

# Evaluation of a Proprietary Slow-Release Oxytocin Formulation on Corpus Luteum Function in Mares

Brendan Sarnecky

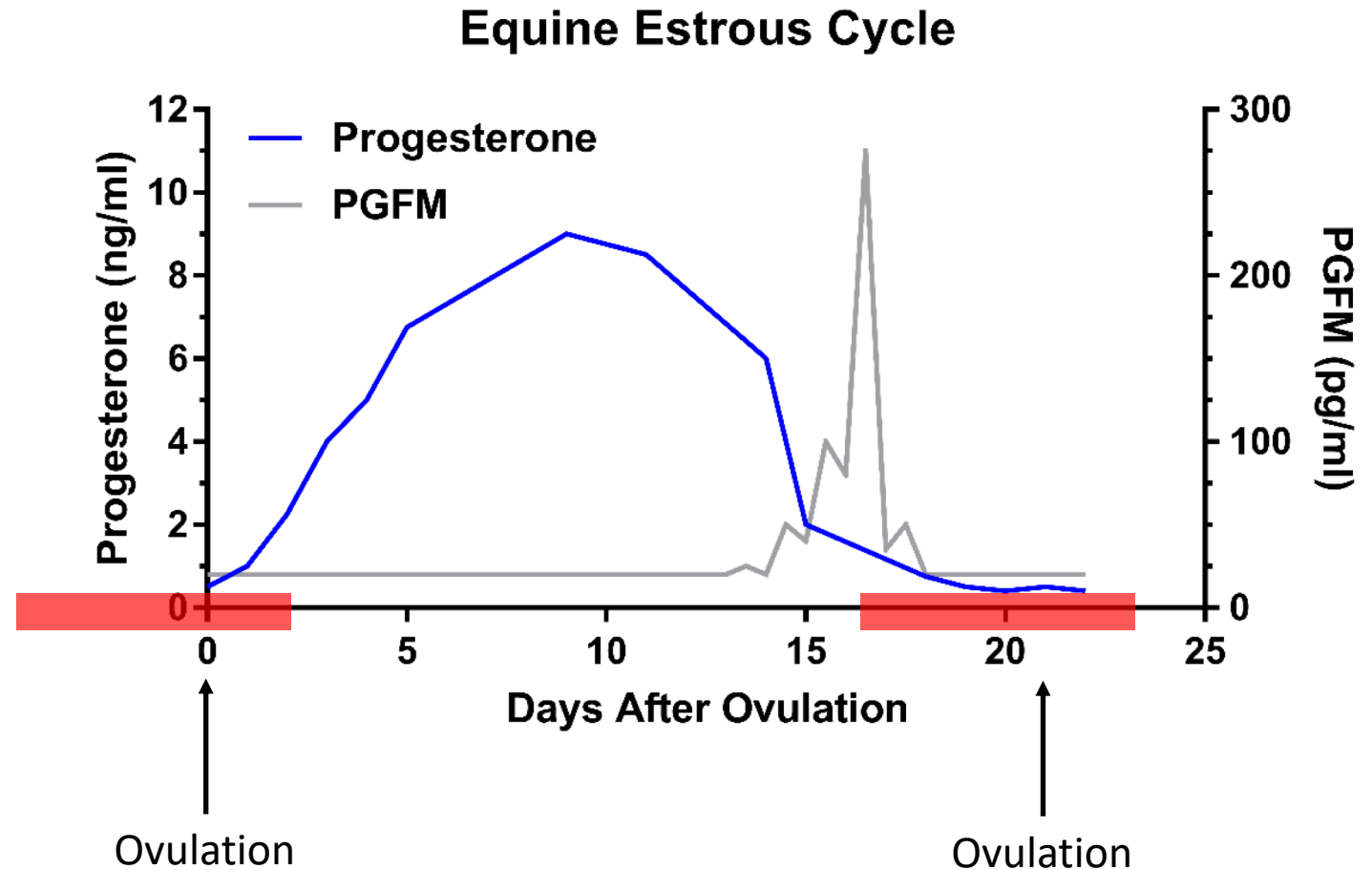
Dirk K. Vanderwall, Holly M. Mason, Stephen M. Kirschner,  
Benson Ambrose, Theda L. Parker



