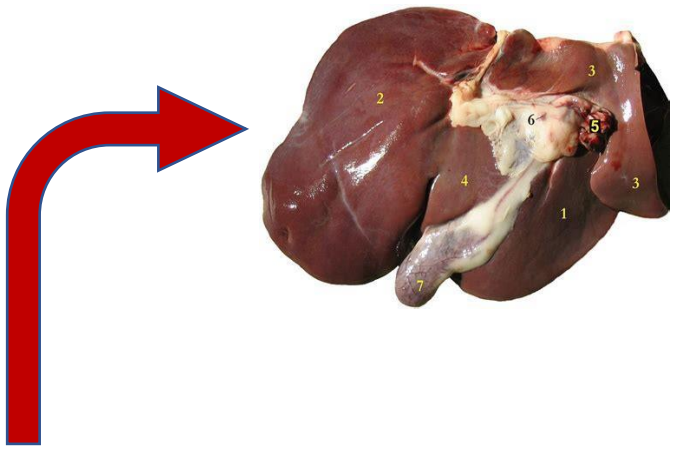
- Healthy animals – CEL-MAX gained 3 kg more
- We did NOT prevent the stress but the animals fed CEL-MAX were RESILIENT. SAME STRESS, DIFFERENT RESULTS.

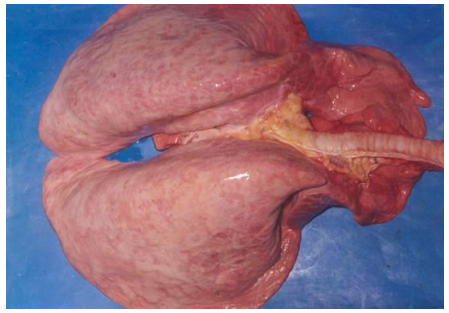
J. Danielo et al. / Domestic Animal Endocrinology 72 (2020) 106427

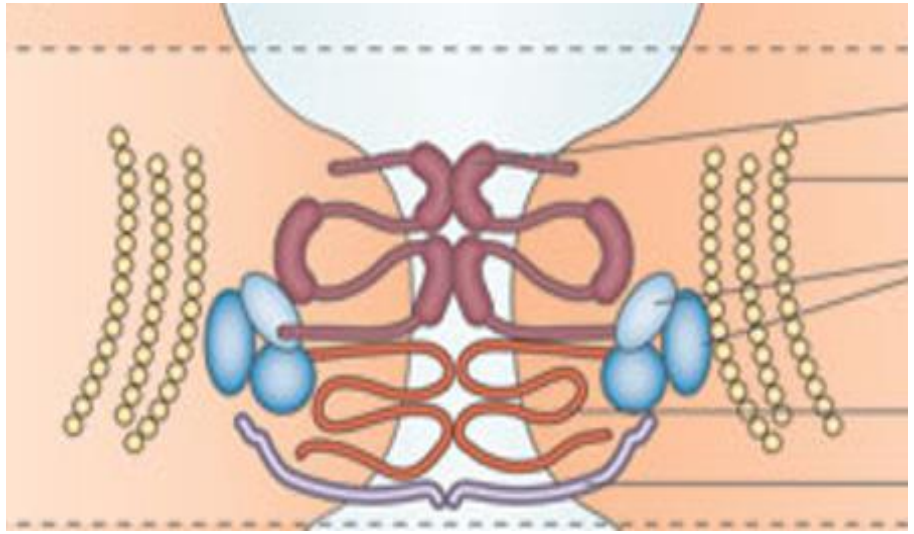
Pathogens, stress, and mycotoxins deplete the first line of defense

