### Theiler’s vs. Tyzzer’s - Equine Liver diseases

**Liver**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Facts/Cause</th>
<th>Presentation/CS</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum hepatitis, Acute hepatitis, Theiler’s diz, Idiopathic hepatitis</td>
<td>- Acute to subacute hepatitis in adult horses - Equine origin biologicals - Tetanus antitoxin, serum of equine origin, pregnant mare serum - Occurs more commonly on certain farms - Occurs in horses hyperimmunized w/ tetanus antitoxin - Diz occurs 4-10 week after last tetanus antitoxin administration - Other cases w/ no equine biologic show similar type of acute hepatic dz (idiopathic hepatitis) - Occur in late summer &amp; fall - Suggested infectious or blood borne agent involved - Seasonal occurrence, multiple horses involved, etc.</td>
<td>- Malaise &amp; weight loss wk-mo before acute signs (liver has to lose more than half its functional capacity before failure signs) - Acute hepatocerebralopathy (incoordination, walk in circles, belligerent to surroundings) - Delirious, head pressing, tail, make repeated attempts to rise, unmanageable - Icterus - Photodermatitis (white muzzle &amp; limbs) - May appear centrally blind - Intravascular hemolysis - Clin. course rapidly progressive - Dying in 2-5 d after initial CS</td>
<td>- Hx, CS - Lab: - ↑ in all liver enzymes - ↑ Bilirubin, glucose variable, clotting profiles prolonged, BSP prolonged - PM (postmortem): - Small, flaccid liver (&quot;dishrag&quot; liver) (swollen acutely) - Microscopically necrosis &amp; bile duct proliferation</td>
<td>Treat as for liver failure: Rompun - Sedate (xylazine) for hepatocerebralopathy - 10% glucose IV (if low blood glucose) - ↓ Blood ammonia (nasogastric tube &amp; mild laxative (mineral oil) + neomycin (but kills GI flora) or lactulose (aids to ↑ ammonia to ammonium) - Correct any acidosis slowly (except hyperammonemia) - Slow 5-10% dextrose drip (↓ hepatic work load) - Dietary management (small meals 4-6 x/d (beet pulp, cracked corn, molasses) - Force feed mixed paste if not eating - IV feeding, but $$$ - Vit. B1, folic acid &amp; Vit. K1 weekly - Protect from sun when grazing</td>
</tr>
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**Ingestion of waste oil** (spread to control dust), tetrachlrobenzodioxin - Tx: Supportive, additionally show acute signs after being exposed fairly recently. Use of intestinal protectants and/or cathartic is indicated

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**Guide to Equine Clinics, vol. 1 Pasquini, 3rd ed.**

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### Theiler's vs. Tyzzer's Equine Liver diseases

#### Tyzzer's Diz, Bacillus piliformis infection, Dead foal diz
- **Bacillus piliformis** (moddie, filamentous, gram (+), spore forming, obligate intracellular bacteria)
- **Fatal diz of foals 7-40 days** (also fatal in lab animals)
- **Focal bacterial hepatitis**
- **Mares m/b carriers**
- **Sporadic, generally only one foal affected**

#### Fetal liver damage
- Infection or toxic damage to foal's liver; EHV (equine herpes virus) - hepatocyte necrosis
- CS: Usually aborted or weak w/ CS or other system
- Dx: Liver lesions (Hepatocyte necrosis, Intranuclear inclusion bodies in hepatocytes)

#### Hepatic neoplasia
- **Uncommon in large animals; 1° Hepatic carcinoma (most common); 1° in yearlings & 2-yr-olds; Lymphosarcoma (2°)**
- **CS: Weight loss, icterus, ↑ hepatic enzymes**
- **Tx:** None

#### Liver abscesses
- **More common in cattle; common incidental finding in horses on necropsy**
- **CS: Similar to other abdominal abscesses (intermittent colic, intermittent fever, weight loss)**
- **Dx:** CS; Can't be palpated per rectum
- **Tx:** Rarely drained to outside or removed; Long term ABs (penicillin or ampicillin - m/b in combined w/ rifampin or metronidazole)

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Pyrrolizidine alkaloid toxicity

- See TOX pg 323
- Poisonous plants: Crotalaria, Senecio, Amsinckia, Heliotropium, Echium - Not very palatable (eaten when thick or other forage sparse [drought]) - 1st cut hay, alfalfa or hay cubes
- Cumulative & progressive - Acute when ingest tremendous amounts - Chronic disorder (more common) - Problem 1-5 months later - Material often no longer on farm to identify - Western US (also in pastures through out US)
- Pathology: - Alkaloids, liver metabolized into pyroles - Pyroles inhibit mitotic division so get megalocytes & death of hepatocytes - Fibrosis replaces cell & liver fails - Marked portal hypertension

