



## Practical Equine Endocrinology

Hambletonian Continuing Education Seminar  
East Rutherford, NJ

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## 14-year-old Arabian gelding



## 14-year-old Arabian gelding

- Owned since birth
- Always an “easy keeper”
- Ridden 3 to 4 times per week
- Used for working cattle
- Has always had a thick neck crest
- Complaint of foot soreness

## Survey Radiographs



## Endocrine disorder?

- Only complaint is foot soreness
- Too young for PPID
- Not sure what “Equine Metabolic Syndrome” means

Frank, et al. *J Vet Intern Med* 2010

## Cushing's: Easily recognizable

- Older (> 15 years) horse with:
  - Long curly haircoat that does not shed
  - Muscle loss
  - Cresty neck and tailhead fat pads
  - PU/PD
  - Laminitis

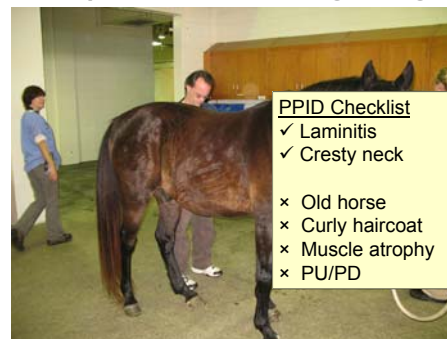


### General appearance

- Too FAT in some places
  - Cresty neck
  - Fat pads at tail head
  - Bulging supraorbital fat
- And too THIN in other places
  - Loss of muscle mass
  - Sway back
  - Ribs easily palpated
- Rounded abdomen (pot-bellied)

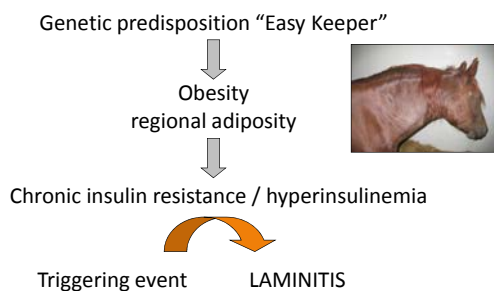


### 14-year-old Arabian gelding



- PPID Checklist**
- ✓ Laminitis
  - ✓ Cresty neck
  - × Old horse
  - × Curly haircoat
  - × Muscle atrophy
  - × PU/PD

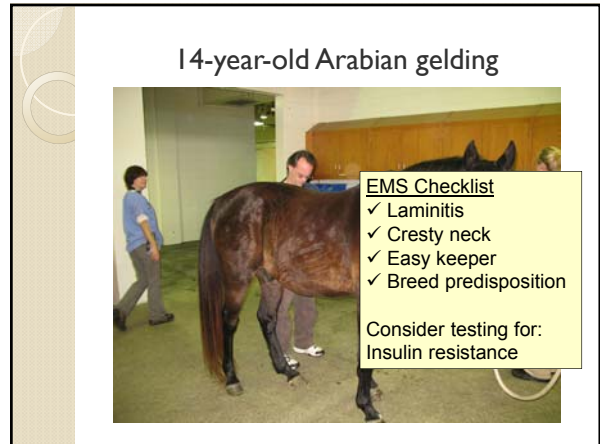
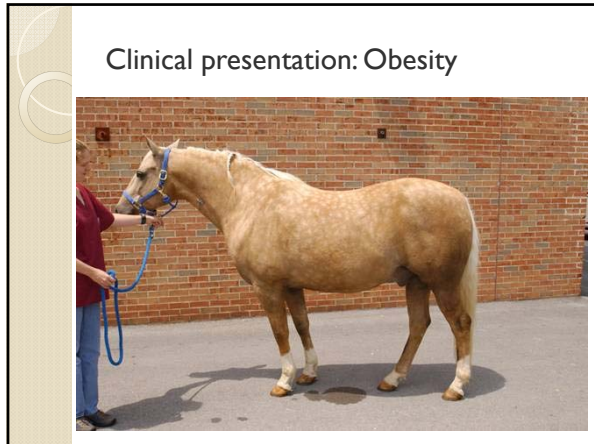
### Equine Metabolic Syndrome (EMS)




### Breed predisposition

- Most commonly affected: Ponies, Morgans, Paso Finos, and Arabians
- Warmbloods, Quarter Horses, Saddlebreds, and Tennessee Walking Horses





### Screening for IR



**Glucose**

- Within reference range in most cases
- Higher in comparison with healthy controls
  - Frank et al. (2006) J Am Vet Med Assoc
  - Treiber et al. (2006) J Am Vet Med Assoc
- Persistent hyperglycemia raises concern
  - Must determine whether transient or persistent
  - Persistent hyperglycemia indicates type 2 DM
    - Durham et al. (2009) Equine Vet J

