Endotoxemia as a model for evaluating naturally occurring and nutritionally-induced variations in the stress and innate immune responses of cattle and swine.

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Seminar Outline

- Introduction
- Natural variations in cattle innate immunity
  - Sexually dimorphic responses
  - Effect of animal temperament
- Nutritionally-induced changes in innate immunity
  - Fishoil supplementation in pigs
  - Chromium supplementation in cattle

Introduction

It has been well-established that an animal's ability to protect itself from diseases and other immunological challenges within its environment depends upon the presence of a well developed and properly functioning immune system.

It is also common knowledge that animals which possess an adequate level of immunological protection exhibit greater reproductive capabilities, enhanced growth, and increased feed efficiency.

Introduction (cont.)

However, even animals which possess an immune system functioning at an optimum level can often become susceptible to disease following exposure to various stressful conditions such as extreme fluctuations in environmental temperature, poor or inadequate nutrition, improper handling techniques, mixing of unfamiliar animals, inadequate ventilation, and unsanitary housing conditions.

AND its important to understand that not all animals response the same to stressful conditions and that the animal's diet can influence its immune system.

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Do cattle exhibit a sexually dimorphic innate immune response following an endotoxin challenge?

Materials and Methods

Twelve purebred Brahman calves (6 bulls and 6 heifers; 269 ± 11.7 kg) that were fitted with: a) rectal temperature (RT) devices that recorded RT at 1-min intervals for 24 h; and b) indwelling jugular catheters.

The next day blood samples were collected at 30-min intervals from -4 to 8 h relative to an i.v. infusion of lipopolysaccharide (LPS; 0.25 µg/kg BW) at 0 h.

Results

Physiological Response

Rectal Temperature

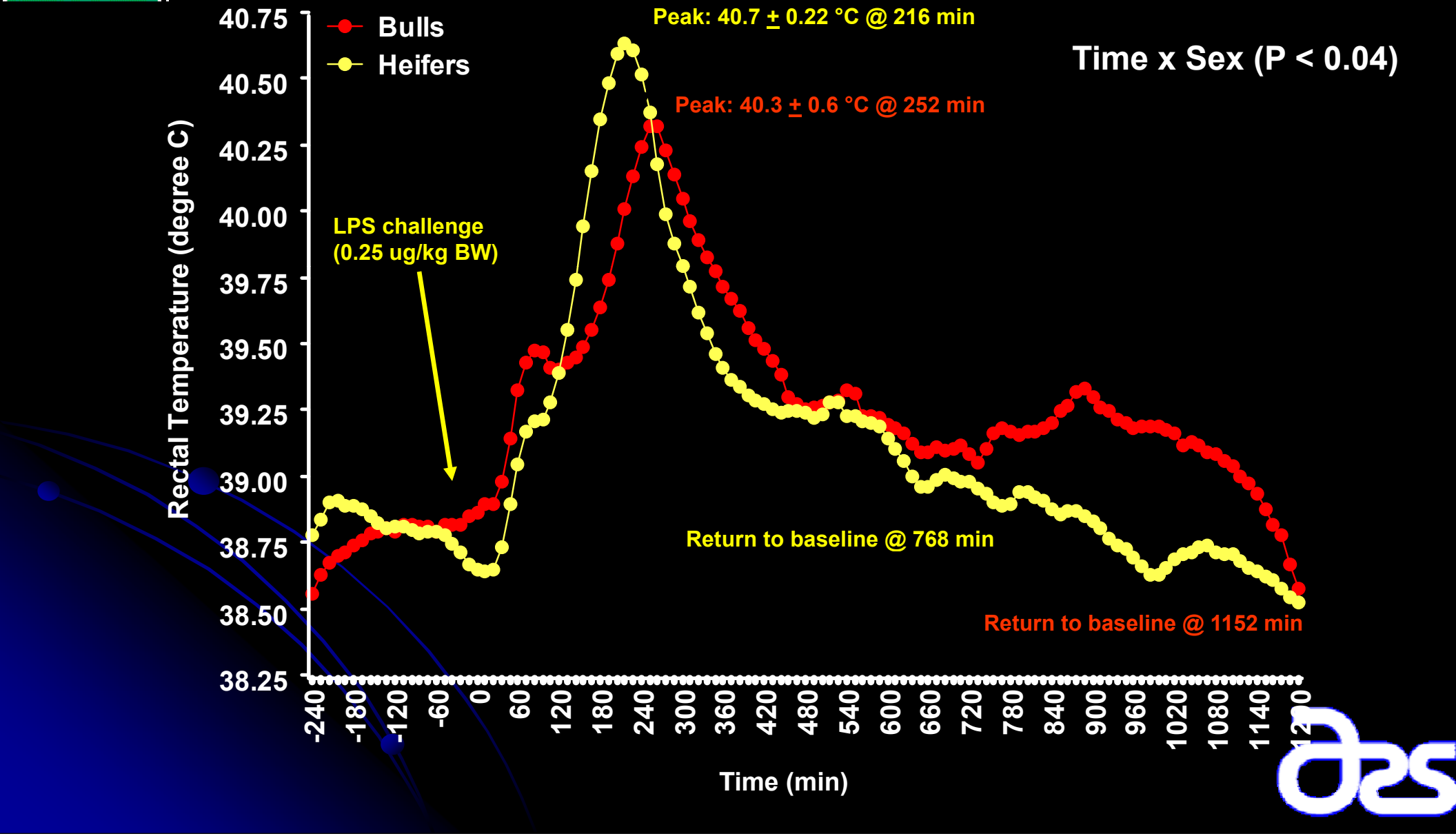
Pro-inflammatory Cytokine Responses

Tumor Necrosis Factor-alpha

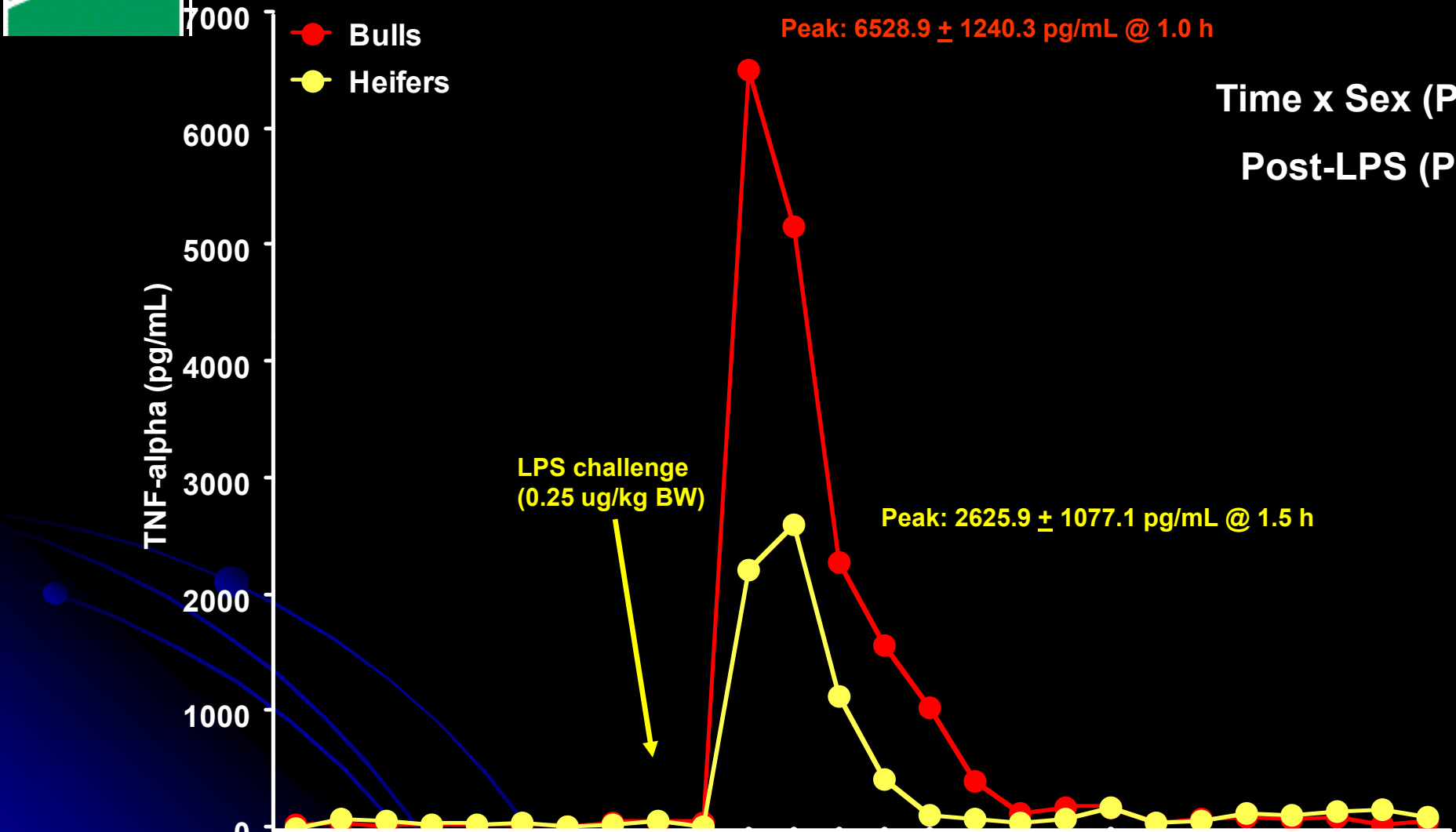
Interleukin 6

Interferon-gamma

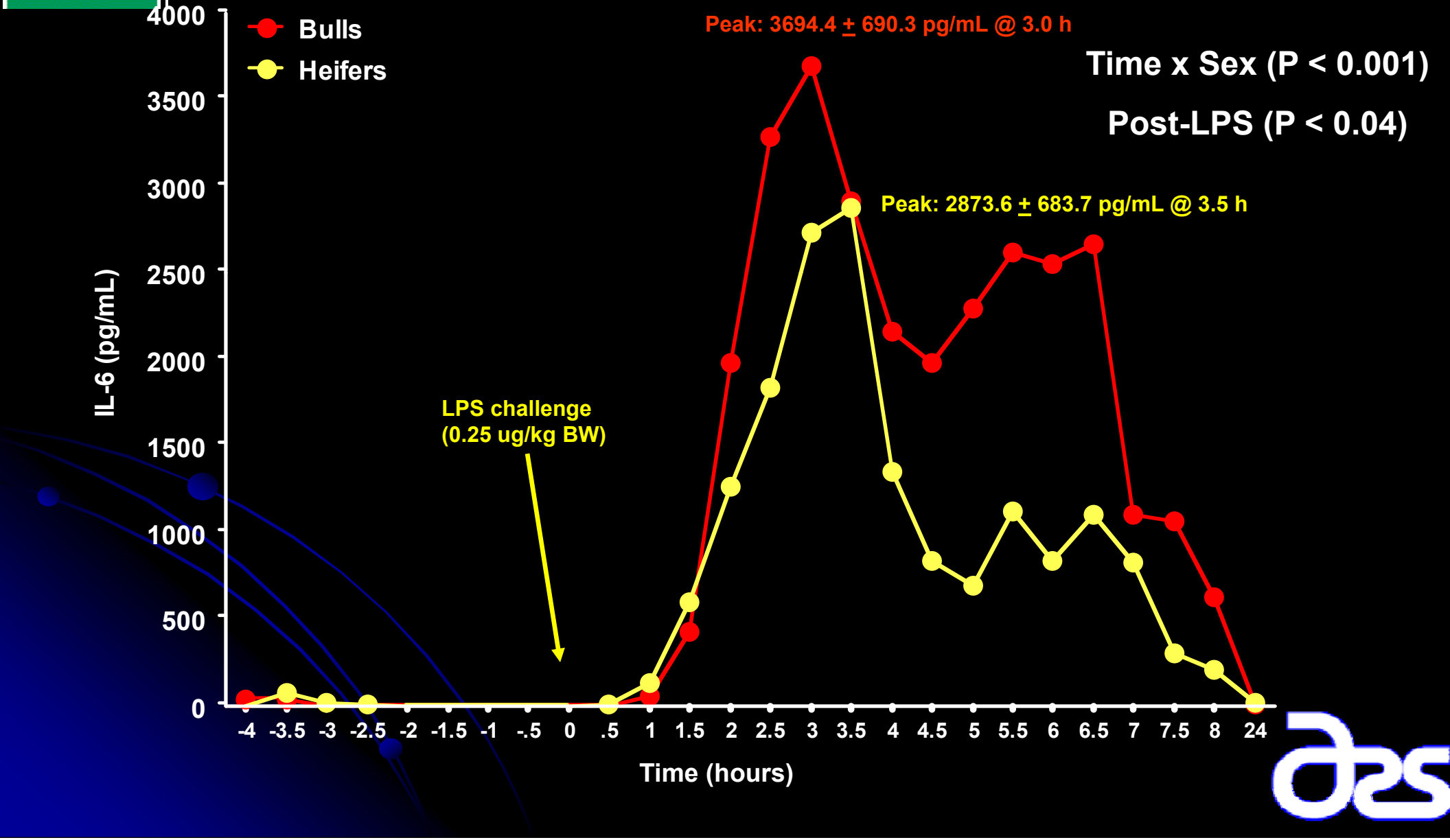
Rectal Temperatures (12-min intervals)