- Liver failure - Onset of CS acute - Weight loss - Hepatomegaly (abnormal behavior, ataxia, wandering) - Icterus (slight to moderate) - Photosensitization (white areas) - Rarely diarrhea - Abortions

- Geographic area or where hay grows, usually not a definitive dx, but suggested - Feed analysis, time consuming & expensive
- Lab: nonspecific - Clotting abnormalities - Liver enzymes normal or elevated - BSP is prolonged
- Liver biopsy (similar to aflatoxins)
  - Triad: Megalocytosis
  - Fibrosis
  - Bile duct proliferation
  - None of above specific for this toxicity so dx difficult if no longer consuming

- Euthanasia: if severe fibrosis liver can’t regenerate so Tx no good
- Remove plant source
- If appetite & little fibrosis
- Treat for liver failure
  - 1st sedate (xylazine) for CNS CS
  - 10% glucose IV + methionine
  - $ blood ammonia: nasogastric tube (mineral oil) + neomycin (but kills GI flora) or lactulose (add GI ammonia to ammonium)
  - Correct any acidosis slowly
  - Slow 5-10% dextrose drip
  - Dietary management
    - Small meals 4-6 x/d
    - Beet pulp, cracked corn, molasses
    - Force feed mixed paste if not eating
    - IV feeding $$
    - Vit. B1, folic acid & Vit. K1 weekly
    - Protect from sun when grazing

Plants
- Tansy ragwort (S. jacobea)
- Groundsel (S. redelli, S. longilobus)
- Fiddleneck (Amsinckia intermedia)
- Rattlebox (Crotalaria)
- Viper’s bugloss (E. plantagineum)
- Common heliotrope (H. europaeum)

DDx
- Other plants
- Fungal hepatotoxins

Tansy ragwort (S. jacobea)
- Description
  - 1-4’ tall
  - Leaves: deeply irregular
  - Flowers: composite, showy, yellow

Prognosis:
- Poor to grave: due to tremendous amount of fibrosis
- Mildly affected cases; use serial liver biopsy & enzyme activity to help w prognosis

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### Liver Disease

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</table>
| Liver disease        | • Liver m/b diseased long before it fails to function  
|                      | • CS not seen in early stages of liver diz      |                  | • History (Hx), CS                | Tx for liver failure:  
|                      | • Loss of 80% of liver before regeneration & recovery impossible |                  | • Lab                              | 1st sedate (xylazine)  
|                      | • Remarkable ability to regenerate               |                  | • Slightly ↑ blood glucose         | 10% glucose IV          |
|                      |                                                  |                  | • Ammonia (4x)                     | Blood ammonia (↑ # of bacteria producing ammonia) |
|                      |                                                  |                  | • ↑ BUN (urea needed)              | Nasogastric tube        |
|                      |                                                  |                  | • Terminally ↑ serum albumin       | Mild laxative           |
|                      |                                                  |                  | • Enzymes:                         | Lactulose               |
|                      |                                                  |                  | • ↑ GGT fairly specific for liver diz | Limit CHO               |
|                      |                                                  |                  | • ↑ ALP in chronic, also in bone, intesine, placenta & macrophages | Correct any acidosis slowly |
|                      |                                                  |                  | • SDH, LDH & GDH                   | Slow 5-10% dextrose drip |
|                      |                                                  |                  | • ↑ in acute diz, normal or ↑ in chronic | Dietary management:       |
|                      |                                                  |                  | • SDH: active hepatocellular necrosis | Small meals 4-6 x/d     |
|                      |                                                  |                  | • Excretion tests                  | Vit. B1, folic acid & Vit. K1 weekly |
|                      |                                                  |                  | • Bilirubin: indicates liver diz, bile blockage, hemolysis, or fasting horse | Fresh plasma transfusions |
|                      |                                                  |                  | • Bile acids: > 15 μm/l indicates hepatic diz, cholestasis or portal systemic shunting | Steroids: if not infectious |
|                      |                                                  |                  | • BSP, normal < 3.5 min            | Protect from sun when grazing |
|                      |                                                  |                  | • Liver biopsy: safe & simple, but avoid if liver abscesses suspected | Colchicin               |
|                      |                                                  |                  | • Hepatomegaly                      | Antibiotics: avoid those metabolized by liver such as tetracycline & chloramphenicol |
|                      |                                                  |                  | • Behavioral changes: docile animal becomes aggressive, aggressive becomes docile | Poor prognostic indicators: |
|                      |                                                  |                  | • Depression, incoordination, aimless walking, head pressing, yawning | • Albumin < 2.5 g/dl &/or ↑ globulin level |
|                      |                                                  |                  | • Multiple causes: low blood glucose levels, ↑ ammonia, altered plasma/ amino acid ratio | • Prothrombin time > 30% of normal |
|                      |                                                  |                  | • Liver biopsy site                | • Greatly ↑ GGT & ALP w/ normal or ↑ SDH or LDH |
|                      |                                                  |                  | • Right 14th ICS (intercostal space) intersection w/ line from tuber coxae to point of shoulder | • BSP half life > 8 min. |
|                      |                                                  |                  |                                     | • Marked fibrosis        |
|                      |                                                  |                  |                                     | Grave w/ pyrrolizidine alkaloid toxicosis, mitotic inhibition |

