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Understanding the Causative Agent, Pathophysiology and Management of the Kentucky Mare Reproductive Loss Syndrome and Related Syndromes

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Gluck Equine Research Center

www.thomastobin.com

University of Kentucky

Monday, October 4, 2010



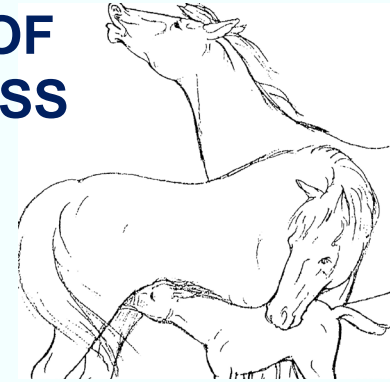
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© Thomas Tobin, September 2012

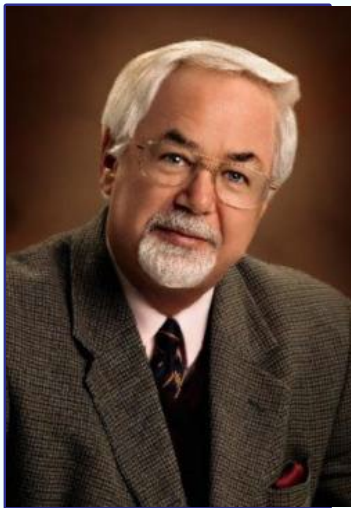
**UNDERSTANDING THE CAUSATIVE AGENT,
PATHOPHYSIOLOGY AND MANAGEMENT OF
THE KENTUCKY MARE REPRODUCTIVE LOSS
SYNDROME AND
RELATED SYNDROMES**

ISER
*Global
Education*

by



**Thomas Tobin, Gabriel Volpato,
Navid Yousefi Mashouf and Kimberly Brewer**



**The Maxwell H. Gluck Equine Research Center
College of Agriculture Food and the Environment
University of Kentucky,
For
The International Symposium of Equine Reproduction
(ISER)**

Questions to ttobin@uky.edu
www.thomastobin.com

THE CAUSE

1/. The **CAUSE** is barbed caterpillar hair
(setae) fragments. →

2/ Demonstrate how **SETAL FRAGMENT
PENETRATION/DISTRIBUTION**
produces MRLS.

3/ Describe the **FIVE** Mare Reproductive
Loss Syndromes.

4/ Review the **EVIDENCE** supporting this
setal mechanism.

5/ Detail **PREVENTION / TREATMENT** of MRLS.



Predictions That Arise From The (Revised) “Setal Emboli Hypothesis”:

Does MRLS follows **PROBABILISTIC** mathematics?

i

Accelerated Failure Time (AFT) analysis of MRLS

Assumed that time until abortion has a log-normal distribution a survival model that well fits the data is an Accelerated Failure Time Model. The model takes the form:

$$T_i = \exp\{\beta_0 + \beta_1 x_{i1} + \dots + \beta_k x_{ik} + \sigma \varepsilon_i\}$$

This model includes an intercept term (β_0) and an error term ($\sigma \varepsilon_i$). T_i is the time that abortion occurs for individual i , and β_1 through β_k are coefficients for covariates that might affect abortion time.

TT → DERBY DAY, 2001

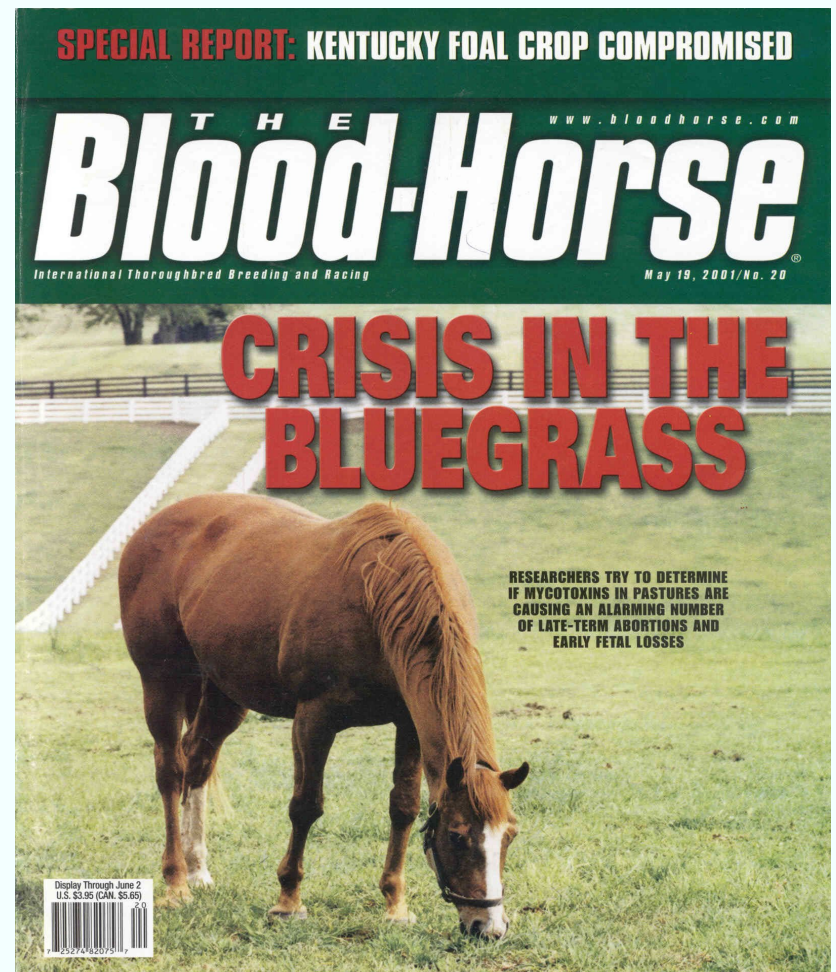
- Derby Day, Thoroughbred Club, Lexington.
- Folks asking why so many trucks at the Veterinary Diagnostic Lab with dead foals ???!
- Monday asked my Chair what was going on.
- He said an abortion storm, not infectious, therefore its a toxin, yours!!!
- (Toxin killing fetuses, bacterial proliferation is secondary!!)



Reproductive LOSS Syndrome

THREE WEEKS ca. Derby Day, May 5th, 2001, KY lost **20-30%** of its in-place foal crops.

Economic loss to KY over 2000-2003 estimated at **~US \$500 million**



FIVE MRLS SYNDROMES

- 1/ **LATE FETAL LOSS**, (**LFL**, 600 to 1,200 cases)
- 2/ **EARLY FETAL LOSS**, (**EFL**, 1,500-2,000 cases)
- 3/ **UNILATERAL UVEITIS** (40)
- 4/ **PERICARDITIS** (60)
- 5/ **ACTINOBACILLUS ENCEPHALITIS** (3)