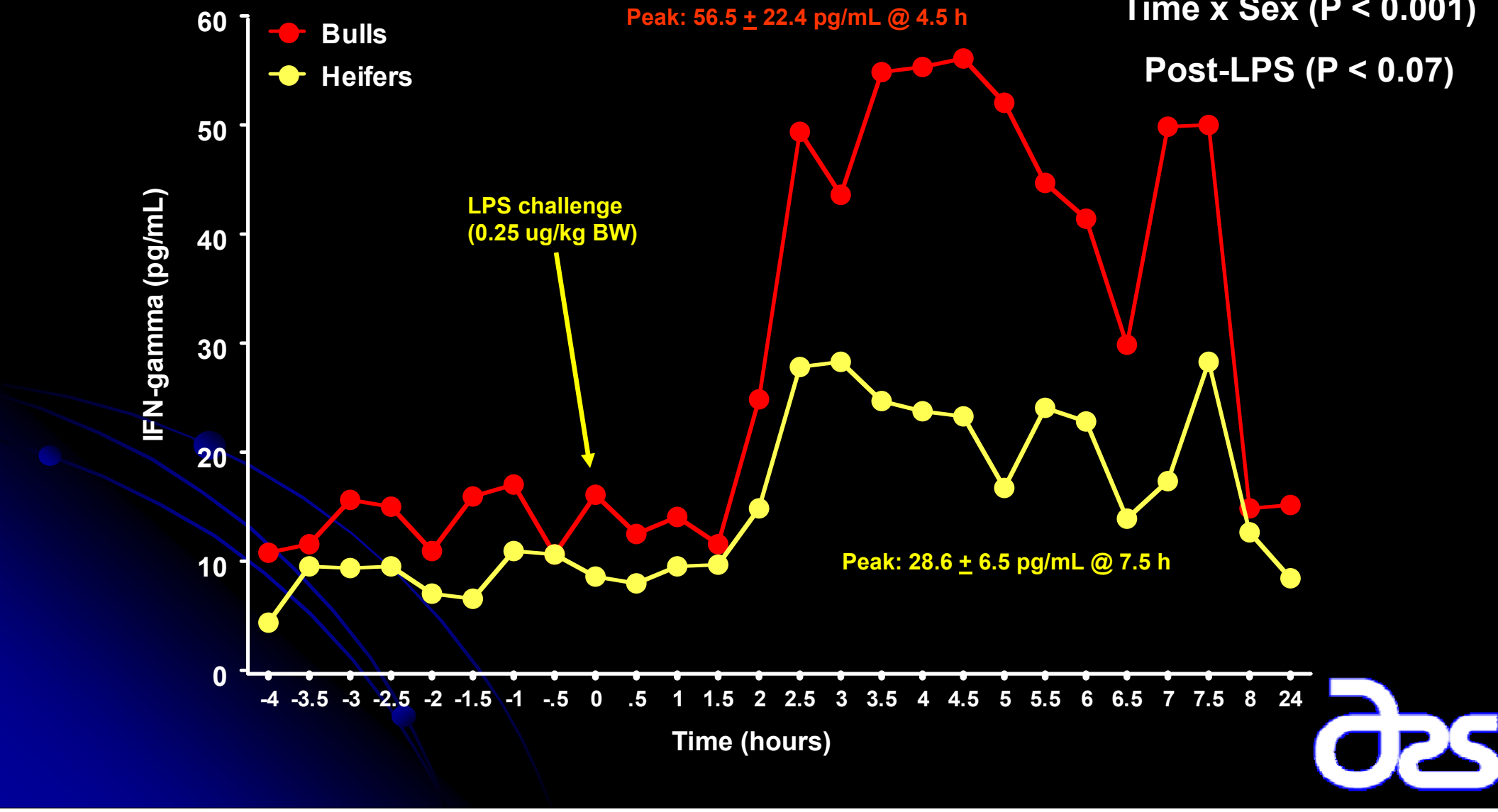
Serum concentration of TNF-alpha



Serum concentration of Interleukin 6



Serum concentration of Interferon-gamma



Summary

Peak rectal temperature occurred 30 min sooner and was 0.4 °C higher in heifer calves as compared to bull calves.

Rectal temperature returned to baseline 6.4 h sooner in heifer calves as compared to bull calves.

Serum TNF-alpha peaked 30 min faster and was ~2.5-fold greater in bull calves as compared to heifer calves.

Serum IL-6 peaked 30 min faster and was ~1.3-fold greater in bull calves as compared to heifer calves.

Serum IFN-gamma peaked 3 h faster and was ~2.0-fold greater in bull calves as compared to heifer calves.

Implications

Collectively, these data suggest that heifers may be more adept at coping with and recovering from an immune challenge as compared to bull calves.

Further studies are needed to determine if the production parameters (i.e., feed intake, body weight gain) recover more rapidly in heifer calves as compared to bull calves.

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Does temperament influence an animal's stress and innate immune responses to an endotoxin challenge?

Temperament Assessment

Subjective Methods

- ✓ Chute Score
- ✓ Pen Score

Objective Method

- ✓ Exit Velocity

In-House Method

Temperament Score = Pen Score + Exit Velocity

Materials and Methods

Twenty-four Brahman bulls were selected from a pool of 60 based on temperament score (average of exit velocity - EV, and pen score - PS) measured 28 days prior to weaning:

8 most Calm (0.89 ± 0.15 EV and 1.00 ± 0.00 PS)

8 most Temperamental (3.70 ± 0.29 EV and 4.88 ± 0.13 PS)

8 Intermediate (1.59 ± 0.12 EV and 2.25 ± 0.16 PS)

Materials and Methods (cont.)

The day prior to the immune challenge, all bulls were fitted with: a) rectal temperature (RT) devices that recorded RT at 1-min intervals for 24 h; and b) indwelling jugular catheters.

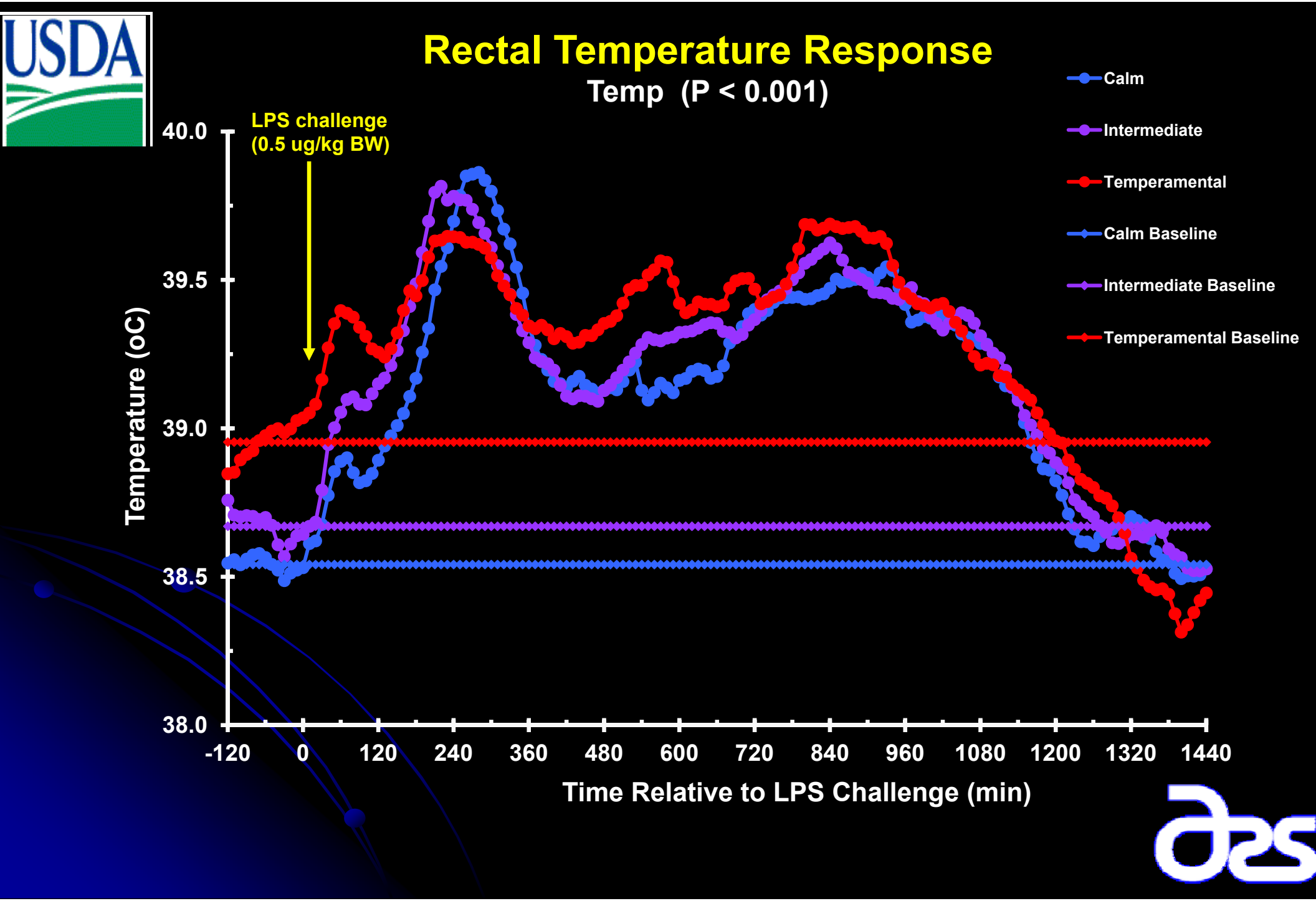
The next day blood samples were collected at 30-min intervals from -4 to 8 h relative to an i.v. infusion of lipopolysaccharide (LPS; 0.5 µg/kg BW) at 0 h.