**Recommendation:**

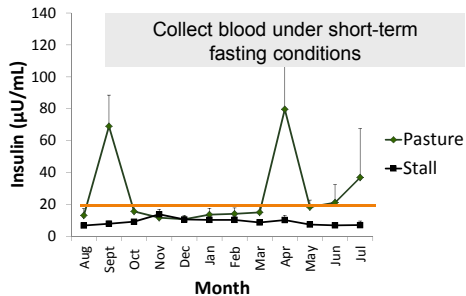
### Resting insulin concentration

- Sample collection
  - Move to stall or dirt paddock
  - Leave only one flake hay in stall after 10 PM
  - Collect blood in the morning to standardize
- Interpretation
  - Fasted samples only
  - Hyperinsulinemia if **> 20 µU/mL** by RIA
  - Use reference range for laboratory if ELISA

### Insulin: Considerations

- Variation among assays and diagnostic laboratories
  - Diagnostic Products Corporation RIA
  - Diagnostic Systems Laboratory Inc. RIA
  - Mercodia Inc. ELISA

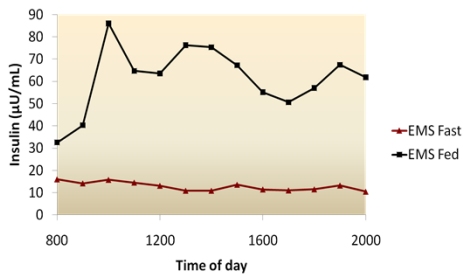
### Insulin responds to diet: Pasture



Collect blood under short-term fasting conditions

Mean ± SE (n = 17)

### Insulin responds to diet: Hay



Mean (n = 6)

### Cornell Diagnostic Laboratory

<http://diagcenter.vet.cornell.edu/>  
Telephone: (607) 253-3900

Tube	Test	Price
EDTA or serum	Insulin	\$17.00
Serum	Glucose	\$8.00
EDTA plasma	Insulin & ACTH	\$38.00


- Grey-topped (oxalate) or serum tube for glucose
- Keep on ice packs or refrigerate
- Centrifuge the same morning or afternoon



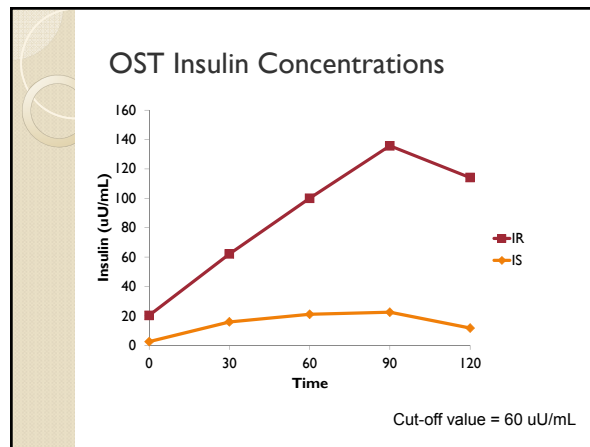
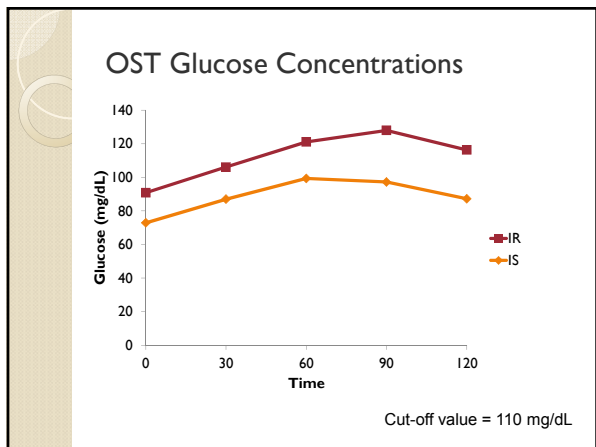
### Dynamic testing

- Research
  - Euglycemic-hyperinsulinemic clamp (EHC)
  - Frequently-sampled intravenous glucose tolerance test (FSIGTT)
- In-house facility
  - Combined glucose-insulin test (CGIT)  
Eiler et al. (2005) Am J Vet Res
- Field practice
  - Oral sugar test (OST)
  - DST with insulin measurements (in development)  
Borer et al. (2010) ACVIM abstracts


