Blister Beetle Toxicosis
The Spanish fly is the emerald-green blister beetle, … which is found in the southern parts of Europe. The dried and crushed body of the beetle was … regarded as a potent aphrodisiac, especially for elderly gentlemen.

The Roman empress Livia (58 B.C. - A.D. 29) purportedly slipped it into the food of other members of the imperial family to stimulate them into committing sexual indiscretions that could later be used against them.

In 1772 the infamous Marquis de Sade doctored some aniseed sweets with Spanish fly and offered this to some prostitutes who took part in a flogging orgy. However, there was no aphrodisiac effect … the girls became very ill, so ill that the Marquis was brought to trial for poisoning.
Synonyms

- Blister Beetle Toxicosis
- Cantharidin Toxicosis
- Striped Beetle Poisoning
Blister Beetle Toxicosis

- Epicauta spp - blister beetles, striped or black beetles
- Leaf and flower eaters move and feed in swarms attracted to alfalfa
- Cutting and crimping hay beetles crushed and baled
- Found in a bale, section of bale not in the entire harvest
Blister Beetle Toxicosis
Cantharidin

- Hemolymph, genitalia
- Extremely irritating
- Acantholysis
- Epidermal vesiculation
- Absorbed through the gut
- Excreted in the urine
Blister Beetle Toxicosis

History

- Sporadic problem
- Single animal
- Same area of barn/pasture
- Fed from the same bale
Blister Beetle Toxicosis

- Severity varies with dosage
  - Horses are particularly susceptible
    - Minimal lethal dose < 1 mg/kg
      - (100-150 beetles/horse)
- Shock, GI tract and Urinary tract irritation
- Initial signs within hours
Blister Beetle Toxicosis

Signs

- Colic most consistent sign
  - Restlessness, irritability, sweating, pawing, grunting, trembling, reluctance to move
  - Rarely gastric reflux
- Frequent attempts urinate
- Pain on urination
- Gross blood clots
- Urine usually looks normal
- Skin irritated - urine contact
Blister Beetle Toxicosis

Signs

- Increased TPR
- Forceful cardiac contractions
- MM dark, congested
- Decreased CRT
Blister Beetle Toxicosis

Signs

- Depression
- Anorexia
- Aggressive behavior, violent seizure-like muscular activity
- Head pressing, abnormal facial expression (grimace)
- Profuse sweating
- Diarrhea rare but severe
Blister Beetle Toxicosis

Signs

- Oral lesions not consistent
  - Gingiva, oral mucosa, tongue
- Profuse salivation
- Place nose in water
- Severe oral lesions - still eat
- Shorten stride – as if myositis
- Synchronous diaphragmatic flutter
  - Associated with low Ca & Mg
Blister Beetle Toxicosis
Laboratory Findings

- Increased PCV - may be >60%
- TP during the first 24 hrs
  - Normal or increased
- TP drops dramatically
- WBC variable
- Neutrophilic leukocytosis
- Cr increased (2-10 mg/dl)
  - Tubular necrosis
Blister Beetle Toxicosis
Laboratory Findings

- Striking decrease Ca-Mg
- Total Ca as low as 4-6 mg/dl
- Mg is <1.5 mg/dl
- Low levels > 48 hrs
- Refractory to therapy
- Ionized Ca normal
- Hematuria, low specific gravity
- CPK elevated in severe cases
Blister Beetle Toxicosis

**Diagnosis**

- Finding blister beetles
- High pressure liquid chromatography
- Gas chromatography - mass spec
- Urine good source for diagnosis
  - Cantharidin levels 8-1,900 μg/kg
- Large volume of stomach contents
  - Cantharidin levels 20-4,800 μg/kg
Blister Beetle Toxicosis

Necropsy Lesions

- Erosions oral cavity
- Erosions of esophagus and stomach
- Sheets of epithelium lift off surface
- GI tr normal to pseudomembranous enteritis
- Hemorrhagic ulcerative cystitis
- Renal tubular necrosis
- Ventricular myocardial necrosis
Blister Beetle Toxicosis

