### ULTRASOUND REPORT

**Medical History / Laboratory & Radiographic Findings:**
Hx of increased ALT/ALKP that responded to antibiotics and fluid therapy. Today, ALT - 2579, ALKP - 2599, cPLi - wnl, vomiting and lethargic.

#### Liver:
- Moderately increased size, moderately rounded shape and moderately coarse hyperechoic echogenicity.
- No focal lesions are appreciated. The gallbladder has a mild amount of unorganized sludge debris and is mildly increased in size. The common bile duct is normal in size and shape.

#### Kidneys:
- Normal size and shape with normal corticomedullary dimensions.

#### Spleen:
- Normal size, shape, and echogenicity. No focal lesions appreciated.

#### Urinary Bladder:
- The bladder is of relatively normal contour and thickness. No overt obstruction, uroliths or neoplasia noted.

#### Adrenal Glands:
- Both adrenal glands were visualized and recognized as having abnormally rounded "plump" shape, increased size (Lt/Rt = 6.8/4.9mm), normal position with stimulated overall echogenicity for this breed. No adrenal invasion into the vena cava, phrenic vein thrombosis, dystrophic mineralization or clinically significant nodular changes were noted.

#### Pancreas:
- No significant findings.

#### Intestinal Tract:
- WNL - normal bowel layering and motility.

#### Lymph Nodes:
- No abnormal visualized.

#### Serosal Surfaces:
- WNL

#### Prostate:
- NA

#### Testicles:
- NA

#### Uterus:
- NA

#### Ovaries:
- NA

#### Cursory Heart:
- NE

### Interpretation:
1) Liver - the findings are moderate - DDx:
   a) Chronic vs. Acute hepatitis or cholangiohepatitis (bacterial vs. sterile vs. toxin)
   b) Steroid hepatopathy / Vacular hepatopathy / Glycogen storage disease / Copper storage disease
   c) Infiltrative neoplasia (lymphosarcoma)
2) Adrenals DDx: bilaterally enlarged and stimulated adrenal glands are suggestive of pituitary-dependent hyperadrenocorticism.

### Recommendations:
1) Consider continued supportive therapy with IV fluids, Actigall, Denamarin, and broad spectrum antibiotics (Ampicillin and Metronidazole)...refer to article below. If minimal improvement, consider fine-needle biopsy of liver.
2) If clinical signs suggest hyperadrenocorticism, consider running an ACTH or LDDS test to confirm hyperadrenocorticism before initiating therapy.

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*Treatment Recommendations for Canine Liver Disease. Updated 7/2010*

1) A lower protein diet to support liver dysfunction such as Hill’s L/D, K/D or Purina CNM-NF is initiated
2) Amoxicillin or ampicillin 10mg/lb bid for potential suppurative hepatitis
3) Metronidazole 3-5mb/lb bid for immunomodulating and anaerobic benefits (avoid with severe hepatic disease)
4) Actigall (urosodiol-Novartis) 15mg/kg sid in 250mg tablets with food to stimulate bile flow, lessen cholestasis, anti copper storage and immune modulating benefits. A drug trial of up to 3 months is recommended. 300mg capsules also available or can be compounded into a liquid formulation as well to dose small patients.

5) Prednisone or prednisolone if biopsy indicates beginning at 2.2 mg/kg/day and tapering over 2-4 weeks to 0.25mg/kg/day once remission has been achieved. Dexamethasone at 0.3 mg/kg PO sid and taper in similar manner in cases of ascites (lacks mineralocorticoid activity.) Eliminate if immuran controls inflammation. Not in cases of hepatic encephalopathy!

6) Azathioprine (immuran) (50-240mg/m²/day) as a long-term alternative for prednisone with minimal side effects. Check cbc and platelet count at 4 and 12 weeks. Taper every 4 wks to lowest effective dose (monitoring transaminase levels).

7) Vitamin E 15U/kg water-soluble form bid, Vitamin C 25mg/kg/day

8) Colchicine 0.03mg/kg/day as an anti-inflammatory, stabilizes membranes, and stimulates collagenase production, hence diminishing fibrosis. Should be used when ascites is present. SE:V,D, Neuropathy.

