

HEPATIC LIPIDOSIS IN A 9 YEAR OLD MAINE COON CAT

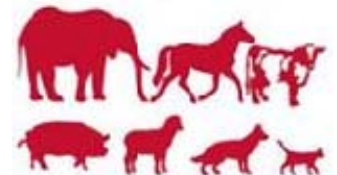
Mila Kundu

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Cornell University
College of
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THE PATIENT

- Approximately 9 year old MC Maine Coon Cat
- Presented on 8/15/13 to the CUHA Emergency Service
- Presenting complaints: vomiting and lethargy



http://www.fantom-xp.com/wp_20__the_Maine_Coon_natural_cat_breeds.html

HISTORY

- Referral: further work-up for elevated liver enzymes (ALP), elevated cholesterol, icterus, lethargy
 - Hospitalized by rDVM 2 nights ago- received fluids (LRS), Cerenia, Famotidine, Ampicillin
- History of vomiting for 7-10 days
 - Usually once daily, consisting of clear liquid
- Lethargic for 1-2 days
- Over the past year he lost approximately 9 pounds
 - His owners were unsure about his appetite and drinking as they have 2 cats and feed free choice

PHYSICAL EXAMINATION

- Quiet but responsive, purring, euhydrated
- Obese (BCS 9/9)
- Severely matted haircoat
 - Difficult to palpate lymph nodes and skeleton
- Severe bruising on limbs where blood had been drawn
- Mild waxy aural discharge
- Dilated pupils
- Icteric mucous membranes, sclera, skin
- Eupneic with normal cardiothoracic auscultation
- Tense, painful abdomen



INITIAL DIAGNOSTICS

- Point of care bloodwork:
 - Anemia
 - Low total solids
 - Icteric plasma
- Gaslyte: Alkalemia
 - Simple metabolic alkalosis with an expected compensatory respiratory response
 - Hypokalemia, hypochloremia
 - Hyperglycemia (mild)
- Urine- orange color
 - USG: 1.014
 - pH: 9
 - Moderate fat drops
- Coagulation panel: normal clotting times



<http://ourworldofcats.com/wp-content/uploads/2012/03/flame-coon->

PROBLEM LIST

- Obesity
- Vomiting
- Anorexia
- Lethargy
- Weight loss
- Icterus
- Bruising
- Tense/painful abdomen
- High ALP
- Bilirubinuria

DIFFERENTIALS FOR ICTERUS

- Pre-Hepatic: Hemolysis
 - Immune-mediated, splenic torsion, zinc toxicity, onion toxicity, Babesia
- Hepatic: Intrahepatic cholestasis
 - Hepatic lipidosis, hepatitis, cholangiohepatitis, neoplasia, infectious disease, drug-induced hepatitis, cirrhosis, toxic (acetaminophen, aspirin, griseofulvin)
- Post-Hepatic: Extrahepatic cholestasis
 - Biliary obstruction (mechanical vs. functional)
 - Extra-hepatic bile duct obstruction (EHBDO), cholecystitis, cholangitis, biliary mucocoele, cholelithiasis, neoplasia, inflammation (pancreatitis, duodenitis), malformations, parasitic infection, extrinsic compression, fibrosis, strictures, abscess, granuloma

