

Tall Fescue Workshop

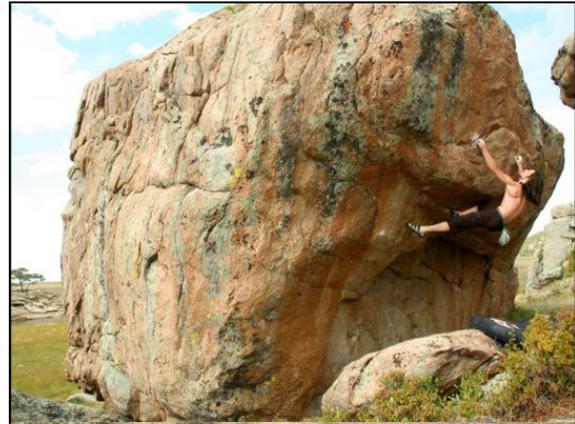
The Effect of Alkaloids in Toxic Tall Fescue on the Animal

 **The Effects of Alkaloids in Toxic Tall Fescue on the Animal**

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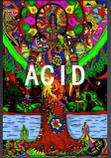
John Studemann, USDA, JPC
Fred Thompson, Vet. Med., UGA
Don Dawe, Vet. Med., UGA
George Rottinghaus, Vet Med., U. MO.
Nik Filipov, Vet. Med., UGA

..... and STEVE



 **Who is Steve?**

1. Rock climber
2. Hippie
3. "Better Living Through Chemistry"
4. Let's see what happens when I drop 'acid' and **GO ROCK CLIMBING !!!!!**

 +  = **BAD News**

 **Candidate Toxins**
(1986)

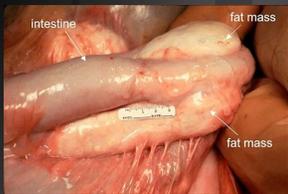
- Loline (n-acetyl and n-formyl) ✓
- Peramine
- Lolitrem (a, b, d, e, etc.)
- Ergot alkaloids (**LSD !!!!!**) ✓

 **Symptoms and Syndromes of Fescue Toxicosis**

Fescue Foot	Summer Slump	Fat Necrosis
Swelling (fetlock, hoof)	< grazing (daytime)	Poor thrift
Lameness	Shade, ponds, streams, wallows	< weight gain
Dry gangrene (ear, tail)	< body weight gain	
Loss of tail switch	Elevated core temperature	
Loss of hooves	Rough hair coat	
	> respiration	
	Excessive salivation	
	Lower serum prolactin	
	Lower milk production	
	Dystocia/abortion	

 **Fat Necrosis**
(prolonged exposure only)

Intestine (blockage)



Kidney (cardiovascular)



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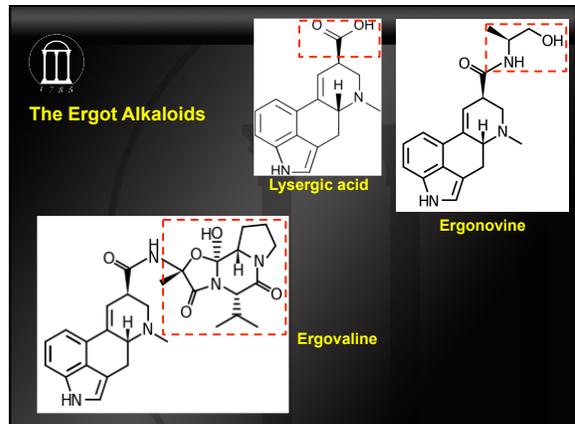
* Associated with vasoconstriction