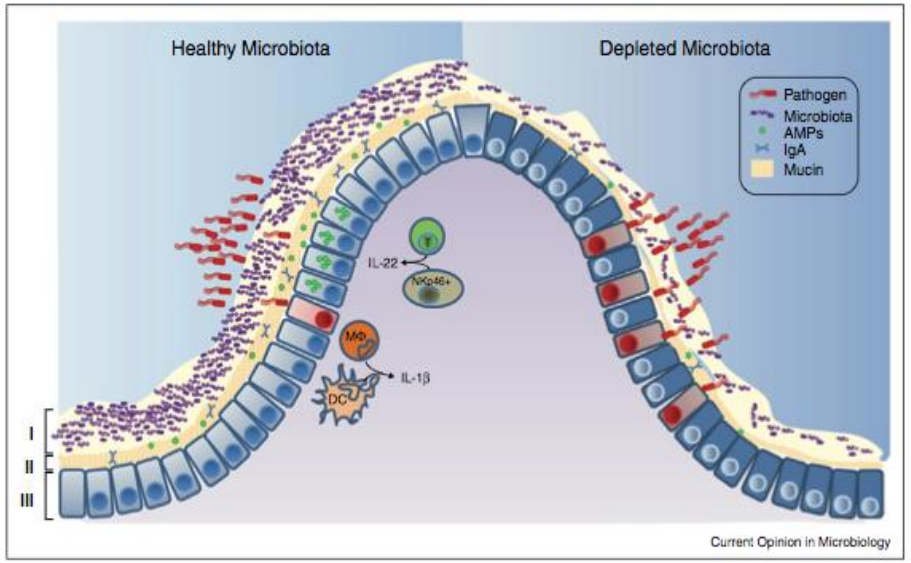


Gut integrity and systemic immune response

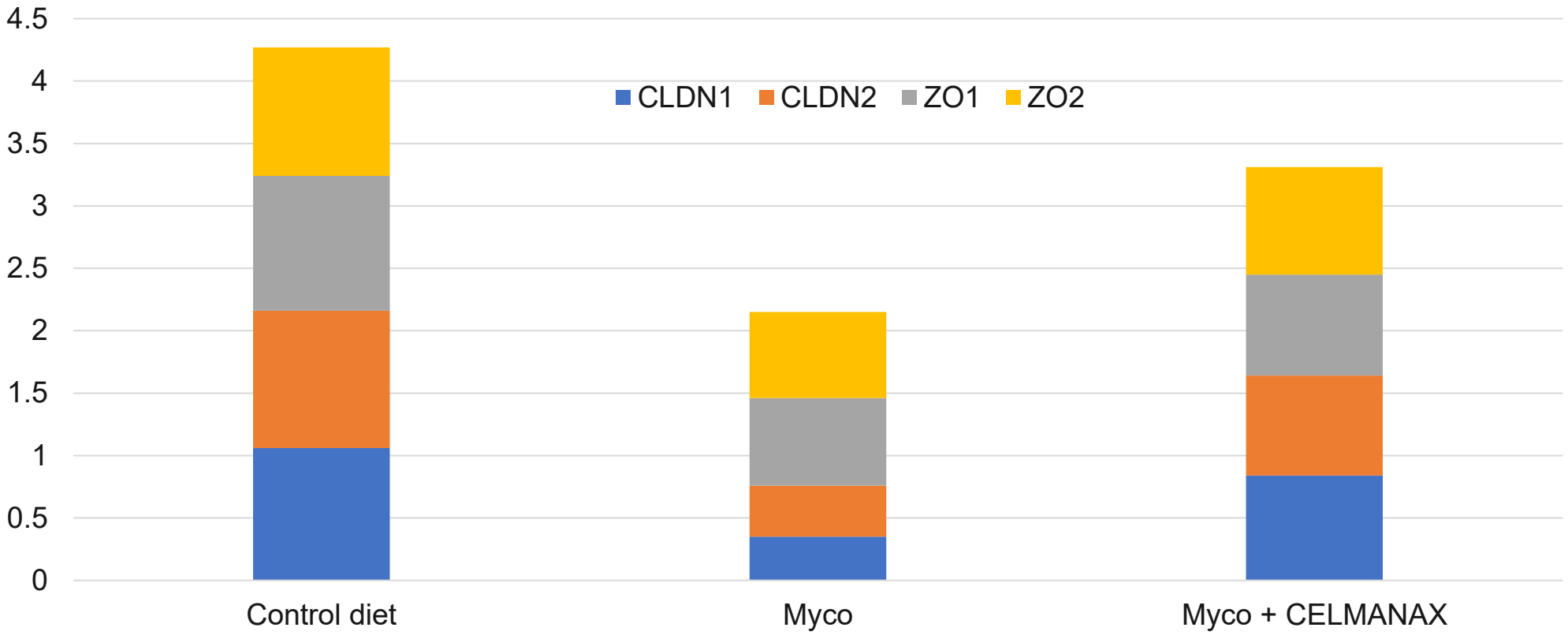








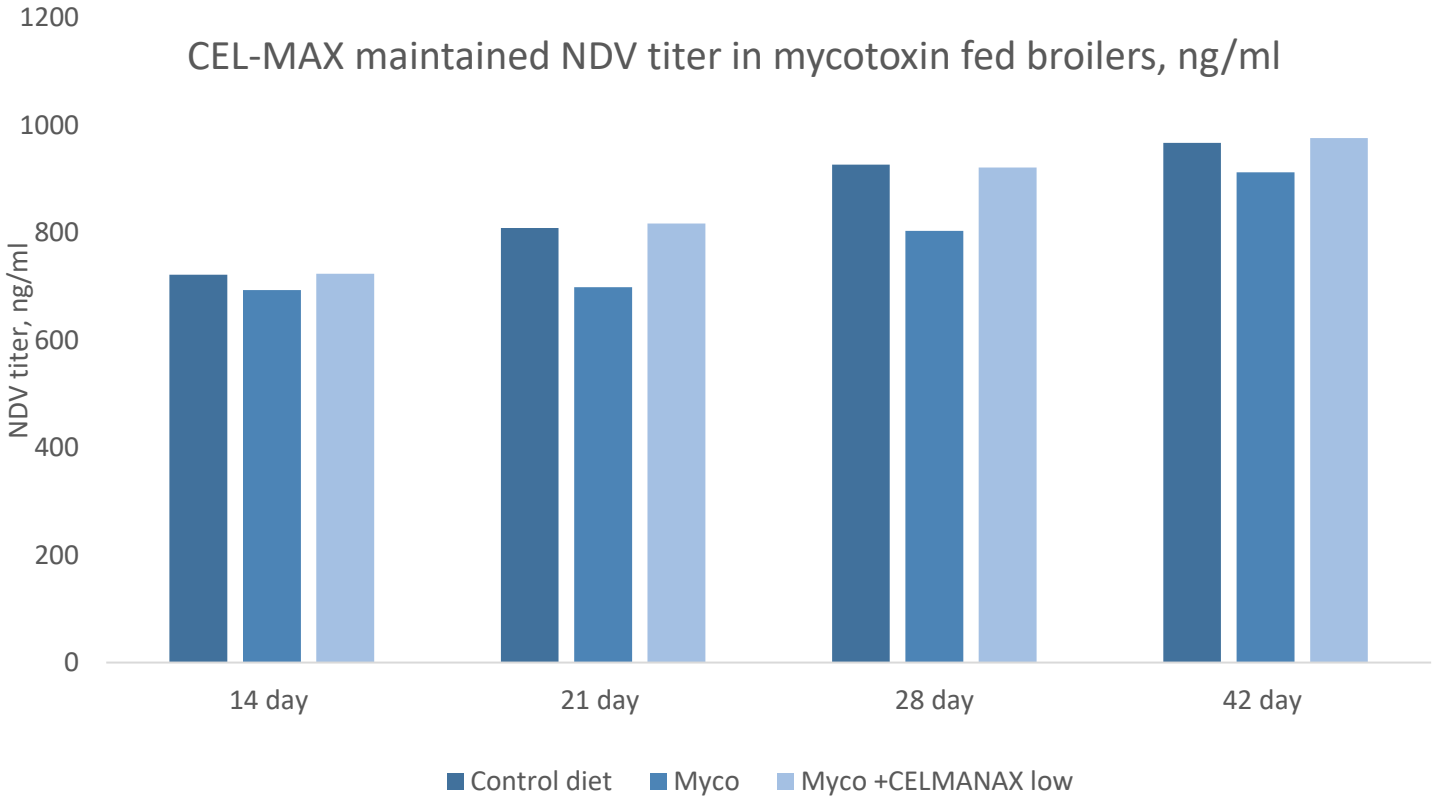
CEL-MAX improved intestinal barrier proteins in the face of MYCOTOXINS