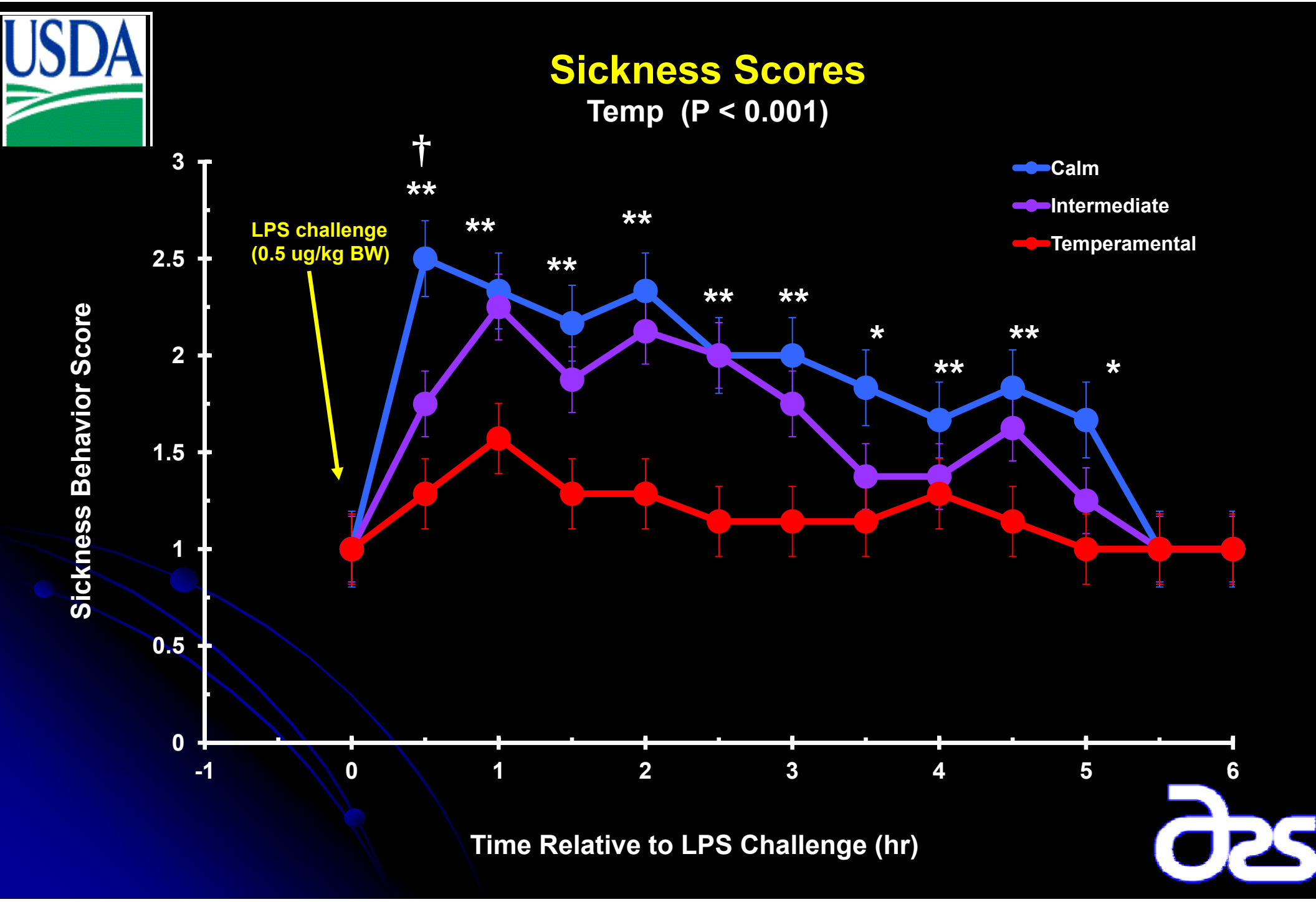
Results

Physiological Response

Rectal Temperature Response to Endotoxin

Sickness Scores


Rectal Temperature Response
Temp (P < 0.001)
LPS challenge
(0.5 ug/kg BW)
Calm
Intermediate
Temperamental
Calm Baseline
Intermediate Baseline
Temperamental Baseline
Temperature (oC)
40.0
39.5
39.0
38.5
38.0
-120
0
120
240
360
480
600
720
840
960
1080
1200
1320
1440
Time Relative to LPS Challenge (min)


Sickness Scores
Temp (P < 0.001)
LPS challenge
(0.5 ug/kg BW)
Calm
Intermediate
Temperamental
Sickness Behavior Score
Time Relative to LPS Challenge (hr)
3
2.5
2
1.5
1
0.5
0
-1
0
1
2
3
4
5
6
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Results

