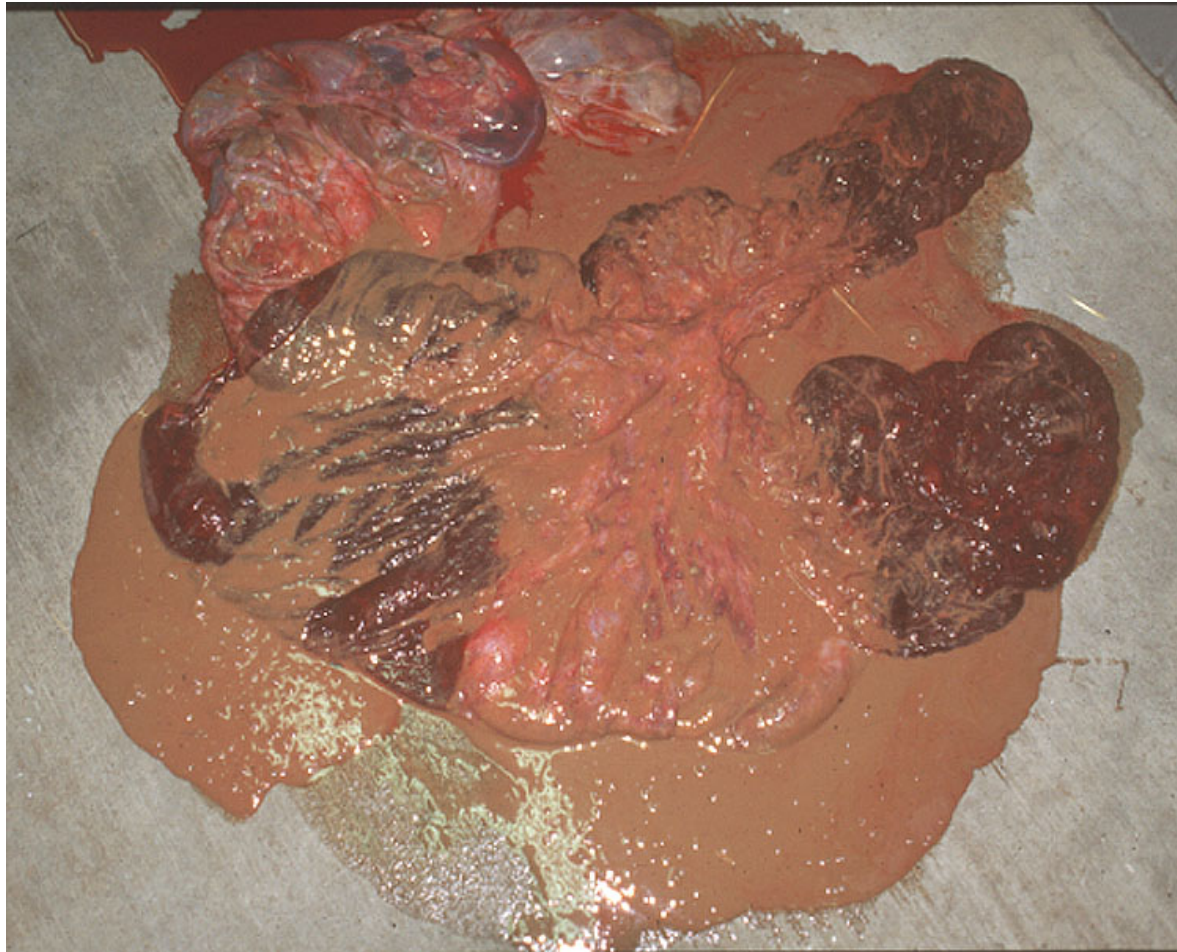


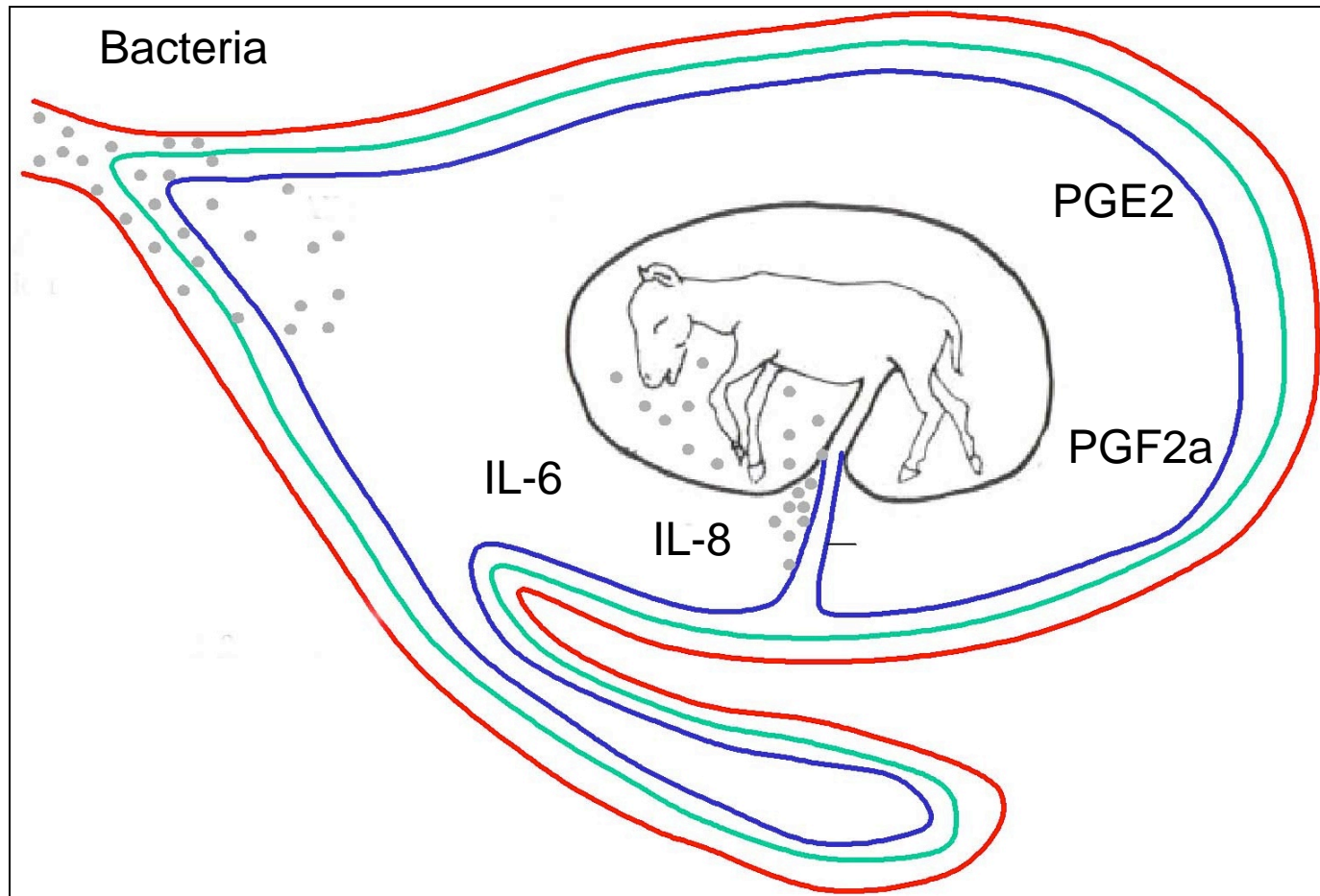


# What's New in the Pregnant Mare

Karen Wolfsdorf DVM Dipl. ACT



# Ascending Placentitis



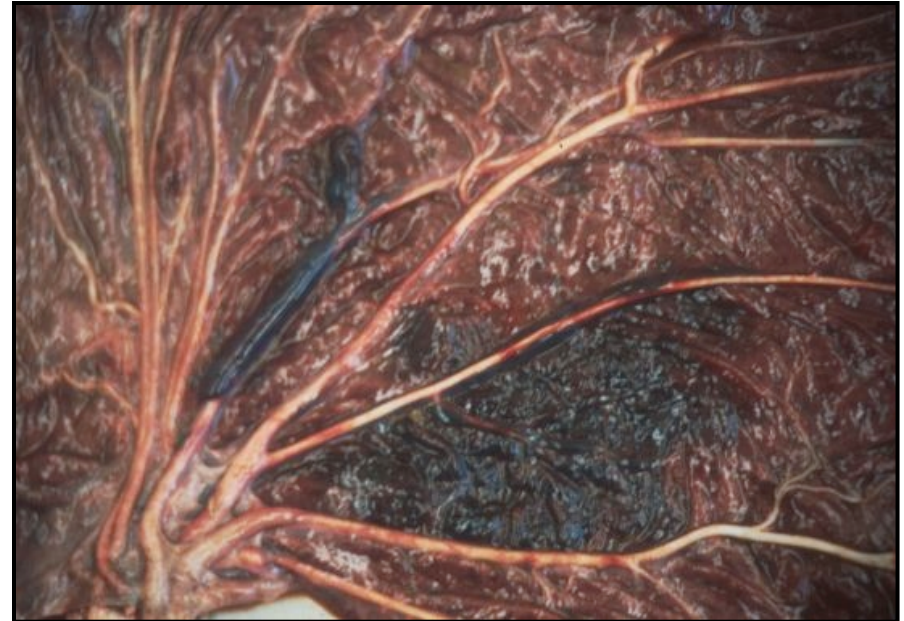


## Ascending Placentitis





## Hematogenous Placentitis



## Focal Muroid Placentitis





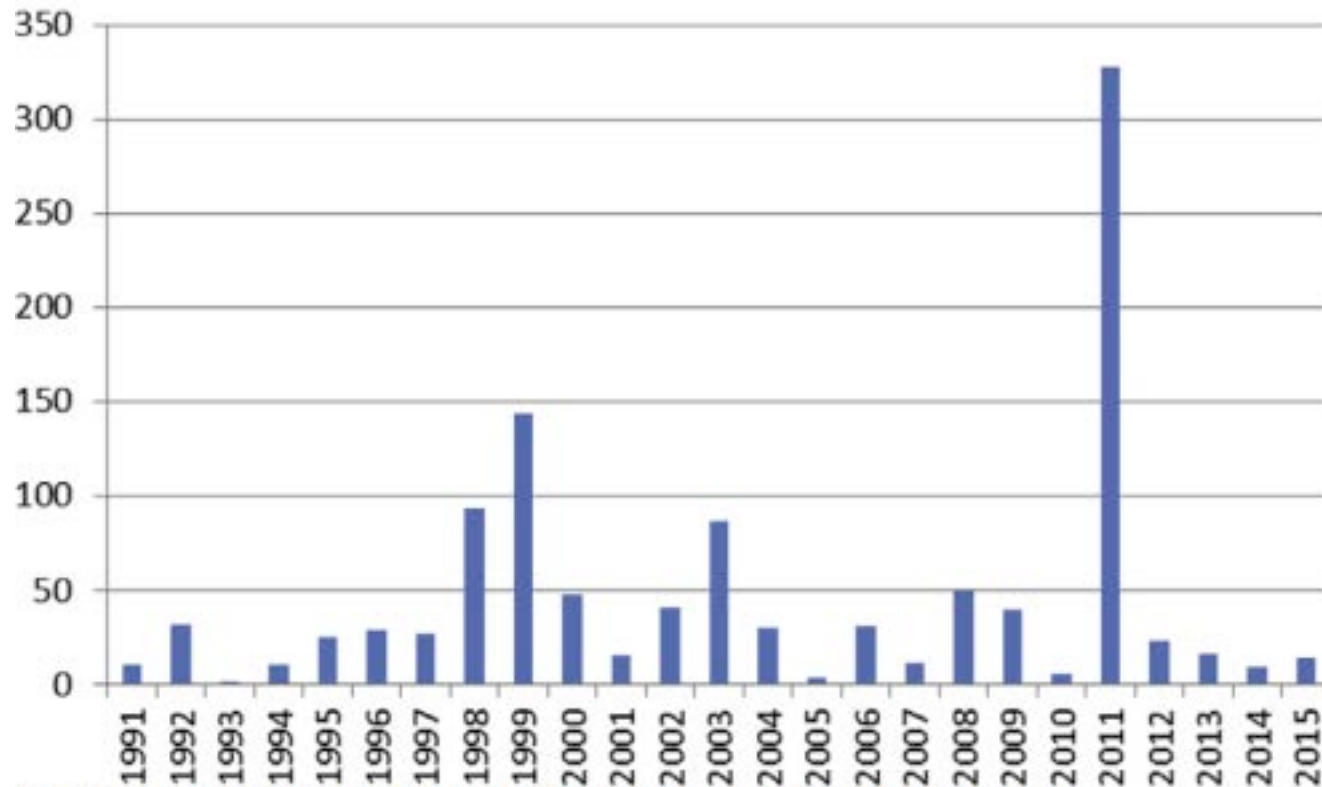
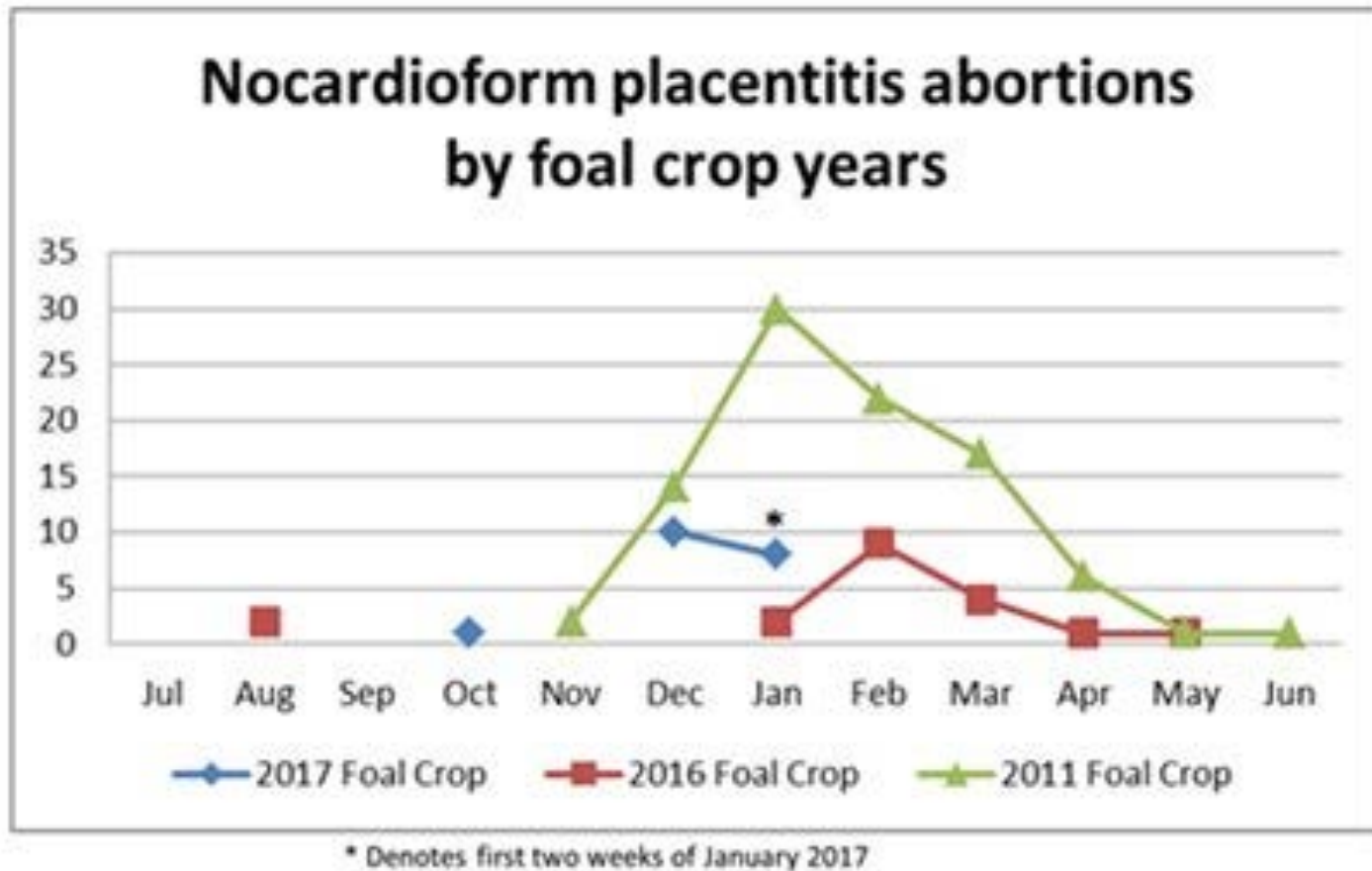