Therapy

- Symptomatic
- Maintain hydration
- Acid base status
- Ca, Mg
- Mineral oil - absorb toxin
- Analgesics
- Remove suspect hay
- Check hay before feeding
Blister Beetle Toxicosis

Prognosis

- Fatality rate as high as 65%
  - With aggressive therapy survival rate 80%
- May be found dead
  - Die within 3-4 hours of onset
  - Die 12-18 hrs. after onset
- If horse survives 72 hrs recovery is likely
Case 1

History

- 4 yr old filly
- TB racehorse
- Racing poorly
- Retired as brood mare
Case 1

- 2 Weeks later foundered
- 5 days later
  - Depressed
  - In pain
  - Diarrhea
  - WBC 3000
  - PCV 47%
  - TP 7.1 gm/dl
Case 1
Physical examination

- Uncontrollable pain
- Temp 101.4
- HR 60
- RR 33
- Ileus - abd distention
- MM injection
- Mouth lesions
- Rectal - fecal balls
Case 1
LAB DATA

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Case 1
Peritoneal Tap

- Protein 1.8 g/dl
- NCC 70,620 /ul
  - Neutr 90%
  - Lymphs 2%
  - Monos 8%
  - Mod toxic changes
Case 1

- Hospital course
- Abdominal pain - 36 hrs
- Depression - 24 hrs
- Diarrhea - PLE
- Bruxism
- Respiratory distress
NSAID Toxicity

- Sensitivity to toxic effects
- Phenylbutazone used for years
  - Before toxic potential realized
- Toxicity near therapeutic dose
  - 8 mg/kg/day >4 days
  - 4 mg/kg/day >50 days
- Experimental
  - 10 mg/kg/day 1-2 wks po
  - 4 mg/kg/day iv
  - > 15 mg/kg/day uniformly fatal
- Ponies are more sensitive
- Flunixin meglumine also toxic
NSAID Induced Ulcers
Gastric Lesions

- Glandular mucosal ulcer
- Esophageal mucosal ulcer
- Protein loosing enteropathy
NSAID Toxicity

Other Lesions

- Colonic and cecal erosions
  - Progressing to ulceration
  - Progressing to necrosis
  - Full thickness
- Chronic right dorsal colitis
- PLE
- Oral ulceration
- Necrotizing phlebitis portal vein
- Renal papillary necrosis
NSAID Toxicity
Right Dorsal Colitis

- **Acute signs**
  - Colic, severe profuse diarrhea, fever

- **Chronic signs**
  - Intermittent colic, soft feces, wt loss, ventral edema

- Often history of dehydration

- Multifocal coalescing ulcerative areas with islands of mucosa

- Colonic stenosis

- Poor response to surgical or medical Rx
NSAID Toxicity
Right Dorsal Colitis - Therapy

Complete rest - no showing, racing, training
No NSAIDs
No long-stem fiber (hay or grass)
Complete pelleted feed
Metronidazole (as an anti-inflammatory)
Psyllium (0.5g/kg 3d/week)
Corn oil (1-2 cups on pellets BID)
Avoid other oral antimicrobials
Misoprostol – PGE₁ analogue
NSAID Toxicity
Clinical Signs

- Oral ulcers
- Depression
- Anorexia
- Colic
- Weight loss
- Diarrhea
  - Cowlike - watery
  - Melena
- Recumbency, weakness
- PLE very common
- Edema
NSAID Toxicity Diagnosis

- History
- Signs
- Oral ulcers
- Low protein
NSAID Toxicity Therapy

- Symptomatic
- Anecdotal reports of use of PGs
  - Efficacy after the lesions develop?
  - Misoprostol (Cytotec®)
  - Reported dose 2.5-5 mcg/kg bid/tid
  - Side effects
    - Colic
    - Diarrhea
NSAID TOXICITY