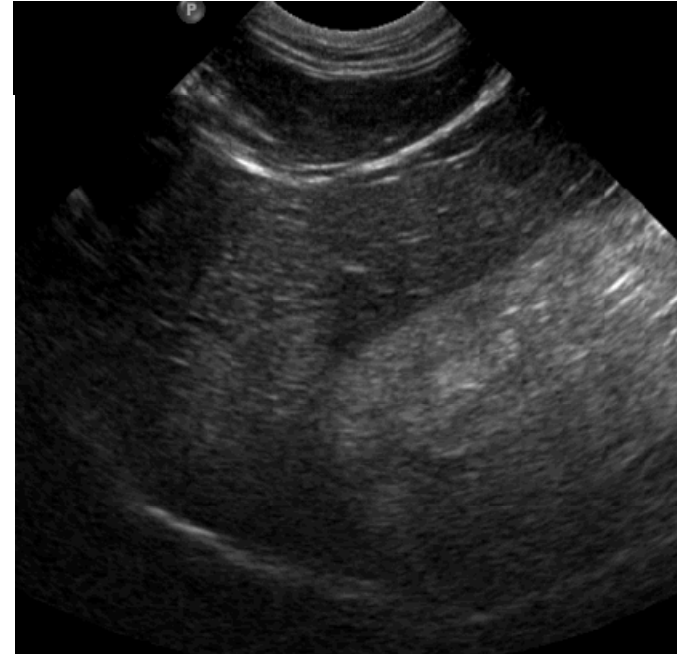
DIAGNOSTICS NEXT DAY

- Fluids overnight → corrected electrolyte imbalances & alkalemia
- CBC: Stress leukogram
- Chemistry: Values consistent with liver and gallbladder disease
- Urine culture: no growth
- PLI: negative for pancreatitis
- Cobalamin: 379 pg/mL (RR 900-3000)
- Folate: 8.26 ng/mL (RR 12-20)
- Ultrasound: evaluate entire abdomen, especially liver, gallbladder, pancreas, bowel (rule out triaditis)

ULTRASOUND FINDINGS



Gallbladder



Liver

- Hyperechoic hepatopathy
- Tiny gallbladder mineral sediment or calculus
- GI hypomotility

DIFFERENTIALS FOR ICTERUS

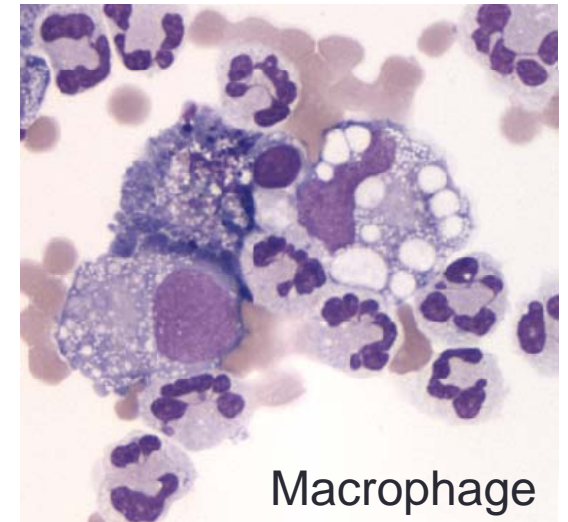
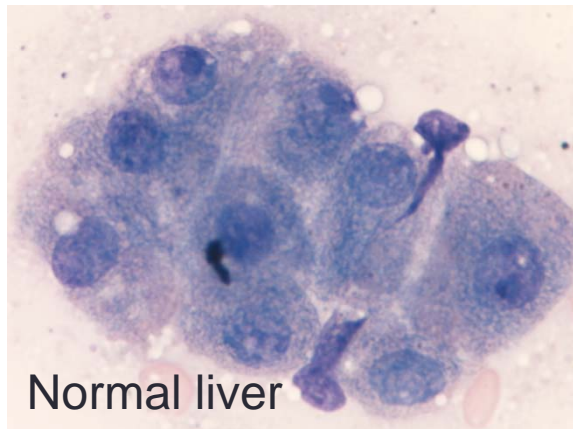
- ~~Pre-Hepatic: Hemolysis~~
 - ~~Immune-mediated, splenic torsion, zinc toxicity, onion toxicity, Babesia~~
- Hepatic: Intrahepatic cholestasis
 - Hepatic lipidosis, hepatitis, cholangiohepatitis, neoplasia (MCT or lymphoma), ~~infectious disease, drug induced hepatitis~~, cirrhosis, toxic (acetaminophen, aspirin, griseofulvin)
- Post-Hepatic: Extrahepatic cholestasis
 - Biliary obstruction (mechanical vs. functional)
 - Extra-hepatic bile duct obstruction (EHBDO), cholecystitis, cholangitis, biliary mucocoele, cholelithiasis, neoplasia, inflammation (pancreatitis, duodenitis), malformations, parasitic infection, extrinsic compression, fibrosis, strictures, abscess, granuloma
- Liver/ biliary disease is likely:
 - U/S: gallbladder sediment
 - ALP is elevated
 - Elevated bilirubin