Figure 1. Twenty-five years of NPA cases (1133) in Kentucky.





## Clinical signs

- Premature mammary gland development
- Cervical softening
- Vaginal discharge

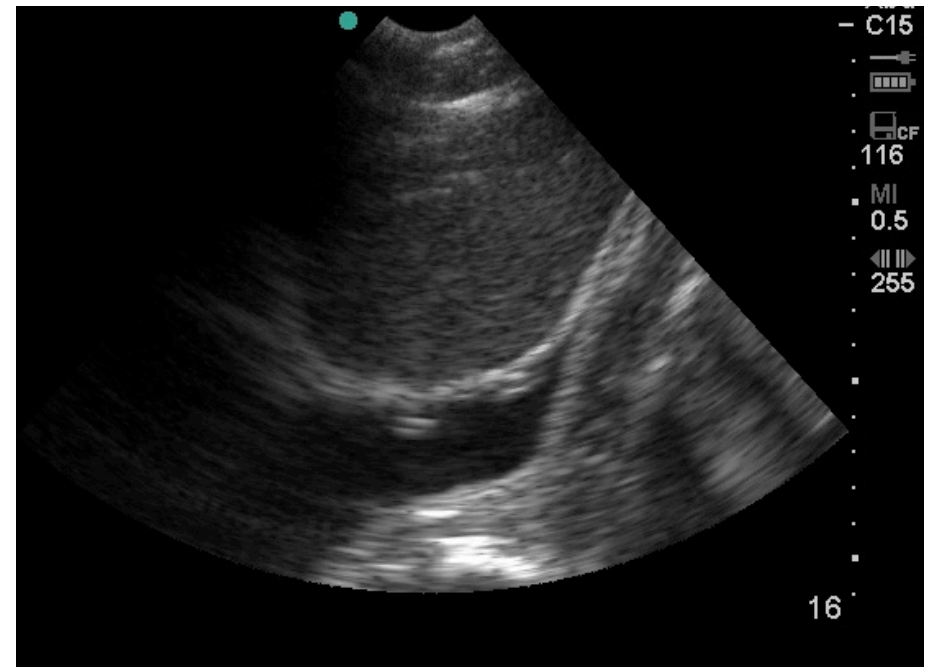


## Diagnostics:

- General physical
- Rectal palpation
- Ultrasound- trans-rectal, trans-abdominal
- Hormone profiles
- Culture(if discharge)
- Pulse wave color doppler
- Leptospirosis titers