### Recommendation: Oral Sugar Test (OST)



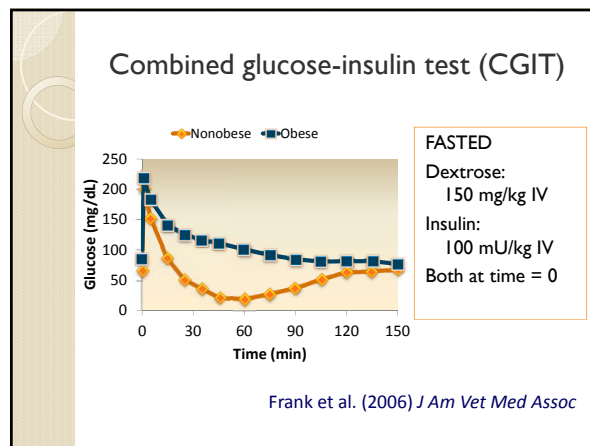
- Karo® Light (not "Lite") syrup
- Contains one gram/mL digestible sugar
- Dosage: 150 mg/kg
- Equal to 0.15 mL/kg (75 mL for 500 kg)
- Test under short-term fasting conditions
- Administer by mouth with a dose syringe
- Measure blood glucose and insulin concentrations 60 to 90 minutes later

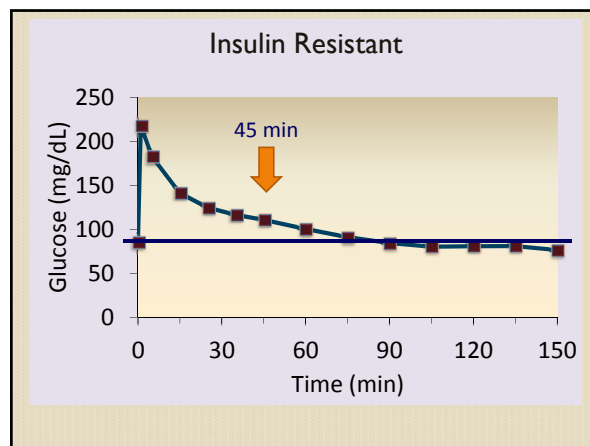
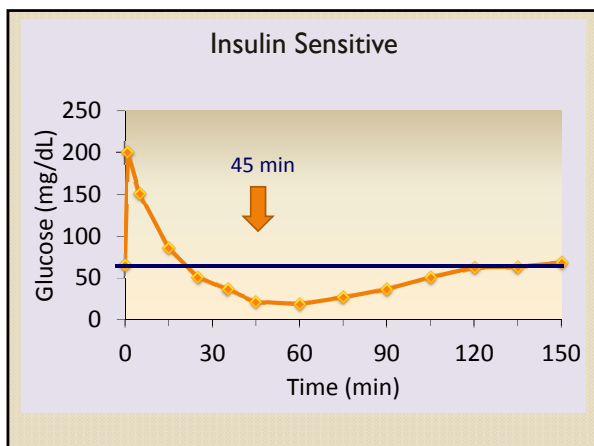


### Simplified OST



- Provide owner with 60 mL syringes
- Owner purchases & administers Karo syrup
- Veterinarian arrives to collect blood 60 to 90 minutes later
- Provisional guidelines for interpretation
  - Insulin resistant if:
    - Glucose > 110 mg/dL
    - Insulin > 60 µU/mL





### 14-year-old Arabian gelding

EMS Checklist

- ✓ Laminitis
- ✓ Cresty neck
- ✓ Easy keeper
- ✓ Breed predisposition
- ✓ **Insulin resistance**

Laboratory Results  
 Glucose: 95 mg/dL (normoglycemia)  
 Insulin: 56 µU/mL (hyperinsulinemia)



### Pathophysiology of PPID

- Pars intermedia is normally in a state of tonic inhibition
- Inhibited by dopamine released from dopaminergic neurons that extend down from the hypothalamus
- Dopamine interacts with D2 receptors on melanotrophs and inhibits their activity

### Pathophysiology of PPID

- Dopaminergic neurons undergo oxidative damage
- Accelerated process in some horses
- As dopaminergic neurons are lost, melanotrophs are less inhibited.
- Hyperplasia develops and melanotrophs secrete more hormones
- Permissive environment for neoplasia, so functional pituitary adenomas develop

*McFarlane et al., J Neuroendocrinol 2005*



### Early PPID

- Important to detect early disease
- Initiate management to prevent laminitis
- ACTH and DST results may be negative
- Key question:  
Wait for positive test results or base diagnosis on clinical judgment?