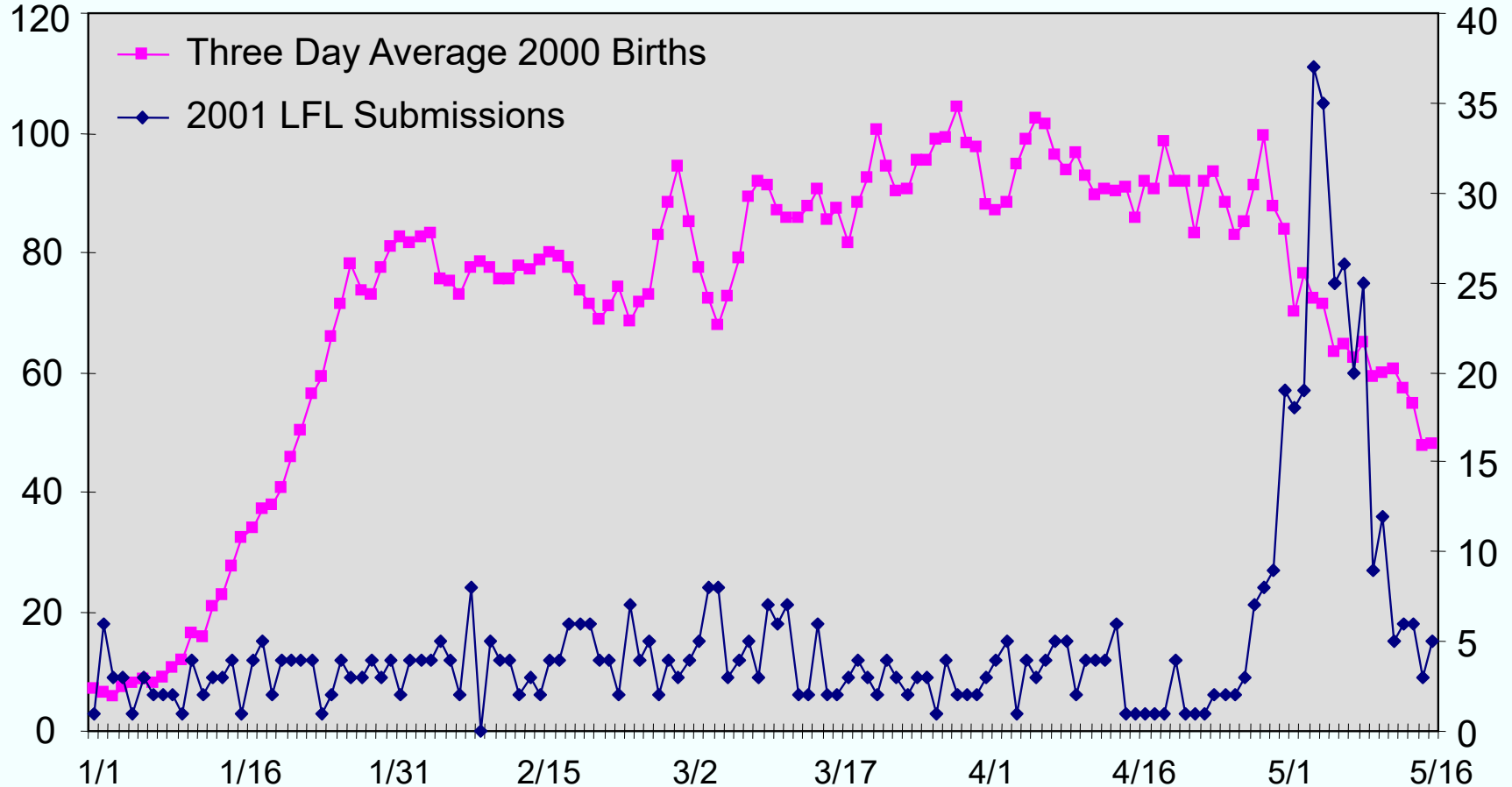


SYNDROME 1: Late Fetal Loss (LFL)

- Near term abortions, “red bag” presentations, weak and still born foals.
- Inflammation of **amnion, umbilicus, (funisitis)**, fetal lungs.
- Estimates: 600-1,200 foals of all breeds affected.
- **Late Fetal Losses** peaked on **Derby Day 5/5/01.**



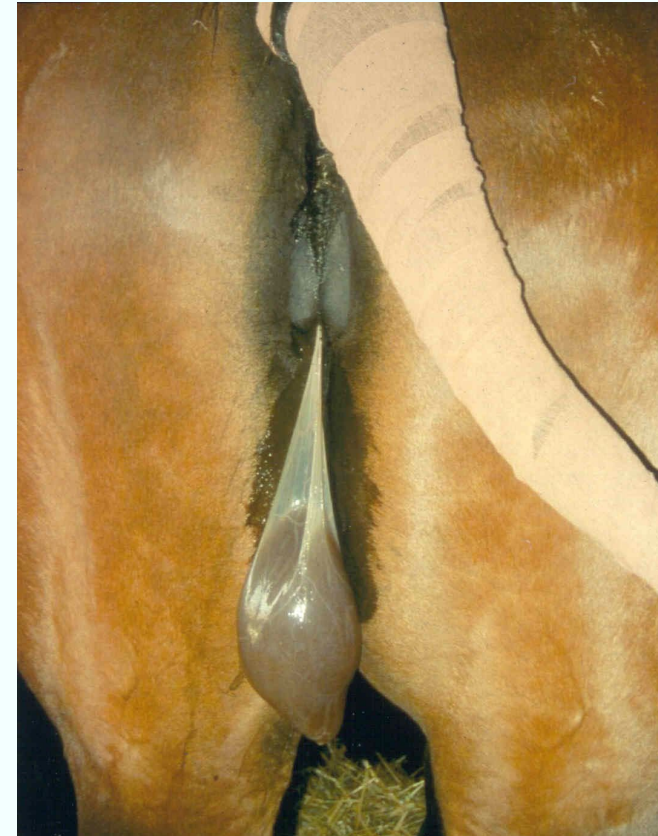
Late Fetal Loss Submissions to Livestock Disease Diagnostic Center



Data provided courtesy of Dr. Albert Kane and Dr. Enzo Campinella, USDA Foaling data provided by The Jockey Club Information Systems

SYNDROME 2: **Early Fetal Loss (EFL)**

- Conceived Feb/March/ unusually high number of fetal deaths.
- First identified **April 26th, 2001**.
- **30-100** day fetuses (Dr. Tom Riddle).
- Fetuses normal on palpation.
- Ultrasound: No fetal heartbeat, “cloudy” echogenic amniotic fluid.
- Death/expulsion of fetus; 1,500-2,000 pregnancies affected.

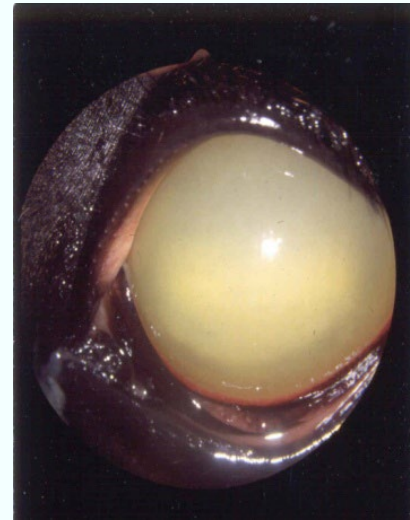


S3: 42 cases of Unique Unilateral Uveitis

- **UNILATERAL hemorrhage and uveitis** (ALL SEXES AGES!)
- Chambers of the eye would fill with fibrin.
- Unresponsive to conventional treatment: Generally, loss of vision in the affected eye, followed by **GLOBAL ATROPHY**.
- None necropsied or cultured.
- **Thought to be an unknown Toxin???????**



SYNDROME 3: Unilateral Uveitis



(Pollards Vision, ran in the 2004 Kentucky Derby!)

*Photographs courtesy of Dr. Stuart Brown, Hagyard-Davidson-McGee;
Dr. David Bolin, LDDC; and Hank Q. Murphy*

S3: Unique Unilateral Uveitis

- An unknown Toxin **??????**
- **46 SINGLE EYES:**

How many systemic small molecule toxins take one eye out completely and absolutely not affect the other?