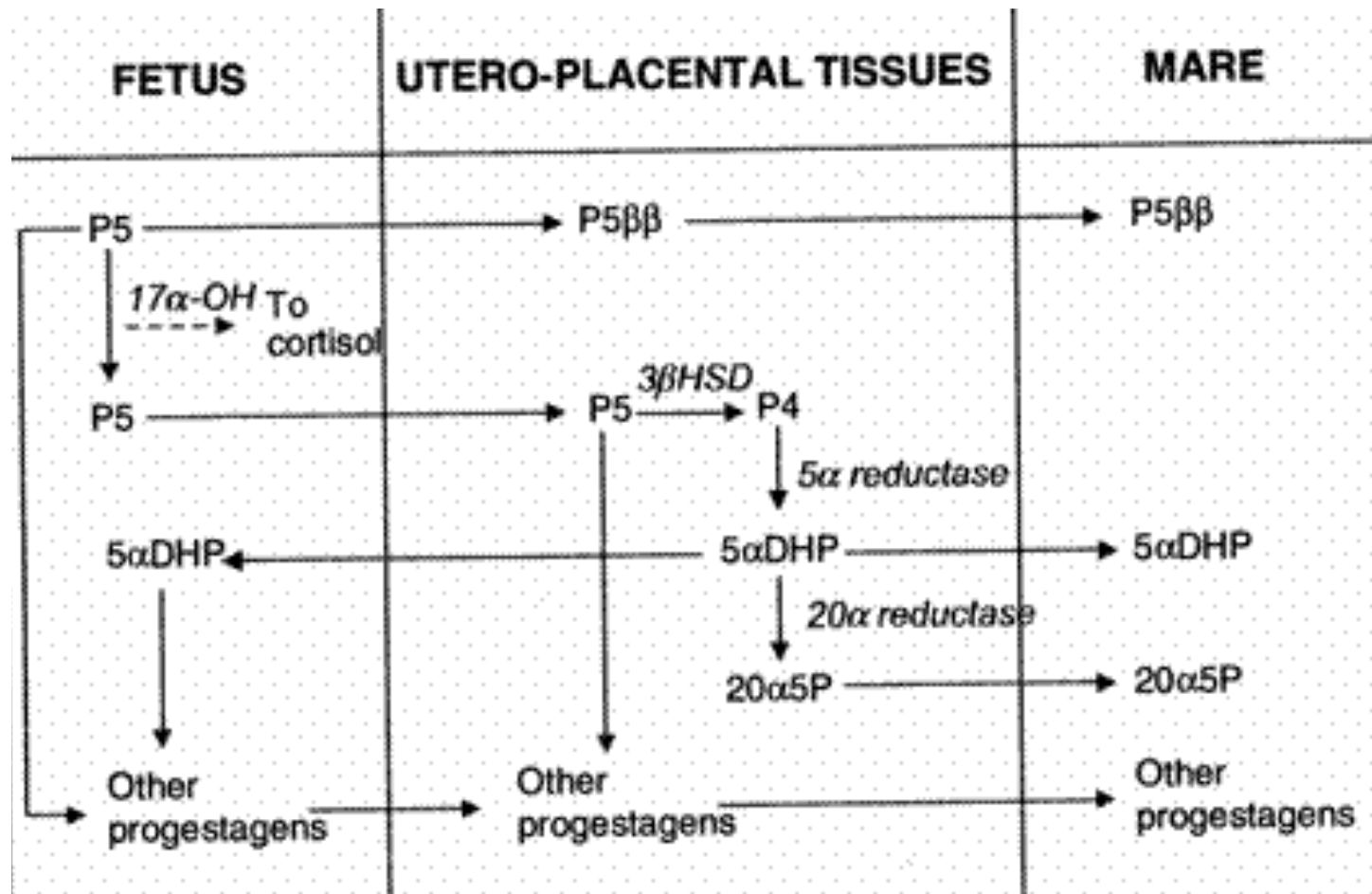


# Placentitis

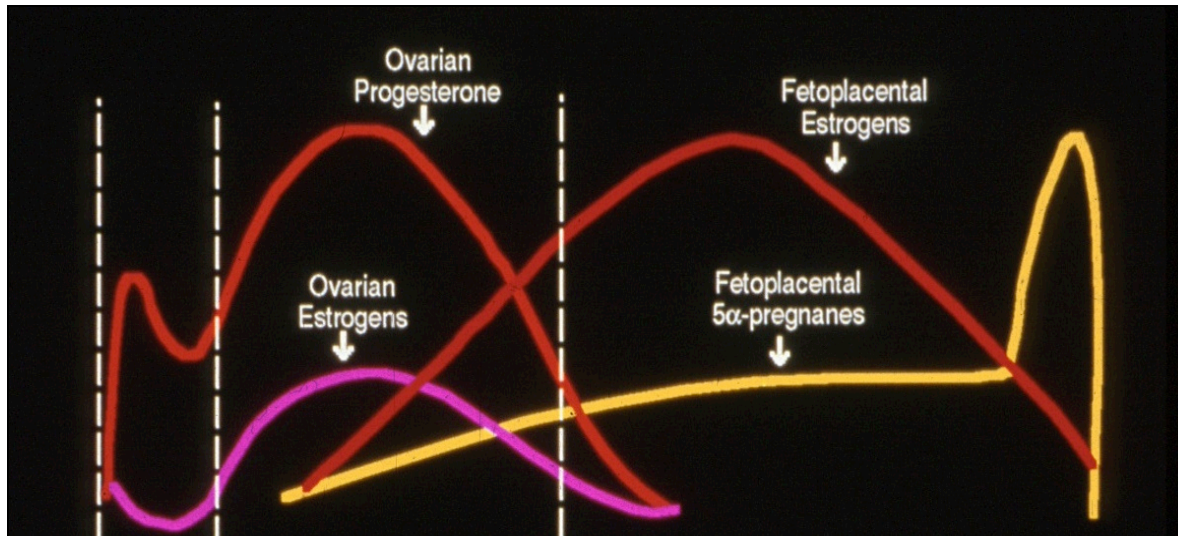




## Placentitis

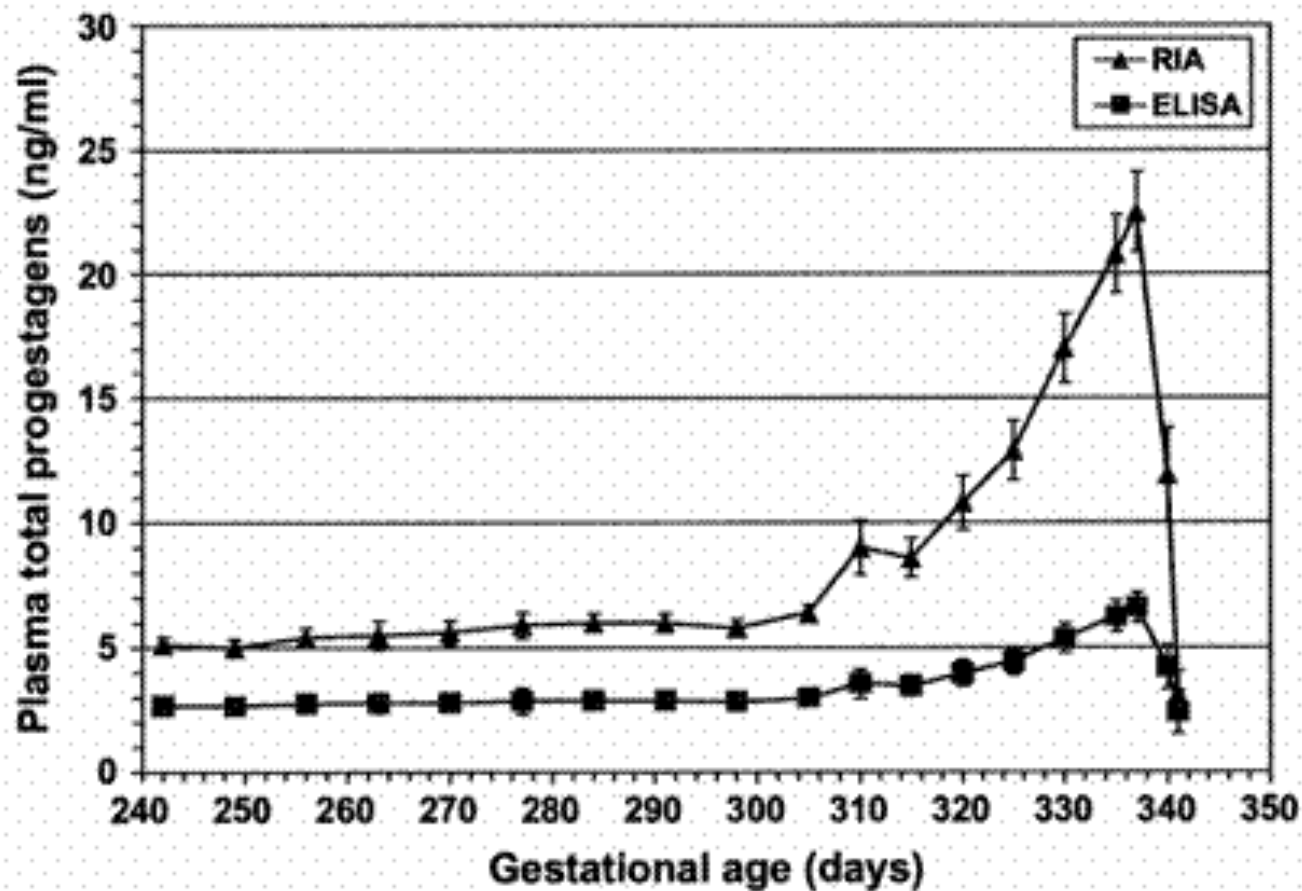


- Some cross-reactivity with P<sub>4</sub> assays
- Concentrations fluctuate
- Progestin assays + CTUP



(Sheerin, Morris 2007)

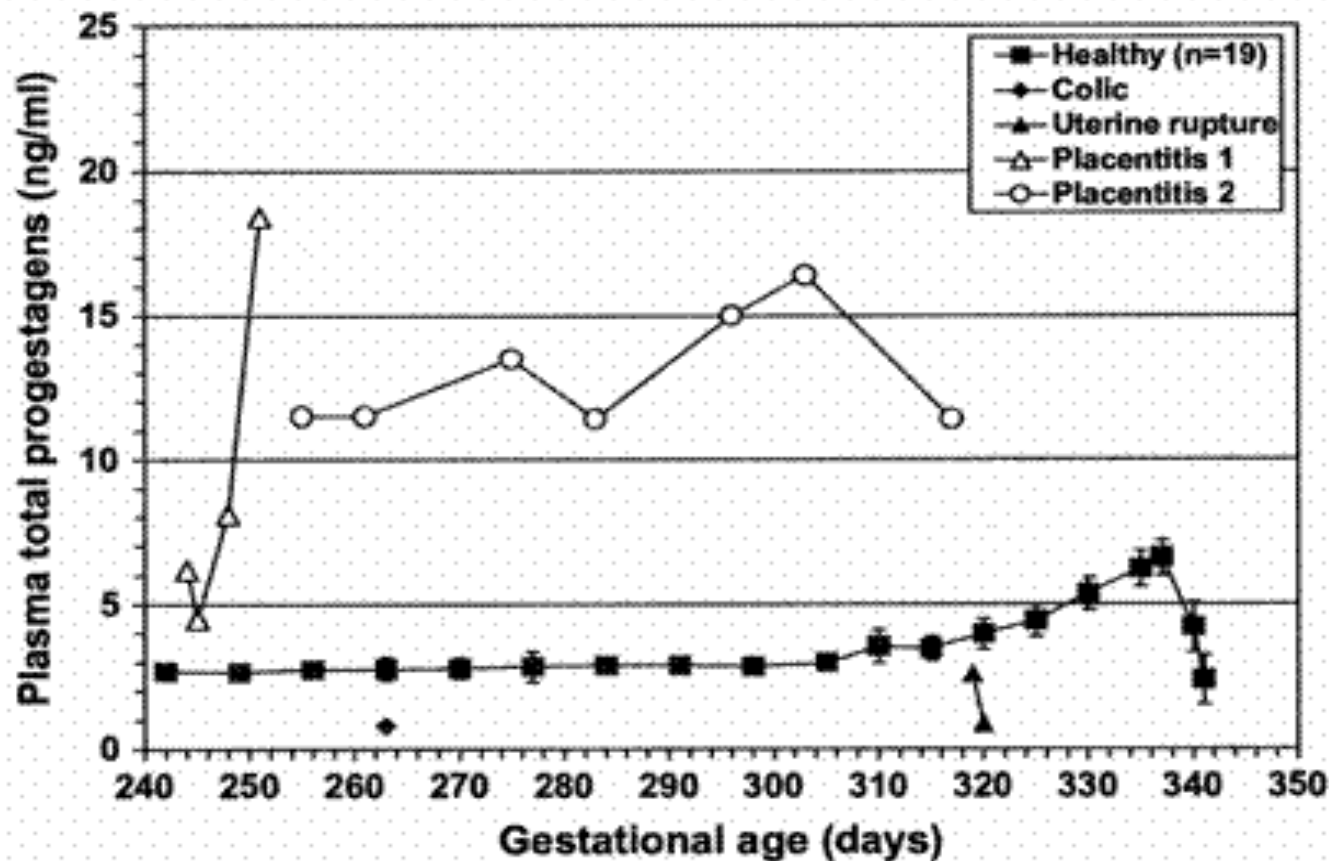
## Progestogens



(Ousey JC. Vet Clin Eq. Practice. ( 2006)22:727-747



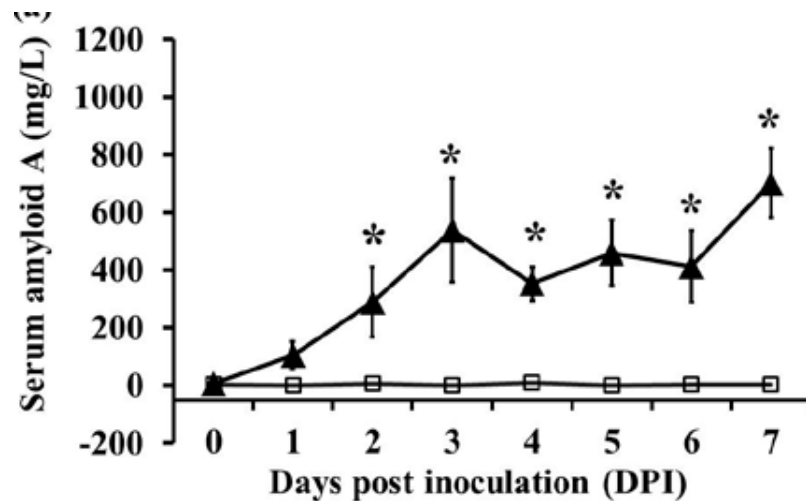
## Progestogens



- Total Estrogens
- Relaxin
- Diagnostic panel??
  - Specific for inflammation and placenta (SAA, Haptoglobin, DHEA, Estradiol 17b, Progestins-5a DHP, 17 Hydroxy DHEA sulfate, Alpha fetal protein)