PROCEDURES- NEXT DAY

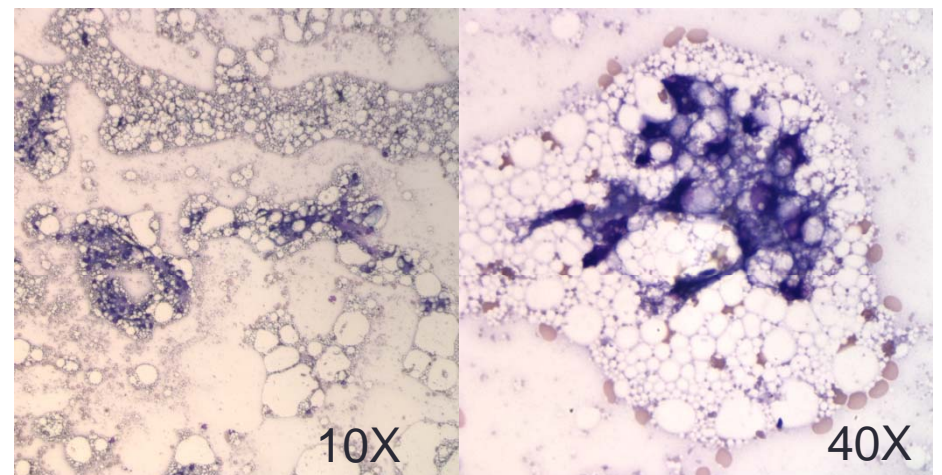
- Under general anesthesia, an esophagostomy feeding tube was placed, with placement verified by radiographs
 - Don't force feed → food aversion
- Ultrasound-guided fine needle aspirates of liver
- Gallbladder aspiration
 - Stone seen
- 1 hour fluid check for bile or blood- none seen on U/S
- Culture of bile + liver aspirates: no growth
- Fed slurry of wet food + water via feeding tube
 - No signs of nausea
 - High protein diet



CLINICAL PATHOLOGY IMAGES



- Majority of hepatocytes markedly distended with cytoplasmic vacuolation
- Occasional hepatocytes contain lipofuscin pigment or rare bile casts (cholestasis)



PATHOLOGY

- Liver is greatly enlarged
- Yellowish discoloration
 - Fat
 - Retention of bile in clogged drainage passageways





DIAGNOSIS:

Feline Hepatic Lipidosis (FHL)

Underlying cause undetermined

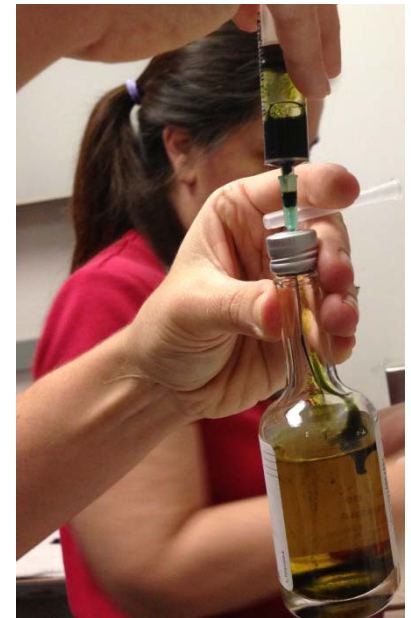
WHAT IS FELINE HEPATIC LIPIDOSIS?