Oral ulcers
French Leave

- 16 year old
- TB geld
French Leave

- Shown Madison Square

Garden 3 wks ago

- Poor ventilation
French Leave

- 1 week later
- Fever not respond to
  - Ampicillin
  - Oxytet
  - TMS
- Others at garden had resp infection
French Leave

- Episodes of anorexia
- Normal appetite between
- Dramatic wt loss
- Ventral edema
- Joint enlargement
French Leave

- 4 CBC'S
  - WBC 6500-7000
- Fibrinogen 500 mg/dl
- TP 6.6 to 7.4 gm/dl
- PCV 28-30 %
- Coggins negative
French Leave

- Temp 102.7
- Pulse 36
- RR 20
- WT loss
  - Triceps, quad, gluteals, neck
- Ventral edema
French Leave

- **WBC**: 7200 /ul
- **SEG**: 73%
- **LYMPH**: 26%
- **EOS**: 1%
- **PCV**: 32%
- **TP**: 7.8 g/dl
- **FIBRIN**: 596 mg/dl
- **CR**: 1.2 mg/dl
- **CPK**: 40 IU/L
French Leave

- Peritoneal fluid
  - TP 4.8 gm/dl
  - WBC 40,590 /ul
    - Neutro 92%
    - Macro 8%
  - RBC 89,760 /ul
French Leave
Hospital Course

- Fever
- Depression
- Not eat well
- Wt loss
Squamous Cell Carcinoma

- Causes gastric ulceration
- Can lead to marked anemia
- 2nd most common internal neoplasm
  (lymphosarcoma is 1st)
Squamous Cell Carcinoma

- Involves esophageal region stomach
  - Cauliflower mucosal mass
  - Mass ulcerates
  - Invades serosa
  - Adhesions to liver and diaphragm
- Also involves esophagus - obstruction
- Effects males > females
Squamous Cell Carcinoma Metastasis

- Diaphragm
- Liver
- Spleen
- Parietal peritoneum
- Omentum
- Kidneys
- Parietal pleura
- Visceral pleura
Squamous Cell Carcinoma Clinical Signs

- Progressive weight loss
- Anemia and melena/occult blood
- Inappetence, dysphagia
- Foul odor from mouth
- Lethargy
Squamous Cell Carcinoma Clinical Signs

- Rectal mass, below left kidney
- Respiratory signs
- Ascites - lymphatic obstruction
Squamous Cell Carcinoma Diagnosis

- Gastroscopy/luminal biopsy
- Peritoneal fluid cytology
- Ultrasound
- Gastric lavage/cytology
- Percutaneous biopsy
- Surgical biopsy
Choke in Horses
Choke in Horses

Causes

- Bad teeth
- Greedy eaters
- Pellets
- Caustics
- Corncob
- Apple
- Wood
Choke in Horses
Location

- Proximal esophagus
- Mid cervical esophagus
- Thoracic inlet
- Heart base
- Diaphragmatic hiatus
Choke in Horses

History

- Sudden onset of signs
- Previous history
- Recent medication in bolus form
- Exposure to caustics
Choke in Horses

Signs

- Salivation
- Retching
- Tense neck muscles
- Sweating over esophagus
- Mass on left neck
  - Palpated in jugular groove
Choke in Horses
Diagnosis

- Physical exam
- Pass stomach tube
- Endoscopic exam
- Barium study
Choke in Horses
Treatment

- External massage
- Pass stomach tube
  - Sedate
  - Be gentle
    - Flush with water (aspiration danger)
- Esophageal contraction/spasm
Choke in Horses

Treatment

- Lidocaine
- Mineral oil
- Atropine
- Analgesics
- Sedatives
- Oxytocin
Choke in Horses
Treatment

- Place in stall without food or bedding
- Give sedatives
- Give analgesics
- IV fluids
- Try to tube again in a few hours
- General anesthesia
  - Intubate
  - Pass tube with head over table
Choke in Horses
Reintroduce Diet

- Grass
- Wet, soupy mashes
- Pellet mashes
- Hay
- No concentrate
Choke in Horses
Search for Cause