# Mare Estrous Cycle

Adapted from Neely, 1985

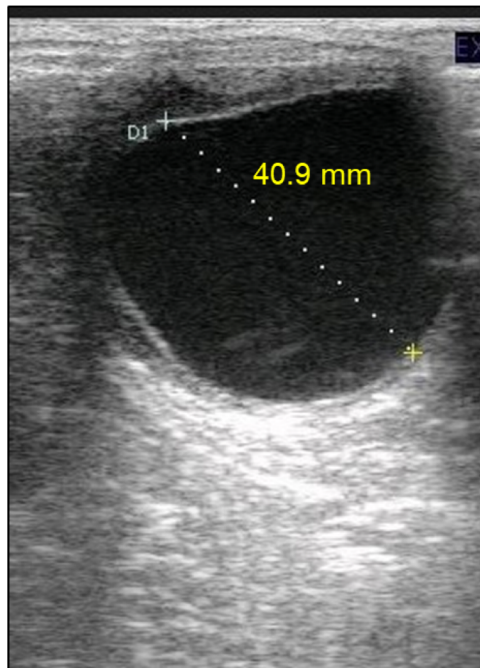
- 21 days
  - 1 week **estrus** (i.e., “heat”)
    - Follicular phase
    - Follicle- **Estrogen**
  - 2 weeks diestrus
    - Luteal phase
    - Corpus Luteum (CL)- **Progesterone**
- Uterus
  - Prostaglandin (PGF2α)
    - Measured as PGFM
  - Luteolysis
- Posterior Pituitary- **Oxytocin**
  - Role in luteolysis



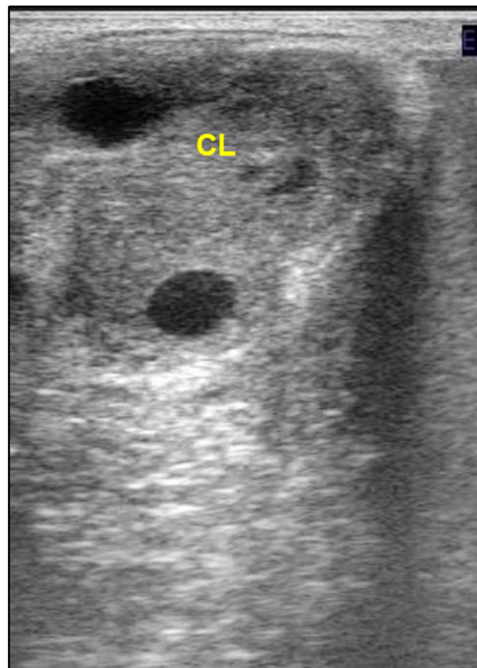
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Images of Ultrasonographic Morphology