- Abnormal accumulation of lipids (usually triglycerides) in hepatocytes
- Most common liver disease in cats
- Primary/idiopathic: seen in obese, indoor cats following a period of stress and anorexia
- Secondary: diabetes mellitus, pancreatitis, diabetic ketoacidosis, inflammatory bowel disease, cholangitis/cholangiohepatitis, neoplasia
 - Diagnostics are important in order to correct the underlying cause
- Cycle of liver damage and hepatic insufficiency
- Treat aggressively- can reverse the damage

DIAGNOSIS OF FHL

- HISTORY!
- Physical exam
- Bloodwork: CBC/Chem; Urinalysis
- Imaging
- FNA of liver (ultrasound-guided)

- Look for a primary underlying disease
 - T4
 - PLI
 - Cobalamin
 - Folate
 - FIV/FeLV

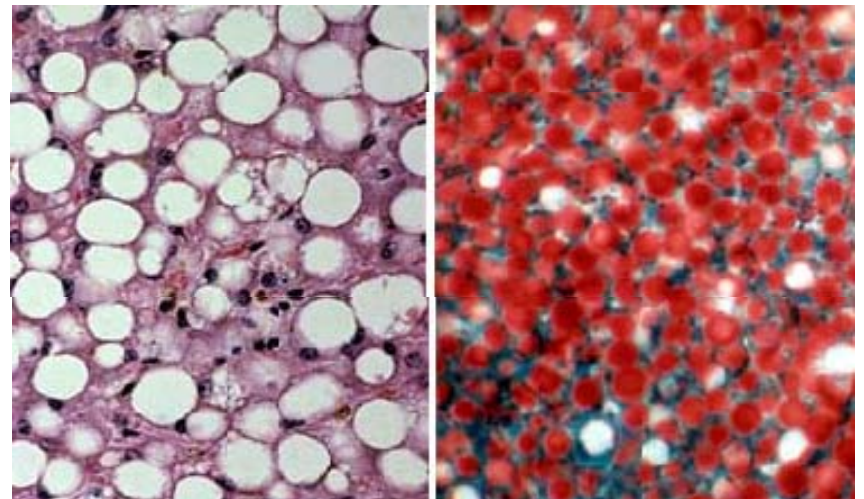


DEFINITIVE DIAGNOSIS

- Liver biopsy
 - Invasive
 - Not recommended if patient is metabolically unstable
 - Suggested to do if patient isn't responding to supportive treatment after 7-10 days
 - Useful to rule out concurrent liver disease
 - Stain with Oil Red O to see triglycerides and lipids on fresh sections

H&E

Oil red O



PATHOPHYSIOLOGY

- May be different for each animal
- During a period of inappetence/anorexia, peripheral lipolysis occurs via stimulation of hormone-sensitive lipase
 - Glucagon, thyroid hormones, epinephrine, norepinephrine, glucocorticoids, and growth hormone
 - (Inhibited by insulin)
- Lipolysis causes increased concentration of free fatty acids (FFA) in blood
- FFA taken up by peripheral cells and later by the liver

METABOLIC ASSOCIATIONS

- Feline-specific nutrition
 - Pure carnivores
 - Require 2-3x more dietary protein than omnivorous species
 - High requirement for essential amino acids and fatty acids
 - Limited ability to adjust metabolic pathways to conserve nitrogen

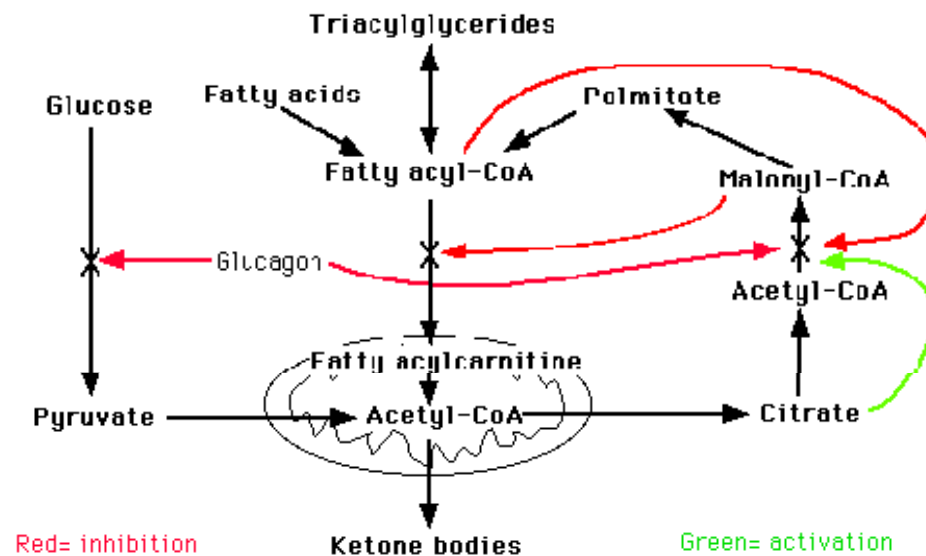


<http://www.cimarronah.com/health-specific-over-the-counter-diets-not-a-gimmick-mostly/cat-eating-food/>