- Stricture
  - Barium study or endoscopy
- Check teeth
- Watch eating habits
- Management factors
Choke in Horses
Damage to Esophagus

- Acute damage
  - Treat with steroids

- Strictures
  - Balloon dilation
  - Esophagostomy

- Adjust diet
  - Grass, sloppy pellets, wet hay, stones
Blister Beetle Toxicosis

I. Introduction
   A. Synonym - CANTHARIDIN TOXICOSIS, striped beetle poisoning
   B. Caused by the ingestion of Epicauta spp - blister beetles
      1. Striped or black beetles
      2. Adults are leaf and flower eaters
      3. Move and feed in swarms
      4. Attracted to alfalfa leaves and blooms
      5. Modern hay harvesting techniques include cutting and crimping hay in one operation
      6. If the beetles are feeding during cutting/crimping they will be crushed and baled with the hay
      7. The beetles will be found in a bale or a section of the bale and not in the entire harvest
      8. Not found in pelleted alfalfa (one poorly documented case in lit.) probably because of inactivation during processing or dilution.
      9. Horses are particularly susceptible to cantharidin with the minimal lethal dose probably less than 1 mg/kg. Four to 6 grams of dried beetles have experimentally induced fatal toxicosis in horses (100-150 beetles).
      10. Other species affected include cattle, sheep, and goat.
      11. Cantharidin is an active ingredient in human wart removal compounds. It is also occasionally used by herbalists.
   C. CANTHARIDIN
      1. Found in hemolymph, genitalia other tissues of beetles
      2. Extremely irritating
      3. Causes acantholysis and epidermal vesiculation on contact with the skin
      4. Absorbed through the Glt and excreted in the urine
      5. The amount of toxin varies between species of beetle, between the sexes, and the time of year. This has resulted in a wide variation in reported toxic doses.
   D. History & Signs
      1. Sporadic problem
         a. single animal
         b. group in same area of barn or pasture
         c. horses fed from the same bale
      2. Severity of disease varies with the dosage of toxin
      3. Signs primarily from shock, Glt and Ut irritation
      4. Initial signs within hours
5. Signs
   a. abdominal pain (colic)
      1. most consistent signs
      2. restlessness, irritability, sweating, pawing, grunting, trembling, reluctance to move
      3. rarely gastric reflux
   b. depression
   c. frequent attempts to urinate
      1. pain on urination
      2. gross blood clots can be seen
      3. despite that urine usually looks normal
      4. skin will be irritated where urine has contacted it
   d. increased TPR - with forceful cardiac contractions
   e. mucus membranes dark, congested
   f. decreased CRT
   g. profuse sweating
   h. profuse salivation
      i. continually place their nose in water and splash
   j. aggressive behavior, violent seizure-like muscular activity
   k. anorexia - but horses w/ severe oral lesions may eat

4. Diarrhea is rare but may be severe with bloody discharge

5. Oral lesions not consistent but may be on gingiva and oral mucosa - especially the tongue; mucous membranes may by injected/irritated

6. Shorten stride may be present but no myositis

7. Synchronous diaphragmatic flutter and muscle fasciculations are common
   a. thought to be associated with low Ca & Mg

8. Other signs which have been attributed to hypocalcemia include: depression, anxiety, decreased sensory awareness, head pressing, abnormal facial expression (tightly clamped jaws with lips drawn back-tetanic facial expression), hind limb ataxia, gate stiffness, laryngeal spasm, dyspnea, dysphagia, and cardiac arrhythmias.