Mixed mycotoxin challenge decreased gut barrier function and supplementation with CEL-MAX partially restored it. **SAME STRESS, DIFFERENT RESULTS.**

CEL-MAX and immune responses in broilers (example of RESILIENCY)

- Mycotoxins cause immunosuppression
- CEL-MAX supplementation can restore immunity and keep animals protected from infections. **SAME STRESS, DIFFERENT RESULTS.**



Zhao, et al. (2021) CAU Data on file

Heat stress mitigation

- Temperature Humidity Index (THI)
- < 20 C: no Heat Stress (HS)
- 20-21.7 C: mild HS
- 22-26 C: mild to moderate HS
- 26.5-32 C: moderate-severe
- 32-37 C: severe HS

Heat stress mitigation

- Acute HS: 1-2 days. Animals develop an adaptive response to manage HS by increasing water intake, respiration rate and sweating to cool.
- Chronic HS: >2 days. Adaptive response cannot be sustained; leads to increase in heart rate, reduced FI, and poor performance. These are all visual……
    - but there are more metabolic and physiologic developments that can be more impactful.

Heat stress

Activation of autonomic nervous system mediated via catecholamines (adrenaline and noradrenaline)

Activation of hypothalamic pituatary adrenal axis and glucocorticoid hormone stimulation (e. g. cortisol)

Increase in panting, in heart rate, in body temp, and decrease in feed intake (FI) and growth

One of the direct effects of increase in panting or breathing rate (BR) is hyperoxia (increase in O_2 in tissues), loss of BLOOD BUFFERING CAPACITY via CO_2 expired

Generates reactive oxygen species (ROS) and increases oxidative stress

Poor gut barrier and morphology

Increase in gram-negative bacterial invasion and endotoximia*

Poor performance/carcass parameters and immune function

Some of the host management mechanisms include:

1. Improve cooling efficiency (increase vasodilation?)
2. Manage oxidative stress
3. Heat shock proteins (HSP): increase in HSP can help develop thermo-tolerance to HS
4. Developing perturbations in post absorptive carbohydrate, protein, and lipid metabolism

Late Day Morbidity and Mortality Challenges in High Performance Cattle Encompass Multiple Cardiopulmonary Disease Phenotypes

Clinical Manifestations

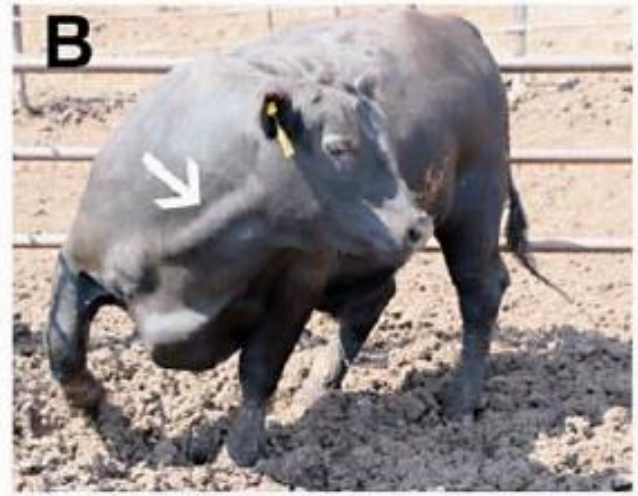
There is considerable overlap between AIP, Feedlot CHF/PH and BRD