Stress Response

Epinephrine

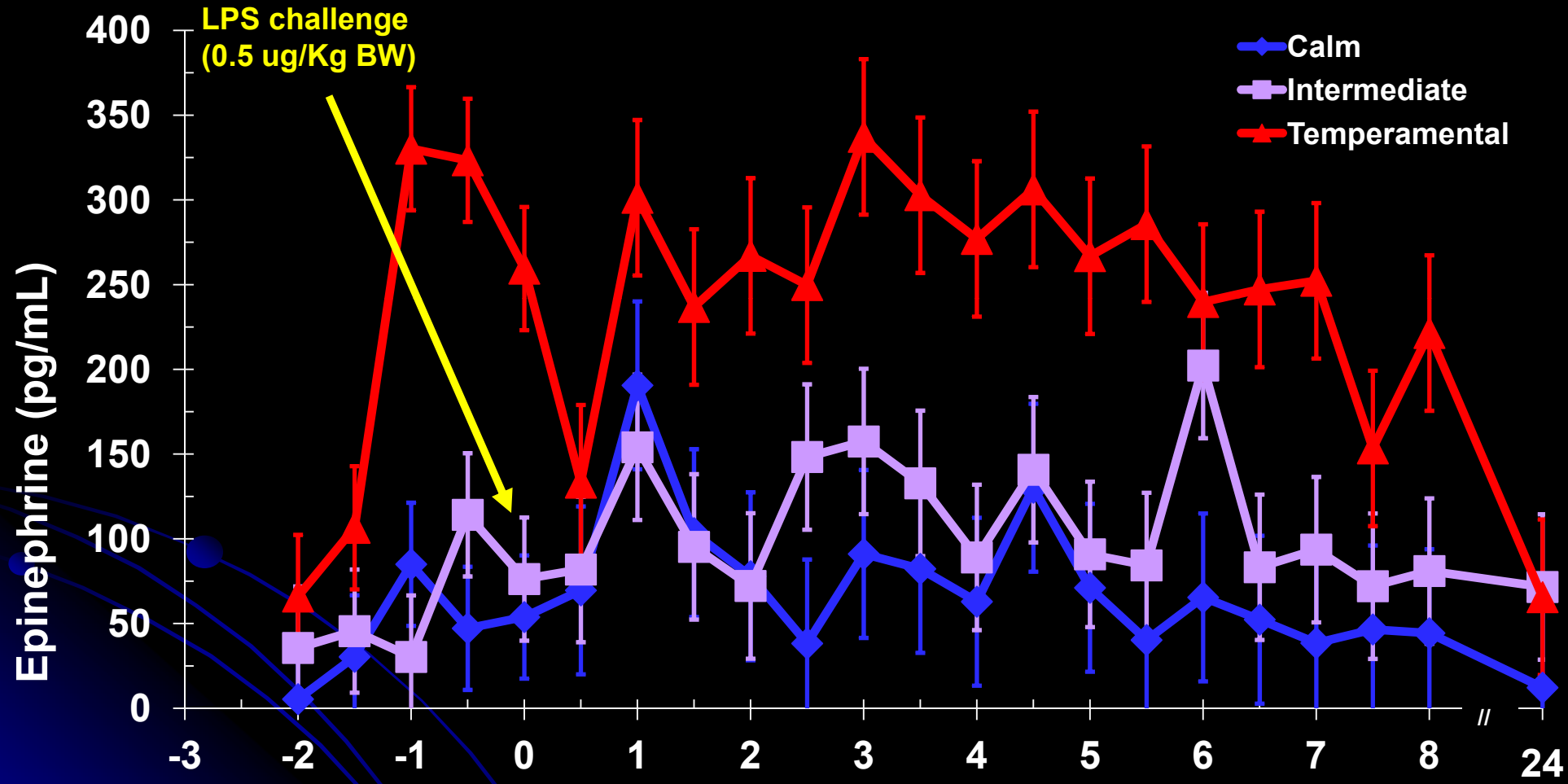
Pro-inflammatory Cytokine Responses

Tumor Necrosis Factor-alpha

Interleukin 4

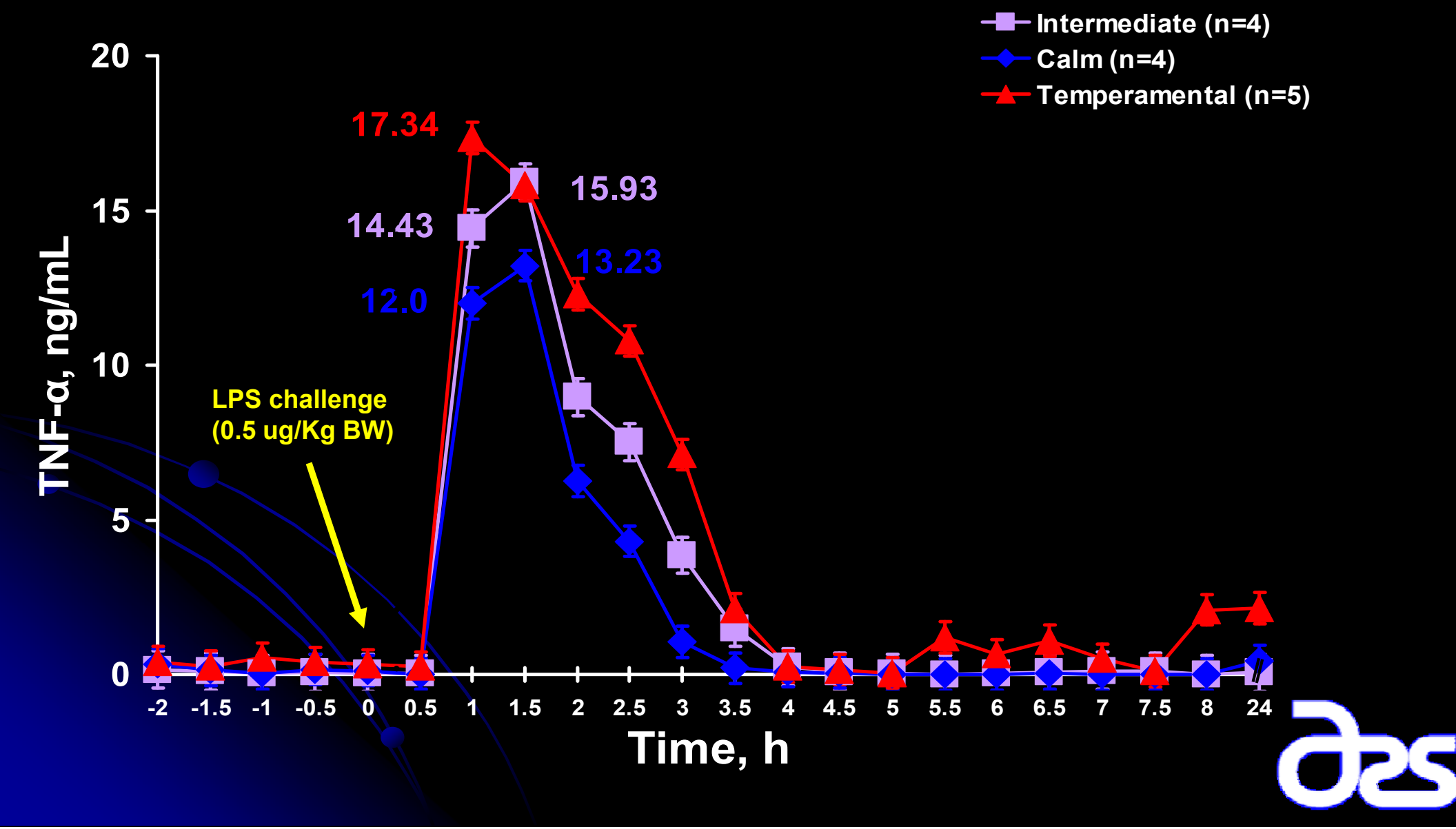
Serum concentration of Epinephrine

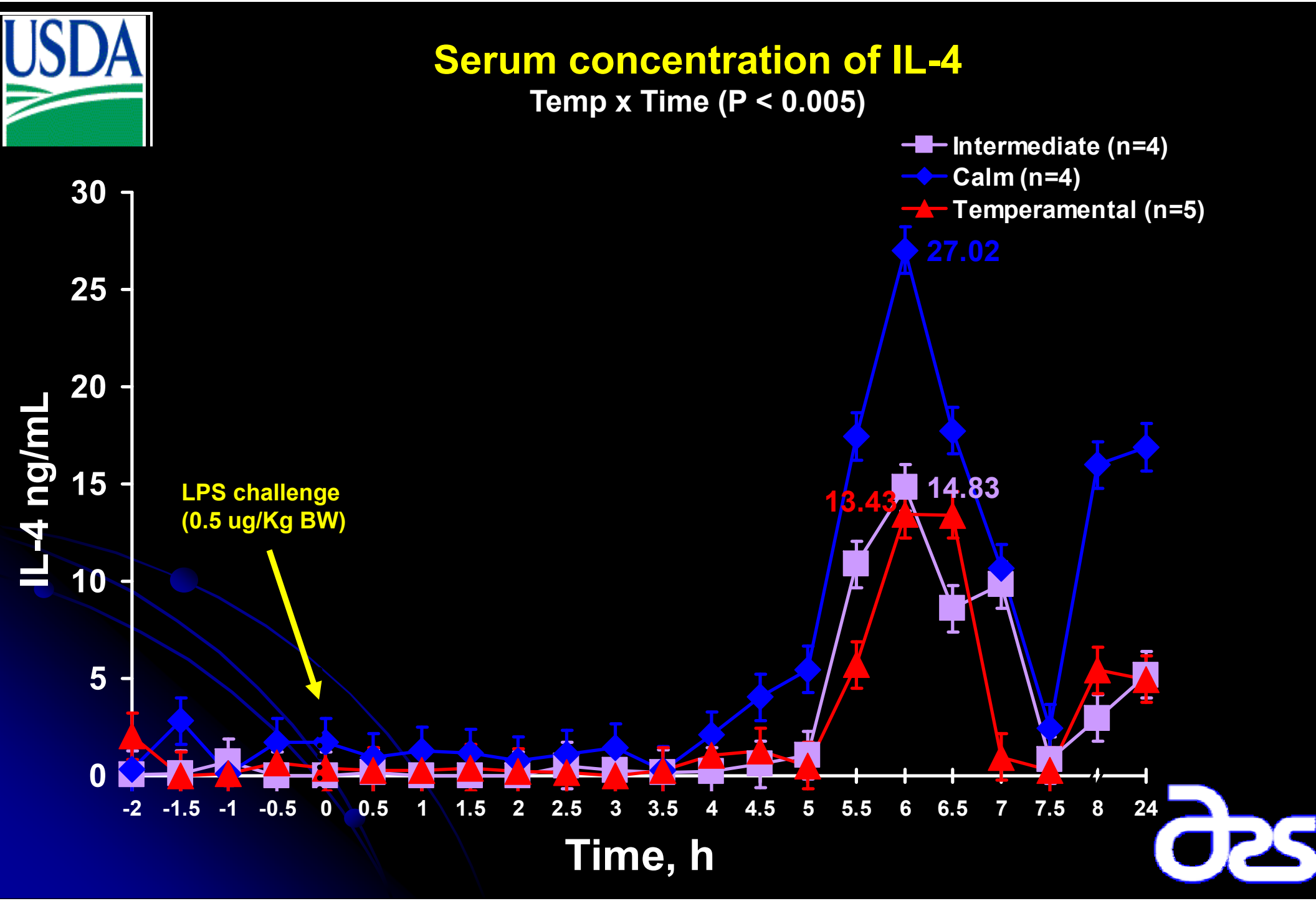
Temp (P < 0.004); Time (P < 0.001)



Serum concentration of TNF-α

Temp x Time (P < 0.005)




Serum concentration of IL-4
Temp x Time (P < 0.005)
Intermediate (n=4)
Calm (n=4)
Temperamental (n=5)
27.02
14.83
13.43
LPS challenge
(0.5 ug/Kg BW)
IL-4 ng/mL
30
25
20
15
10
5
0
-2
-1.5
-1
-0.5
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
5.5
6
6.5
7
7.5
8
24
Time, h

Summary

Temperamental bulls had higher basal RT compared to Intermediate and Calm bulls, and displayed less of a peak febrile response.

Temperamental bulls displayed less visual signs of sickness following the LPS challenge compared to Intermediate and Calm bulls.

Epinephrine concentrations were greater in the Temperamental bulls throughout most of the study.

LPS-induced TNF-alpha concentrations were greater in the Temperamental bulls compared to the Calm bulls.

LPS-induced IL-4 concentrations were lower in Temperamental bulls compared to the Calm bulls.

Implications

Collectively, the findings from this study clearly demonstrate that animal temperament can significantly influence the stress and innate immune responses in cattle exposed to a provocative immune challenge.

Future studies are planned to determine if the production parameters (i.e., feed intake, body weight gain) recover more rapidly in Temperamental as compared to Calm cattle.

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Does fish oil supplementation alter the young pig's immunological response to an endotoxin challenge?

Materials and Methods

Twenty-four crossbred male pigs were weaned at 18.7 ± .13 days of age and placed on a complex nursery diet containing 30% lactose and 7% plasma protein with 6% corn oil as the fat source (Cont, n=12) or with 5% fish oil and 1% corn oil as the fat source (FO, n=12) for a period of 15 days.

On d15 all pigs were non-surgically fitted with an indwelling jugular catheter. On d16 pigs received an i.v. injection of either saline (n=6 pigs/dietary group) or lipopolysaccharide (LPS; 150 ug/kg body weight; n=6/dietary group) and blood samples were collected at 30-min intervals for a period of 5h.

Results

Physiological parameter:

Body weights

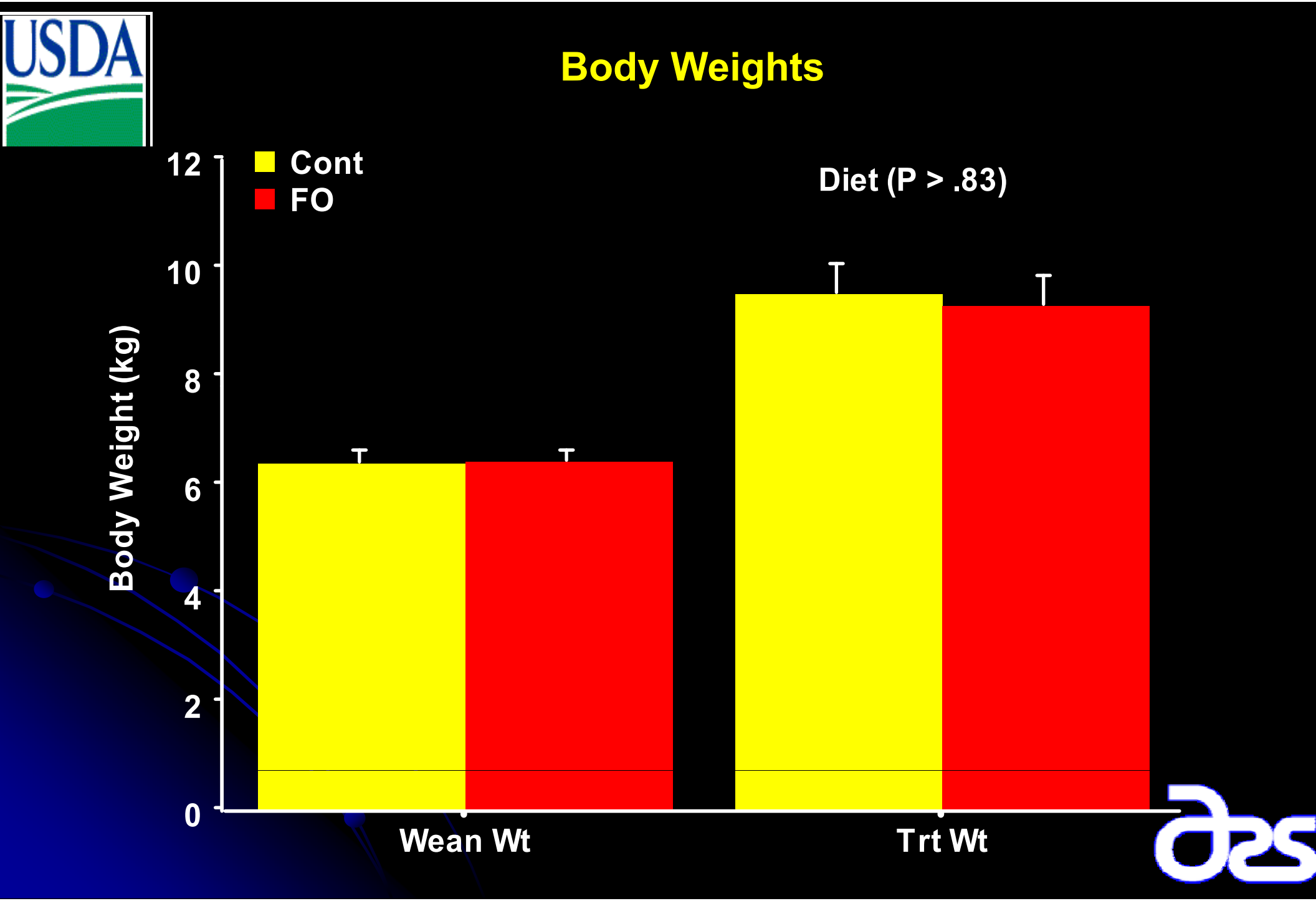
Activation of the Stress axis:

Serum cortisol

Activation of the immune system:

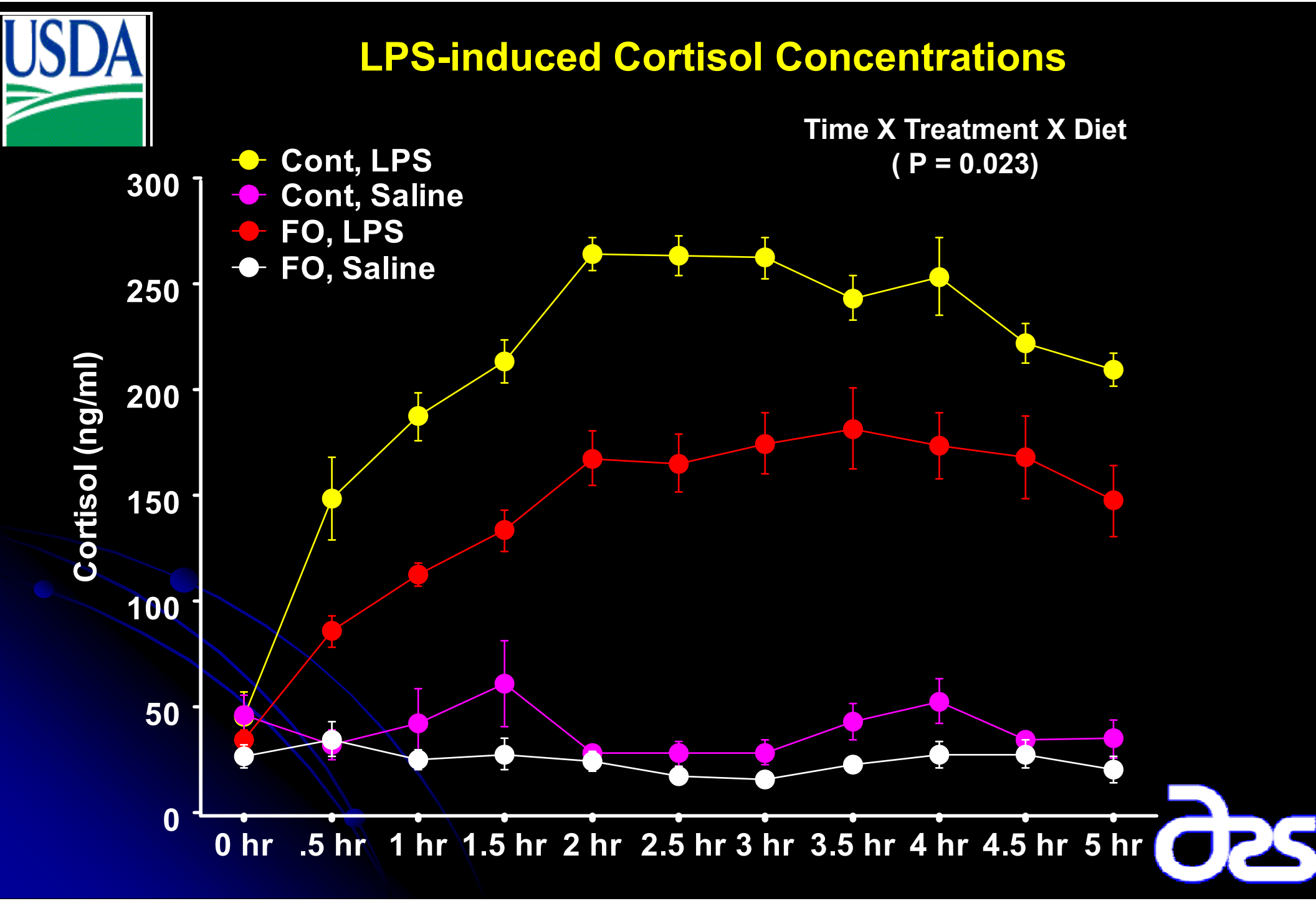
Serum TNF-α and IFN-γ

Body Weights

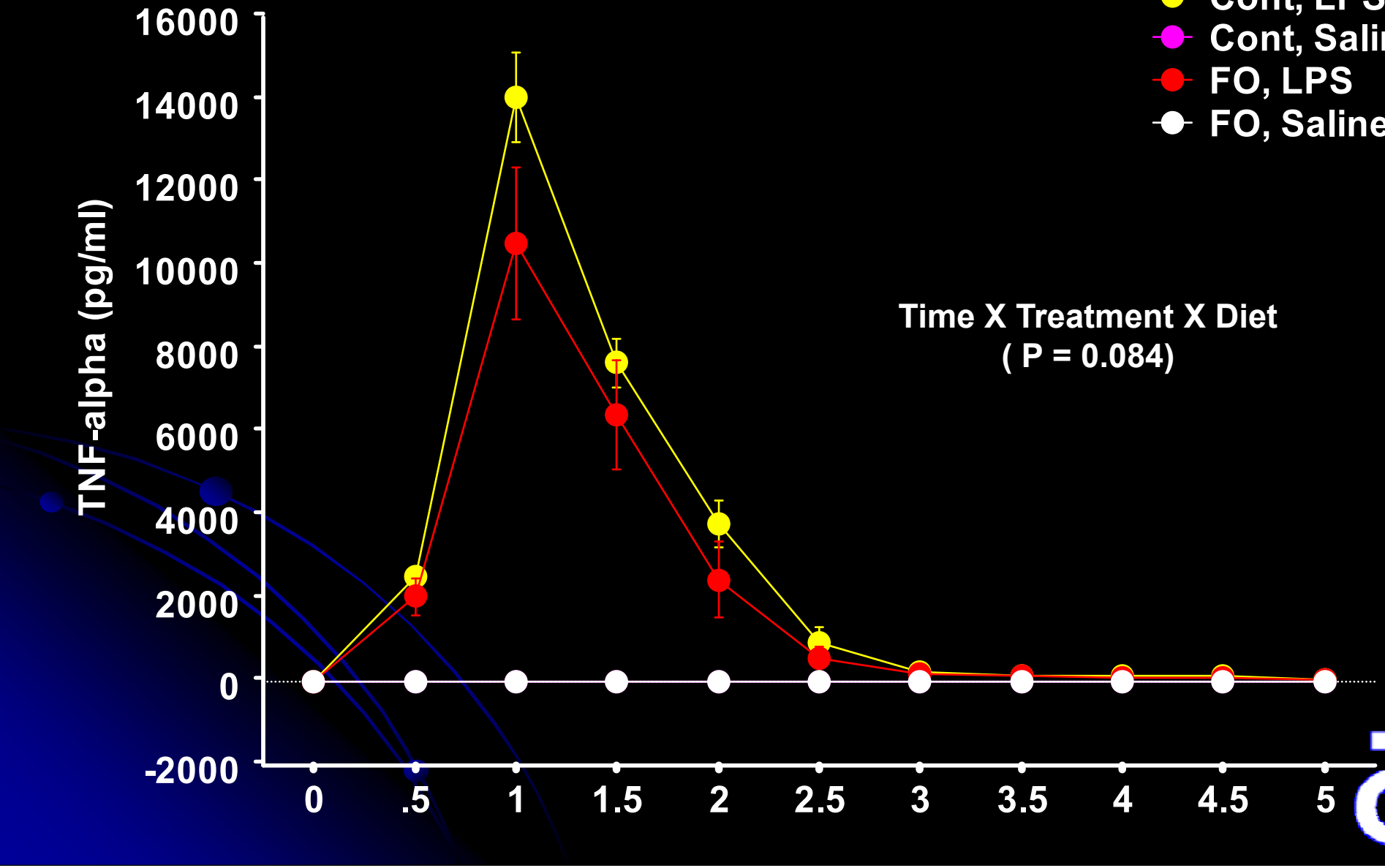


Basal Concentration of Cortisol

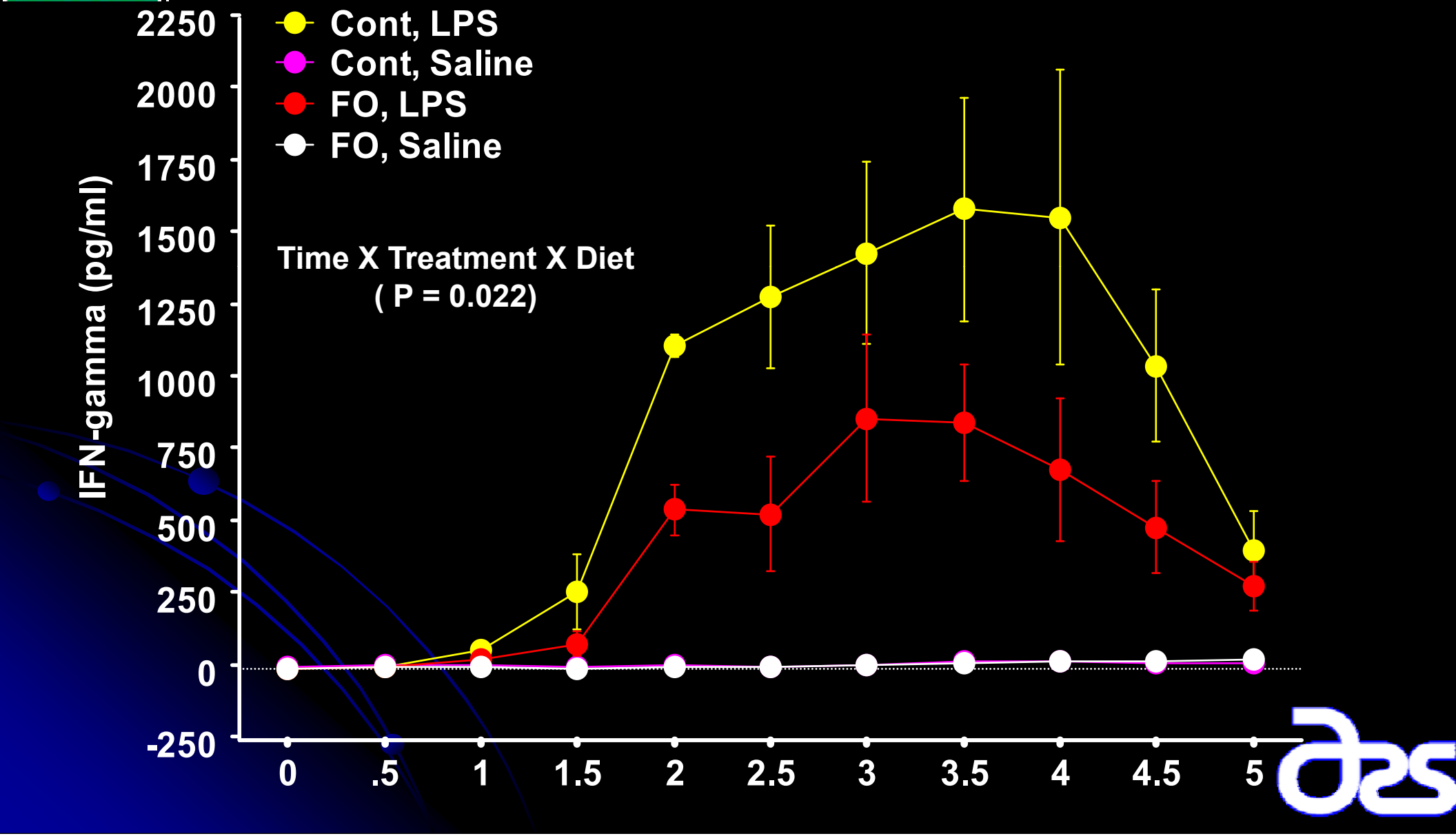
LPS-induced Cortisol Concentrations



LPS-induced TNF-alpha Concentrations



LPS-induced IFN-gamma Concentrations



Summary

Supplementing the weaned pig's diet with fish oil as a source of omega-3 fatty acids did not alter post-weaning gain over a 15 day period.

Fish oil supplementation tended to reduce basal cortisol and significantly lowered the cortisol response to to an LPS challenge.

Serum TNF-alpha following the LPS challenge tended to be reduced by dietary supplementation with fish oil.

LPS-induced IFN-gamma was significantly reduced in the fish oil supplemented pigs.

Implications

Utilizing nutritional supplements such as fish oil as a dietary source of omega-3 fatty acids clearly alters immunological parameters in a manner which could potentially have a beneficial impact on the young pig's overall health.

Future studies need to evaluate the possible beneficial effects of fish oil supplementation following a live pathogen challenge.

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Can dietary chromium alter the innate immune response of cattle to an endotoxin challenge?

Materials & Methods

Twenty crossbred steers (235 ± 4 kg BW) were placed on 1 of 2 dietary treatments (n=10/trt) and fed for 55 days:

Control (0 ppb chromium supplemented as chromium propionate)

Chromium (200 ppb chromium supplemented as chromium propionate)

On day 56, all steers were fitted with: a) rectal temperature (RT) devices that recorded RT at 1-min intervals for 24 h; and b) indwelling jugular catheters.