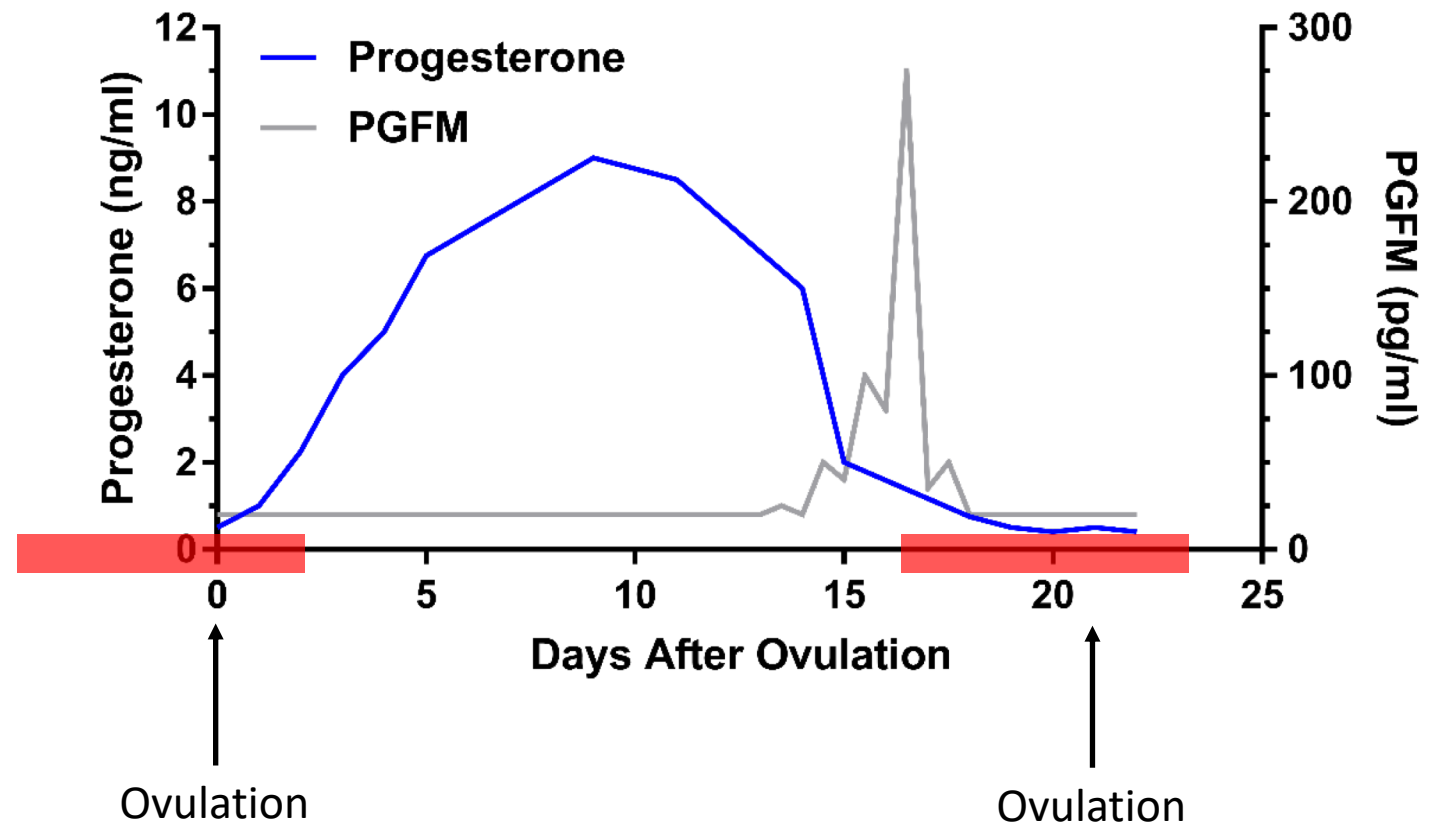


Follicle



Corpus Luteum

Equine Estrous Cycle



# Estrous Behavior (i.e., in heat)



Courtesy of Dr. Vanderwall



The Horse Magazine: March 2017



# Estrous Behavior (i.e., in heat)



Courtesy of Dr. Vanderwall



The Horse Magazine: March 2017



# Estrus Suppression in the Performance Mare



[https://cdn.shopify.com/s/files/1/0002/0899/4306/articles/GuerdatSteveSUI-WEG18brinkman9-19jRE2-9561\\_720x.jpg?v=1537455575](https://cdn.shopify.com/s/files/1/0002/0899/4306/articles/GuerdatSteveSUI-WEG18brinkman9-19jRE2-9561_720x.jpg?v=1537455575)



The Horse Magazine: March 2017

# Methods of Estrus Suppression

- Administration of exogenous progesterone/progestins
  - E.g., Oral Altrenogest
- Extending the functional span of the corpus luteum (CL)
  - Intrauterine glass ball
  - Oxytocin





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Courtesy of Dr. Vanderwall



# Oxytocin

- Released from the posterior pituitary gland
- Pulsatile nature
- Very short half-life
- Functions
  - Milk let-down
  - Stimulates uterine contractions
  - Oxytocin-Prostaglandin luteolytic pathway
- Therapeutic use to prolong CL function
  - 8-Day Protocol (1x daily: days 7-14)
  - Slow-release Oxytocin (SR-OT: two treatments)





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Original Research

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# Hypothesis

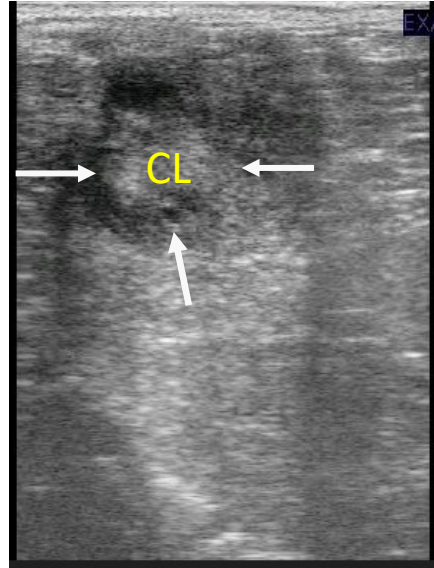
- A two-injection proprietary SR-OT protocol will deliver an appropriate amount of oxytocin for a sufficient duration of time to inhibit luteolysis