Panting scores, edema, jugular distention/pulse, shoulder spreading, cyanosis

- AIP = Acute Interstitial Pneumonia

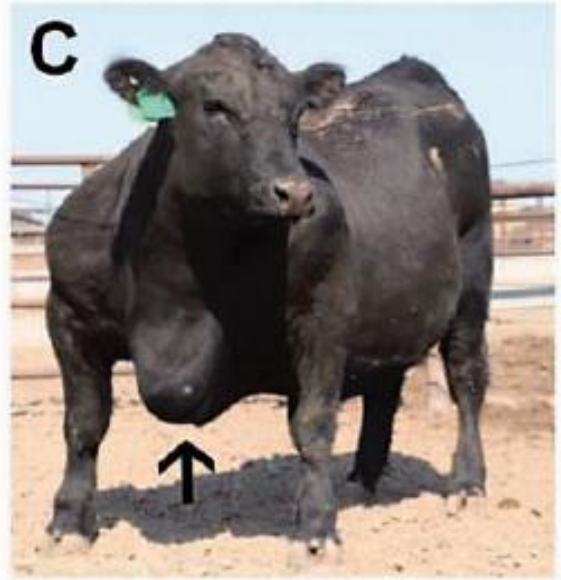
Unaffected Pen-Mate

Symptomatic



Jugular Distension

Intermandibular Edema



Sternal Edema

RTI Research Project

Project Objective

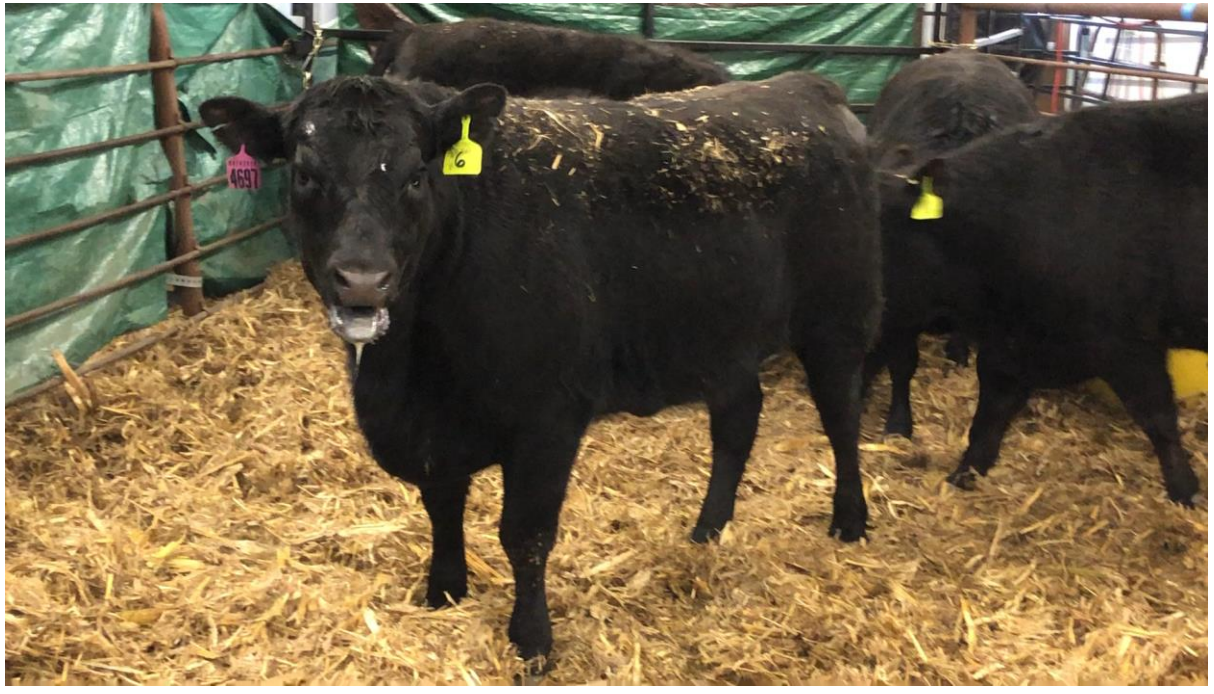
The objective of this study is to investigate immune effects of the combination of in-feed CERTILLUS and CEL-MAX in reducing effects on cardiopulmonary disease associated with heat stress in feedlot heifers.

Design

- The trial consisted of two treatment groups:
  - control – heat stress and no in-feed product
  - treatment – heat stress with in-feed product
- Trial phases:
  - day 0-20 – acclimation, background testing – SNP genotyping (ARRDC3 and NFIA genes) = **susceptible to AIP**
  - day 21-26 – heat stress – THI 60-90 adjusted based on panting score
    NOTE: **heat stress for 6 days only**
  - day 27-35 – post heat-stress recovery

Short term responses to heat stress and short term "recovery"