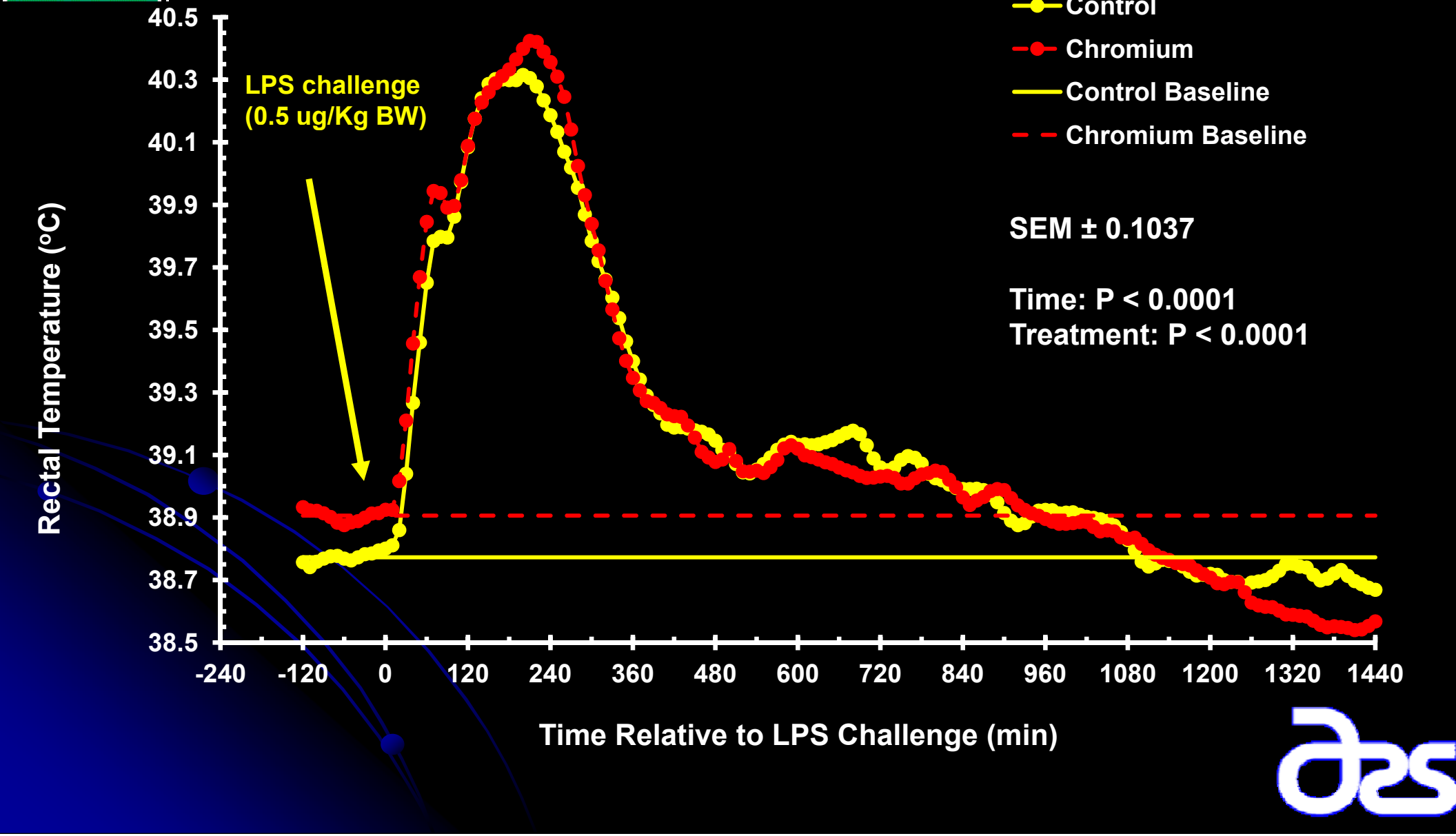
The next day blood samples were collected at 30-min intervals from -4 to 8 h and at 24 h relative to an i.v. infusion of lipopolysaccharide (LPS; 0.5 µg/kg BW) at 0 h.

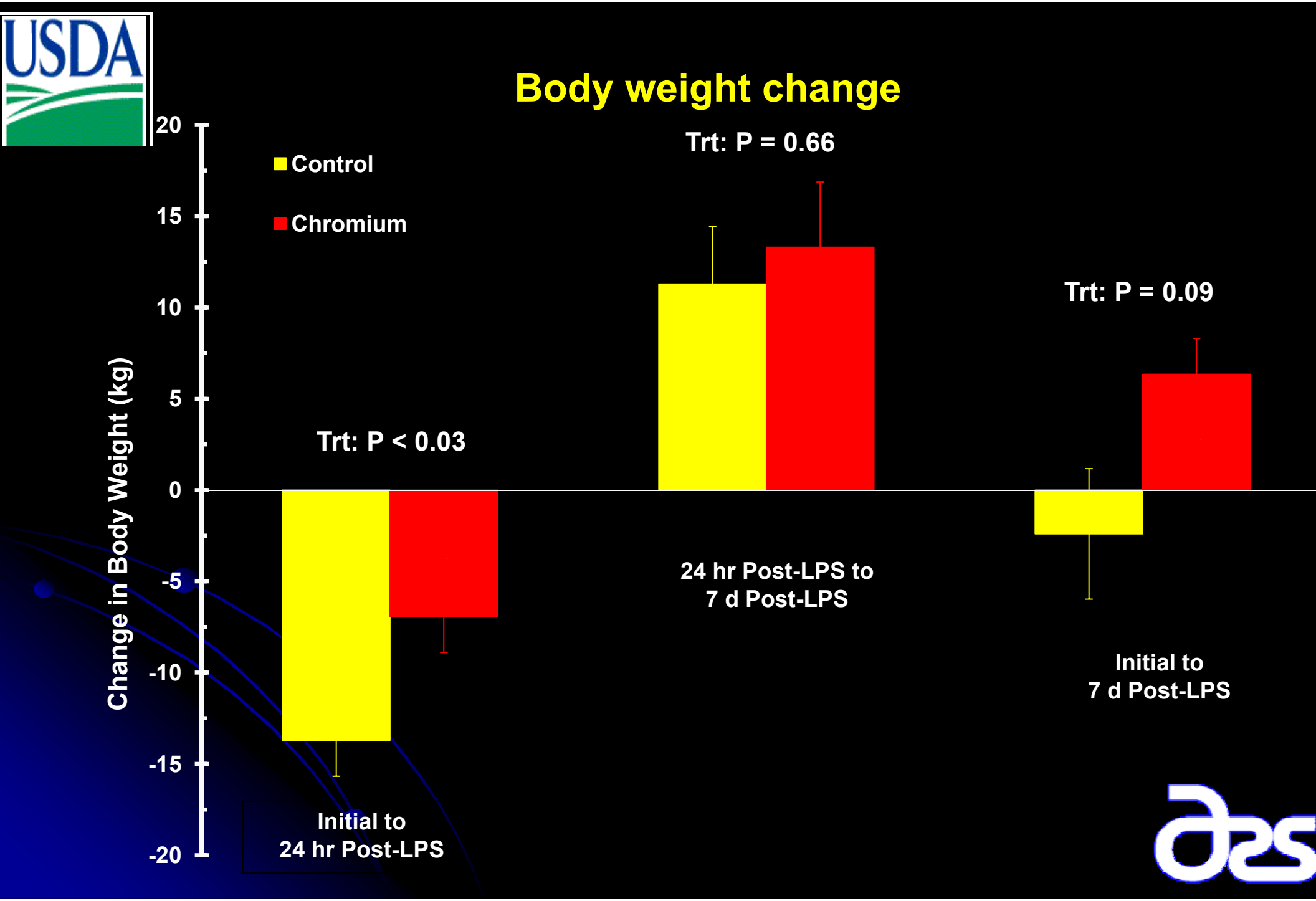
Physiological Results

Rectal Temperature

Body Weight Change

Rectal Temperature Response




Body weight change
Control
Chromium
Change in Body Weight (kg)
20
15
10
5
0
-5
-10
-15
-20
Trt: P < 0.03
Trt: P = 0.66
Trt: P = 0.09
Initial to
24 hr Post-LPS
24 hr Post-LPS to
7 d Post-LPS
Initial to
7 d Post-LPS