## Acute phase proteins:

- Serum Amyloid A



★Placentitis



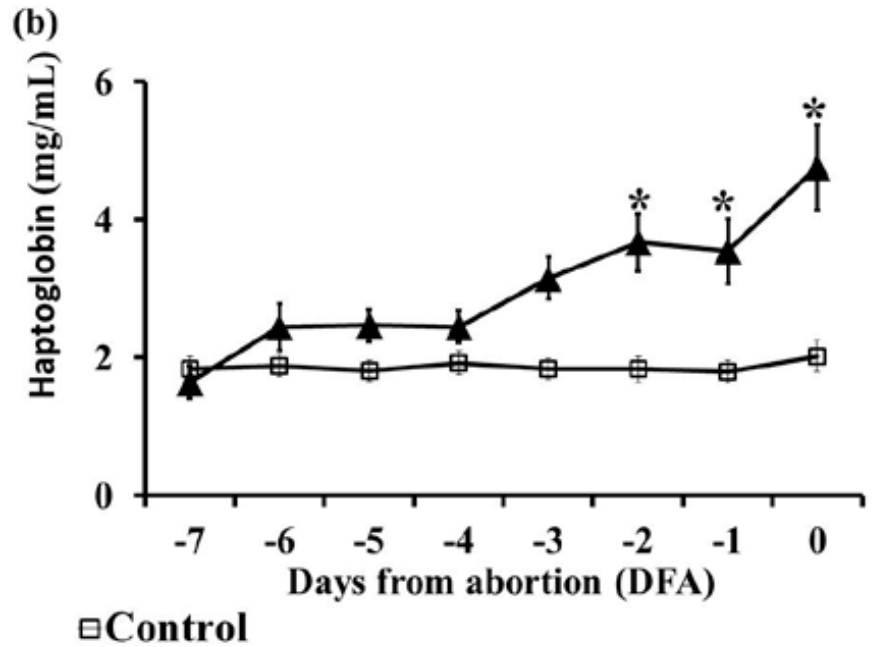
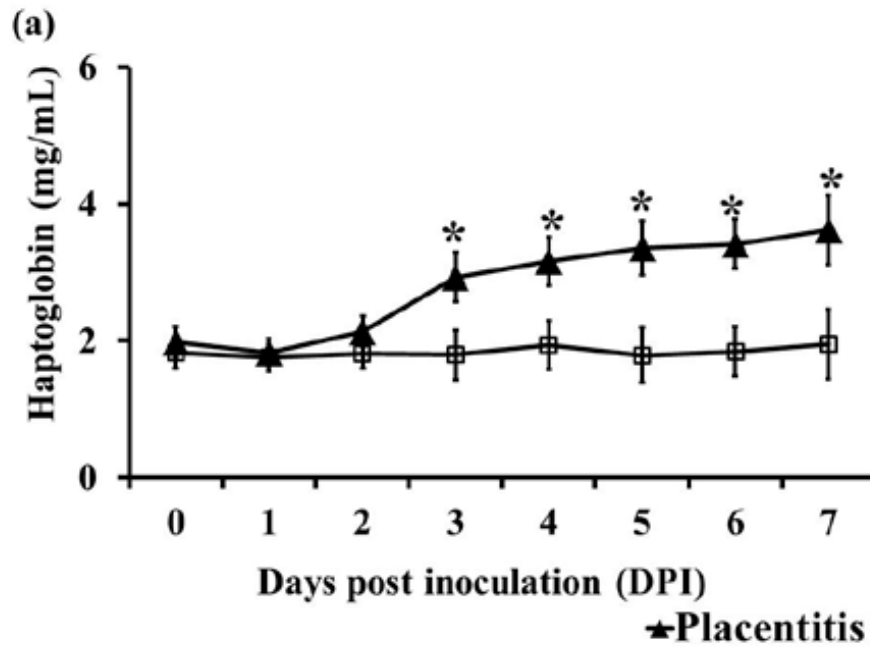
□Control

*Coutinho de Silva 2013, Christofferson 2010, Canisso 2014*

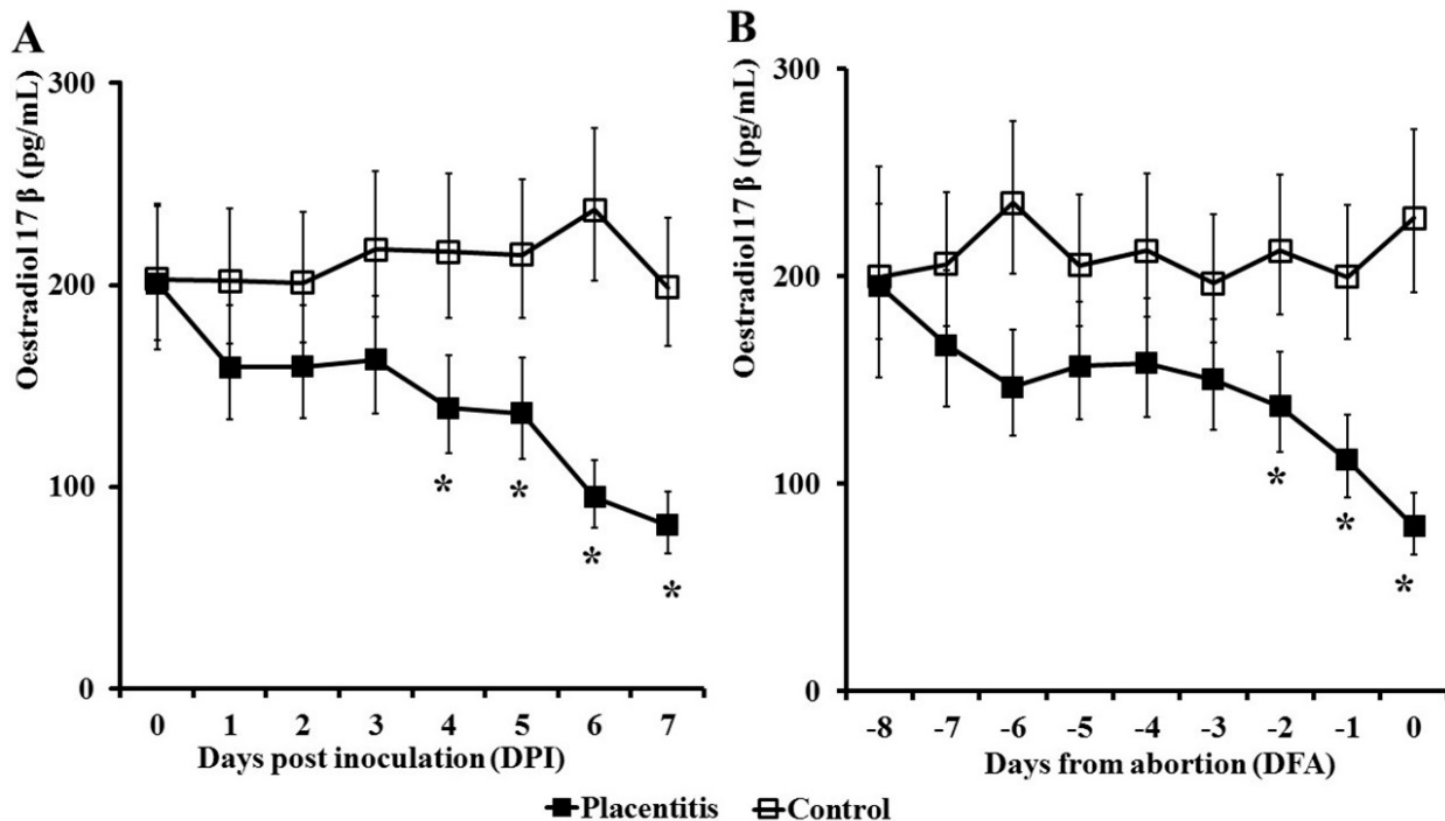


## Acute phase proteins:

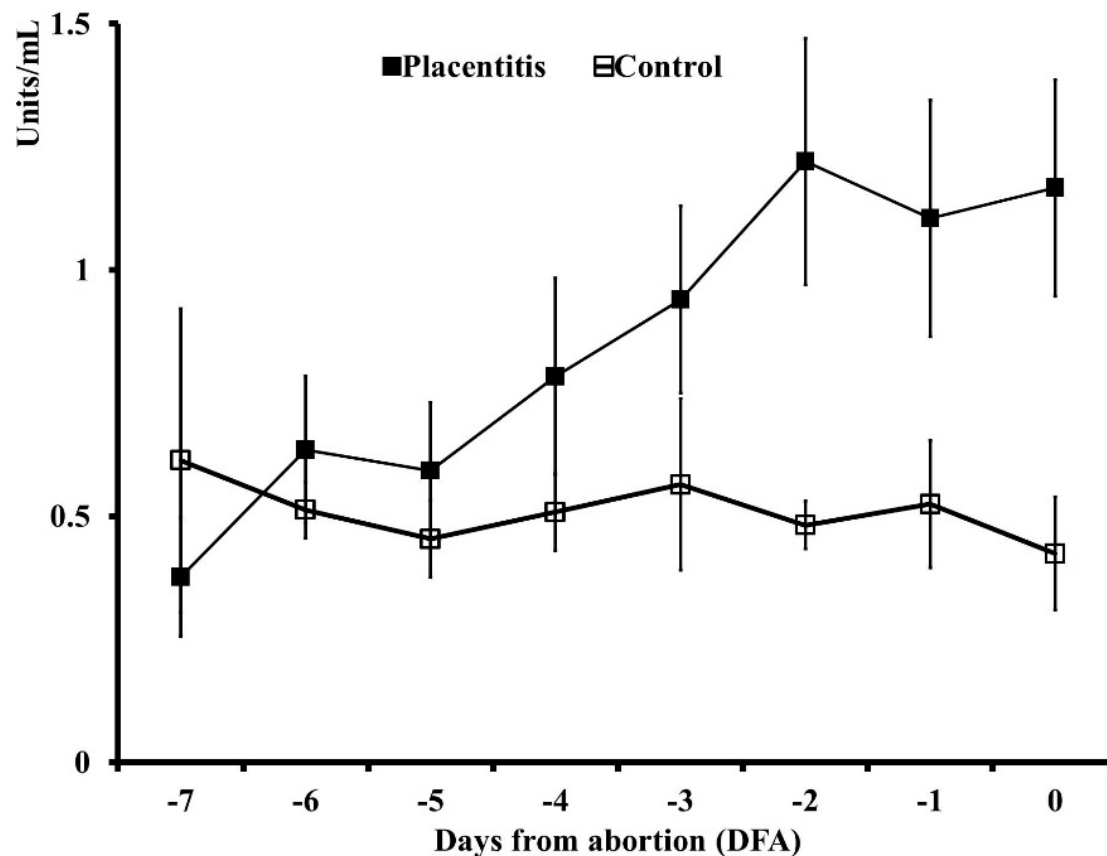
- Haptoglobin



## Estradiol 17 $\beta$



## Alpha Fetal Protein (AFP)



*Canisso 2014*

Field Study (700 mares)- within 7 days of abortion:

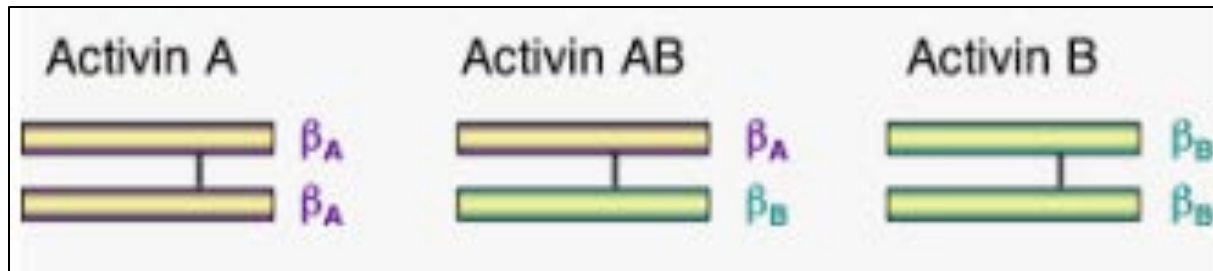
- AFP increased
- Estradiol-17 $\beta$  decreased
- Progesterone not significantly associated with pregnancy outcome



## Maternal serum and allantoic fluid concentrations of activin A in experimentally induced equine placentitis

Harutaka Murase, Kristen Scoggin, Barry Ball

Gluck Equine Research Center, University of Kentucky, Lexington, KY



- Activin A--acute mediator of inflammation
- Hypothesis--Activin A is increased in serum and fetal fluids of pregnant mares with placentitis.
- Objective--determine maternal serum and allantoic fluid concentrations of Activin A in mares with experimentally induced placentitis.

270 d gestation

14



placentitis

- Serum and allantoic fluid daily
- Actvin A determined at -8, -6, -4, -2, -1, and 0 days preceding abortion

15



control

- ↑ Serum concentrations in placentitis mares, day 6 prior to abortion.
- ↑ Allantoic fluid concentrations in placentitis mares day 5 after inoculation.