9) S-Adenosylmethionine (SAMe by Nutramax FDA regulated or human equivalents nutritional supplement not regulated) 20mg/kg/day Sid in 90 mg tablets not to be broken. Adenosyl replenishes glutathione and aids in cellular detoxification. Has antiarthritic activity.

10) Milk thistle can be administered at a dosage of 100mg for each 25-50 pounds of body weight. Dosage may be increased 2-3X for serious conditions, with no risk of toxicity, but with increased efficacy.

11) Lactulose (0.5 ml/kg PO bid/tid) is used to manage hepatic encephalopathy by combining with gut ammonium.

12) L-Carnitine, normally synthesized by the liver, enhances ammonia elimination and is indicated in cases of hepatic encephalopathy and lipoidis. Must be in the -form. SE:expense.

Copper storage disease verified on biopsy and quantitative/qualitative copper stain (frequent in terriers Dalmatians, Dobermans, 40-70% in Belington’s) This pathology will resemble chronic active hepatitis. Peaks at 5-6 yrs of age. Dx = copper level > 400ng/dl


14) Penecillamine (alternate to Suprine): frequent vomiting side effects

15) Zinc gluconate: 1.5-2.5mg/kg tid. May be used solely in mild cases or in combination with Suprine in moderate/severe cases. Goal to reach serum levels of 200-600ug/dl measured every 4-6 months. Give on empty stomach or with tuna fish to avoid vomiting. Binds with intestinal copper to avoid absorption.

Suggestions based on clinical and pathological information:

General liver support tx :1,2,5,8,11; fibrosis: add 6, 9, 10; ALT elevation: add 3, 4, 9, 10, 11, (6,7 if significant lymph/plasmacell infiltration on bx); ALKP +/- Tbillev elevation, congestion on bx: 5, 10; Hepatic encephalopathy: 4, 12, 13 and w/d diet or equivalent, H2 blockers for GI bleeds. Ascites: Spironolactone 1-2 mg/kg/sid/bid, spiro-hydrochlorothiazide (1mg each component bid), lasix 0.5-1mg/kg for quick fix only! (causes azotemia, hypokalemia, and hypomagnesemia.

Common drugs to avoid in hepatic disease:
Halothene, sulphonamides, diazepam, azole antifungals, Phenobarbital, tetracyclines, erythromycin or Baytril combo with theophylline or cisapride, cimetidine with theophylline, metronidazole or ciprofloxacin. May be used alone or in combination. Ensure patient is on a liquid diet when starting.

Try to wean to immuran from initial pred to avoid side effects. For financial concerns eliminate SAMe first and Actigall second. The remainder of the medications is financially contained. Copper storage is long term management if not indefinite and requires follow-up biopsy to quantify success of treatment over a 3-6 month period.

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Updated 7/2010

Diagnosing Canine Cushing’s Syndrome
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Hyperadrenocorticism (HAC) is the term used to describe the clinical and laboratory changes associated with chronic exposure to glucocorticoids. A synonym for HAC is Cushings syndrome. Hyperadrenocorticism can be either spontaneous (naturally occurring) or iatrogenic. There are two forms of spontaneous HAC. Pituitary dependent (PDH) is the most common form (80-85% of cases) and is due to hyperplasia of the adrenal cortex resulting from inappropriate release of adrenocorticotropic hormone (ACTH) by a pituitary tumor (usually benign). The other form of HAC is adrenal dependent (ADH) (15-20% of cases), which is due to a functional tumor of the adrenal cortex. The tumor secretes cortisol independent of the normal pituitary control (feedback) process. Adrenal tumors can be either benign or malignant. Iatrogenic HAC results from chronic administration of glucocorticoids (oral, parenteral or topical, including otic and ophthalmic).

Clinical Signs
Typical clinical findings include polydipsia, polyuria, polyphagia, excessive panting, pot-bellied appearance, bilaterally symmetrical alopecia (hair loss/thin hair coat-typically, non-pruritic and predominantly truncal), thinning of the skin, muscle wasting, weakness, and lethargy. Less frequent clinical signs include comedones, calcinosis cutis and a plantigrade stance. Common complications of HAC include pyoderma, urinary tract infection, proteinuria, hypertension, diabetes mellitus and thromboembolism.
Laboratory Findings
The CBC reveals a "stress leukogram" (mature neutrophilia, monocytosis, lymphopenia and eosinopenia), mild polycythemia and thrombocytosis. Typical changes in the serum biochemistry panel include increased alkaline phosphatase activity, increased alanine transaminase activity (usually less than twice the upper limit of the reference range), increased triglyceride concentration, increased cholesterol concentration and slightly decreased urea nitrogen concentration.