PATHWAYS OF FATTY ACIDS

- In hepatocytes, fatty acids follow two main pathways

Regulatory Interactions of Fatty Acid Synthesis and Oxidation in Liver



OXIDIZED IN MITOCHONDRIA

Fatty
Acids

Acetyl-
CoA

ENERGY!

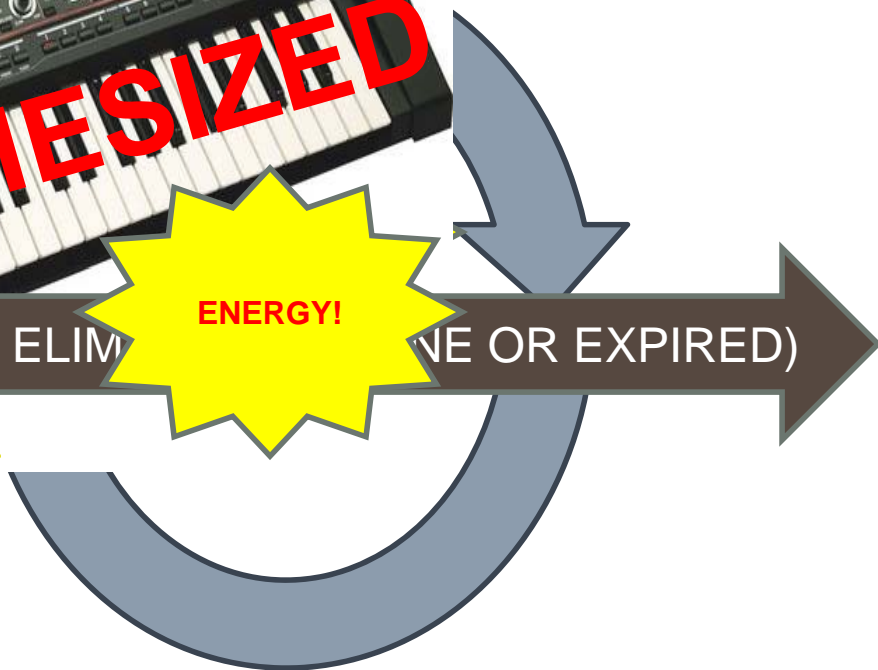
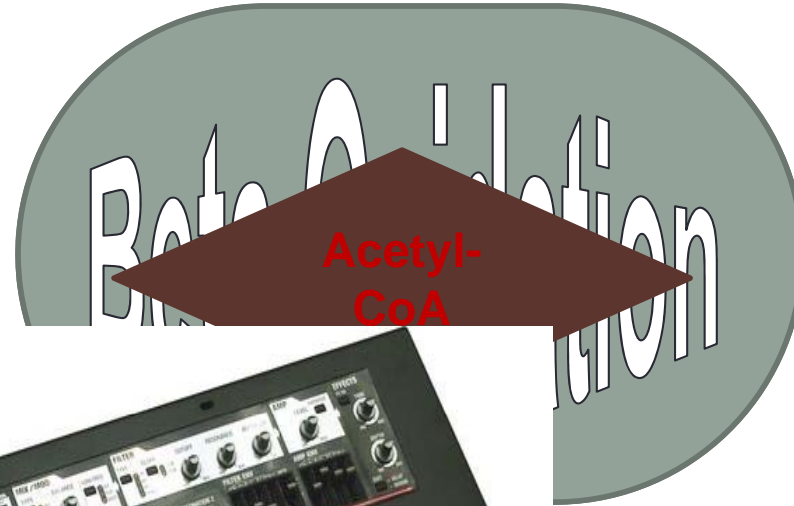
SYNTHESIZED