[Toxin dose contains about 10 to the power of 16 molecules]



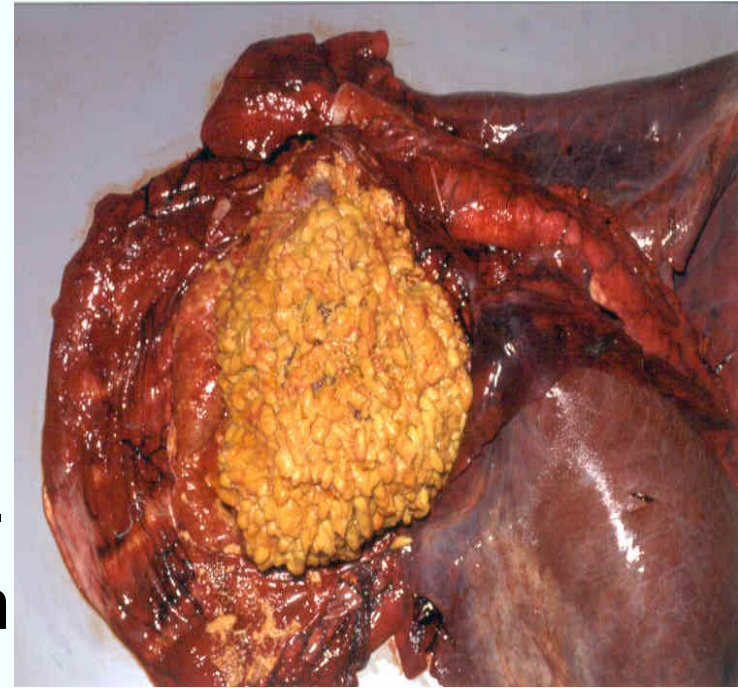
SYNDROME 4: 60 Pericarditis Cases



Photographs courtesy of Dr. Stuart Brown, Hagyard-Davidson-McGee; Dr. David Bolin, LDDC; and Hank Q. Murphy

Syndrome 4: Pericarditis

- 60 cases of pericarditis observed around this period (ALL SEXES AGES!).
- **Epicardium** (CLUE?) covered with fibrin (Clumps of fibrin ?).
- Excessive fluid in pericardial sac.
- Fluid Low white cell#/high protein
- Fluid often **sterile**; when bacteria cultured tended to be typical of MRLS



BACTERIAL ISOLATES IN FETAL LOSS CASES

- Non-beta hemolytic streptococci
- Actinobacilli
- Actinobacilli and non-beta hemolytic streptococci
- SERRATIA MARCESCENS (CLUE!)

THEORY → TOXIN kills fetus, bacterial invaders secondary.

9/15/2022

(c) T Tobin 2022

Bacterium isolated	Number (%) of fetuses
	2001
Non-beta hemolytic streptococci	223 (51.5)
Actinobacilli	74 (17.1)
Actinobacilli and non-beta hemolytic streptococci	8 (1.8)
Escherichia coli	7 (1.6)
Pantoea agglomerans	4 (0.9)
<u>SERRATIA MARCESCENS</u>	2 (0.5)
Aeromonas spp.	4 (0.9)
Enterobacter spp.	0
Acinetobacter spp.	4 (0.9)
Beta-hemolytic streptococci	2 (0.5)
Staphylococcus spp.	1 (0.2)
Other coliforms	4 (0.9)
Other bacteria	4 (0.9)
No significant bacteria	70 (16.6)
Overgrown by saprophytes	26 (6.2)
TOTALS	433 (100)

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Assessment of the Syndromes: May 2001, chairing Mid-Week Meeting of Toxicology Working Group

- Estrogenic mycotoxicosis considered less likely

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- Moving towards ergot alkaloid/plant endophyte theory.
- Dr. Neil Williams: 'Pathology absolutely inconsistent with endophytes'; silence.

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- Estrogenic mycotoxicosis considered less likely
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- Prof. Jim Henning suggested **CATERPILLARS**; resounding silence. Meeting ended.



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- Moving towards ergot alkaloid/plant endophyte theory.
- Dr. Neil Williams: ‘**Pathology absolutely inconsistent with endophytes**’; silence.
- Prof. Jimmy Henning suggested caterpillars; resounding silence. Meeting ended.
- Sat. 7:00 AM, **Henning/Tobin**: Richmond Rd. McDonalds: Prof. Henning, eyes bright: ‘it’s the Cherry trees/ caterpillars/ [**CYANIDE?**]!’



(c) T Tobin 2022

9/15/2022 "Personally checked the trees/ pastures!!". (cyanide measured in Illinois)

Late May 2001, Official “Working Hypothesis” Cherry trees/Caterpillars/Cyanide

- Became the official **WORKING HYPOTHESIS** of the MRLS group.
- **Caterpillar control measures were recommended/** instituted, including **removal of Black Cherry trees.**
- Other possible toxins were still pursued.



Test the Hypothesis: Epidemiological Survey, 2001 (Roberta Dwyer)

133 Farms, 17,000 Horses, Multiple breeds,
Multiple counties in central Kentucky.

High Risk of MRLS:

- **CHERRY TREES** and seedlings
- Trees stripped of leaves
- **Moderate to heavy CATERPILLAR PRESENCE**

Low Risk of MRLS:

- 10-20% clover in pasture
- Spring fertilization
- 40% or more of any of:
fescue, orchard grass,
bluegrass, clover or other
grasses

- Offered **strong independent support for “caterpillar”** hypothesis.
- **FORCED EVERYBODY TO TAKE THE CATERPILLARS SERIOUSLY**
- Enabled industry to focus on caterpillar prevention.

Spring 2001 → Early Spring 2002

- Numerous toxins/theories tested:
 - Nitrate/nitrite
 - Mycotoxins
 - Plant estrogens
 - Hemlock
 - Cyanide [TT and colleagues] **NO PREGNANT HORSES ABORTED**
- **ALL TOXIN EXPERIMENTS NEGATIVE.**

Spring 2002 The Caterpillars Return

- Pregnant mares + caterpillars->
EFL ABORTIONS Dr. Bruce Webb, Dr. Bill Bernard.
- TT: **Late Term** pregnant mares administered caterpillars: INTUBATED → first abortions in **72 hours**
- **SPEED** of **LFL** abortions **impressive !**



Flip the Hypothesis: 'Bacterial Proliferation First Analysis'

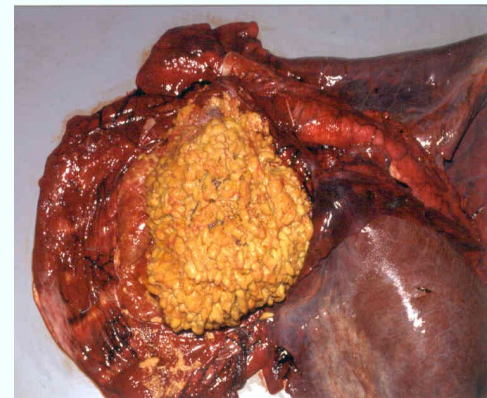
- LATE fetal abortions **RAPID** after caterpillar exposure
- Bacterial **PROLIFERATION** came **PRIOR** to cessation of fetal heartbeat and death of fetus.
- [Previously, thought bacterial proliferation followed TOXIN induced death of fetus].
- **BACTERIAL PROLIFERATION** now appears to be the critical **DRIVING STEP** in MRLS.