Symptoms and Syndromes of Fescue Toxicosis

Summer Slump

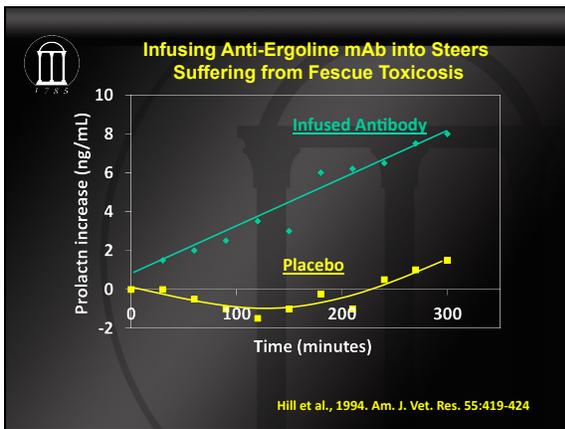
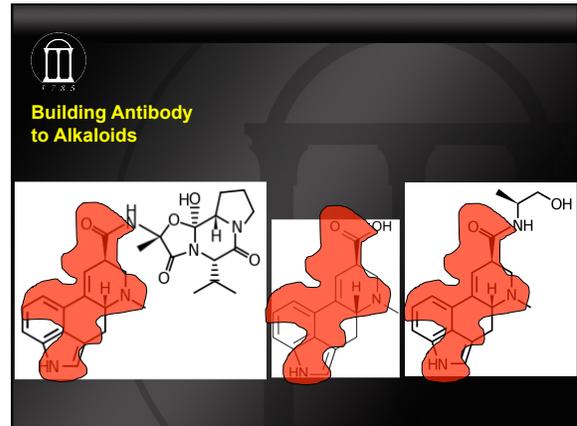
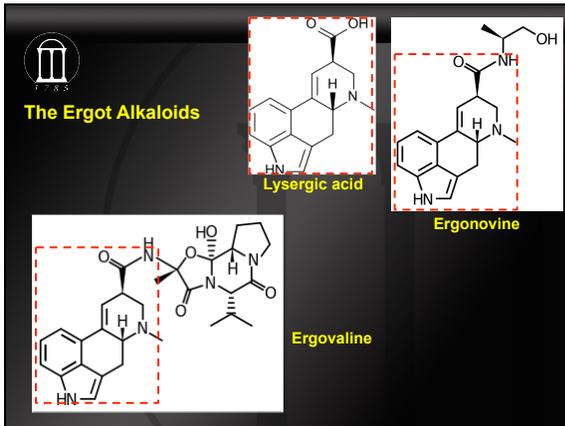
- < grazing (daytime)
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- Elevated core temperature
- Rough hair coat
- > respiration
- Excessive salivation
- Lower serum prolactin*
- Lower milk production
- Dystocia/abortion

* a physiological marker



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Mechanism of Ergot Alkaloid Action

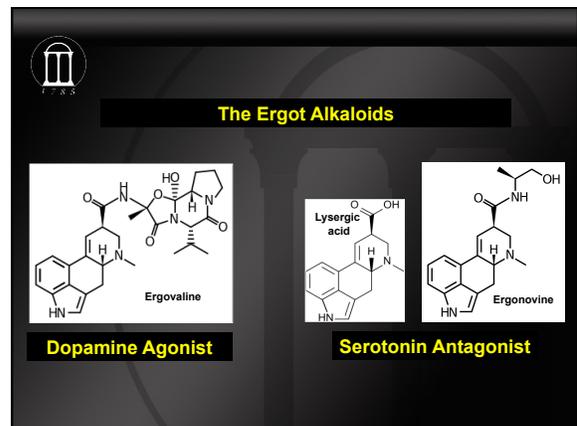
Dopamine Agonist (stimulant)
 Produced in pituitary
 Produced in GI track (80%)

- Causes smooth muscle constriction (high doses)
- Vaso – poor blood flow (blood pressure)
- Gastric – poor gut motility - compaction

Mechanism of Alkaloid Action

Serotonin Antagonists (suppressant)
 Produced in pituitary/hypothalamus (brain)
 Transported to, and impacts, the in GI track
 Product of tryptophan metabolism

- Causes mood disorders
- Eating disorders (common in anorexic individuals)
- Gastric – effective treatment for constipation



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How Do We Analyze for Alkaloids?

We Sieve

Large

Medium

Small

Ergovaline

Ergonovine

Lysergic acid

Testing for Toxins - HPLC

Little Stuff

Big Stuff

Lysergic acid

Ergovaline

Testing for Toxins - HPLC

E+

low EV

high EV

Ergovaline + at least 5 other ergot alkaloids.

In other words, figuring this out won't be easy!