Acetone

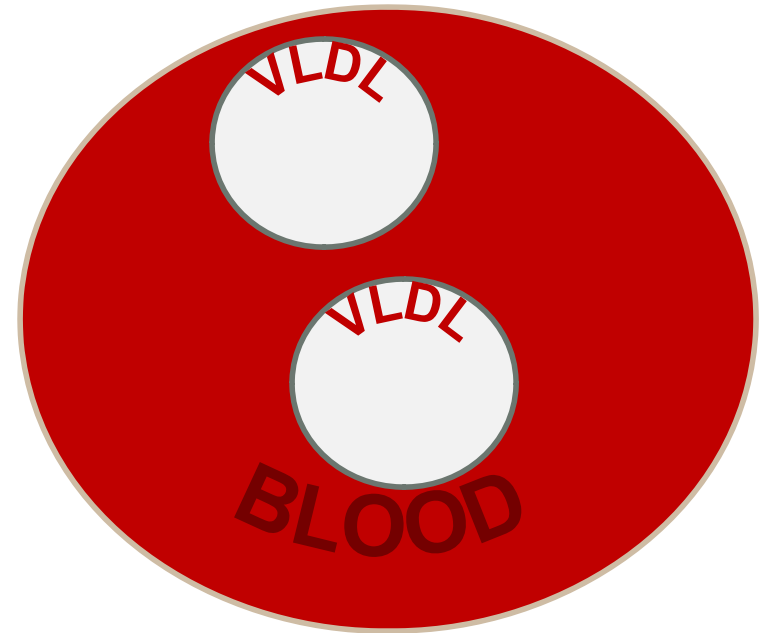
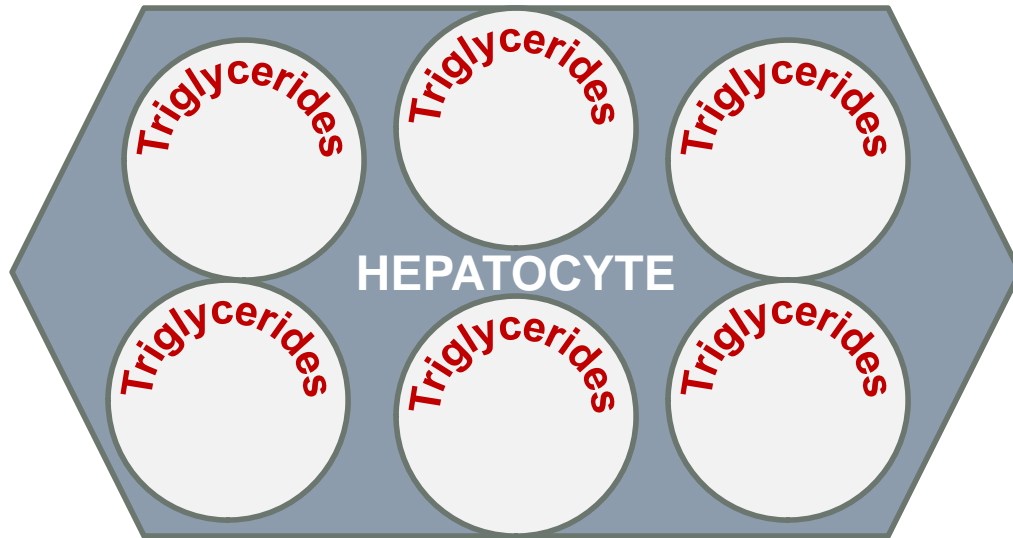
ELIM

ENERGY!