HOW DOES EXPOSURE TO THE CATERPILLARS LEADS TO RAPID DISTRIBUTION OF BACTERIA TO:

1/ THE FETUS



2/ THE HEART



3/ A SINGLE EYE

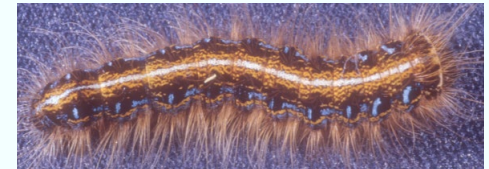
Let's look at the

CATERPILLARS ->



Data: Eastern Tent Caterpillar (ETC)

Very Much Present at Scene



REVISIT Caterpillar Setae Electron Micrograph From 2001

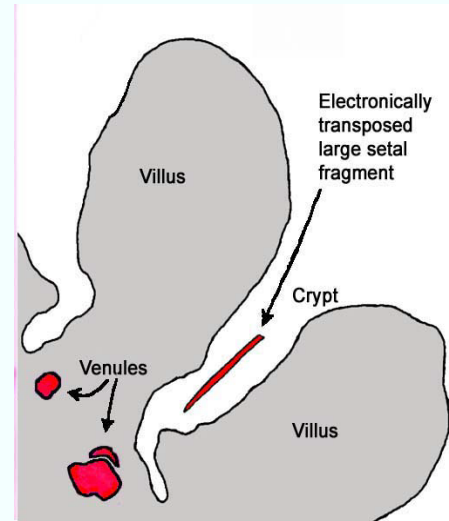
- **Pat Van Meter** and I had looked at the caterpillars by Electron Micrography.
- Setae of the Eastern Tent Caterpillars were clearly mechanically “barbed”.
- The barbs pointed out, away from the caterpillar, which seemed (?) unusual.
- An important finding, implications not realized at the time.



(Note: No toxin/venom occurs with the ETC setae)

Revised Hypothesis (July 10, 2002) ... The “Setal Emboli Hypothesis”

1/ Barbed setal fragments penetrate the intestine. Some **enter blood vessels** and **RANDOMLY DISTRIBUTE** → **SETAL EMBOLI**



3/ Carry bacteria thru body

4/ Fetus large volume, poorly immune protected
->**EFL and LFL**

5/ Eye, small volume, poorly immune protected
>**unique single eyes**

6/ All fragments go thru the heart ->**pericarditis**

Predictions That Arise From The (Revised) “Setal Emboli Hypothesis”

- 1/ **Setal fragments** should present in blood / tissues.
- 2/ It is a probabilistic mechanism; Does MRLS follow **PROBABILISTIC** mathematics?
- 3/ **Mechanical** properties of setal fragment drive this syndrome: Similar caterpillar syndromes in other locations??
(**Australia, 2004, → Caterpillar abortions, Saskatchewan, 2017 → Caterpillar driven pericarditis cases.**)

ETC – ‘Exposed to Caterpillars’

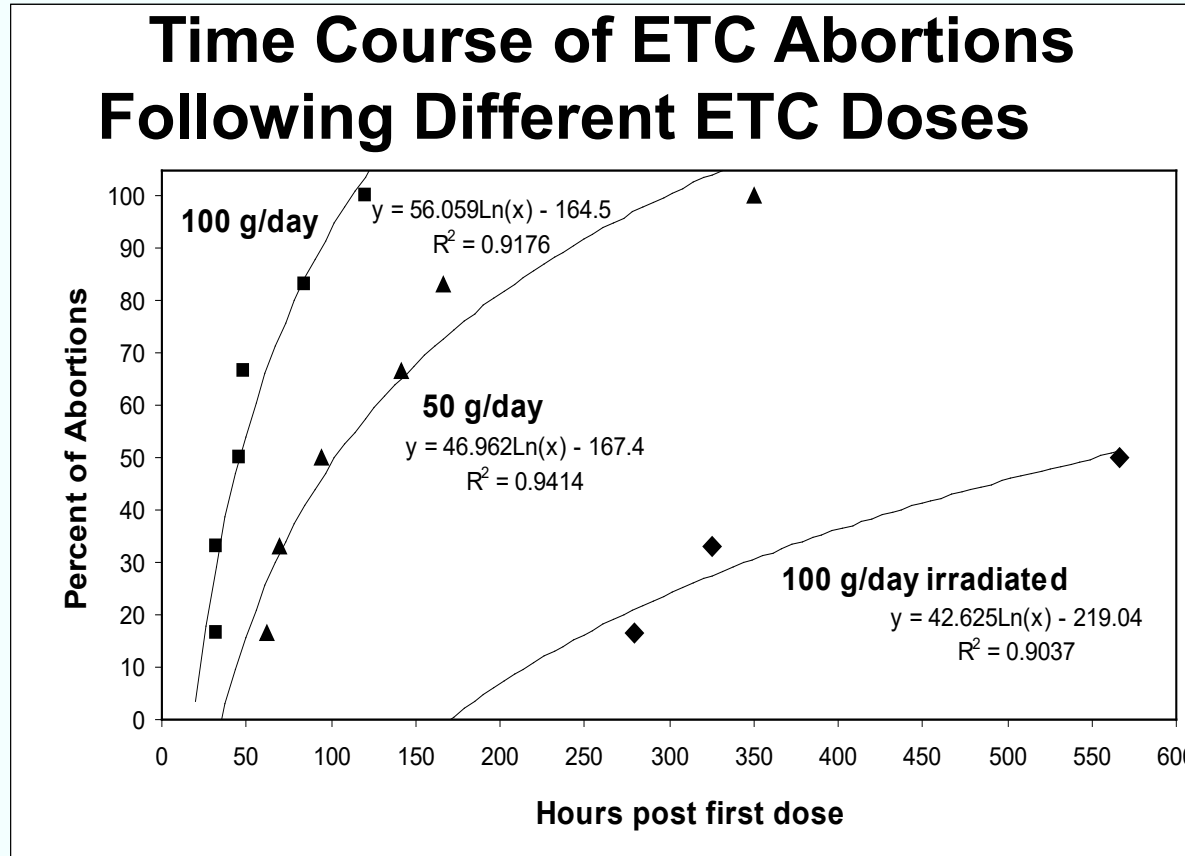


Figure 1. Time course of abortions following intubation of mares with 50 and 100 (nonirradiated or radiated) g of Eastern tent caterpillars (ETCs)/day for 10 days. The solid lines are the best fit regressions for the data points. The calculated x-axis intercepts (apparent lag times) are 20 (100 g), 37 (50 g) and 193 hours (100 g irradiated) after the first dose of ETCs.

Does MRLS follows **PROBABILISTIC** mathematics?

Accelerated Failure Time (AFT) analysis of MRLS

Assumed that time until abortion has a log-normal distribution a survival model that well fits the data is an Accelerated Failure Time Model. The model takes the form:

$$T_i = \exp\{\beta_0 + \beta_1 x_{i1} + \dots + \beta_k x_{ik} + \sigma \varepsilon_i\}$$

1/ Sebastian MM, Gantz M, **Tobin T**, Harkins JD, Bosken JM, Hughes CG, Harrison LR, Bernard WV, Richter D and Fitzgerald TD: 2003 "[The mare reproductive loss syndrome and the eastern tent caterpillar: A toxicological/statistical analysis with clinical, epidemiologic, and mechanistic implications](https://www.researchgate.net/publication/8568892_The_mare_reproductive_loss_syndrome_and_the_eastern_tent_caterpillar_A_toxicological_statistical_analysis_with_clinical_epidemiologic_and_mechanistic_implications)". *Veterinary Therapeutics* **4** (4): 324–39.

https://www.researchgate.net/publication/8568892_The_mare_reproductive_loss_syndrome_and_the_eastern_Tent_Caterpillar_A_toxicokineticstatistical_analysis_with_clinical_epidemiologic_and_mechanistic_implications#fullTextFileContent

Does MRLS follows **PROBABILISTIC** mathematics?