The Ergot Alkaloids

"The chemical diversity of ergot alkaloids corresponds to the diversity of the biological activities of these compounds. It is probably correct to state that there are few chemical groups which comprise substances with such diversified actions. It has been accurately said that ergot alkaloids have been a treasure chest to pharmacologists and a treasure house for drugs."

Berde and Sturmer, 1978.

Ruminal Metabolism of Ergot Alkaloids

Metabolism of ergot alkaloids - Site of absorption Ayers et al., 2008

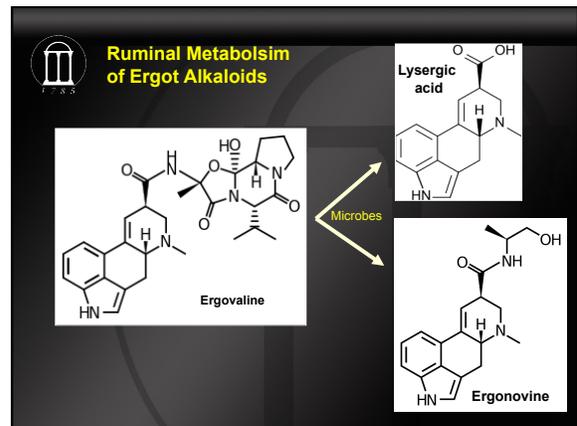
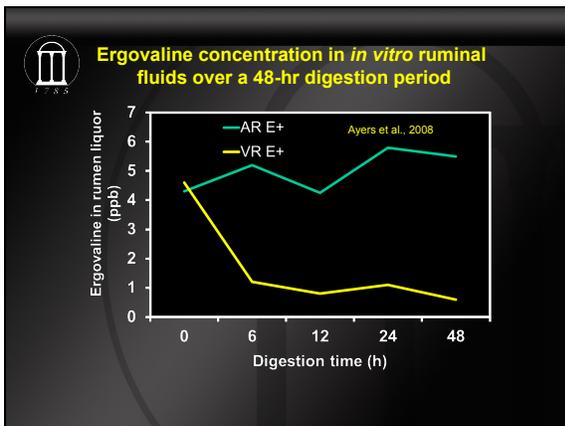
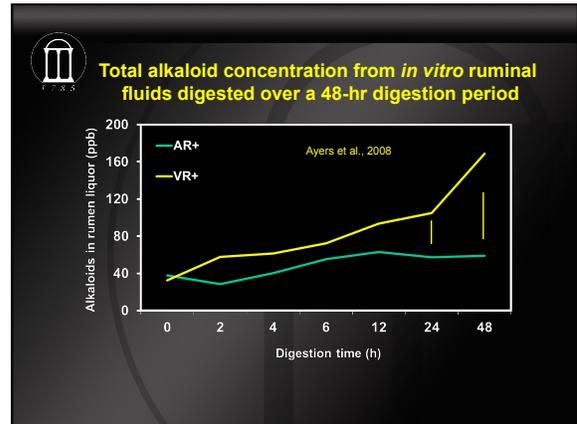
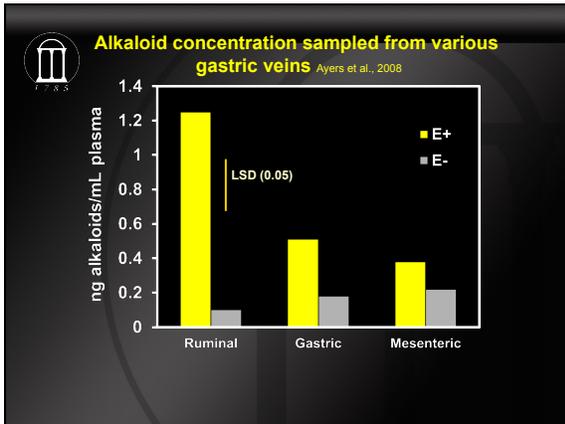
Ruminal