(NE OR EXPIRED)



STORAGE IN HEPATOCYTES OR EXPORTED TO TISSUES



FATTY ACIDS IN FHL

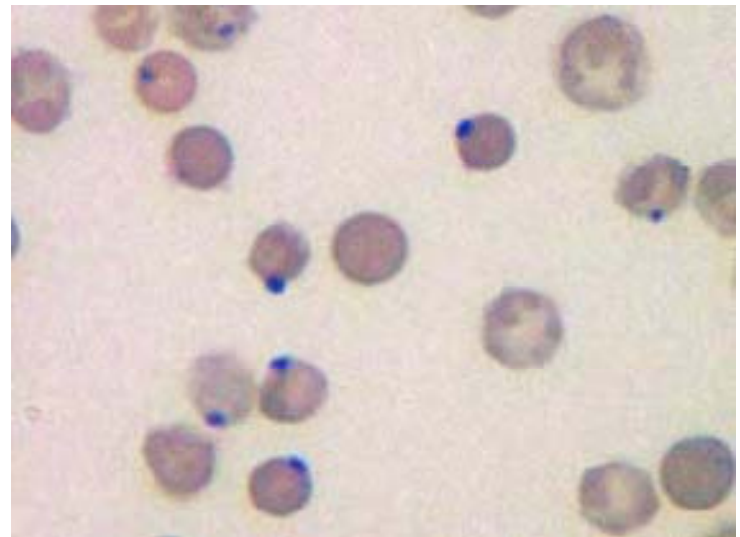
- Increased delivery to hepatocytes
- Decreased export to tissues
- Decreased oxidation in mitochondria
- **Increased storage as triglycerides in vacuoles**

COAGULATION DISORDERS

- Liver disease is associated with coagulation abnormalities and increased risk of bleeding
- Site for production of clotting factors
- Responsible for vitamin K-dependent carboxylation of clotting factors
- Don't do cystocentesis or aspirates until 12h after vitamin K supplementation is given
- Hepatic lipidosis
 - 4%- prolonged PT
 - 25%- prolonged APTT
 - 75%- increased PIVKA clotting times
 - PT/APTT may not reflect entire impairment of hemostasis

OXIDATIVE DAMAGE

- Cats are susceptible to oxidative injury due to a deficiency in Glutathione (GSH)
- Lipid peroxidation affecting cellular membranes
- Heinz body anemia



TREATMENTS- OUR PATIENT

- Fluid therapy: 0.9% NaCl + 20 mEq KCl
 - Avoid lactated ringers and dextrose
 - Potassium supplementation <0.5mEq/kg/h
- Pantoprazole
- Antibiotics: ampicillin, metronidazole
- Vitamin K: 3 doses, q 12h
 - Start early
 - Careful dosing: too frequent can cause hemolytic reactions
- Potassium phosphate
- Antioxidants
 - N-acetylcysteine
 - S-adenosylmethionine (SamE)
 - L-carnitine
 - B vitamins in fluids
 - Vitamin B12 & thiamine
 - Vitamin E

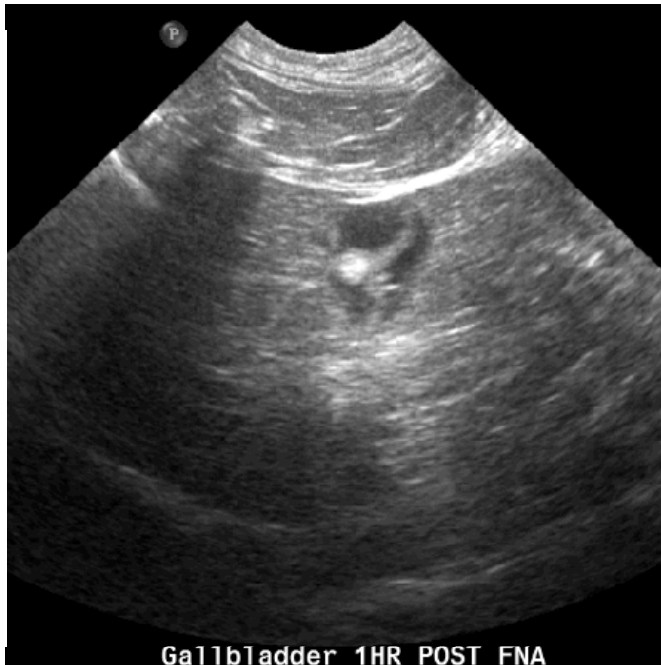
REFEEDING PHENOMENON

- Rapid shift from purely catabolic state
- Insulin surge
- Translocation of potassium and phosphorus into cells
 - Hypokalemia
 - Hypophosphatemia
 - Phosphate is component of cell membranes and nucleic acids, is involved in glycolysis, and is part of ATP
 - Hemolytic crisis if $<2\text{mg/dL}$
 - Seen 48 hours after initial feeding
 - Anticipate and supplement at time of re-feeding
 - KPO_4 in fluids