RTI Research Project



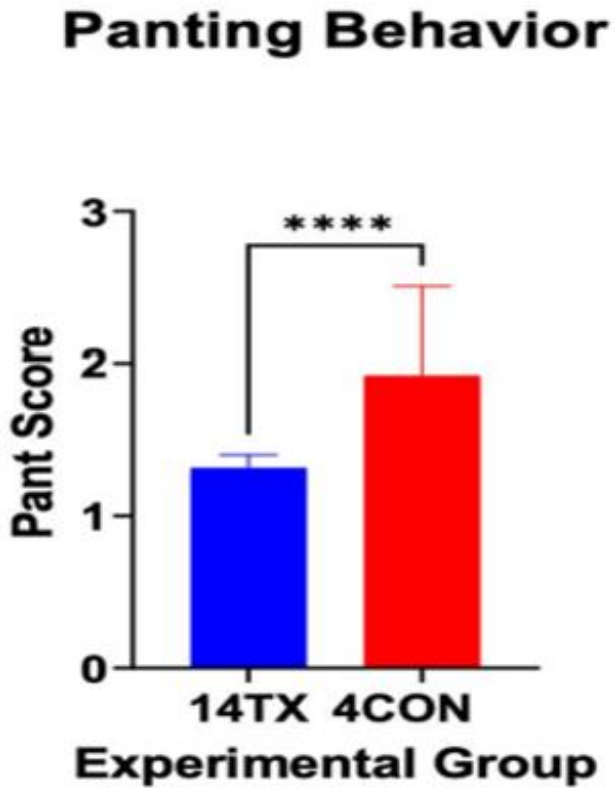
Control response to heat stress

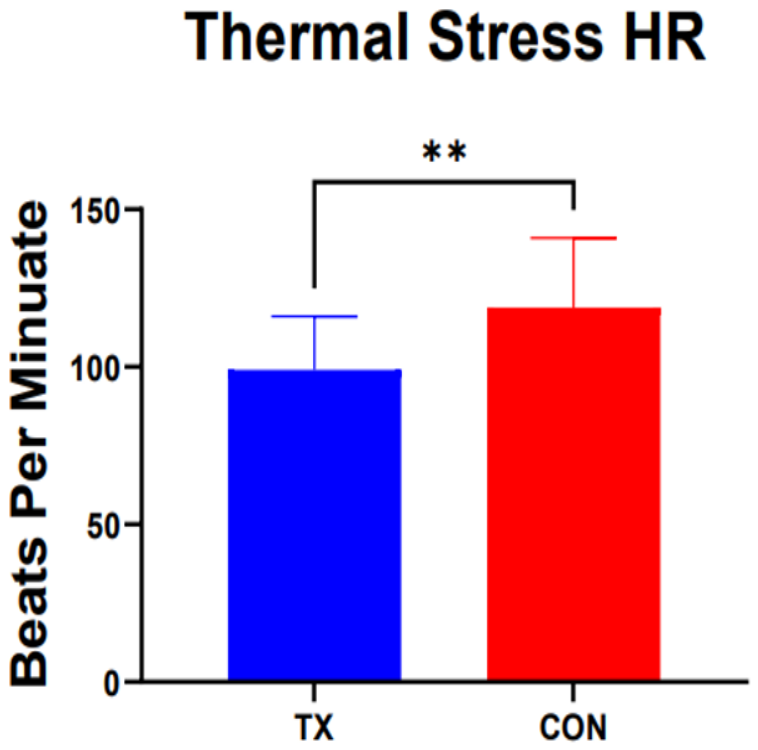
Treated response to heat stress

Control response to heat stress

Treated response to heat stress

CEL-MAX + CERTILLUS: finishing cattle response to heat stress





SAME STRESS, DIFFERENT RESULTS.

FIGURE 5: ANIMAL 4, CON, LONG RUMEN PAPILLA, 200X

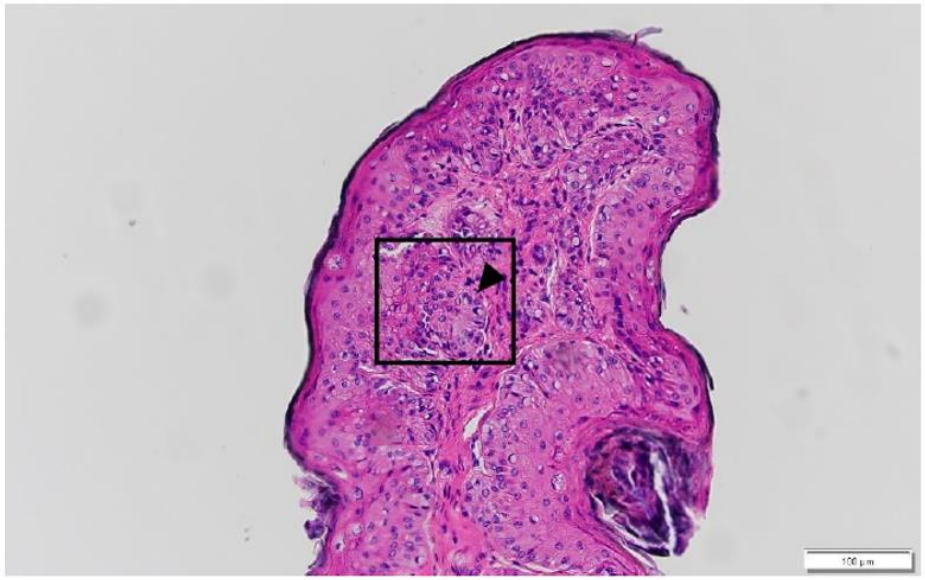
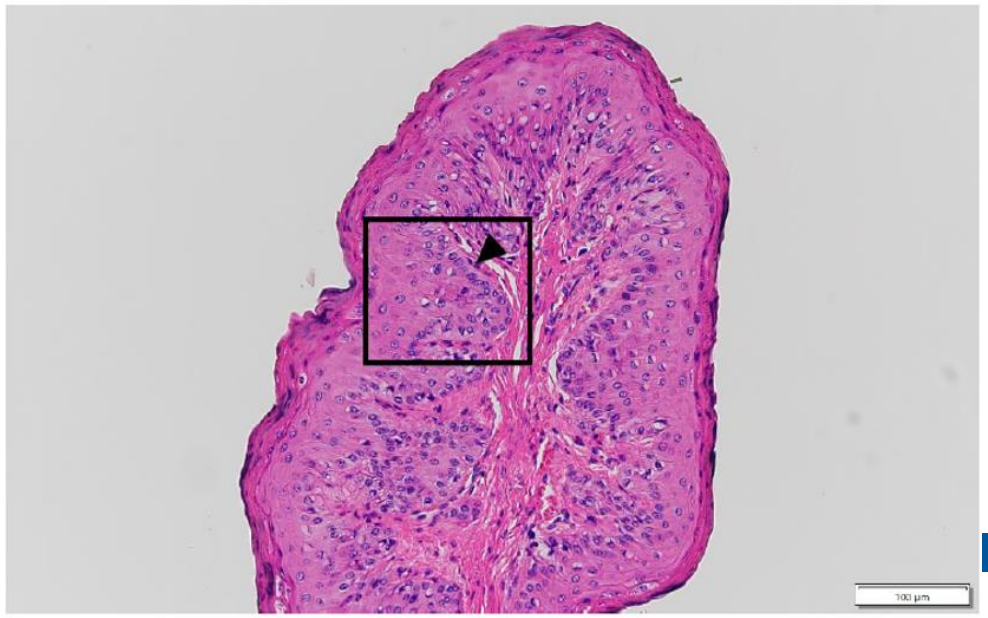