## **Fetal and maternal immune response to ascending placentitis**

Carleigh Fedorka, Barry Ball, Kirsten Scoggin, Shavahn Loux, Mats Troedsson, Amanda Adams  
Department of Veterinary Science, University of Kentucky, Lexington, KY

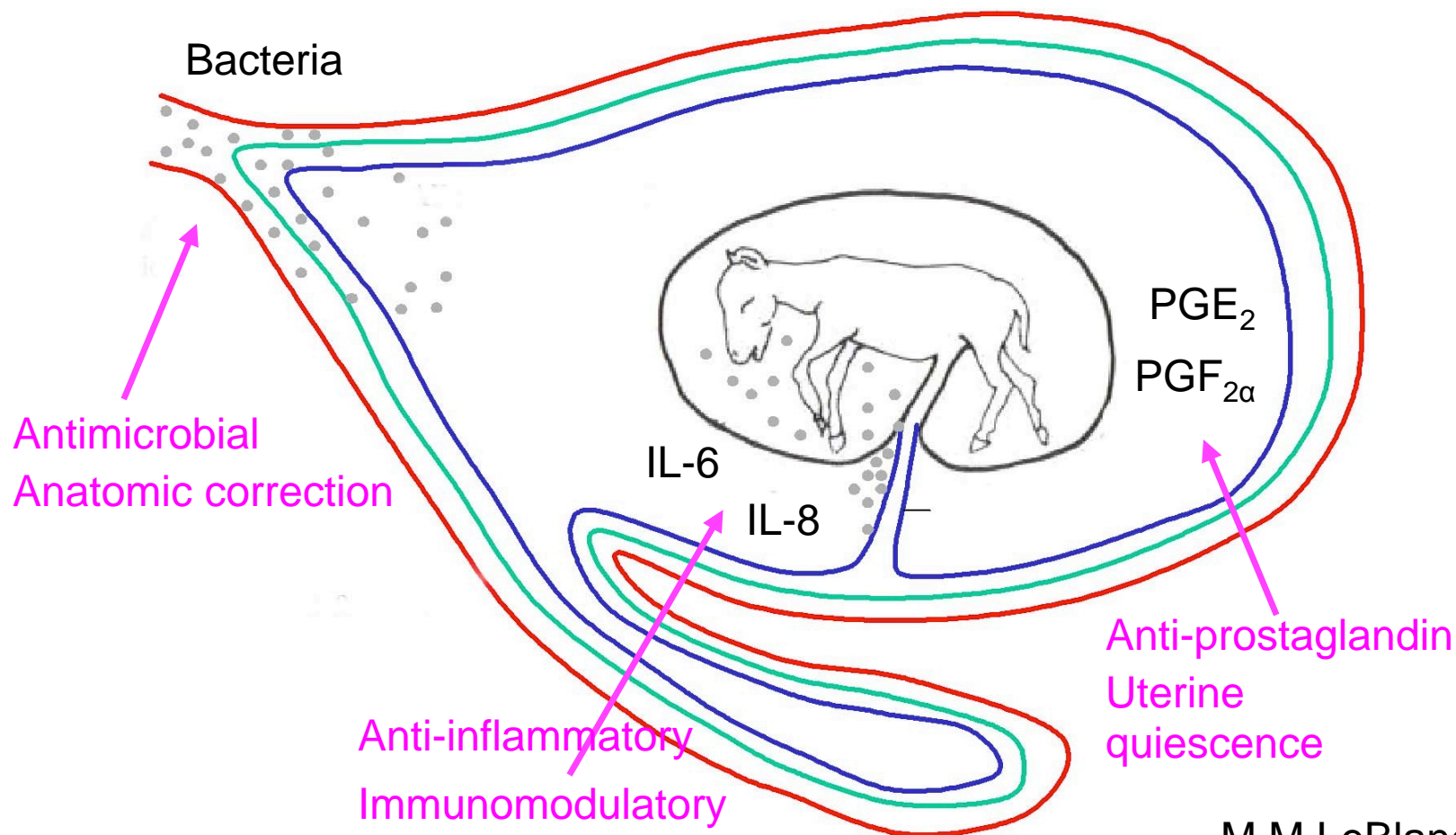
Hypothesis--induction of ascending placentitis →  
significant increase in inflammatory markers in fetal fluid  
compartments and associated tissues.

*Clinical Therio (2019)11:3;433*

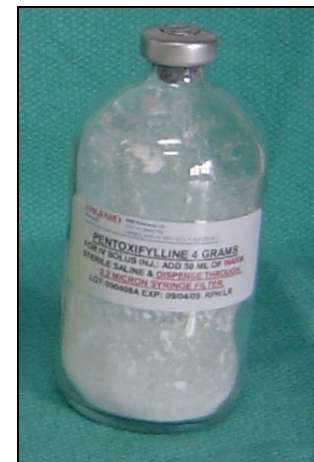
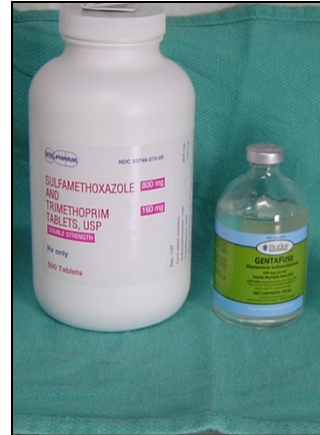
- Of the fluids studied, only effect of inoculation on amniotic fluid-- ↑ IL1 $\beta$ , IL6, IL10, and GRO in placentitis.
- Inflammation localized to the amniotic fluid, minimal effect on allantoic fluid or serum of inoculated.
- Maternal response → pro-inflammatory
- Fetus has a regulatory role inflammation
- ↑ amniotic IL6 and IL10 – diagnostic predictors for microbial invasion of the amniotic cavity in humans
- Amniotic fluid sampling may be more predicative of placentitis than serum or allantoic biomarkers.



## What can we do?



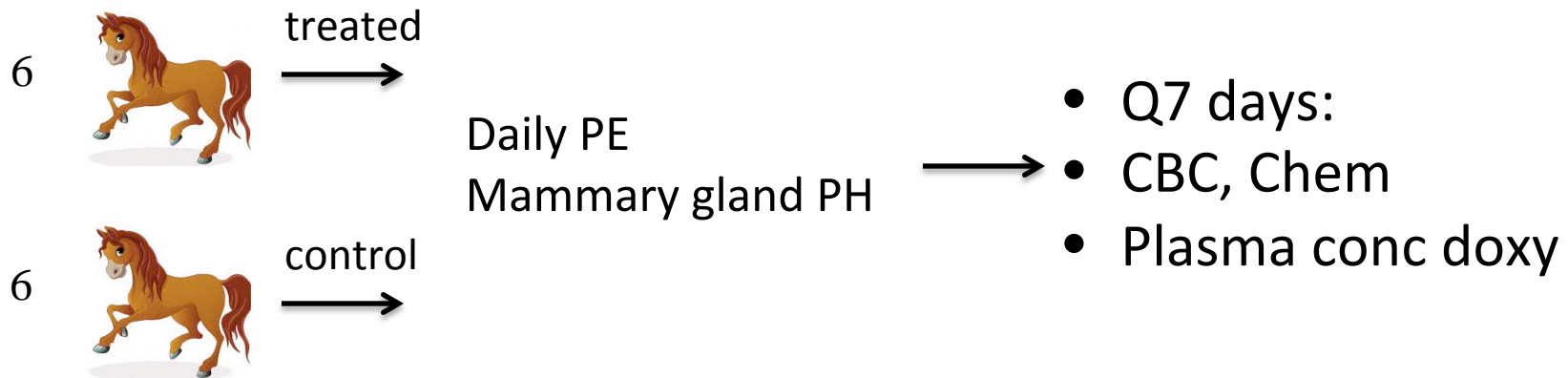
- Antibiotics
- Progesterone supplementation
- Non-steroidal anti-inflammatories
- Rheostatic agents



**Doxycycline diffused to fetoplacental unit and with no apparent complications to resulting foal**  
Fernand Dantas,<sup>a</sup> Igor Canisso,<sup>b</sup> Zhong Li,<sup>c</sup> Lorena Feijó,<sup>a</sup> Carlos Nogueira,<sup>a</sup> Augusto Postal,<sup>a</sup> Josiane Feijó,<sup>a</sup> Bruna R Curcio<sup>a</sup>

- Antimicrobial resistance
- Doxycycline
  - Broad spectrum antimicrobial
  - Treat intracellular microorganisms: High cellular penetration.
- Limited knowledge-toxicity and ability of tetracyclines to diffuse to the fetoplacental unit.

- Study aim: Assess doxycycline diffusion to fetoplacental unit during late pregnancy and potential toxicity to foal.







- Allantoic & Amniotic fluid
- CBC, Chem both mare/foal
- Exam 2x/day
- Conc of doxy in plasma mare/foal
- Conc of doxy in fetal fluids

### Results:

- Doxycycline concentrations in **allantoic fluid > amniotic fluid**
- **Doxycycline detected in foals plasma** immediately after birth.
- **No clinical signs** suggestive of doxycycline toxicity (e.g. diarrhea and jaundice).
- **No differences** in CBC or Chemistry

### Conclusion:

- Doxycycline to late term pregnant mares did not result in apparent clinical
- Doxycycline **crosses** the equine placenta and achieves high concentrations in the fetoplacental unit.



Table 1: Antimicrobial susceptibility patterns of nocardioform actinomycetes isolated from placentas during 2010/2011 foaling season and 2019/2020 foaling season\*

Drugs	2010/2011 foaling season (% of susceptibility)				2019/2020 foaling season (% of susceptibility)			
	<i>Amycolatopsis</i> species (n=38)	<i>C. equi</i> (n=22)	Other actinomycetes (n=10)	Total (n=70)	<i>Amycolatopsis</i> species (n=9)	<i>C. equi</i> (n=8)	Other actinomycetes (n=4)	Total (n=21)
Amikacin	86.8	0	80	58.6	55.5	0	25	28.6
Amox/Clav. Acid	78.9	100	50	81.4	55.5	62.5	75	61.9
Cefepime	28.9	22.7	30	27.1	11.1	0	0	4.7
Cefoxitin	13.2	0	20	10	NI	NI	NI	NI
Ceftriaxone	92.1	95.5	40	85.7	77.8	87.5	100	85.7
Ciprofloxacin	36.8	4.5	20	24.3	22.2	0	0	9.5
Clarithromycin	71.1	13.6	50	50.0	55.5	0	25	28.5
Doxycycline	73.7	95.5	90	82.9	88.9	100	100	95.2
Imipenem	55.3	59.1	70	58.9	44.4	12.5	0	23.8
Linezolid	92.1	95.5	100	94.3	100	100	100	100
Minocycline	68.4	90.9	90	78.6	88.9	100	75	90.4
Moxifloxacin	Not tested	Not tested	Not tested		100	100	50	90.4
Tobramycine	18.4	4.5	70	21.4	22.2	0	0	9.5
TMP/SMX	89.5	100	40	85.7	77.8	100	100	90.4

\*: Numbers represent percentage of susceptibilities. As there are no interpretative criteria for antimicrobial susceptibility of nocardioform actinomycetes, the criteria have been extrapolated from human *Nocardia* species, closely related microorganisms. It should be kept in mind that these results are only *in vitro* test results and may not necessarily be applied to actual clinical cases.