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**Diagnosis of liver diz:**
- **History**
- **Lab:**
  - Slightly ↓ blood glucose (gluconeogenesis)
  - Ammonia (4x) (urease of liver needed to convert)
  - ↑ of ammonia doesn’t correlate to level of CNS signs
  - ↓ BUN (urease needed)
  - Terminally ↓ serum albumin (liver makes albumin, long half life)
- **Enzymes:**
  - ↑ GGT in chronic diz fairly specific (gamma glutamyl transferase)
  - Found in biliary tract (cholestatic instead of hepatocellular)
  - Also in pancreas, lungs & kidney (renal diz, not ↑ because excreted in kidney)
  - ↑ ALP in chronic (alkaline phosphatase)
  - Also in bone, intestine, placenta & macrophages
  - SDH, LDH & GDH (sorbitol dehydrogenase, lactate dehydrogenase & glutamate dehydrogenase)
  - ↑ in acute diz; normal or ↓ in chronic
  - SDH, liver specific, good indicator of active hepatocellular necrosis
- **Excretion tests** (checks liver’s excretory function)
  - Bilirubin: from heme, mainly from RBCs, unconjugated bilirubin is converted by liver to conjugated which is secreted by bile system into intestine where it is converted into urobilinogen.
  - Liver diz - mostly unconjugated (Indirect reacting)
  - Direct to total ratio usually < 0.3
  - Bile blockage or intrahepatic cholestasis
  - ↑ Conjugated (direct reacting) & unconjugated
  - Direct to total ratio > 0.3
- **Bile acids** - synthesized by liver from cholesterol & excreted in bile
  - Bile acids > 15 um/l indicates hepatic diz, cholestasis or portal systemic shunting
- **BSP** (sulfobromophthalain) dye, clearance (halftime) used in lg. animals more than retention test. Inject IV & blood samples taken 5 times in 12 min.
  - Normal < 3.5 min
- **Liver biopsy** - safe & simple
  - Do not do if liver abscesses suspected
  - Diffuse or zonal lesions seen in most toxic infections & metabolic liver diz - usually Dx by biopsy
  - Easily miss focal lesions - abscesses, granulomas, neoplasia & liver flukes

**DDx:**
- Icterus - fasted 48 hours (must be acutely off food; therefore icterus & ↑ unconjugated bilirubin doesn’t mean liver diz.

**Treatment for Liver Failure**
- 1st Sedate (xylazine) for hepatonecephalopathy
- Diazepam, chloralhydrate or barbiturates
- 10% glucose IV (if low blood glucose)
- Blood ammonia (↑ ↑ of bact. producing ammonia)
- Nasogastric tube
  - Mild laxative (mineral oil) + neomycin or lactulose
  - Neomycin (may induce diarrhea, so not commonly used)
  - Lactulose (↑ acidity in GI to incr. amount of ammonia converted to ammonium, therefore not absorbable)
- Limit CHO, low protein diet to minimize ammonia
- Correct any acidosis slowly (exacerbates hepatonecephalopathy)
- Slow 5-10% dextrose drip (decr. hepatic work load)
- **Dietary management**
  - Small meals 4-6 x/d, beet pulp, cracked corn, molasses
  - Force feed mixed paste if not eating (by rehydrating pellets & nasogastric tube)
  - Dextrose to water (ready source of energy)
  - 14 feeding expensive. Amino acid supplementation
  - Vit. B1 folic acid & Vit. K1 weekly
- **Fresh plasm transfusions** for clotting abnormalities & m/b Vit. K
- **Corticosteroids:** if suspect acute hepatitis not due to infectious agent, & in chronic w/ unknown cause (prednisolone doesn’t require hepatic transformation)
- Grazing, protect from sun
- Colchicine - used empirically in chronic liver emphysema to ↓ fibrosis, but may cause laminitis
- **Antibiotics:** w/ liver biopsy & positive results of bacteria
  - Culture & sensitivity should be done
  - Avoids those metabolized by the liver, such as erythromycin, tetracycline, chloramphenicol