E. Laboratory findings
   1. Increased PCV - may be >60%
   2. TP may be normal or increased during the first 24 hrs but the drops dramatically
   3. WBC variable, usually neutrophilic leukocytosis
   4. Cr (2-10 mg/dl) and BUN (50-70 mg/dl) maybe elevated with tubular necrosis
5. Electrolytes
   a. striking decreases in Ca and Mg
   b. Ca may be as low as 4-6 mg/dl (usually 6-8 mg/dl)
   c. Mg is <1.5 mg/dl
   d. low levels persist for at least 48 hrs and are refractory to therapy
   e. recent evidence indicates that ionized Ca levels may be normal despite the low total Ca levels

6. urinalysis - hematuria, low specific gravity (despite hemoconcentration)

7. CPK elevated in severe cases

**F. Diagnosis**

1. Tentative diagnosis by finding blister beetles in uneaten hay or around manger
2. Definitive diagnosis
   a. high pressure liquid chromatography (HPLC)
   b. gas chromatography - mass spec
   c. urine is the best source for diagnosis (>500ml) – cantharidin levels 8-1,900 µg/kg
   d. large volume of stomach contents – cantharidin levels 20-4,800 µg/kg

3. Necropsy lesions - acantholytic lesions
   a. erosions oral cavity
   b. even if no lesions in oral cavity often erosions of the esophagus and stomach
   c. sheets of epithelium may be lifted off from the surface with normal epithelium in between
   d. intestine/colon range from normal to ulcerated to a pseudomembranous enteritis
   e. hemorrhagic ulcerative cystitis
   f. renal tubular necrosis
   g. lesions generally mild in upper Ut but ulcerative lesions in the bladder may be dramatic
   h. ventricular myocardial necrosis
   i. some horses may have no gross lesions

**G. Therapy**

1. Largely symptomatic and supportive
2. Maintain hydration
3. Acid base status, Ca, Mg
4. Mineral oil and/or activated charcoal may absorb toxin
5. Analgesics - use with care to avoid exacerbation of ulcerative lesions
6. Remove suspect hay and check hay before feeding
H. Prognosis
   1. Fatality rate can be as high as 65%, with aggressive therapy survival rate 80%.
   2. May be found dead, die within 3-4 hours of onset; may die 12-18 hrs. after onset.
   3. If horse survives the first 72 hrs then recovery is likely

**NSAID Toxicity**

A. Sensitivity to toxic effects
   1. Phenylbutazone can be used for years without any apparent ill effects
   2. Toxicity at doses near therapeutic dose
      a. 8 mg/kg/day for more than 4 days
      b. 4 mg/kg/day for more than 50 days
      c. Experimental
         1. 10 mg/kg/day for 1-2 weeks po reliably results in toxicity
         2. 4 mg/kg/day IV
         3. > 15 mg/kg/day uniformly fatal for horses
      d. Ponies are more sensitive to low levels developing severe lesions and even dying
      e. Flunixin meglumine will also cause toxicity
   3. Gastric lesions
      a. Glandular mucosal ulceration
      b. Esophageal mucosal ulceration
      c. Protein loosing enteropathy (PLE)
   4. Right Dorsal Colitis - may be only lesion found
      a. acute signs - colic, severe profuse diarrhea, fever, depression, endotoxic shock
      b. chronic signs - intermittent colic, soft feces, wt. loss, ventral edema
      c. often history of dehydration when NSAID given
      d. multifocal to coalescing ulcerated areas with islands of mucosal regeneration
      e. colonic stenosis may develop
      f. responds poorly to medical or surgical therapy
         1. PG therapy has been suggested - response??
         2. Suggested therapy for management
            a. complete rest (no showing, racing, training, etc.)
            b. no NSAIDs
            c. no long-stem fiber (hay or grass)
            d. complete pelleted feed
            e. metronidazole (as an antiinflammatory)
f. psyllium (0.5g/kg 3d/week)
g. corn oil (1-2 cups on pellets BID)
h. avoid other oral antibiotics

5. Other lesions
   a. Colonic and cecal erosions progressing to ulceration
   b. PLE
   c. Oral ulceration
   d. Necrotizing phlebitis of the portal vein
   e. Renal papillary necrosis

6. Clinical signs of toxicity
   a. Depression, anorexia, weight loss
   b. Colic
   c. Diarrhea - cowlike to watery +/- melena
   d. Oral ulcers
   e. Recumbency, weakness
   f. PLE very common
   g. Edema