FIGURE 4: ANIMAL 14, TX, LONG RUMEN PAPILLA, 200X



CEL-MAX + CERTILLUS on rumen papillae in heat stress

SAME STRESS, DIFFERENT RESULTS

FIGURE 13: ANIMAL 4, CON, DUODENUM, 40X

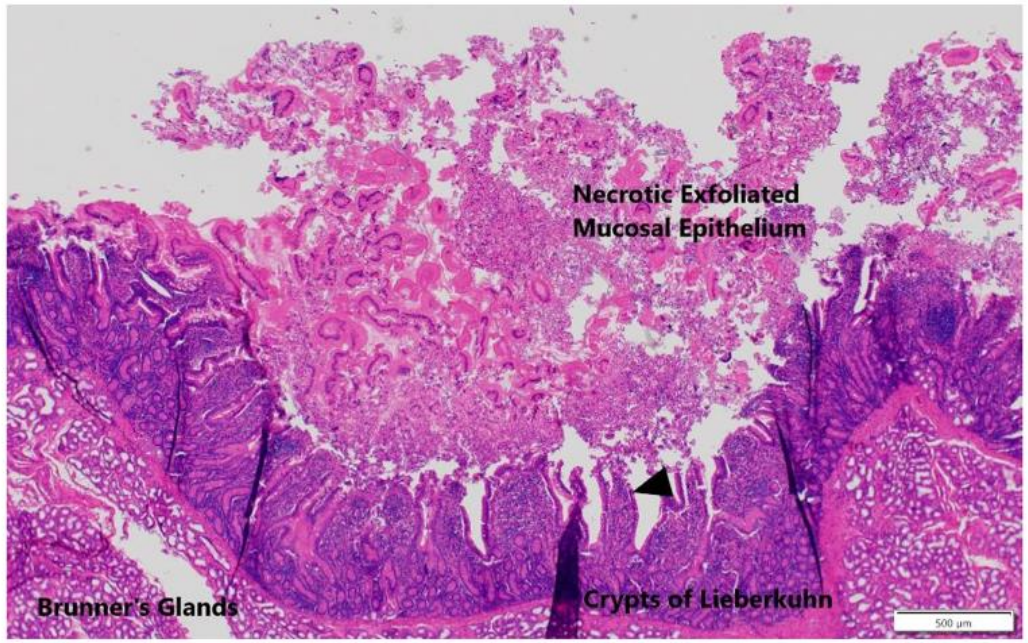
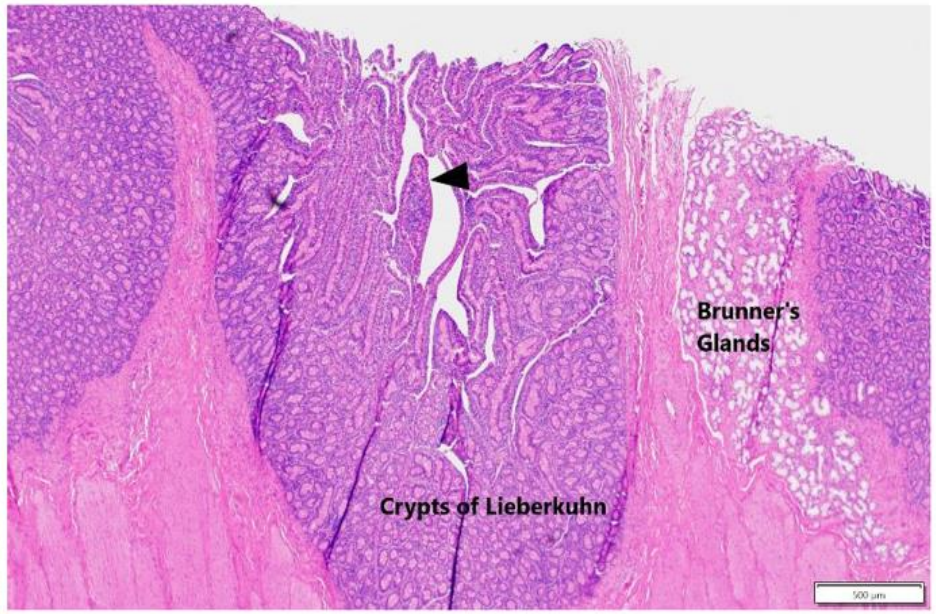