Proinflammatory Cytokine Response

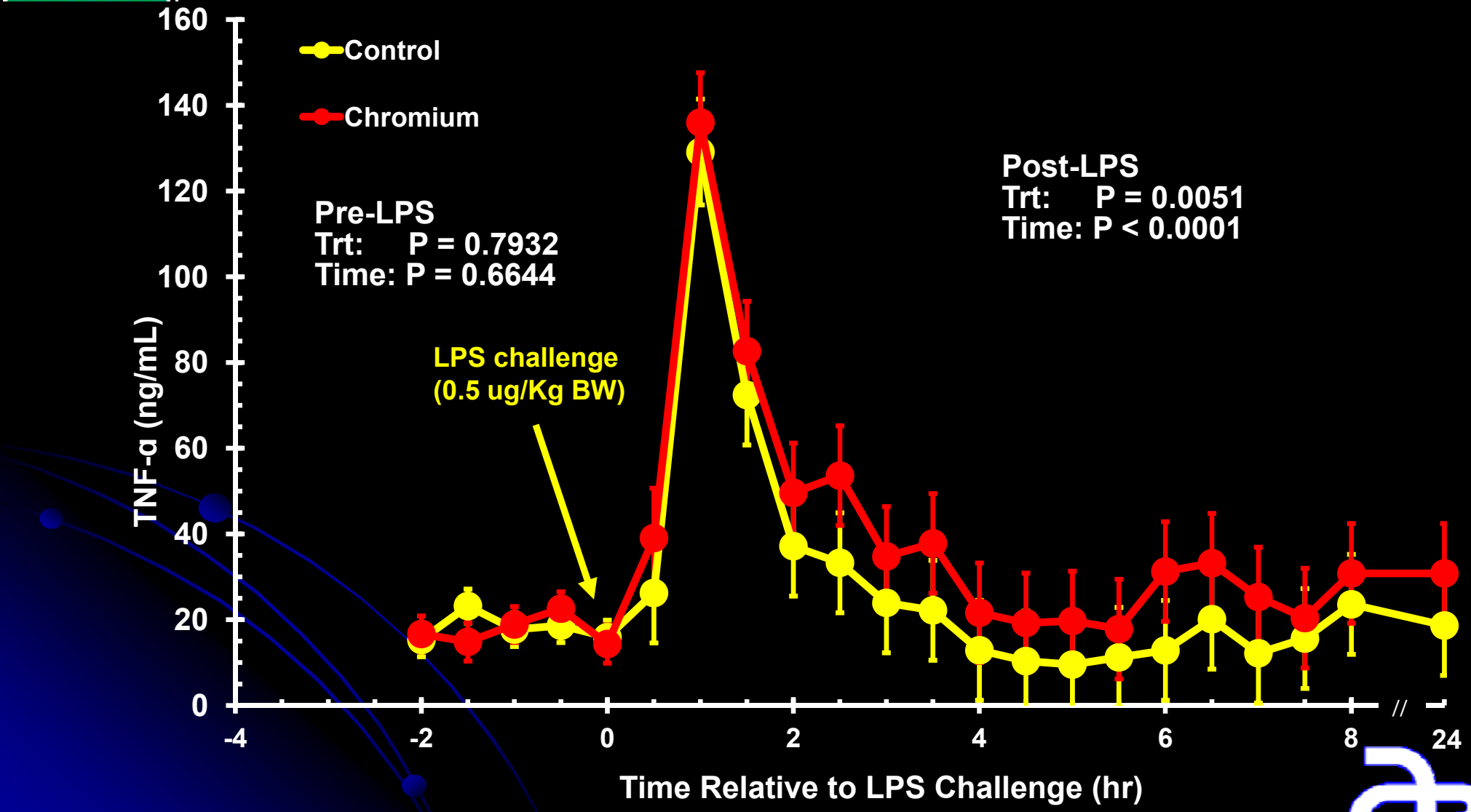
TNF-α

IFN-γ

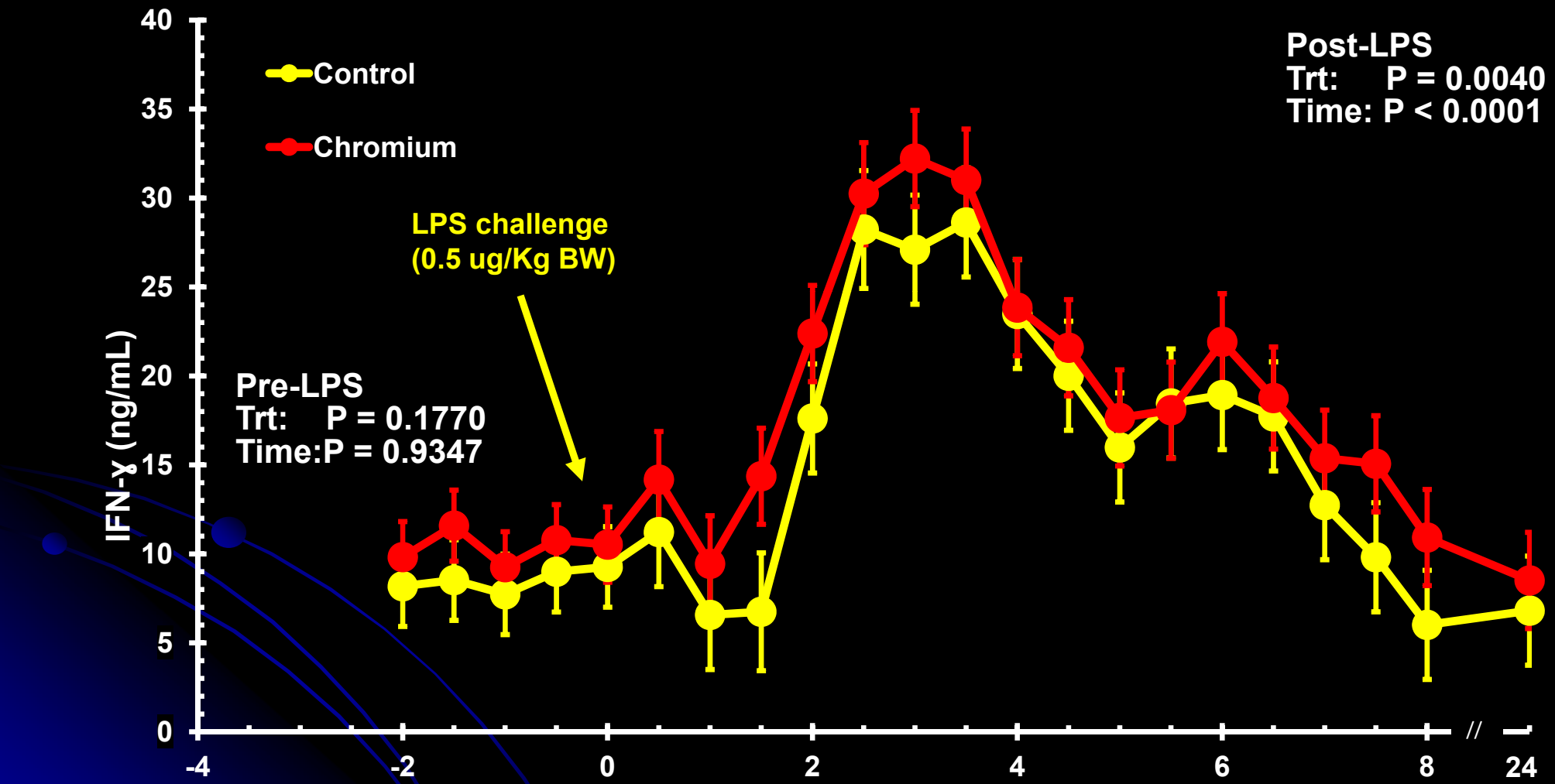
IL-6

B.