# Objectives

- Determine if IM administration of 2,400 IU of SR-OT once on days 7 and 10 after ovulation would prolong CL function in treated mares compared to a non-treated control group
- Reduce number of injections from previous aqueous oxytocin methods

## Ovulation

Detected via trans-rectal  
ultrasound/palpation



**Groups**  
Control n=8 mares  
SR-OT Treatment n=8 mares

## Collect Blood

3 times per week  
Until day 50

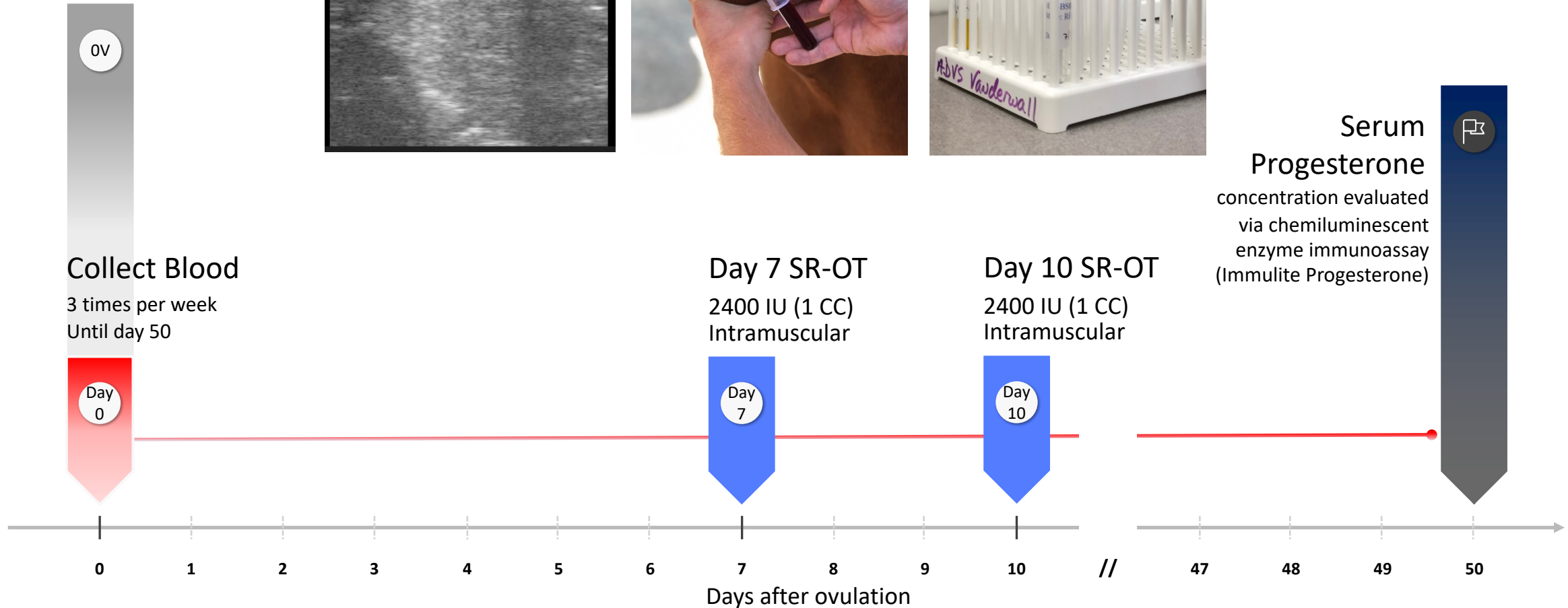
## Day 7 SR-OT

2400 IU (1 CC)  
Intramuscular

## Day 10 SR-OT

2400 IU (1 CC)  
Intramuscular

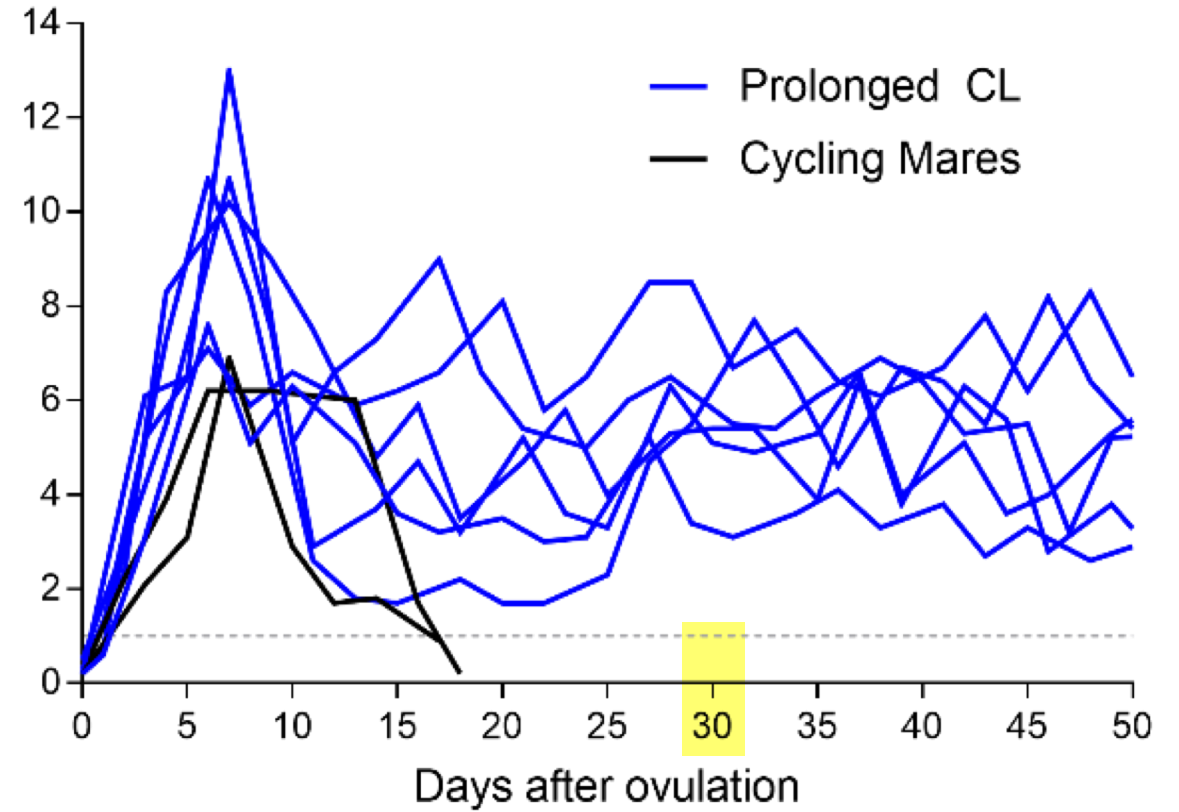
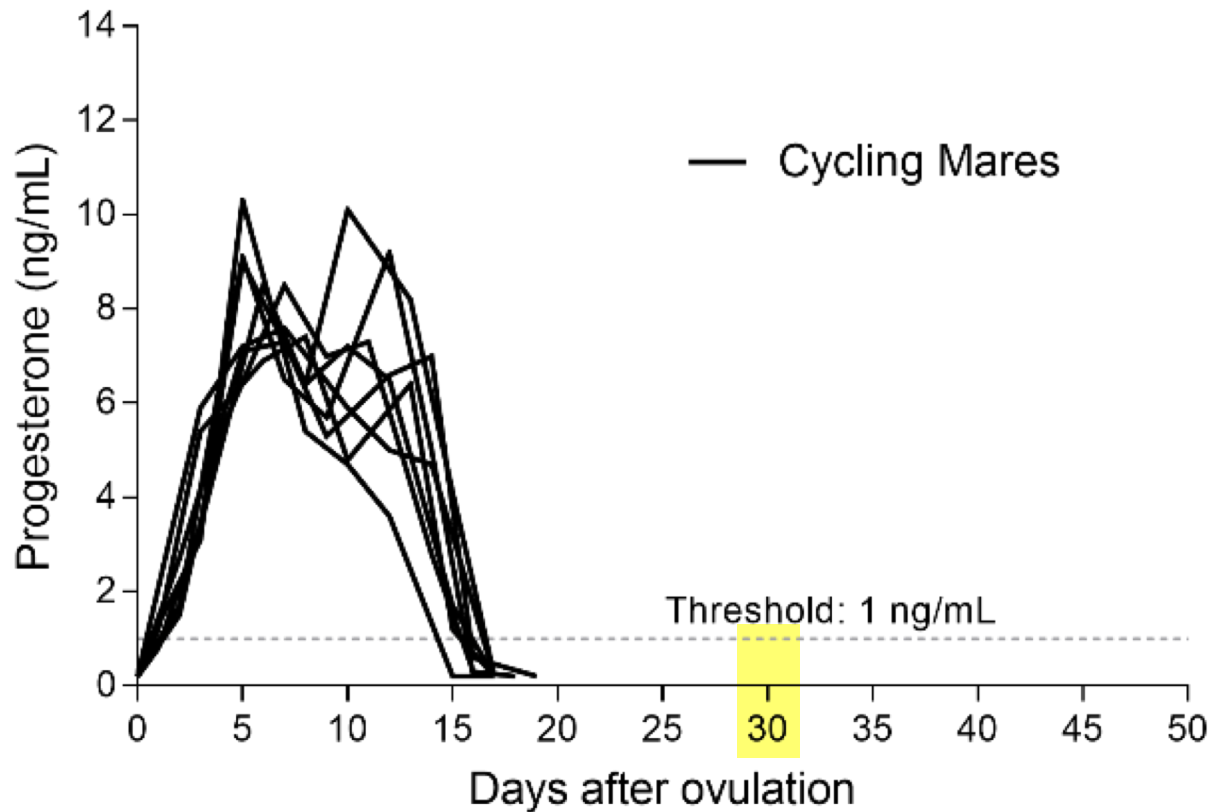
**Serum  
Progesterone**  
concentration evaluated  
via chemiluminescent  
enzyme immunoassay  
(Immulite Progesterone)