FIGURE 11: ANIMAL 14, TX, DUODENUM, 40X

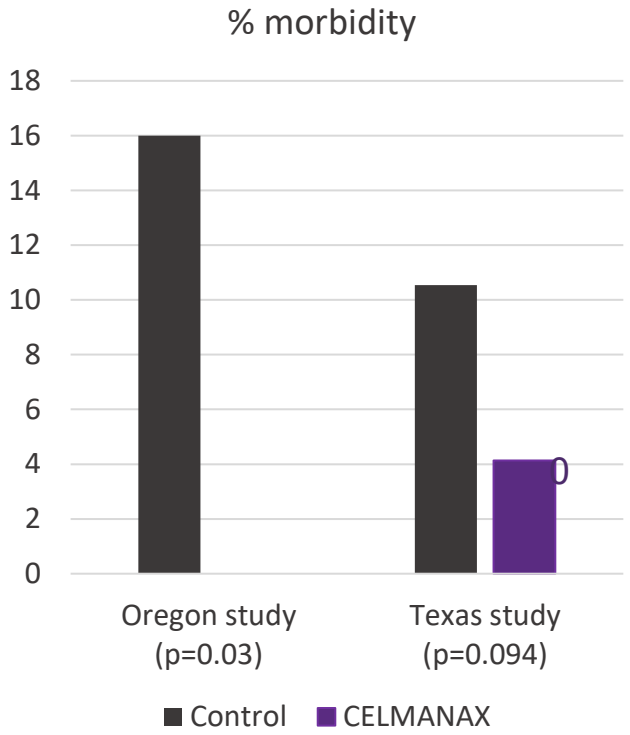


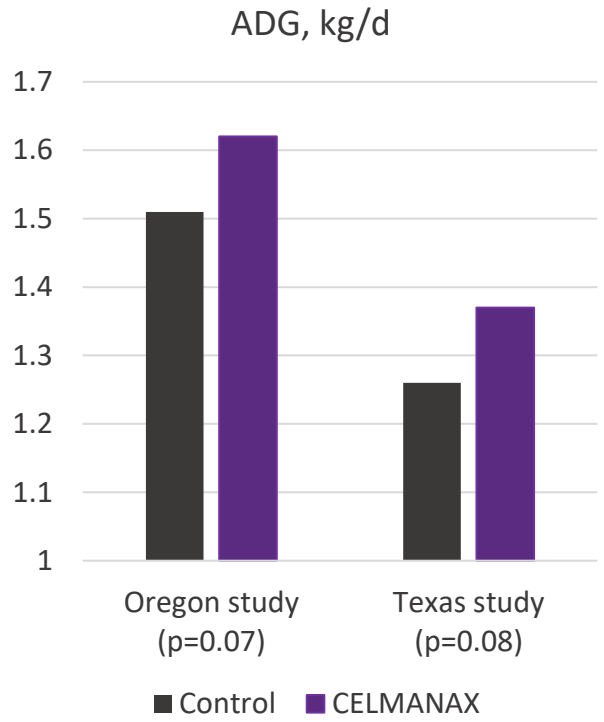
CEL-MAX + CERTILLUS on intestinal response to heat stress

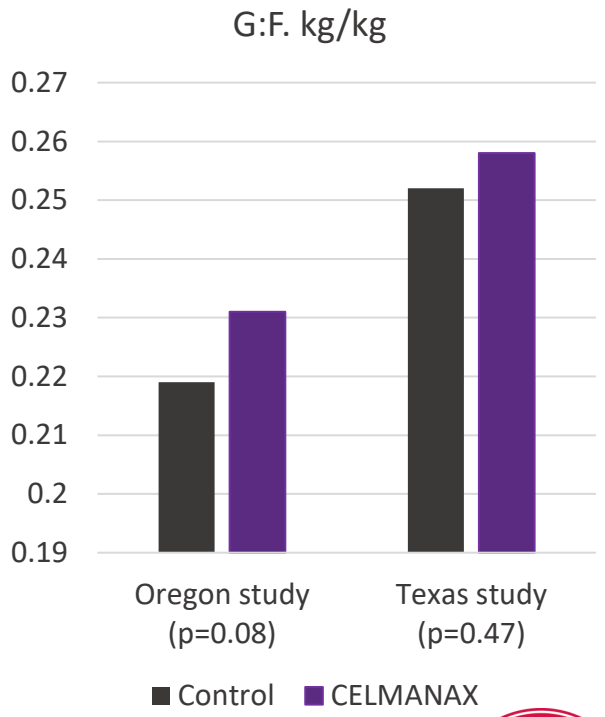
SAME STRESS, DIFFERENT RESULTS

CEL-MAX reduced morbidity and mortality related to respiratory disease – SAME STRESSORS, DIFFERENT OUTCOMES

- Two separate studies show CEL-MAX supplementation in the receiving phase reduces BRD morbidity and improves ADG and feed efficiency.







Oregon study: Schubach et. al. Proceedings, Western Section , American Society of Animal Science, Volume 68, 2017
Texas study: Ponce et. al. *The Professional Animal Scientist* 2012;28:618-622.

BRD feedlot study: objective

- Demonstrate ability for CEL-MAX to reduce morbidity and mortality associated with Bovine Respiratory Disease (BRD) in newly received cattle in a large, commercial receiving yard.

Trial overview

- ~3,000 head of receiver cattle assigned to 20 pens with 10 pens control and 10 pens treated (CEL-MAX @ 2g/head/day)
  - about 150 cattle/pen and 1,500 head per treatment group
- Cattle are sourced as weaned calves from multiple sources (auction)
- Control was compared to treatment for morbidity and mortality as well as growth performance efficiency
- Success is declared if performance and/or health metrics will result in a positive ROI

Baseline and ancillary production and performance data summary

Production Variable	Experimental Group		SEM	*P* – value
	CEL-MAX	CNTL		
Number of Pens	10	10		
Head in Pen	150.5	149.6	3.7	0.870
Allocation Weight (kg)	271.3	269.5	4.2	0.212
Final Weight (kg)	**361.5**	**351.8**	**5.5**	**0.035**
Days on Feed	66.6	66.6	0.8	0.511
Daily Dry Matter Intake kg/animal day)	7.35	7.29	0.20	0.561
Average Daily Gain (kg)	**1.37**	**1.25**	**0.08**	**0.043**
Dry Matter Intake to Gain Ratio	**5.36**	**5.83**	**0.26**	**0.077**