B. Diagnosis
   1. History
   2. Signs
   3. Low protein

C. Therapy
   1. Symptomatic
   2. Anecdotal reports of use of PGs - efficacy after the fact?
Squamous cell carcinoma

A. Introduction
1. Second most common internal neoplasm of the horse (lympho 1st)
2. Generally involves the esophageal region of stomach
   a. Often cauliflower mucosal mass which ulcerates
   b. Invades serosa and may result in adhesions to the liver and diaphragm
3. Causes gastric ulceration with significant bleeding which can lead to marked anemia
4. Metastasis
   a. Diaphragm
   b. Liver
   c. Spleen
   d. Parietal peritoneum
   e. Omentum
   f. Kidneys
   g. Parietal pleura
   h. Visceral pleura
5. Affects males more often than females

B. Clinical signs
1. Progressive weight loss
2. Anemia and melena or occult blood positive feces
3. Inappetence, dysphagia, esophageal obstruction, foul odor from mouth
4. Lethargy
5. Rectal mass, below left kidney
6. Increased BSP
7. Lipemia
8. Respiratory signs
9. Ascites secondary to lymphatic obstruction

C. Diagnosis
1. Gastroscopy and luminal biopsy
2. Ultrasound exam of anterior abdomen
3. Peritoneal fluid cytology
4. Surgical or percutaneous biopsy
Choke in Horses

A. Introduction
   1. causes
      a. bad teeth
      b. greedy eaters
      c. pellets
      d. caustics
      e. corncob
      f. apple
      g. wood
   2. location
      a. pharyngeal area at most proximal part of the esophagus
      b. mid cervical esophagus
      c. at thoracic inlet
      d. at heart base
      e. at diaphragmatic hiatus

B. History
   1. sudden onset of signs
   2. previous history of choke may be present
   3. recent medication in bolus form or exposure to caustics

C. Signs
   1. salivation
   2. retching
   3. tense neck muscles

D. Sweating on one side of the neck

E. Lump on left neck may be palpated in jugular groove

F. Dx
   1. physical exam
   2. pass stomach tube and meet an obstruction
   3. endoscopic exam
   4. barium study

G. Rx
   1. external massage - breakup of impacted ingesta
   2. pass stomach tube
      a. sedate with xylazine to get head down
      b. be gentle
      c. flush with water but watch out for aspiration
      d. food on top of obstruction is easily removed
      e. esophageal contraction/spasm at site of obstruction makes it difficult to dislodge by flushing
      f. do not force tube
      g. use lidocaine 10 cc in 50 cc of water through stomach tube to help relax esophagus
h. mineral oil - its use is questionable because of the real danger of aspiration
3. atropine has been used to decrease esophageal spasm but problems associated with secondary ileus make its use questionable
4. analgesics (i.e. NSAID)
5. sedatives

6. **TIME TIME TIME** never force the situation - if you are not making progress back off; if you continue you may do more harm than good - one exception to this rule if there is indication of **necrosis or exposure to caustics** then more aggressive techniques (e.g. surgery) are needed
   a. place in stall without food or bedding
   b. give sedatives
   c. give analgesics
   d. +/- IV fluids
   e. try to tube again in 12 hours
7. place under general anesthesia
   a. intubate
   b. pass tube with head over table
   c. surgery may be required
8. Reintroduce diet after obstruction is relieved
   a. grass - very good because of high water content
   b. wet, soupy mashes - pellet mashes
   c. hay - no concentrate

H. Follow up
1. search for cause
   a. stricture - barium study or endoscopy - can miss with either procedure
   b. check teeth
   c. watch eating habits
   d. look into management factors
2. damage to esophagus
   a. endoscopic exam
   b. barium swallow
   c. if acute damage is present can treat with steroids
   d. strictures can be dilated
   e. esophagostomy
   f. adjust diet - grass, sloppy pellets, wet hay, stones