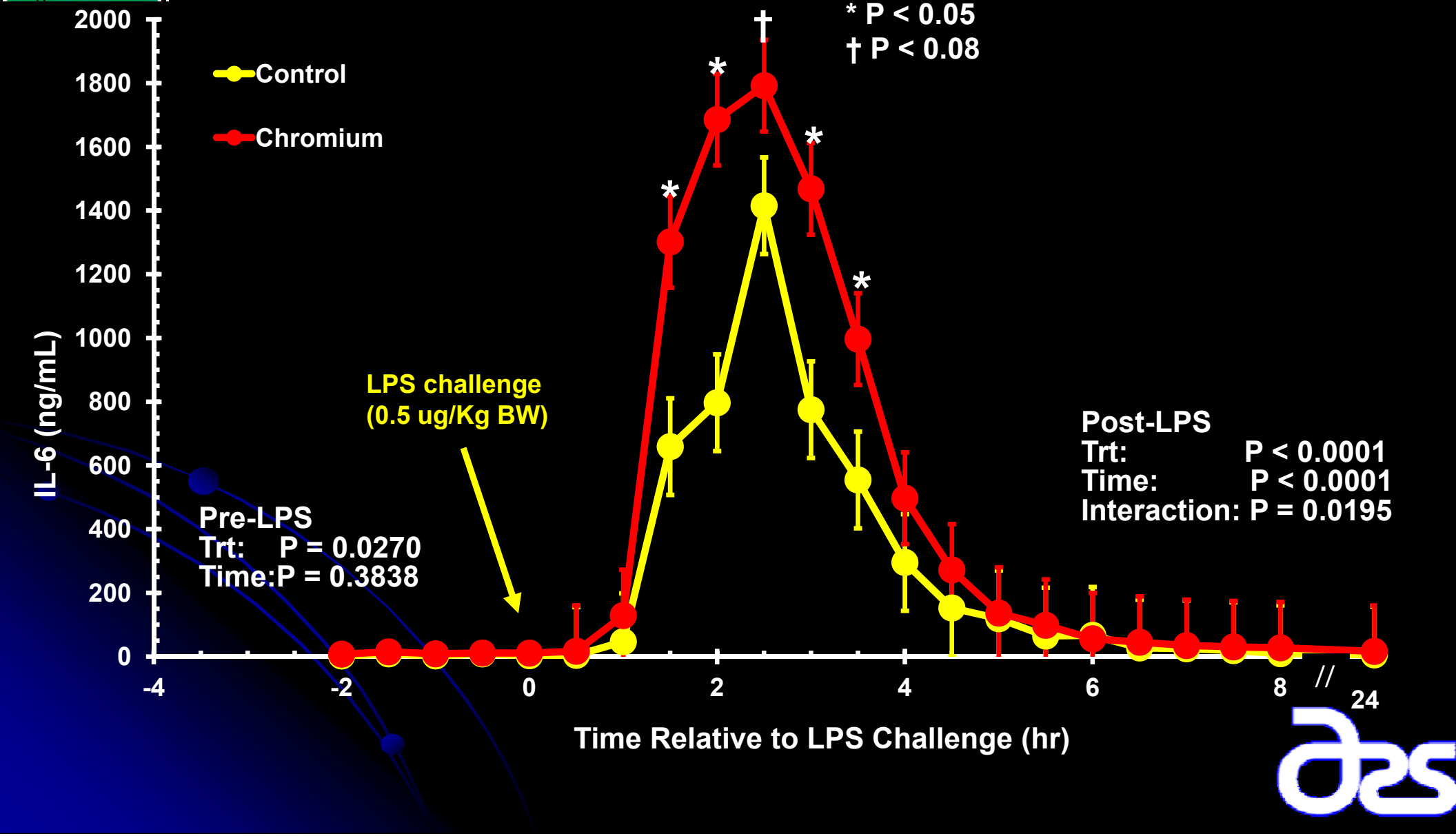
Serum concentration of TNF - alpha



Serum concentration of Interferon - gamma



Serum concentration of Interleukin - 6



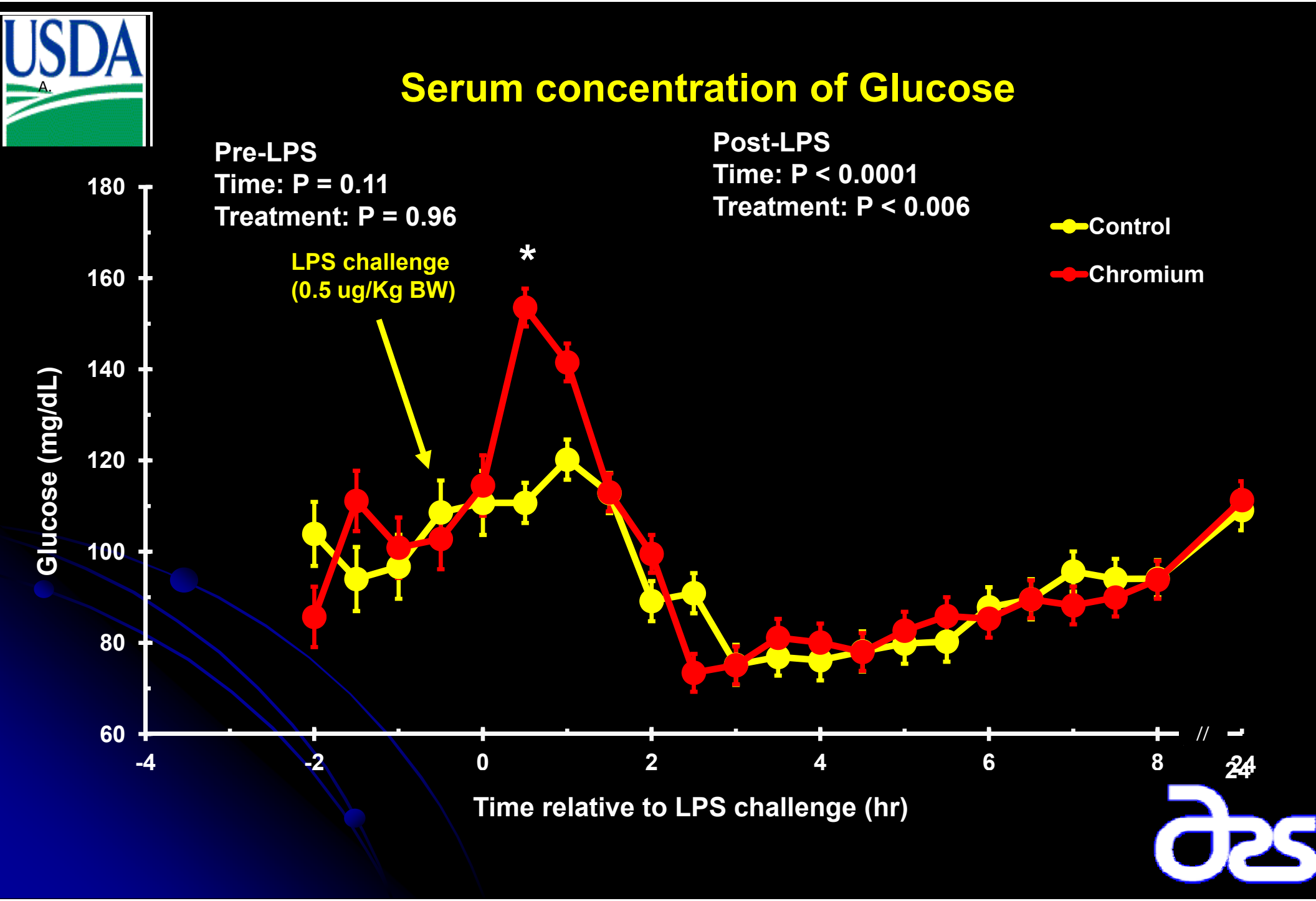
Metabolic Indicators

Glucose

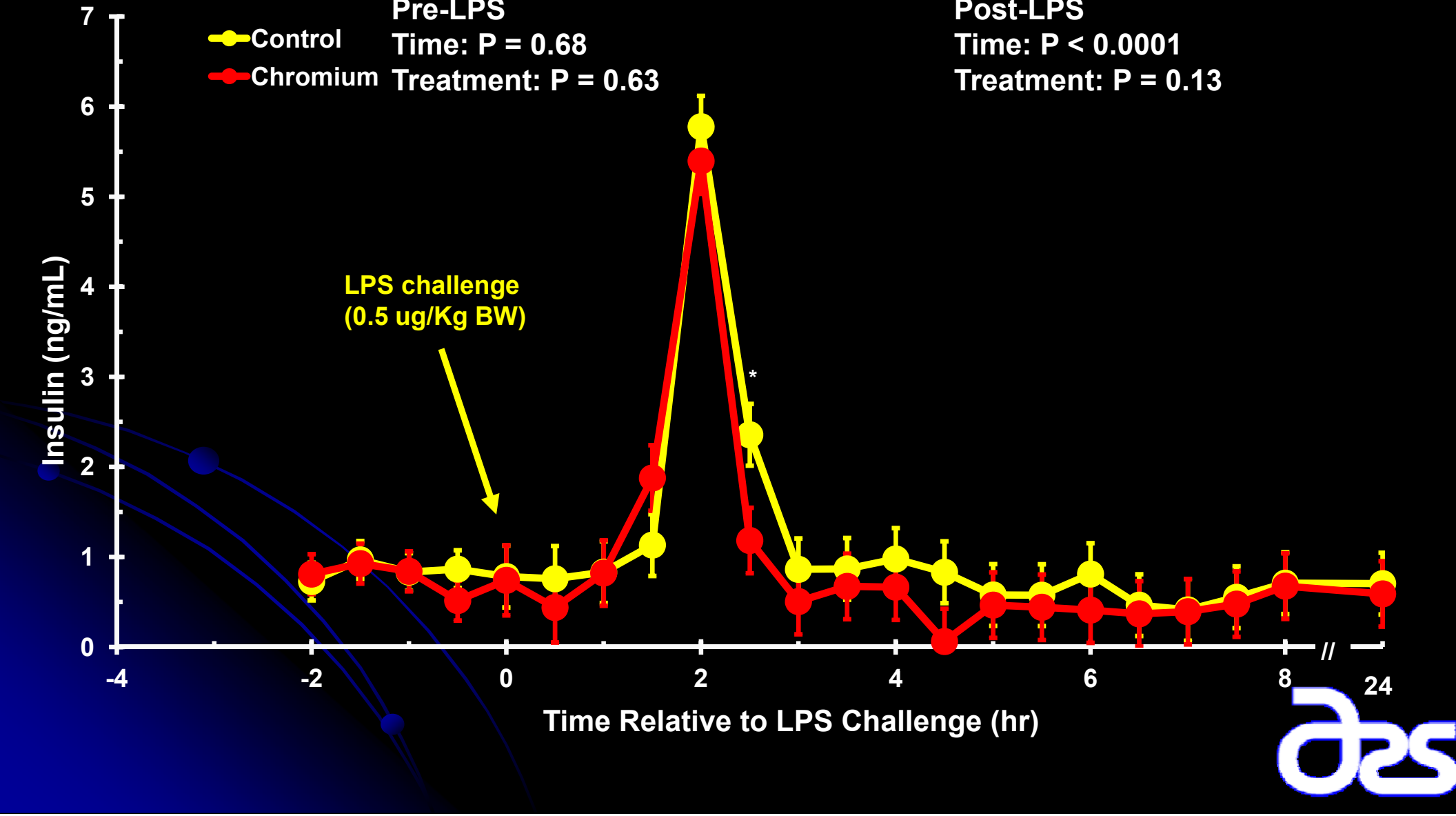
Insulin

NEFA

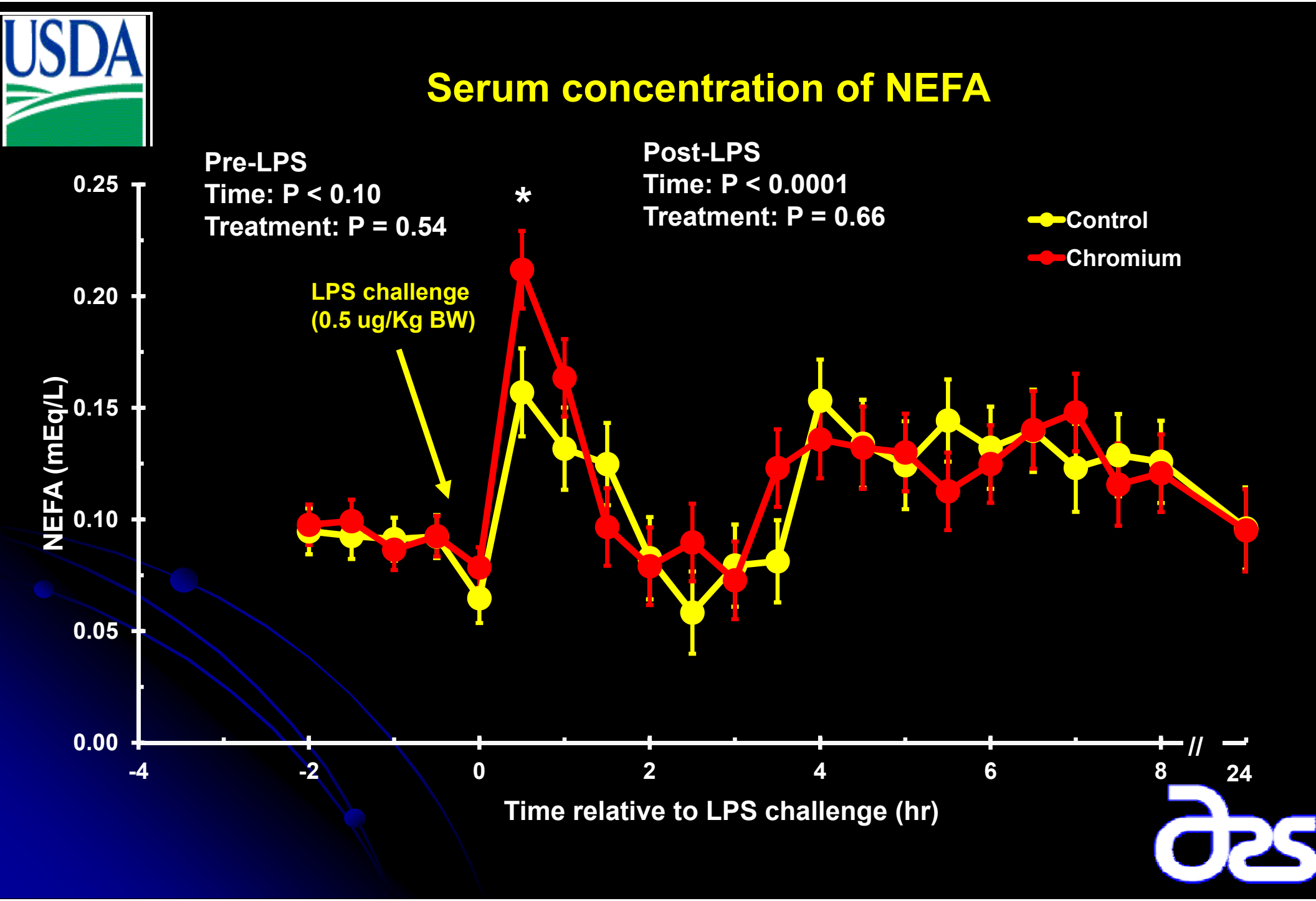
Serum concentration of Glucose



Serum concentration of Insulin



Serum concentration of NEFA



Summary

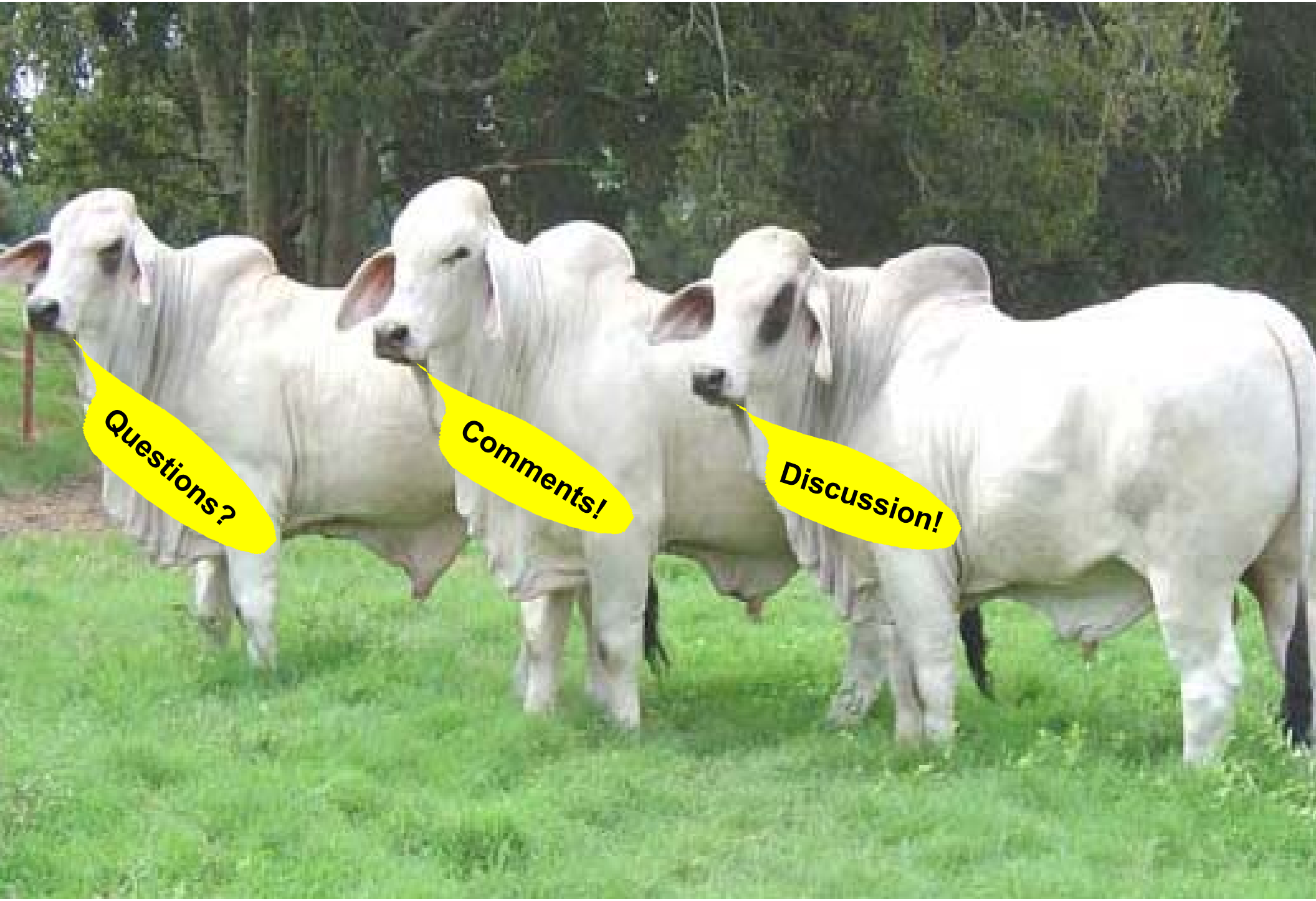
Chromium supplementation reduced the febrile and sickness behavior responses, and enhanced the cytokine response to LPS challenge.

These data suggest that feeding chromium supplemented as chromium propionate can enhance the acute phase response of steers to immune challenge, which may expedite recovery.

Overall Conclusion

Collectively, these data clearly demonstrate the existence of both naturally occurring and nutritionally induced changes in the stress and innate immune response of livestock. Additionally, these data highlight the need to extend our understanding and knowledge base with regard to the regulation of these systems within the production animal, as well as research animals.

Further elucidation of these biological systems in livestock will undoubtedly increase our capability of developing novel management practices that enhance production efficiency and overall health.


Questions?
Comments!
Discussion!