Percent Aborted by Hour and Dose, Accelerated Failure Time Model

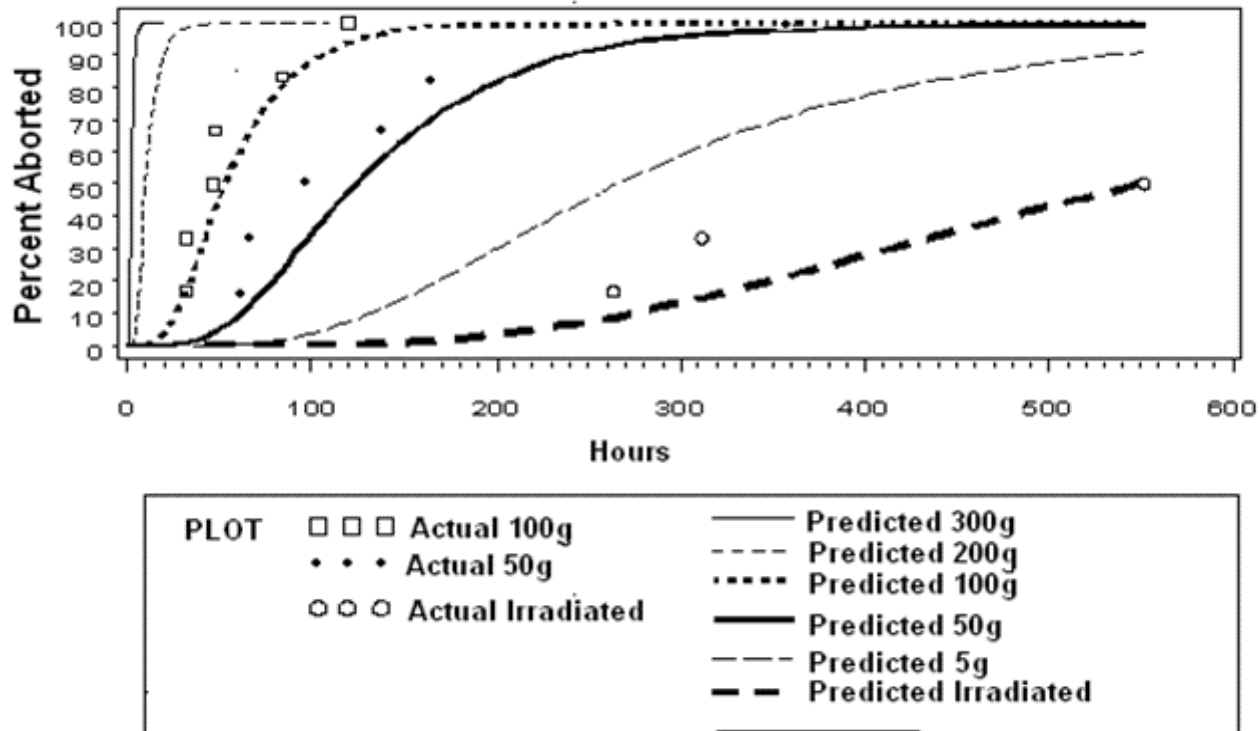


Figure 2. Actual abortion rates following dosing with Eastern tent Caterpillars (ETCs) at 50 and 100 (nonirradiated and irradiated) g/day for 10 days and predicted abortion rates by the accelerated failure time model for doses of 5, 50, 100 (nonirradiated and irradiated), 200 and 300 g ETCs/day. The estimated lag time for the actual ETC doses administered are **10** (100 g), 20 (50 g), and 80 (100 g irradiated) hours.