### Early PPID

1. Delayed shedding of winter hairs (compare to other horses in the barn)
2. Increase in calorie demands; a transition from "easy keeper" to regular horse
3. Loss of muscle mass (epaxial muscles)
4. Deterioration in glucose and insulin values (exacerbation of IR in well regulated horse)

### Recommendation:

#### Resting ACTH concentration

##### Sample collection

- Use plastic EDTA tube
- Keep on ice packs or refrigerate
- Centrifuge same morning or afternoon

##### Interpretation

- Positive if **> 35 pg/mL** by chemiluminescence

### Advances in resting ACTH

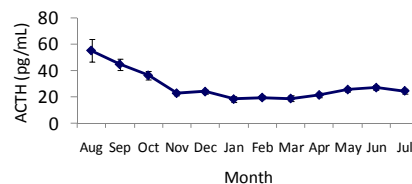
#### Limitations

- Healthy horses have higher ACTH concentrations in late summer/fall
- Within-horse variability

#### Recommendations

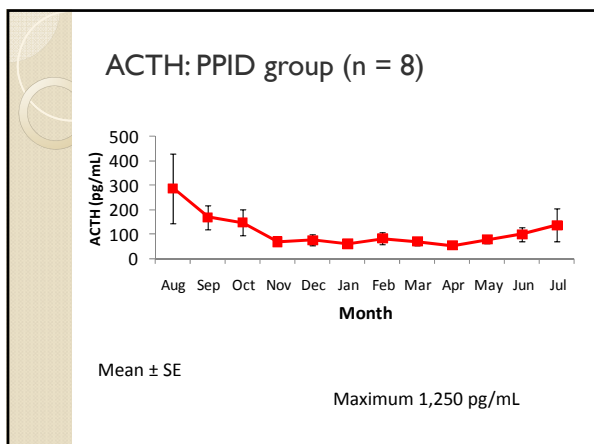
- Adjust reference range to < 50 pg/mL in August, September, and October
- Use the seasonal rise as a dynamic test
- Take multiple samples in suspected cases

### ACTH: Control group (n = 9)



Mean ± SE

Maximum 105 pg/mL



Recommendation:  
**Overnight DST**

Procedure

- Measure cortisol at 0 and 24h (or just 24h)
- Inject 0.04 mg/kg dexamethasone IV (20 mg for a 500-kg horse)

Interpretation

- Positive if > 10 ng/mL (1.0 µg/dL) at 24h

Limitation

- Owner concerns about laminitis

### TRH Response Test

Procedure

- Measure ACTH at 0 and 30 min (\$22 each; \$44)
- Inject 1.0 mg TRH intravenously at time = 0

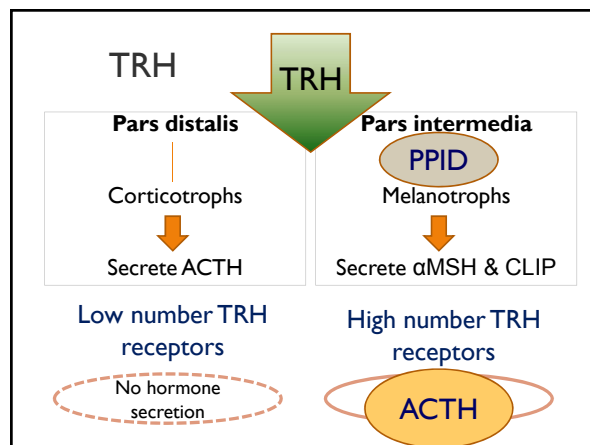
Interpretation

- Positive if > 35 pg/mL at time = 0 or 30 min
- Affected by fall season

Limitation

- TRH available as medical grade (\$600/test)
- Research centers purchase reagent grade TRH and prepare a solution (\$25/test)

Beech et al. J Am Vet Med Assoc 2007



### 14-year-old Arabian gelding

EMS Checklist

- ✓ Laminitis
- ✓ Cresty neck
- ✓ Easy keeper
- ✓ Breed predisposition
- ✓ **Insulin resistance**

PPID Checklist

- ✓ Laminitis
- ✓ Cresty neck
- ✓ Delayed shedding
- ✓ **Positive DST**

Laboratory Results

Glucose: 95 mg/dL  
 Insulin: 56 µU/mL  
**Positive DST**

Equine Metabolic Syndrome	PPID Cushing's
<ul style="list-style-type: none"> <li>• Weight loss if obese</li> <li>• Exercise</li> <li>• Low soluble carb diet</li> <li>• Limit pasture access</li> </ul>	<ul style="list-style-type: none"> <li>• Drug therapy (Pergolide)</li> <li>• Weight maintenance</li> <li>• Manage complications</li> </ul>