Unpublished data Dr. E. Erol



A	B	C	D	E
January 2020 Nocardia Isolates	1	2	3	% Sensitive
Amikacin	S	R	R	33
Ampicillin	R	R	S	33
Naxcel	R	S	S	67
Ciprofloxacin	S	R	R	33
Doxycycline	S	S	S	100
Gentamicin	S	R	R	33
Imipenem	S	S	S	100
Furacin	S	S	S	100
Tetracycline	S	S	S	100
Timentin	I	S	S	67
SXT	S	S	S	100

**Enrofloxacin crosses equine placenta in early pregnancy without inducing gross lesions in fetus**

Robyn Ellerbrock,<sup>a,c</sup> Igor Canisso,<sup>a</sup> Patrick Roady,<sup>a</sup> Elizabeth Uhl,<sup>c</sup> Gioria Podico,<sup>a</sup> Zhong Li<sup>b</sup>

<sup>a</sup>Department of Veterinary Clinical Medicine

<sup>b</sup>Roy Carver Biotechnology Center, University of Illinois, Urbana IL

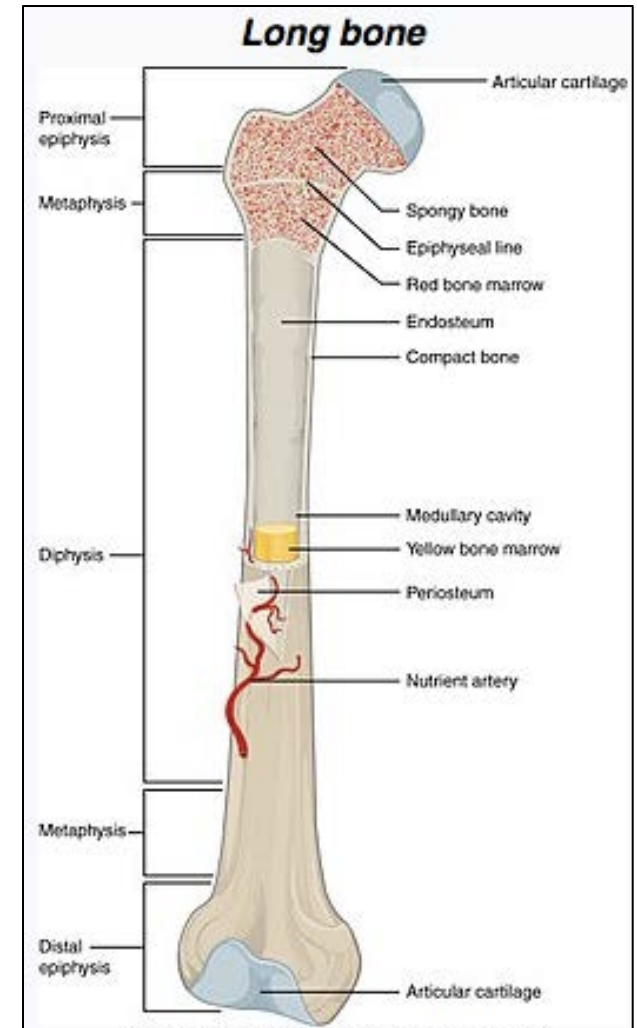
<sup>c</sup>College of Veterinary Medicine, University of Georgia, Athens, GA

*Ellerbrock R et al. Clin Therio (2019)119:3;451*

### Hypothesis:

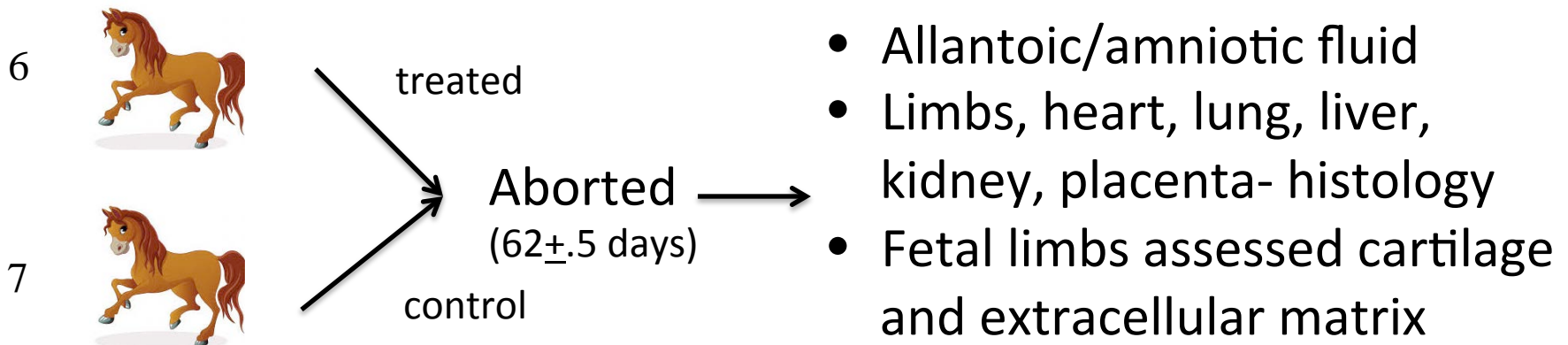
- Enrofloxacin administration to early pregnant mares  
→ high concentrations of enrofloxacin/metabolite ciprofloxacin in fetal fluids
- Fluoroquinolone exposure in early pregnancy induces chondrotoxic lesions in the 60 day fetus.

Ellerbrock R et al. Clin Therio (2019)119:3;451



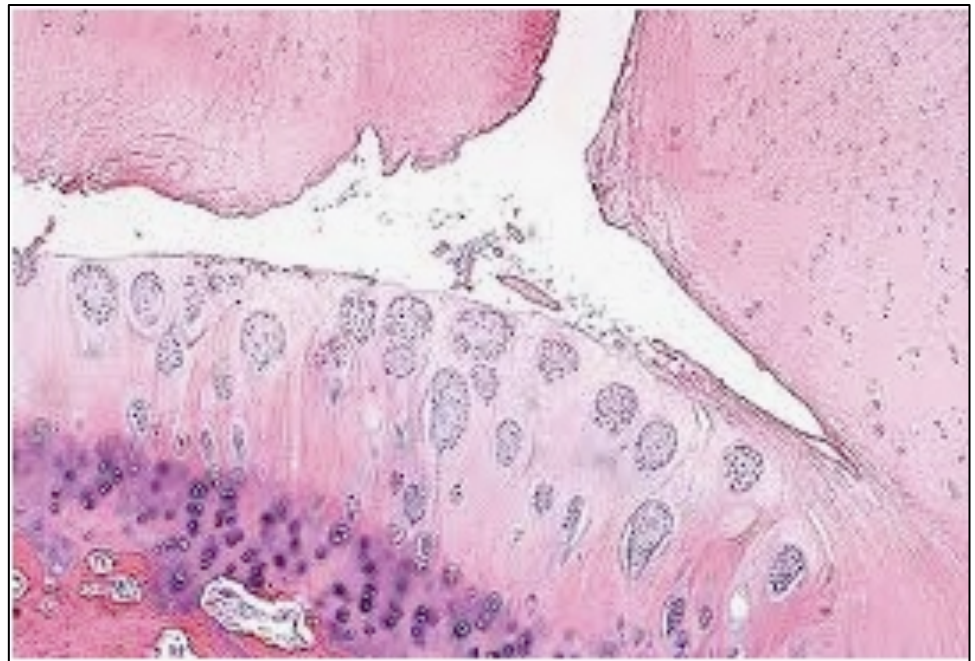
### Objective:

- Determine enrofloxacin/ciprofloxacin in fetal fluids during early pregnancy
- Compare endochondral ossification of long bones from fetuses with gestational age matched controls.



### Results:

- Enrofloxacin and ciprofloxacin in both amniotic and allantoic fluids
- No differences in histological features of front or hind limbs.





- Short term administration of enrofloxacin in early pregnancy did not result in pathologic lesions in the equine fetus.
- Further research- assess other stages of pregnancy, longer durations, long term foal outcomes

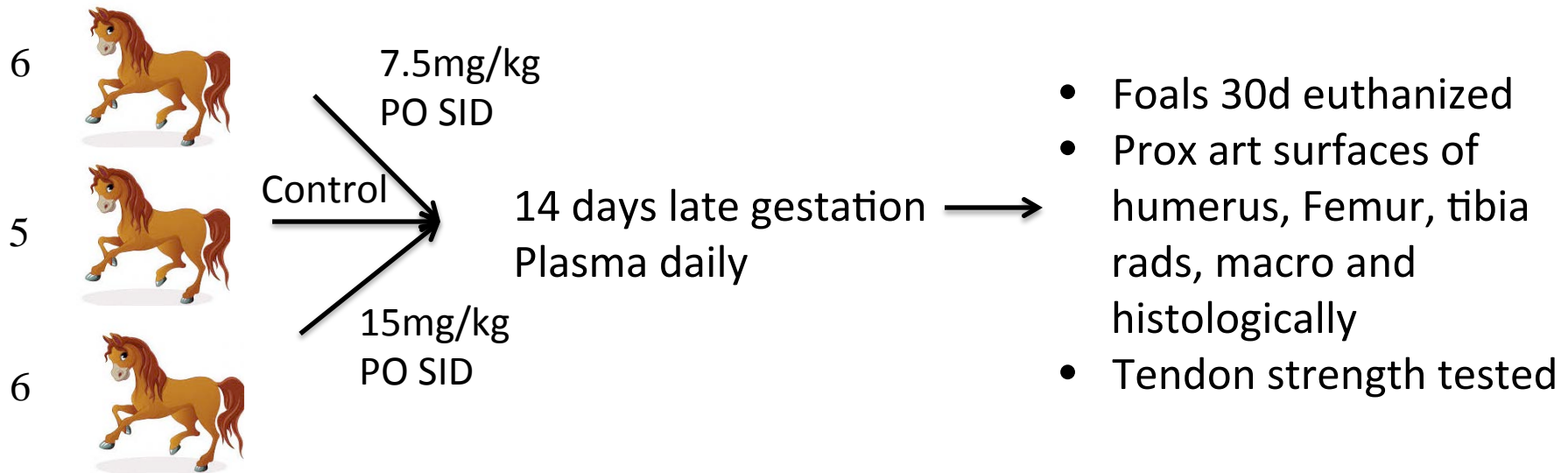


\*\*\*Enrofloxacin **may be** useful to treat select severe bacterial infections in pregnant mare\*\*\*

## Foals Born from Mares Treated with Enrofloxacin During Late-Term Pregnancy

Robyn E. Ellerbrock, DVM, PhD, DACT+;  
Igor F. Canisso, DVM, MSc, PhD, DACT, DECAR\*; Peter Larsen, PhD;  
Katherine Garrett, DVM, DACVS; Giorgia Podico, DVM, MS; and  
Bronwen Childs, DVM, MS, DACVR

*Ellerbrock RE et al, AAEP proc (2019)65;63*

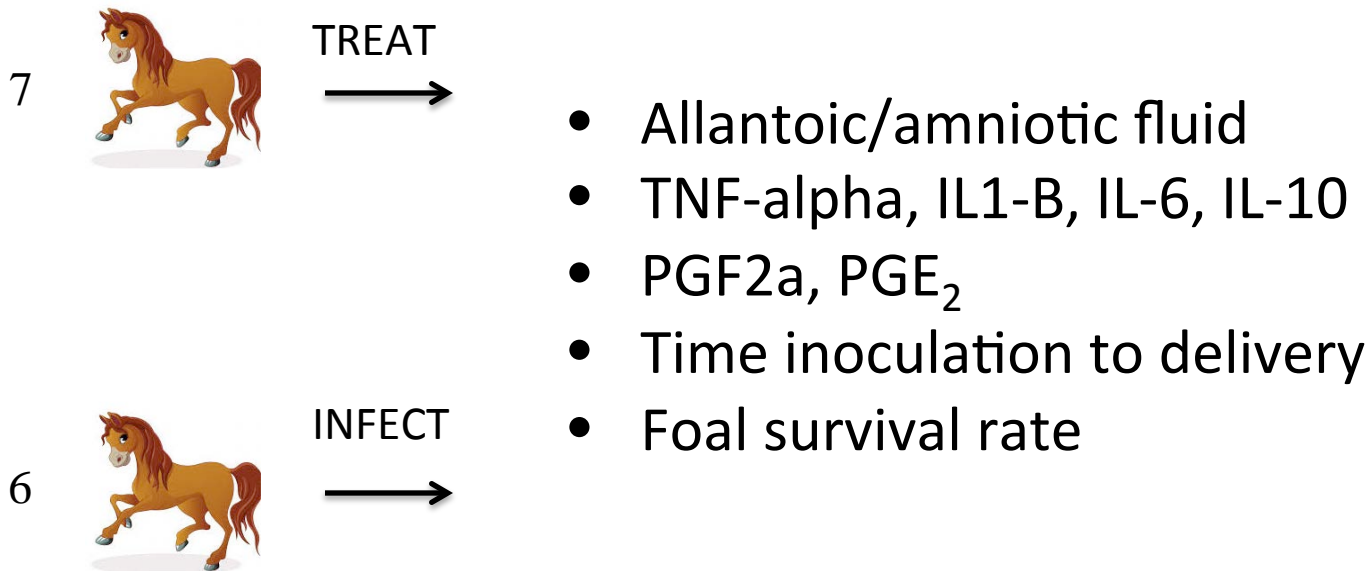


- No clinical lameness noted by 30 days of age
- No difference in tendon tensile strength
- Osteochondral changes similar in txn and non txn