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CATERPILLAR DOSE AND TIME COURSE OF ABORTIONS

Effect of ETC Dose on Time Course of Abortions

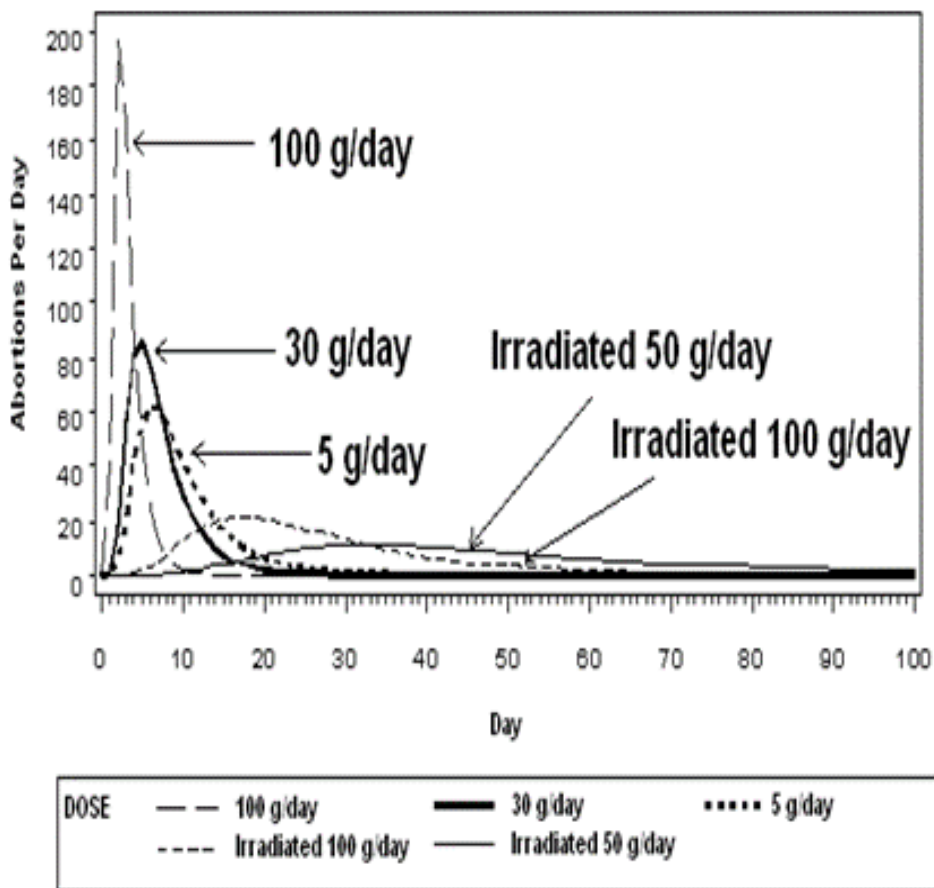


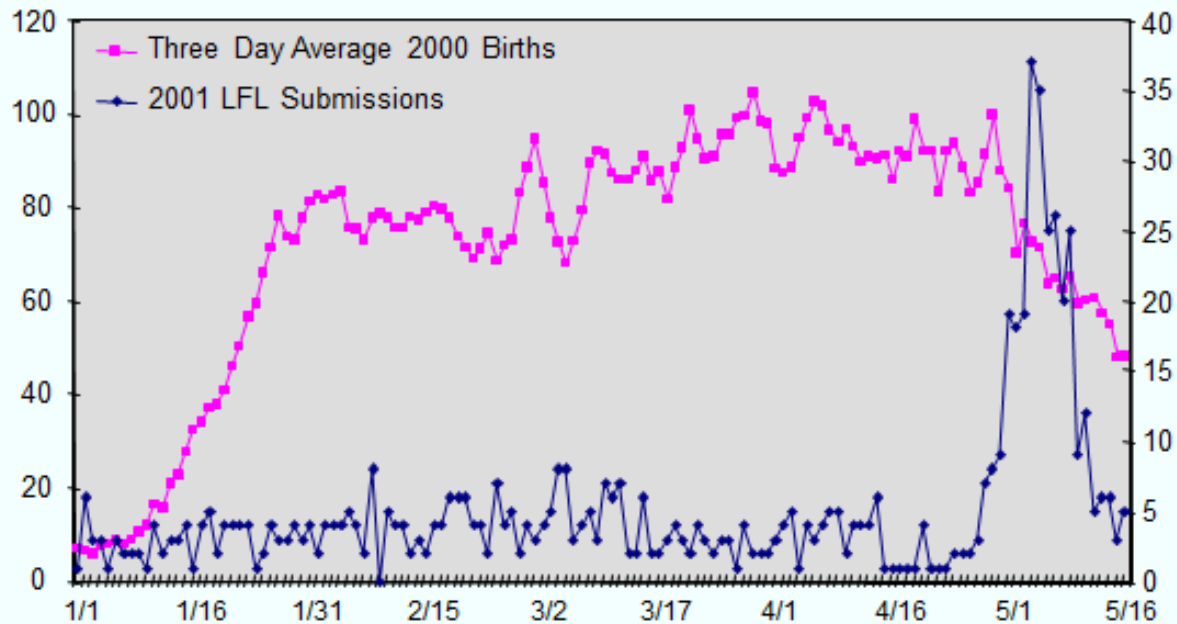
Figure 5. Effect of dose on daily abortion rates as a function of daily exposure to Eastern tent caterpillars (ETCs) for 600 mares. At 100 g of ETCs/day, the abortions occur rapidly, peaking approximately 3 to 4 days after exposure, and virtually all susceptible mares exposed will abort by Day 10. At 30 g/day, the abortions peak about 6 days after exposure and are largely complete within approximately 18 days. If the abortigenic dose of caterpillars is reduced to an amount equivalent to that present in the irradiated caterpillars, the first abortions do not begin to appear until about Day 8, and the abortions will not peak until Day 20. The model assumes that there are 600 mares in each group and that all mares dosed with ETC will eventually abort.

THE FIRST TIME THAT THE SYNDROME WAS LINKED TO THE CATERPILLAR WAS IN 2001, WHEN THE CATERPILLARS WERE UNDERFOOT IN LARGE NUMBERS DURING THE OUTBREAK (30 GRAM DAY CURVE !!).

IN ALL PREVIOUS YEARS THE ABORTIONS WERE NEVER LINKED TO THE CATERPILLARS BECAUSE THE CATERPILLARS STAYED UNDER THE RADAR, SO TO SPEAK. (50 GRAM/DAY IRRADIATED CURVE)

Does MRLS follows **PROBABILISTIC** mathematics?

Late Fetal Losses of Thoroughbred Mares Submitted to Livestock Disease Diagnostic Center



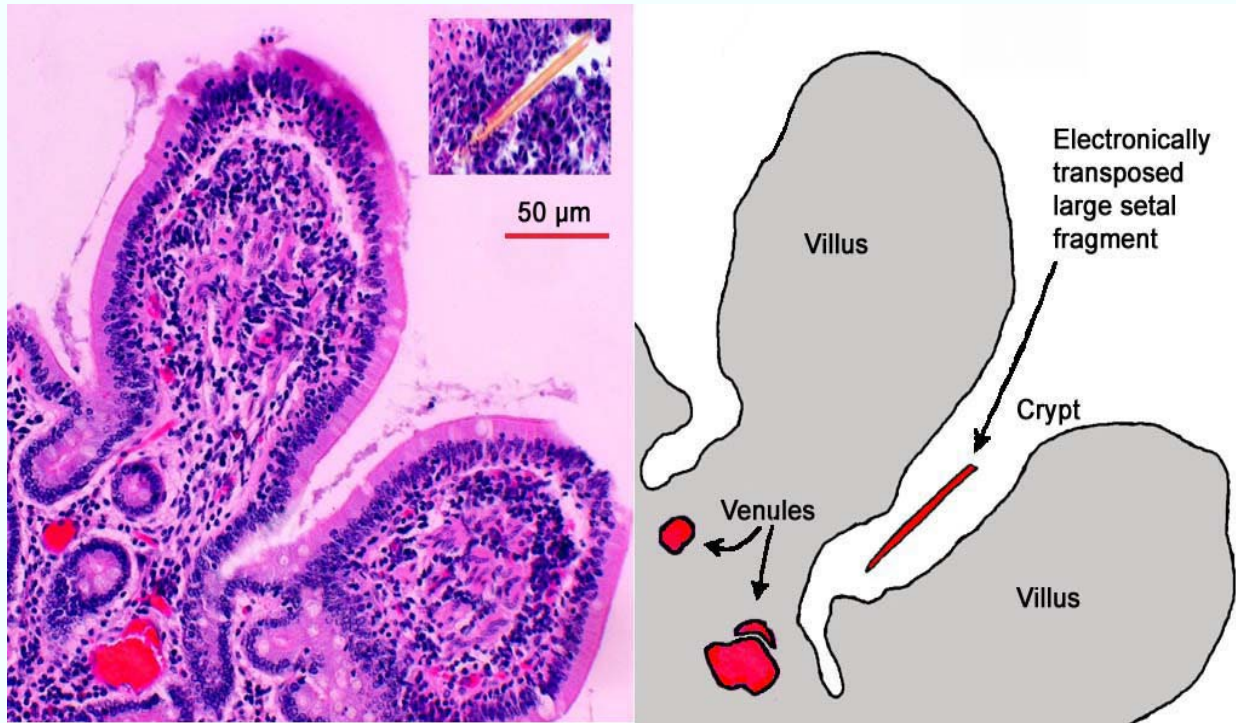
Data provided courtesy of Dr. Albert Kane and Dr. Enzo Campinella, USDA
10/12/2019
Foaling data provided by The Jockey Club Information Systems
(c) T Tobin

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Interpretation: The **PROBABILISTIC** analysis supports the Setal Emboli Hypothesis

Testable Predictions re The “Septic Penetrating Setal Emboli Hypothesis”:

1/ Setal fragments in tissues?

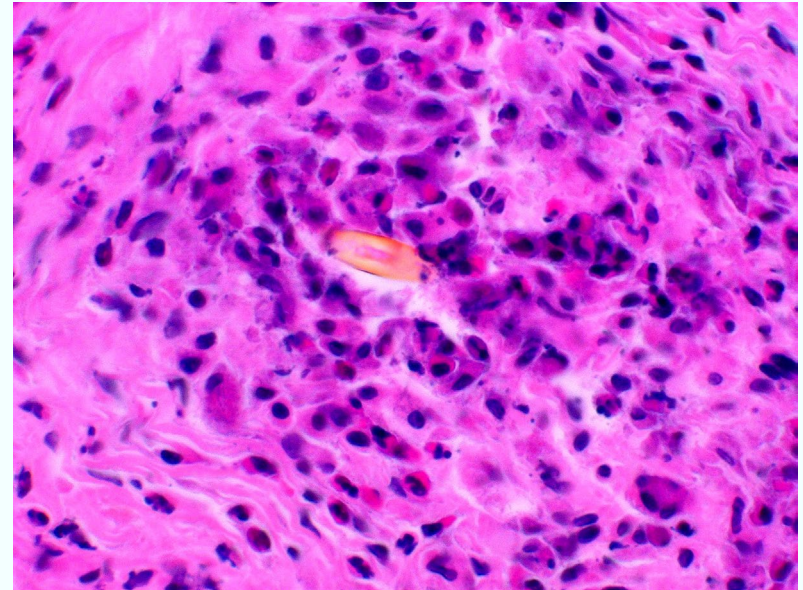
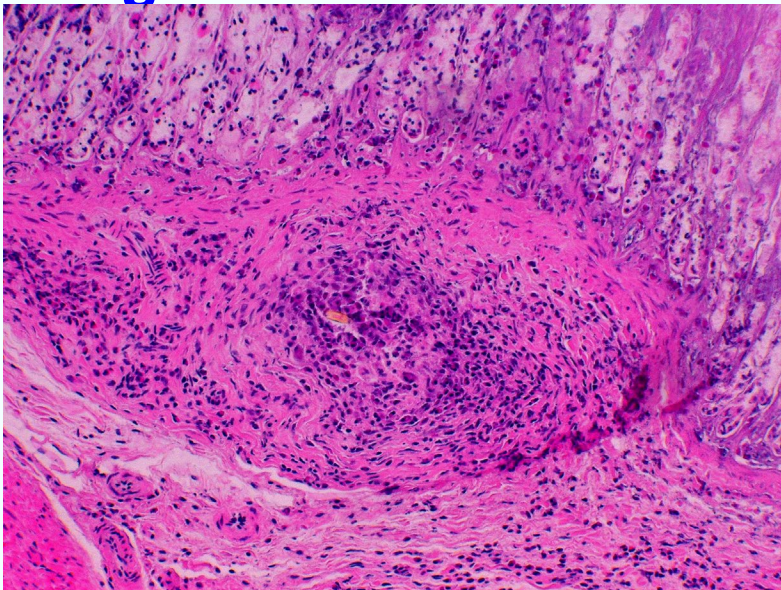