Gastric

Mesenteric

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Ergot Alkaloid Transport



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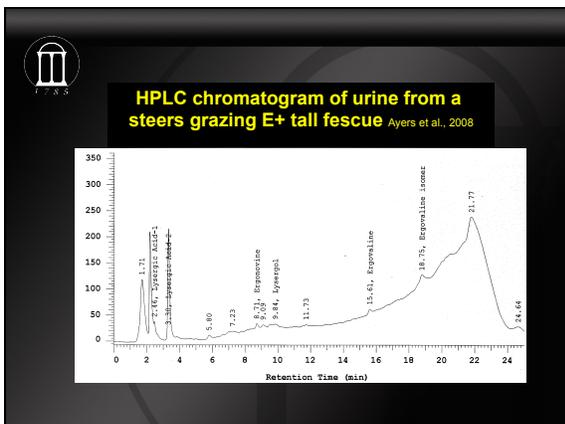
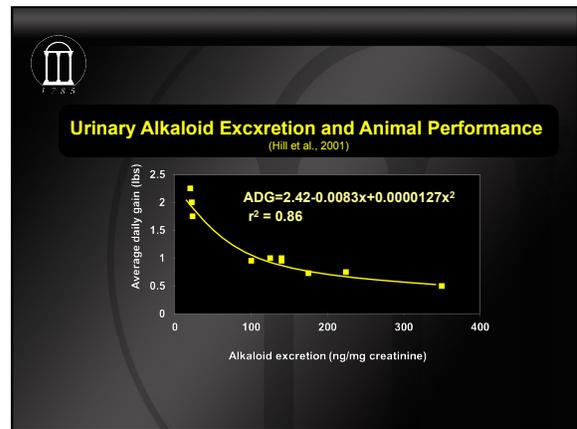
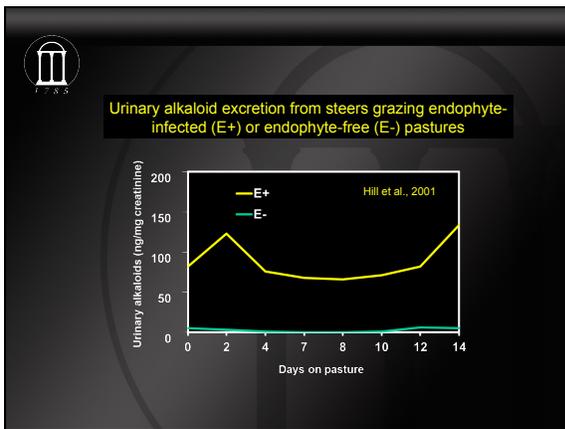
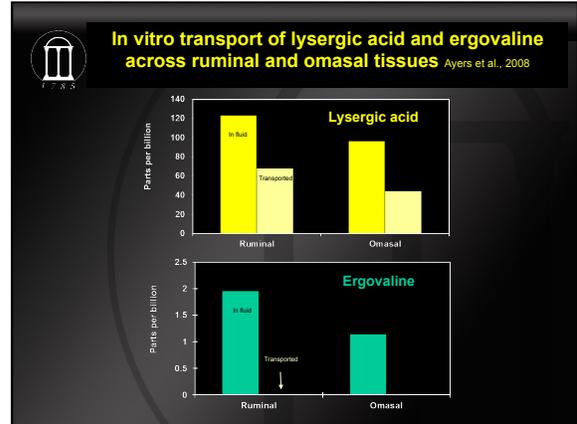
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Mucosal side-ergot alkaloids in KRPG

Serosal side-equal amount of KRPG

Tubes to bubble 95% O₂ and 5% CO₂

Water Bath 39°C

Truth is rarely pure and never simple.
 - Oscar Wilde

..... And neither is fescue toxicosis.

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Metabolomics – A New Research Tool
(Current research - Filipov, Jones, Hill)



Toxic Endophyte Tall Fescue **Non-toxic Endophyte Tall Fescue**



Metabolomics – A New Research Tool
(Current research - Filipov, Jones, Hill)

Sample Blood, Plasma, Urine From Cattle Grazing
Toxic, Non-Toxic Tall Fescue

- Screen for chemical changes in each (including ergot alkaloids)
- Circulating toxins – lysergic amides, no ergovaline
- Appears that vasoconstrictive effects are not directly due to alkaloids, but a result of other alkaloid-induced metabolic changes