# Results

- 0/8 control mares with prolonged luteal function\*
- 6/8 treated mares with prolonged luteal function\*



- Prolonged luteal function defined as >1 ng/ml for over 30 days
- \* Prolonged function compared with Fisher's exact test;  $P < .01$

# Conclusions

- SR-OT administered on days 7 and 10 is an effective method of prolonging luteal function
- This proprietary SR-OT formulation provides a 75% reduction in number of treatments needed in previous aqueous oxytocin methods

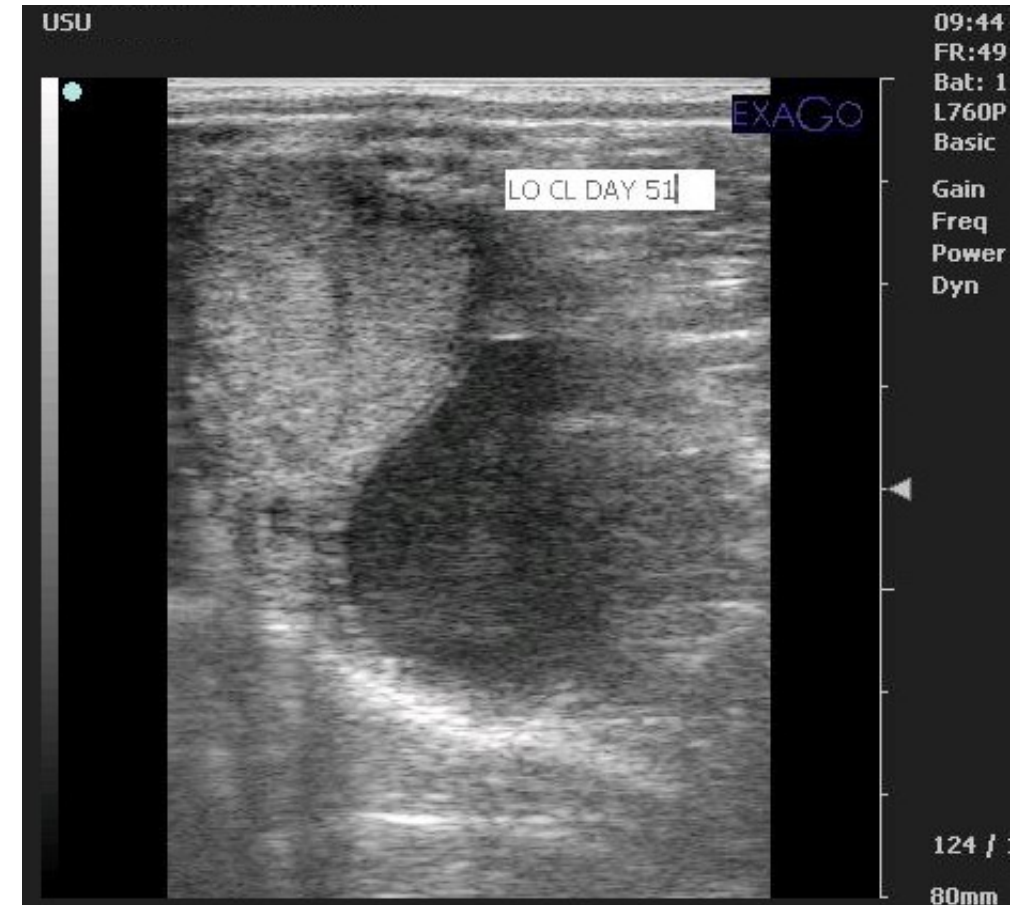


# Acknowledgements

- Utah Agricultural Experiment Station (Project # UTA01157)
- Wildlife Pharmaceuticals, Windsor, CO.
- JoAnna Buschmann, Ashlee Buist, Sherrie Petty, and Bettina Conrad

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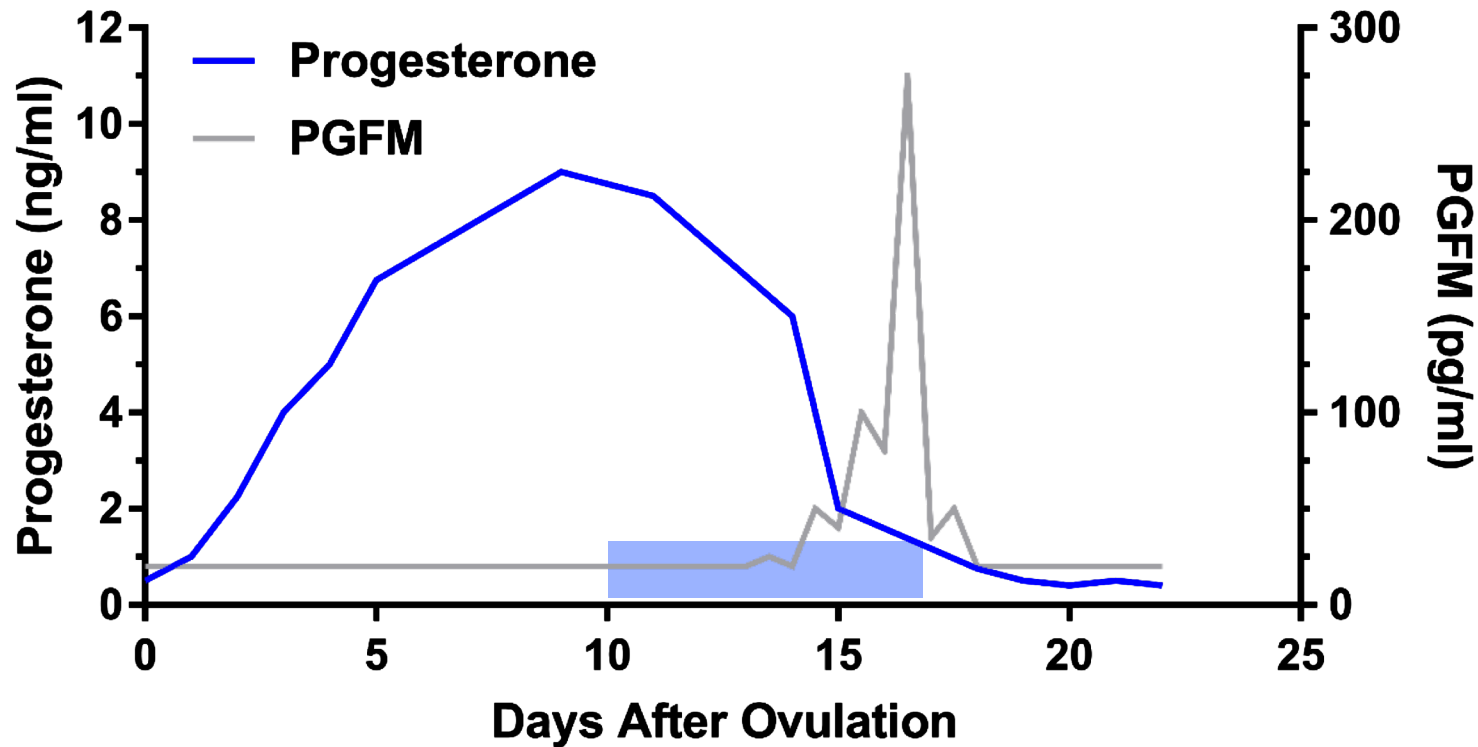