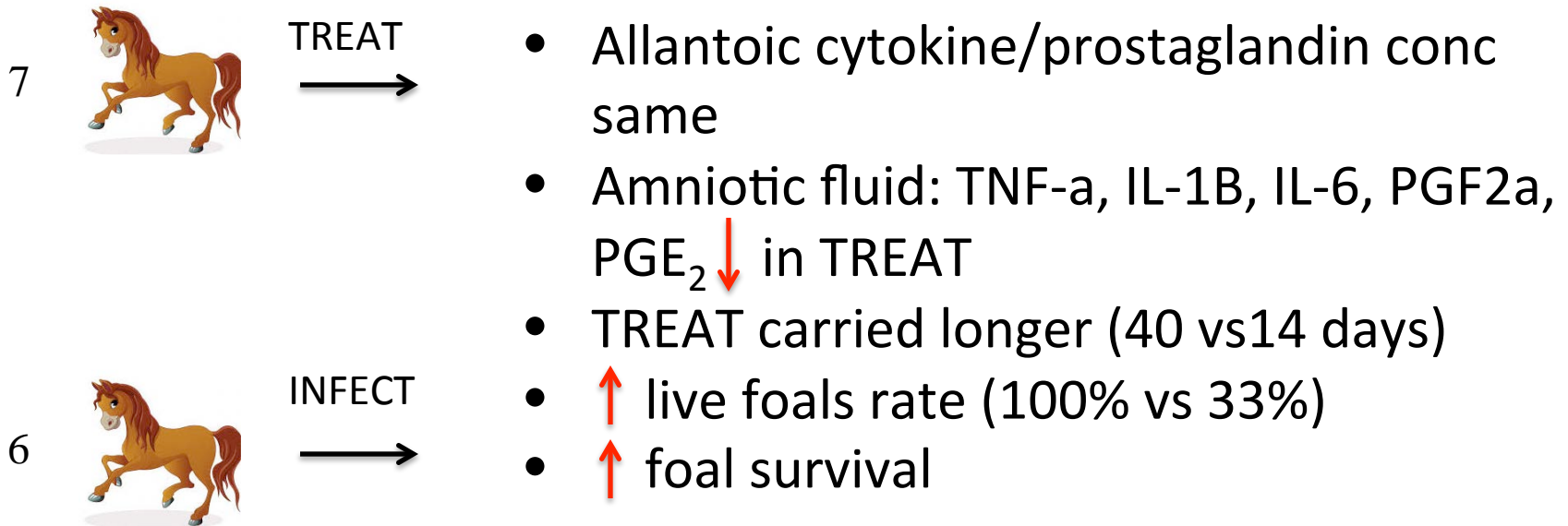
**\*Long term studies needed to determine affect for first year of life\***

Effects of Firocoxib, Trimethoprim  
Sulfamethoxazole, and Altrenogest on  
Inflammation and Foal Survival After  
Administration to Mares with Experimentally  
Induced Placentitis

- Characterized anti-inflammatory effects of firocoxib, TMS and altrenogest in fetal fluids in mares with placentitis
- Live foal delivery rates compared in treated/infected vs untreated/infected mares.







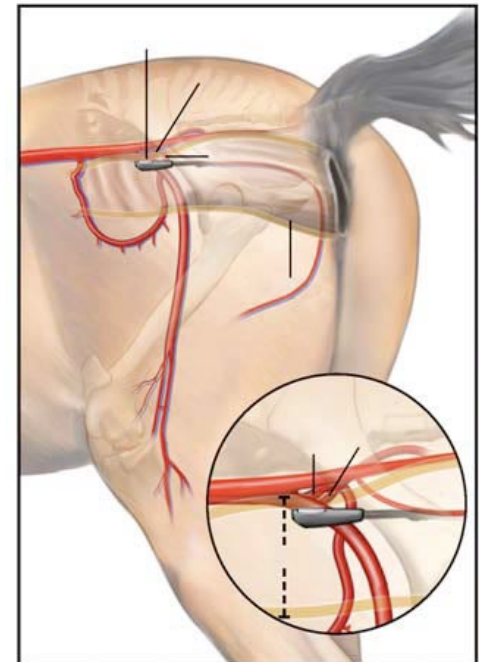
- Suppressive effect of firocoxib, TMS and altrenogest on proinflammatory mediators
- Treatment with firocoxib, TMS and altrenogest ↑ pregnancy maintenance and foal outcome



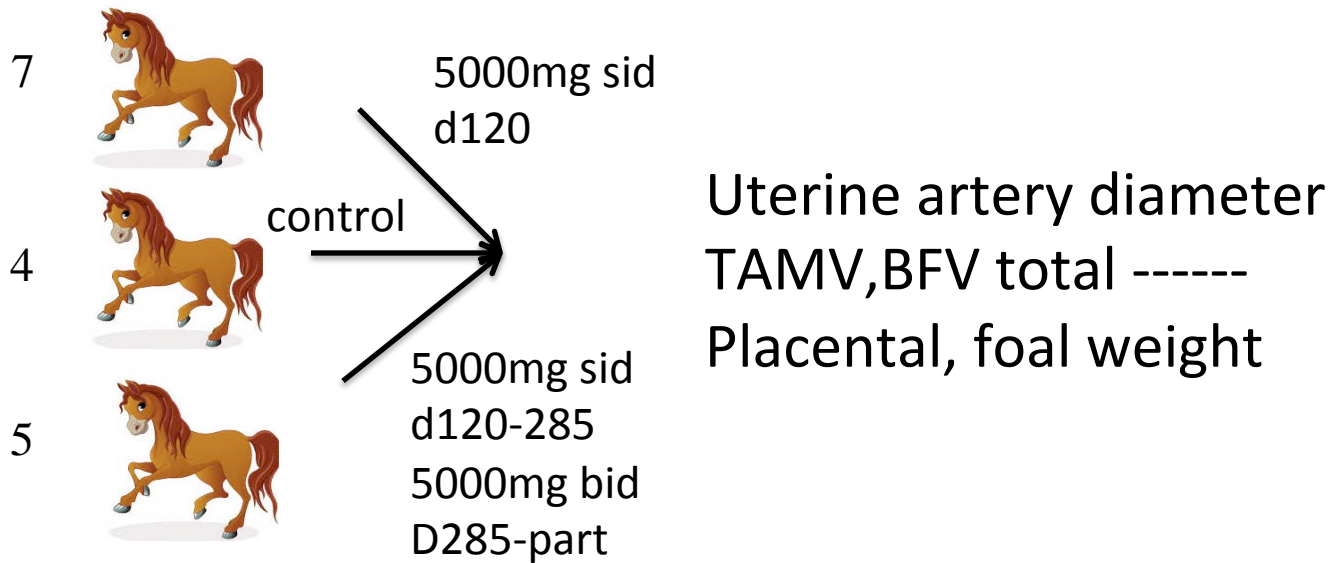
## Effect of Acetylsalicylic Acid on Uterine Blood Flow and Feto-Placental Development in Pregnant Mares

J. Sielhorst;U. Bücken;A. Kahler;K. Rohn;R. Koch;C. Pfarrer;H. Bollwein;H. Sieme;

J of Eq Vet Science (2018)66:233



- Rise in uterine blood flow in pregnancy
- ASA inhibits platelet aggregation and ↑ blood flow in women
- Aim: analyze effect of ASA on uterine blood flow, placental development and foal weight in normal and abnormal pregnancies



- Foals birth weight positively correlated with mare's parity
- Foal and placental weight not influenced by treatment
- BFVtotal sig varied between treatment groups
- During late pregnancy TAMV was higher in ASA bid



## Equine placentitis is associated with a downregulation in myometrial progesterin signaling

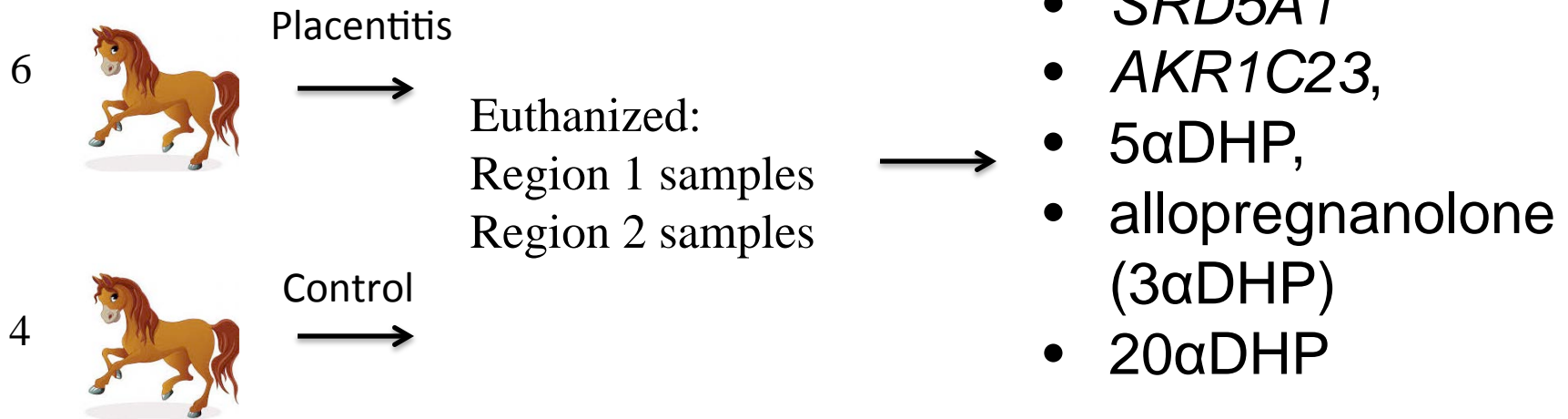
Hossam El-Sheikh Ali, Erin L Legacki, Shavahn C Loux, Alejandro Esteller-Vico, Pouya Dini, Kirsten E Scoggin, Alan J Conley, Scott D Stanley, Barry A Ball ✉