Diagnosis
Hyperadrenocorticism is diagnosed based on the Presence of clinical signs, suggestive findings on CBC and serum biochemistry profiles and a positive confirmatory screening test (ACTH stimulation test, low dose dexamethasone suppression test-LDDST or urinary cortisol:creatinine test-UCCR).

There is no perfect screening test for the diagnosis of HAC. Many veterinary endocrinologists recommend the LDDST as the initial test however, the choice of which screening test to use is influenced by several considerations including the following:

1. Number and severity of clinical signs suggesting HAC
2. Ongoing or recent treatment with glucocorticoids
3. Strength of suspicion of an adrenal gland tumor
4. Potential presence of concurrent non-adrenal illness

Results of the ACTH stimulation test will be in the normal range (false negative) in roughly 20% of dogs with HAC. The false negative rate for the LDDST is lower; however, the specificity of the LDDST is poor (between 44%/o and 73%/o). In general, if a patient has serious non-adrenal disease, the more likely the LDDST will be falsely positive. The urinary cortisol to creatinine ratio (UCCR) is best used to rule out HAC. Nearly 100/o of dogs with HAC have an increased (positive) UCCR. Unfortunately, many dogs with an increased UCCR do not have HAC. If the results of one of the specialized endocrine tests are normal, but clinical suspicion of HAC is high, consider performing the other screening endocrine test.

<table>
<thead>
<tr>
<th>TEST</th>
<th>SENSITIVITY* (%)</th>
<th>SPECIFICITY^ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH Stim</td>
<td>Less than ideal</td>
<td>Good</td>
</tr>
<tr>
<td>(80-95)</td>
<td>(86-91)</td>
<td></td>
</tr>
<tr>
<td>LDDST</td>
<td>Excellent</td>
<td>Poor</td>
</tr>
<tr>
<td>(85-100)</td>
<td>(44-73)</td>
<td></td>
</tr>
<tr>
<td>UCCR</td>
<td>Excellent</td>
<td>Poor</td>
</tr>
<tr>
<td>(75-100)</td>
<td>(24-77)</td>
<td></td>
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</tbody>
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*Sensitivity > per cent of positive tests in dogs with HAC

^Specificity > per cent of negative tests in dogs without HAC

ACTH Stimulation Test-The forms of corticotropin (ACTH) historically used for testing are corticotrophin gel (Acthar) or synthetic corticotrophin (cosyntropin). Many veterinary endocrinologists use Cortrosyn (cosyntropin manufactured by Amphastar Pharmaceuticals, Rancho Cucamonga, CA). Cortrosyn is sold in packs of 10 or as a single vial of 0.25 mg (250 ug). Cosyntropin can be reconstituted and stored frozen (-20°C) in plastic syringes for up to 6 months. The dose for dogs is 5 pg/kg IV or IM (maximum dose per dog 250 pg). A pre-ACTH sample is collected, ACTH is injected IV and one post-ACTH sample is collected one hour later.

Four compounded ACTH formulations sold to veterinarians have been tested in normal dogs. These four formulations consistently stimulated increased cortisol concentrations at one hour, but yielded variable results at two hours.

LDDST-Either dexamethasone sodium phosphate or dexamethasone in polyethylene glycol can be used, but the dose is based on the amount of active dexamethasone. For example, a 4 mg/mL solution of dexamethasone sodium phosphate contains about 3 mg/ml of active dexamethasone. In order to give the correct dose in small dogs, make a 1:20 dilution by mixing 0.2 mL of dexamethasone with 3.8 mL of sterile water or saline. For example, for Azium@ a 1:20 dilution will make the final solution 0.1 mg/ml dexamethasone. In order to make a diagnosis of HAC, the dog must have clinical signs consistent with the disorder. If a dog has a positive screening test but doesn’t have clinical signs of HAC, the dog either does not have HAC or it may have subclinical HAC. In the latter case, monitoring for the development of clinical signs and repeat endocrine testing are recommended.