# Supporting Slides

# Pro- vs Anti-Luteolytic Functions of Oxytocin

## Equine Estrous Cycle



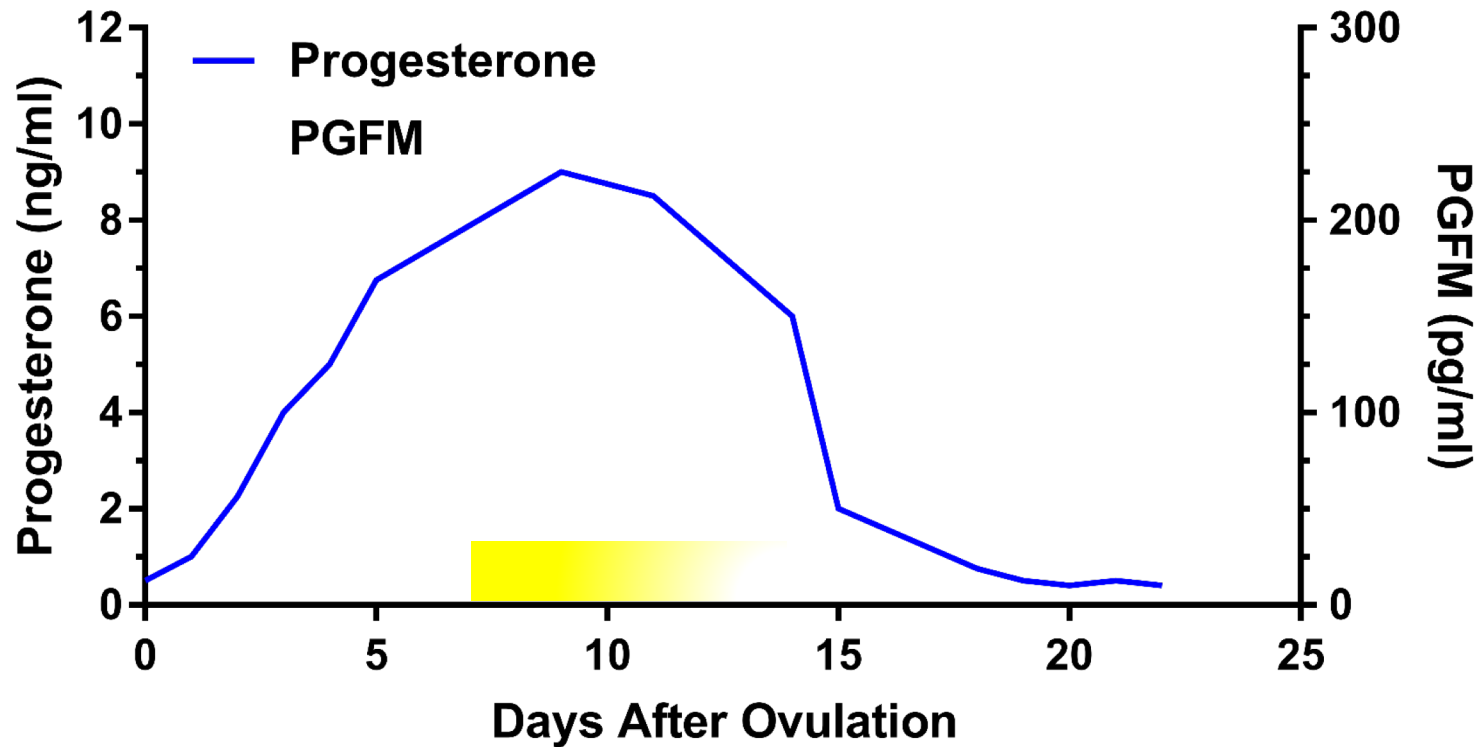
### Pro-Luteolytic

- Oxytocin after day 10
  - Binds to oxytocin receptor at endometrial epithelium
  - Stimulates secondary messengers associated with PGF2 $\alpha$  synthesis
    - COX II
  - PGF2 $\alpha$  circulates through the blood stream and targets the CL
  - CL undergoes luteolysis

Adapted from Neely, 1985

# Pro- vs Anti-Luteolytic

## Equine Estrous Cycle



### Anti-Luteolytic

- Oxytocin administered **before day 10 and continued**
  - Binds to oxytocin receptor at endometrial epithelium
  - Lack of secondary messenger
  - Inhibits the upregulation of secondary messengers
    - Specifically COX II
  - No “spontaneous” luteolysis
  - CL has prolonged function
    - Up to 90 days

Adapted from Neely, 1985