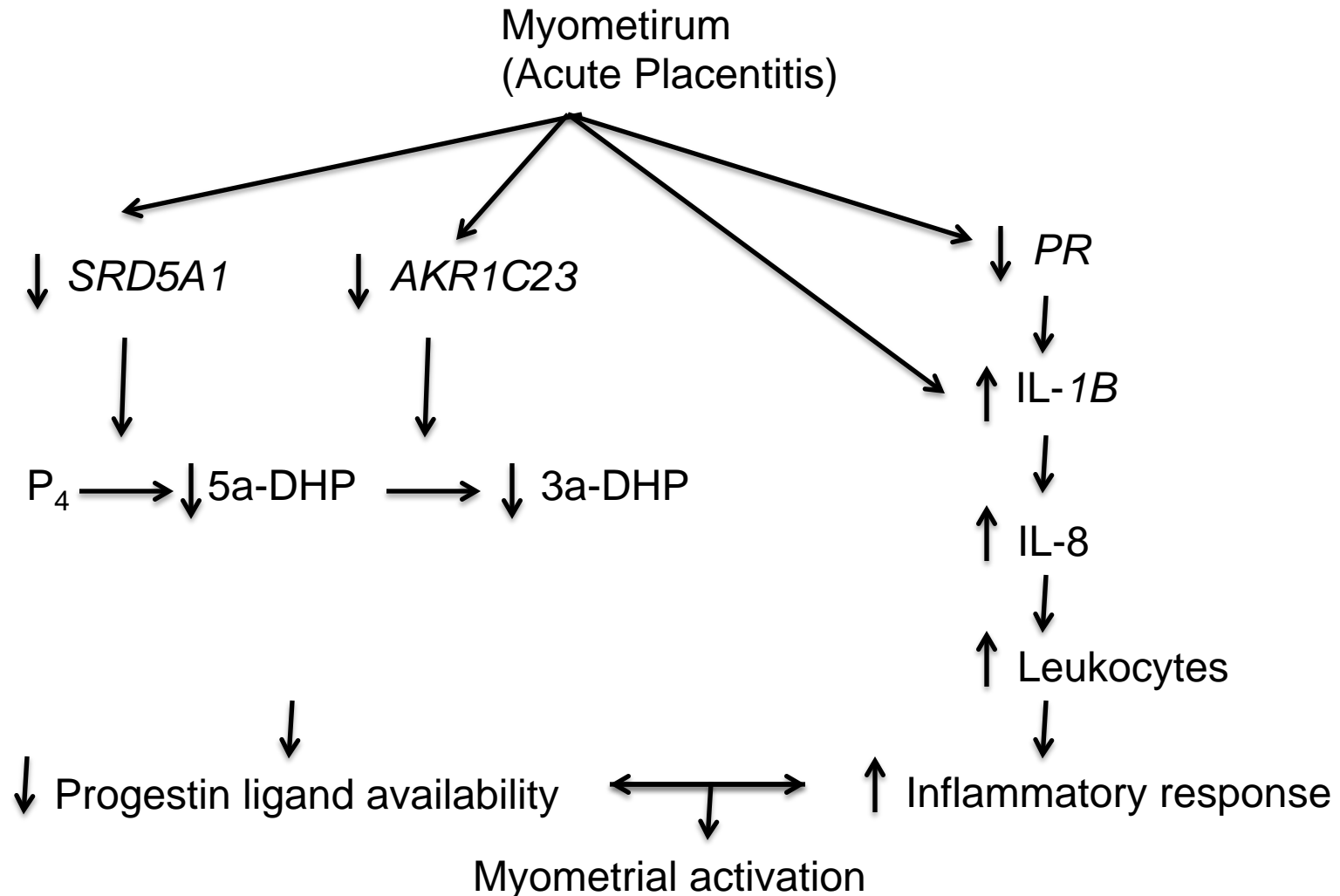
*Biology of Reproduction*, Volume 101, Issue 1, July 2019, Pages 162–176, <https://doi.org/10.1093/biolre/ioz059>

**Published:** 10 April 2019    **Article history** ▼

- Study aim-- elucidate the mechanisms underlying myometrial activation during equine placentitis related to progestogens and the progesterone receptor signaling pathways

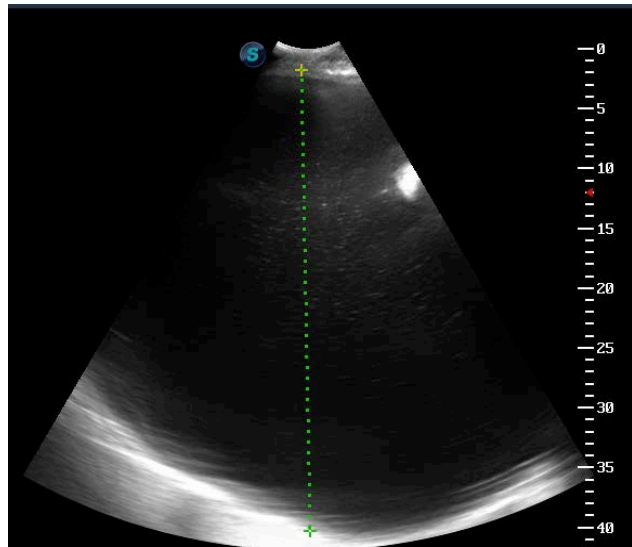
290 d gestation





## Hydrops Allantois

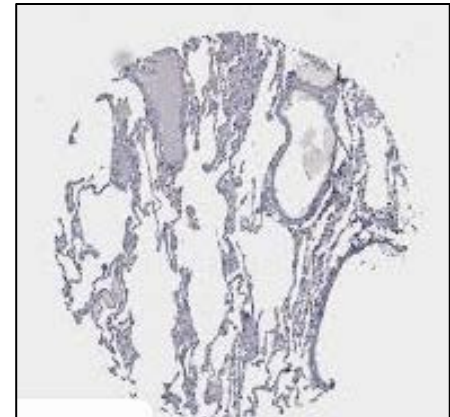
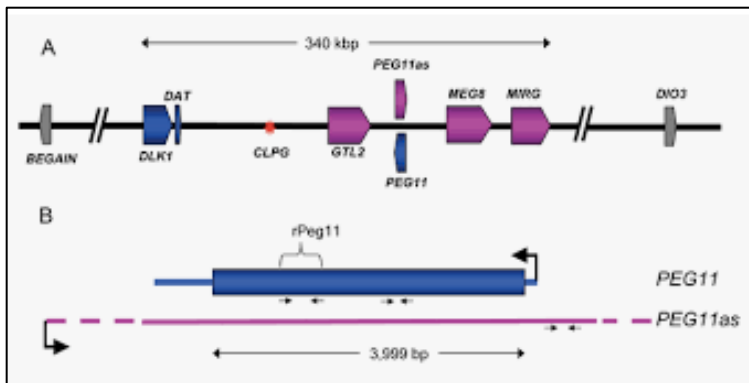
- Excessive accumulation of allantoic or amniotic fluid
- Last trimester of gestation
- Postulated associated with structural/functional changes in the chorioallantoic membrane such as dysfunction of chorionic ion pumps



## Hydrops Allantois

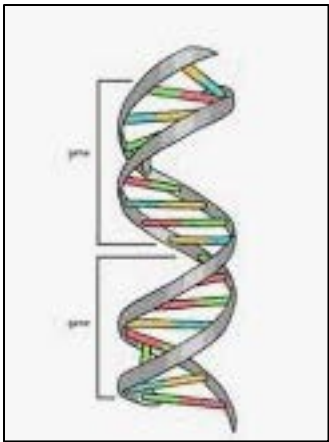
### Evaluation of angiogenesis in equine hydrops

Pouya Dini,<sup>a,b</sup> Peter Daels,<sup>a</sup> Mariano Carossino,<sup>d</sup> Alan Loynachan,<sup>c</sup> Karen Wolfsdorf,<sup>e</sup>  
El-Sheikh Ali,<sup>b</sup> Kirsten Scoggin,<sup>b</sup> Barry Ball<sup>b</sup>



- Hypothesized that the expression of angiogenic genes and the number of chorioallantoic (CA) capillaries are altered in hydrops placentae.
- Evaluated angiogenesis in the hydrops placenta.





10



Hydrops

4



Normal

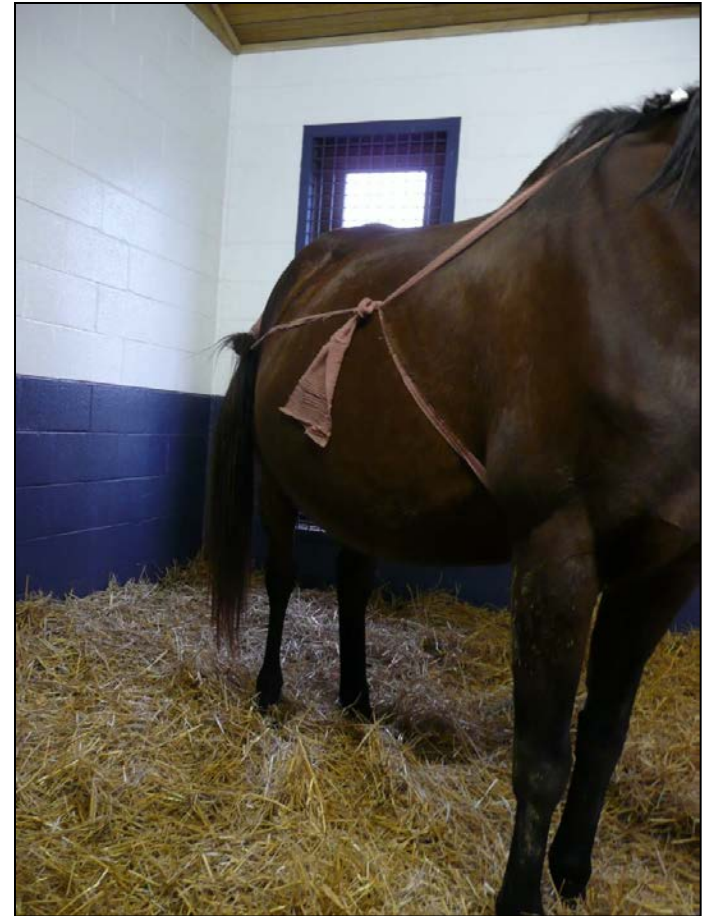
Protein exp of RTL1---  
Immunohistochemistry

Vascular density---  
Immunostaining

- 4 differentially expressed transcripts

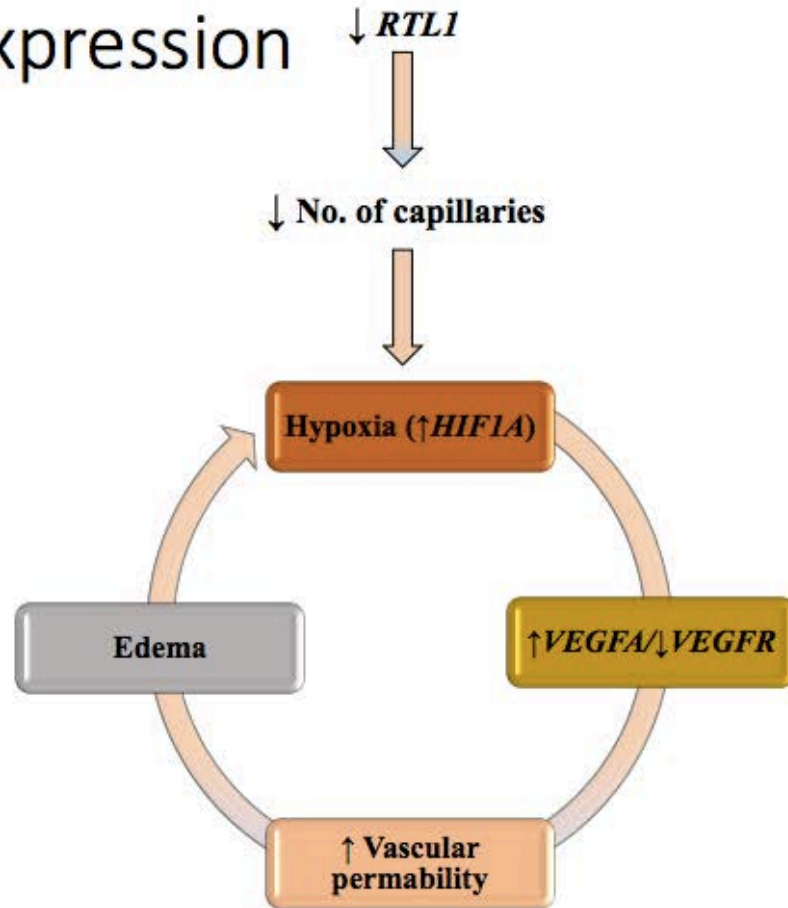
## Hydrops Allantois

- Protein expression of RTL1 and the number of vessels were **lower** in hydrops samples.
- **Conclusion-- alteration in expression of select angiogenic genes and disruption in capillary vessel formation.**



## Hydrops Allantois

Abnormal RTL1 expression  
is associated with  
hydrallantois



Thank You!