## Limited pasture grazing

### Goals

1. Prevent obesity from developing again
2. Stop sugars in the grass from exacerbating insulin resistance

### Concerns

- Stress of confinement
- Recent findings suggest that paddocks preferable



## Hay and Ration Balancer Diet



Wk	Percent of body weight	Body weight (lb)	Amount hay fed (lb)	Approximate amount (1 flake = 3lb)
0-2	1.5%	1,200 (current)	18 lb	6 flakes
2-6	1.5%	1,000 (ideal)	15 lb	5 flakes
>6	1.0%	1,000 (ideal)	10 lb	3 flakes

## Medical treatment

- Not a substitute for diet, exercise, and management changes.
- Two indications:
  1. Short-term (3 to 6 months) treatment while instituting the diet/exercise plan
  2. Refractory cases

### Recommendation:

#### Levothyroxine Sodium (Thyro-L®)



- Reserve for obese horses
- Accelerate weight loss; 3 to 6 months
- Administer 0.1 mg/kg (48 mg/day)
- Increase to 72 mg/day in extreme cases
- Cost (Thyro-L®) is < \$1/day
  - \$25 for 1lb (83 teaspoons/lb)
  - \$175 for 10lb
  - < \$1/day at the 48 mg/day dosage

### Recommendation:

#### Metformin

##### Mechanisms of action

- Activates AMP kinase
  - Inhibits gluconeogenesis and lipogenesis
  - Increases fatty acid oxidation and lipolysis
- Increases insulin sensitivity
  - Increases GLUT4 within membranes
  - Enhances glucose uptake
- Acts at the post-receptor level in tissues



### Recommendation:

#### Metformin

- Administer 30 mg/kg PO q12h
- Purchase generic tablets in bulk
- Cost is approximately \$5/day
  - Wedgewood Pharmacy; (800) 331-8272
  - [www.wedgewoodpharmacy.com](http://www.wedgewoodpharmacy.com)
  - \$17 for 100 tablets (1,000 mg tablets)
  - Giving 15 tablets twice daily
  - Will use 900 tablets/month; \$153/month



Recommendation:**Pergolide**

Type:	Dopamine agonist
Action:	Inhibition of PI cells
Dose:	One mg total dose/day (up to 5 mg)
Response:	Improved "energy", muscle mass, haircoat
Side-effects:	Transient anorexia and depression

Recommendation:**Pergolide – Compounded**

- Administer 1-5 mg PO q24h (Pony: 0.5 mg)
- Granules have better stability
- Suspension is easy to administer; lasts 30 days
- Cost is approximately **\$1/day** at lowest dosage
  - Wedgewood Pharmacy; (800) 331-8272  
[www.wedgewoodpharmacy.com](http://www.wedgewoodpharmacy.com)
  - Granules cost \$36 for one month supply (30 scoops; one mg per 5 mL scoop)
  - Suspension costs \$30 for one month supply (30 mL; one mg per mL)

Recommendation:**Pergolide – FDA approved product**

- A product is currently under FDA review
- We can expect FDA-approved pergolide to be available within the next year
- No information on cost or formulation

**Monitoring**Resting ACTH concentrations

- Recheck after 30 days
- Ideally increase dosage if > 35 pg/mL
- Low sensitivity, so use clinical judgment

Dexamethasone suppression test

- Should return to normal within 30 days
- Increase dosage if still fails to suppress

Recommendation:**Refractory PPID Cases****Advanced PPID**

- Pergolide 3 mg/day
- Cyproheptadine 0.25 mg/kg PO q12h

**Diabetes mellitus**

- Persistent hyperglycemia
- Glucosuria
- Hyperlipemia if become anorexic

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## Oral Domperidone Challenge Test

### Procedure

- Measure ACTH at 0 and 2h; \$22 each
- Administer one syringe (25 mL gel; 2.75 grams) domperidone (Equi-Tox®) orally at time = 0
- Purchase from [www.equitox.com](http://www.equitox.com); (864) 646-6599
- Currently \$225 for 6 syringes; \$38 each

### Interpretation

- Positive if:
  - > 35 pg/mL at time = 0
  - > 75 pg/mL at 2h (can use a single measure)
- Affected by fall season

Miller et al. *Vet Pathol* 2008

## Dopaminergic Control

- Pars intermedia is under dopaminergic control
- Dopamine released from neurons that extend down from hypothalamus to the pars intermedia
- Dopamine interacts with D2 receptors on melanotrophs and inhibit their activity
- Domperidone is a D2 receptor blocker
- Allows melanotrophs to be more active
- If there are cells secreting ACTH, they secrete more after domperidone administration