PROGNOSIS

- Must discuss the likelihood of an underlying primary disease and the importance of supportive care with owner
- HL rarely reoccurs
- Treatment may require weeks to months of assisted alimentation and metabolic support as well as concurrent management of underlying medical conditions
- Recovery rate over 85% if the primary disease is identified and treated and the patient survives the initial 72-hours of critical supportive care

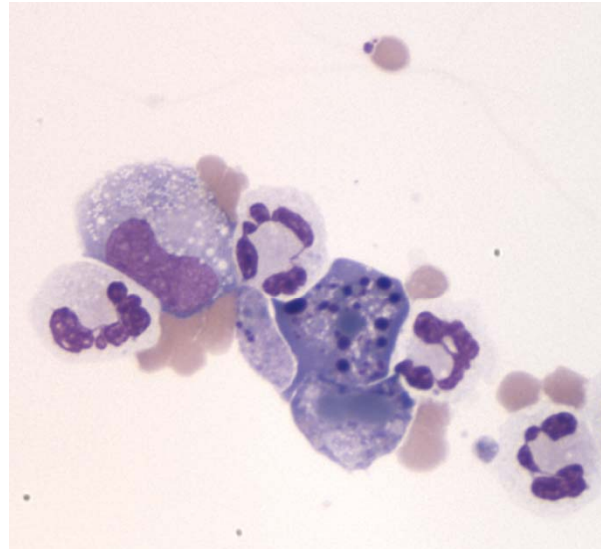
BILE PERITONITIS



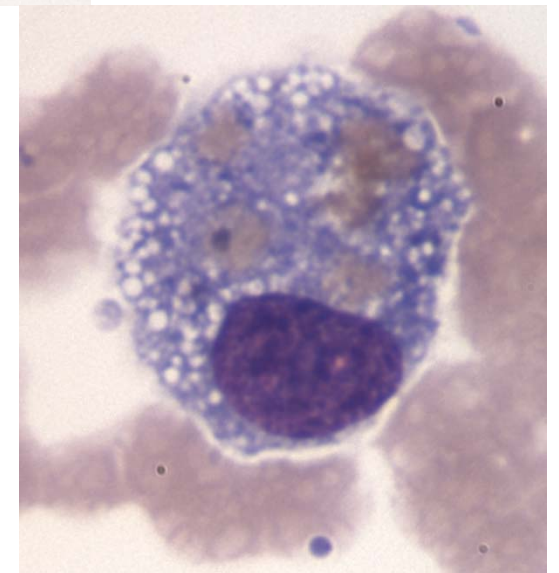
- Bile peritonitis occurs when there is rupture of the gall bladder
- “Chemical” peritonitis
- Iatrogenic: rupture or leakage caused by needle puncture during aspiration
 - Prevent by complete drainage of gall bladder
 - Fluid check one hour post FNA
- Treatment for rupture of biliary tract is surgery
 - Primary repair, biliary diversion or **cholecystectomy**
- Survival rate ~50%

PERITONEAL FLUID ANALYSIS

- Bile peritonitis
 - Tan pigment seen free in background or engulfed by macrophages
- Our patient: abdominocentesis on day 2 and 3 after initial U/S-guided FNA
 - Euthanized due to poor prognosis



Apoptotic cell



Macrophage with bile

SUMMARY OF COSTS

- Imaging (ultrasound, radiographs, fluid check, FNA): \$621
- Clinical pathology: \$625
- Diagnostic lab: \$270
- Esophagostomy tube with anesthesia: \$393
- Inpatient care: \$1500

- Total: \$4,394.60

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- Internal Medicine Department



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QUESTIONS?