Testable Predictions re The “Septic Penetrating Setal Emboli Hypothesis”:

- If SPSE is correct, **why no MRLS peritonitis??**
- Non-distributing fragments obviously do not penetrate the intestinal tract (stop at connective tissue layer(?)).

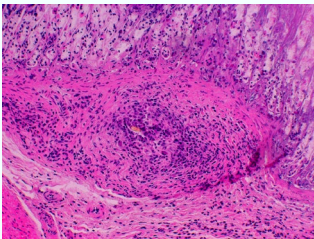
Predictions From The “Septic Penetrating Setal Emboli Hypothesis”:

- If SPSE is correct, **why no MRLS peritonitis??**
- Non-distributing fragments obviously do not penetrate the intestinal tract (stop at connective tissue layer(?)).
- Sept 03 or so Dr. Neil Williams, reviewing intestinal tissues from ETC dosed pigs, **observed numerous intestinal microgranulomas containing setal fragments.**

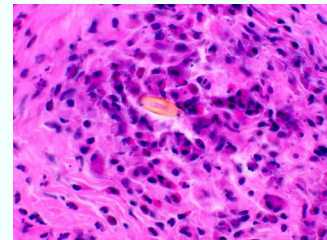


Testable Predictions That Arise From The “Septic Penetrating Setal Emboli Hypothesis”:

- If SPSE is correct, **why no MRLS peritonitis??**
- Non-distributing fragments obviously do not penetrate the intestinal tract (stop at connective tissue layer?).
- In or about Sept 03 Dr. Neil Williams, reviewing intestinal tissues from ETC dosed pigs, **observed numerous intestinal microgranulomas containing setal fragments.**



GAME OVER



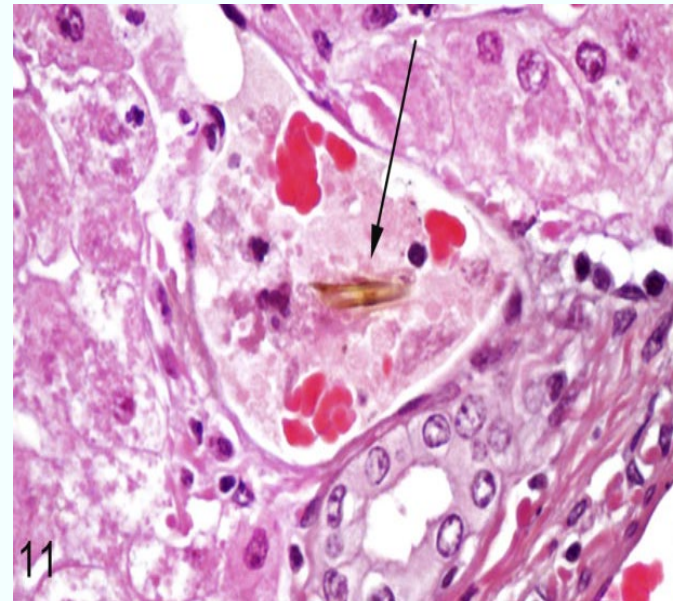
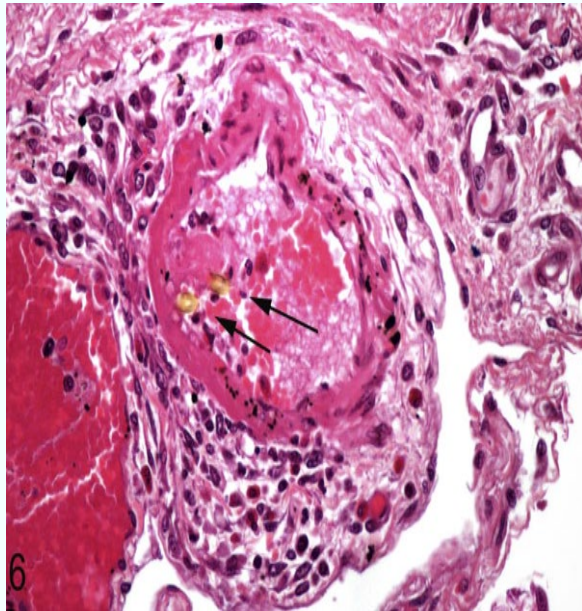
- Subsequent experiments in rats, pigs and apparently horses have shown numerous intestinal setal fragments in ETC dosed animals, and also in the equine uterus.

Australia, 2004, Todhunter, Perkins et al,

- 2004: **Equine Abortions in Hunter Valley, NSW**, TT asked to review MRLS with NSW vets.
- Advised Dr. Nigel Perkins, Experimental priority #1, **Caterpillars**, other possibilities, priority #2.
- Colloquially “**Bag-shelter moth caterpillars**”
- **Processionary Caterpillars** have **barbed hairs**, abortion syndrome named **Equine Amnionitis and Fetal Loss, EAFL**.
- Caterpillar administrations showed setal fragments in blood vessels and many **setal fragments in affected uteri**.
- Researchers consider that EAFL setal transfer is **direct transperitoneal migration from intestine to the uterus**.
- Risk period, February to September, peaks in May.
- Interval from exposure to abortion can be days or months, (consistent with random slow setal fragment migration).
- EAFL may be 1/3 of regional Thoroughbred abortions.

Testable Predictions That Arise From The “Septic Penetrating Setal Emboli Hypothesis”:

- A similar syndrome, EAFL, identified in Australia in 2004
- Administered caterpillars to pregnant mares
- Observed barbed setal fragments in blood vessels.
- Note: Speed of delivery to uterine membranes critical.



New Syndrome linked to “Septic Penetrating Setal Emboli”:

INTERSTITIAL SUPPURATIVE PLACENTITIS, ISP

- The placentitis associated with MRLS is also unique
- Not an ascending placentitis through the cervix
- Not a hematogenous placentitis; no inflammation of the villi
- Has been tentatively named an **INTERSTITIAL SUPPURATIVE PLACENTITIS, ISP**.
- Equine Amnionitis and Fetal Loss is a correct description of the fetal portions of this syndrome.