Animal health data summary

Animal Health Variable	Experimental Group		*P* – value
	CEL-MAX	CTRL	
Head in Pen	153.4	153.5	0.986
Total cattle in 10 pens per group	1534	1535	
Head Treated (%)	**32.28**	**42.43**	**0.002**
All Treatments (%)	**48.34**	**69.22**	**0.005**
Morbidity (%)			
Initial UF Treatment (BRD)	**28.79 (n=442)**	**41.97 (n=644)**	**0.002**
First UF Relapse(% of initial)	**21.66 (n=96)**	**28.25 (n=182)**	**0.089**
Second UF Relapse	46.16	31.27	0.250
Mortality (%)			
BRD Mortality	0.92	0.68	0.447
Histophilosis Mortality	0.73	0.72	0.980
Other Mortality	0.35	0.26	0.466

Economic evaluation: performance

PERFORMANCE		
Days of study	66	
Number of cattle per treatment	1505	
Beef price (CAD/lb)	$3.82	
CEL-MAX cost (per head/day)	$0.06	
	Control	**CEL-MAX**
Initial weight (lbs)	593.0	596.9
Final weight (lbs)	773.9	795.4
Gain (lbs)	180.9	198.5
	Difference (lbs)	17.6
CEL-MAX Advantage for Performance (CAD)	(1505 x 17.6 lbs x $3.82/lb)	**$101,184.16**

Economic evaluation: animal health

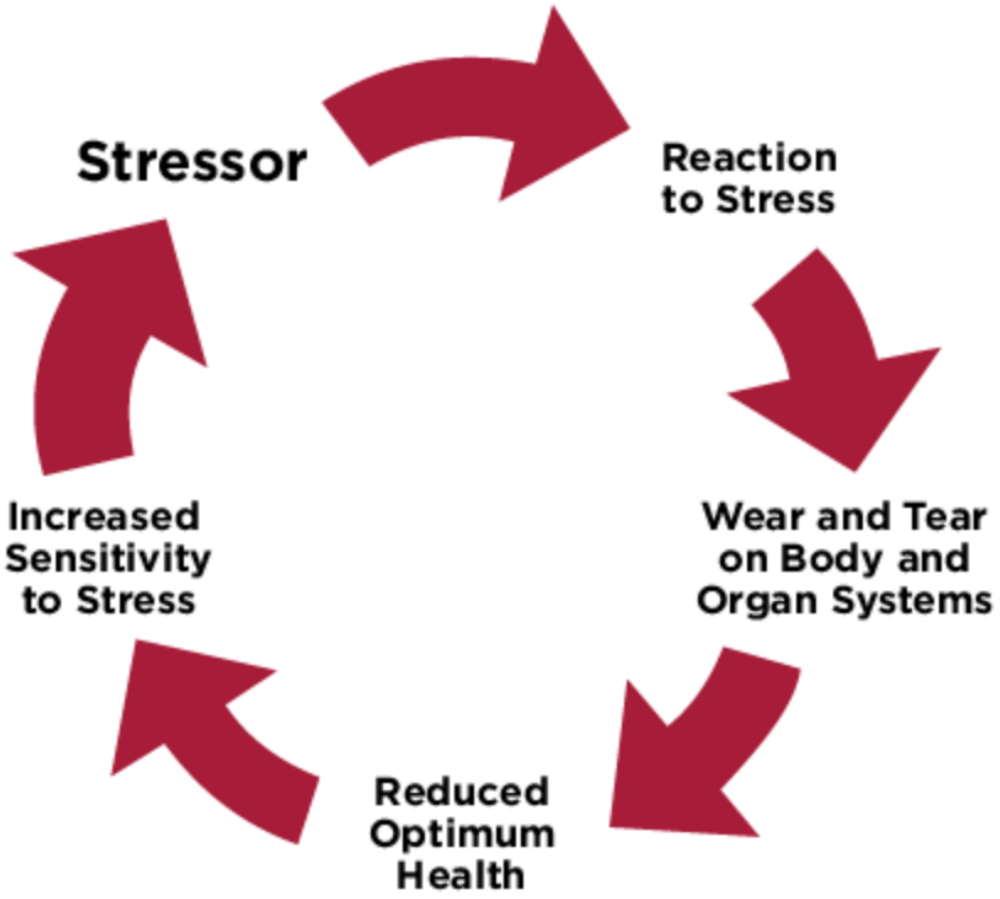
ANIMAL HEALTH		
Labor cost (CAD) per treatment	$12.29	
Initial UF treatment (CAD)	$41.00	
First UF relapse treatment (CAD)	$31.11	
Second UF relapse treatment (CAD)	$28.22	
	Control	**CEL-MAX**
Initial UF treatment (no of animals)	644	442
First UF relapse	182	96
Second UF relapse	57	44
Total treatment cost (CAD)	$44,526.63	$29,493.02
CEL-MAX Advantage for Treatment Costs (CAD)		**$15,033.61**

Economic evaluation: ROI

RETURN ON INVESTMENT		
CEL-MAX Cost (CAD) @ 2g/h/d	$0.06	
Total CEL-MAX Cost (CAD) ($0.06 x 66 days x 1505 head)	$5,959.80	
	ROI for Health Benefits	**2.5:1**
	ROI for Performance Benefits	**17:1**
	ROI for Both Combined	**19.5:1**

STRESS IN ANIMAL SYSTEMS

- acute or cumulative stress WILL results in productive losses and health issues
- some stresses can be minimized via good management but the stressors are still present
- we can intervene to protect animal systems and improve resiliency



Take home message

- ✓ minimize stress and diseases (clinical and subclinical)
  - ✓ stress and disease causes inflammation and tissue damage, which alters function
  - ✓ alters partition of nutrients to favor control of infection and tissue repair in place of tissue accretion
  - ✓ priority shifts from production/growth to survival
  - ✓ creates long-term negative effects on production and reproduction
  - ✓ CEL-MAX is one potential tool to minimize the effects of stress and risks for disease