FOREST TENT CATERPILLARS IN SASKATCHEWAN : SEPTIC FIBRINOUS PERICARDITIS

- Spring 2007: Chapuis et al, 2020: Saskatchewan outbreak of **Forest Tent Caterpillars**
- **4 horses** presented to Univ Saskatchewan Coll of Vet. Med. with right sided heart failure due to **Septic Fibrinous Pericarditis**.
- Clinically similar to MRLS pericarditis cases.
- **“Refractile yellowish brown foreign material”** noted in center of colonic lesions in one case suggesting involvement of caterpillar setae
- Clinical condition challenging and expensive to treat, with poor long term poor prognosis.

SUMMARY

- MRLS is caused by tissue distribution of barbed Septic Penetrating Setal Fragments.
- Clinical outcomes occur only in **poorly immune protected tissues.**
- The largest poorly immune protected tissue in horses is the **Late Term Fetus, [LFL]** next is the **Early Fetus [EFL]. Fetus LFL + [EFL] => MRLS**

SUMMARY

Probabilistic Implications

- MRLS events are probabilistic, and MRLS strictly follows probabilistic mathematics.
- OCULAR and CARDIAC syndromes are fragment distribution outcomes in all horses.
- The EYE data allow estimation of the mean number of distributing setal fragments; in the order of 10/day.

SUMMARY

- 1/ Mechanical** properties of the **BARBED** setal fragment drive the syndrome:
- 2/ July 10, 2002 Prediction:** It should occur with similar caterpillar setal structures **in other places**

Tobin T, Harkins JD, VanMeter PW, Fuller TA: 2004; The Mare Reproductive Loss Syndrome and the Eastern Tent Caterpillar II: A Toxicokinetic/Clinical Evaluation and a Proposed Pathogenesis: Septic Penetrating Setae. Int J Applied Res in Vet Med, Vol 2 No2 p 142 -158.

https://uknowledge.uky.edu/cgi/viewcontent.cgi?article=1029&context=gerc_facpub

SUMMARY

Similar Caterpillars **in other places**

- 2004: **Australian** Equine Amnionitis and Fetal Loss, EAFL, also caterpillar driven (Case **NUMBERS SMALL** relative to Kentucky!) Neundorf, F.(2007) Caterpillars are aborting our mares. *Australian Performance Horse*, January, pp 56-8.
- 2013: **Gabriel Volpato**: “Duda” syndrome in **Western Sahara** camels, **LONG KNOWN** to be caterpillar driven (“**Everybody knows!**”,).
- 2017: Caterpillar associated Fibrinous Pericarditis cases in Saskatchewan, Forest tent caterpillars.

Prevention / Treatment

PREVENTION, PREVENTION, PREVENTION :

- 1/ Keep pregnant horses away from caterpillars.
- 2/ Remove Black Cherry trees from equine pasture areas.
- 3/ Remove caterpillars eggs/caterpillars from affected trees.
- 4/ Muzzle horses if potential exposure to caterpillars is unavoidable.

TREATMENT

- 1/ Treatment is challenging given that MRLS occurs in poorly immune protected tissues.
- 2 / Make sure the foal gets its Colostrum
- 3/ Treatment is basically symptomatic, i.e., broad spectrum antibiotics.
- 4/ Treatments as required by the clinical condition.

CLOSING SUMMARY

The Septic Penetrating Setal Hypothesis explains:

- 1/ The Four related syndromes defined as MRLS.
- 2/ The probabilistic mathematics underlying MRLS.
- 3/ The lack of systemic symptoms in affected horses.
- 4/ Why the syndrome resisted identification until 2001.
- 5/ The range of bacteria associated with the syndrome.
- 6/ The *Serratia marcescens* caterpillar intubation link.
- 7/ The pathologically unique placentitis associated with MRLS.
- 8/ Predicted similar caterpillar associated syndromes elsewhere.
- 9/ As we speak, seems to be well under control in Kentucky.

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REFERENCES

1/ Sebastian MM, Gantz M, **Tobin T**, Harkins JD, Bosken JM, Hughes CG, Harrison LR, Bernard WV, Richter D and Fitzgerald TD: 2003 "[The mare reproductive loss syndrome and the eastern tent caterpillar: A toxicological/statistical analysis with clinical, epidemiologic, and mechanistic implications](#)". *Veterinary Therapeutics* 4 (4): 324–39.

https://www.researchgate.net/publication/8568892_The_mare_reproductive_loss_syndrome_and_the_easte rn_Tent_Caterpillar_A_toxicokineticstatistical_analysis_with_clinical_epidemiologic_and_mechanistic_implic ations#fullTextFileContent

•
2/ **Tobin T**, Harkins JD, VanMeter PW, Fuller TA: 2004; The Mare Reproductive Loss Syndrome and the Eastern Tent Caterpillar II: A Toxicokinetic/Clinical Evaluation and a Proposed Pathogenesis: Septic Penetrating Setae. *Int J Applied Res in Vet Med*, Vol 2 No2 p 142 -158.

https://uknowledge.uky.edu/cgi/viewcontent.cgi?article=1029&context=gerc_facpub

3/ Neundorf, F.(2007) Caterpillars are aborting our mares. *Australian Performance Horse*, January, pp 56-8.

4/ **Volpato G**, Di Nardo A, Rossi D, Saleh SM, Broglia A. 'Everybody knows', but the rest of the world: the case of a caterpillar-borne reproductive loss syndrome in dromedary camels observed by Sahrawi pastoralists of Western Sahara. *J Ethnobiol Ethnomed*. 2013 Jan 10;9:5. doi: 10.1186/1746-4269-9-5. PMID: 23305273; PMCID: PMC3561205. <https://pubmed.ncbi.nlm.nih.gov/23305273/>

5/ Todhunter KH, Perkins NR, Wylie RM, Chicken C, Blishen AJ, Racklyeft DJ, Muscatello G, Wilson MC, Adams PL, Gilkerson JR, Bryden WL, Begg AP. Equine amnionitis and fetal loss: the case definition for an unrecognised cause of abortion in mares. *Aust Vet J*. 2009 Jan-Feb;87(1):35-8. doi: 10.1111/j.1751-0813.2008.00386.x. PMID: 19178475. <https://pubmed.ncbi.nlm.nih.gov/19178475/>

6/ https://hoofbeats.com.au/sneakpeekNEW/newspeak/march18_hairycaterpillars.html

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REFERENCES

7/ Chapuis RJJ, Ragno VM, Ariza CA, Movasseghi AR, Sayi S, Uehlinger FD, Montgomery JB. Septic fibrinous pericarditis in 4 horses in Saskatchewan following an outbreak of forest tent caterpillars in 2017. *Can Vet J.* 2020 Jul;61(7):724-730. PMID: 32655155; PMCID: PMC7296872.

8/ Slovis, N. (2011) Pericarditis: A clinical perspective during an epidemic of fibrinous pericarditis in central Kentucky: *Equine vet. Educ.* 23 (2) 69-72.

9/ McDowell KJ, Webb BA, Williams NM, Donahue JM, Newman KE, Lindemann MD, Horohov DW. Invited review: the role of caterpillars in mare reproductive loss syndrome: a model for environmental causes of abortion. *J Anim Sci.* 2010 Apr;88(4):1379-87. doi: 10.2527/jas.2009-2584. Epub 2010 Jan 15. PMID: 20081071.

10/ Burns SJ, Westerman AG, Harrison LR. Environmental influences on mare reproductive loss syndrome: Do they fit with a toxin as the causative agent? *J Equine Vet Sci.* 2022 Apr 28;114:104001. doi: 10.1016/j.jevs.2022.104001. Epub ahead of print. PMID: 35490973.