



Hepatic Lipidosis in Llamas and Alpacas Part 1. Recognizing the Disease

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Excessive accumulation of fat in liver cells (i.e., hepatocytes) is a disease process termed hepatic lipidosis, fatty infiltration, or fatty liver (see Figure 1) and is associated with well-known disease syndromes in cats, cows, sheep, goats, ponies, and humans. Although there are differences in conditions that initiate hepatic lipidosis between these species, a common theme is a period of inadequate energy intake (i.e., negative energy balance [NEB]) initiating body fat mobilization. Unfortunately for llamas and alpacas, the disease outcome is nearly fatal in all cases if not recognized and aggressively treated early in disease development.

Hepatic lipidosis in llamas and alpacas has not been frequently reported in the veterinary literature, but is increasingly recognized in cases of camelid illness and death. A large majority of cases submitted to veterinary diagnostic laboratories report some degree of fatty liver infiltration in llamas and alpacas submitted for necropsy. Whether hepatic lipidosis was the primary lesion causing the death of the animal, or a secondary lesion to some other disease process is not always clear. Veterinarians and owners are becoming aware of the serious nature of this problem and seeking ways to treat when recognized or prevent it entirely. Many owners have a horror story to tell about the loss of one or more females to this disease. In this column I will review the current state of knowledge about hepatic lipidosis in camelids and provide some background to its cause and early

recognition. A second column will detail treatment and prevention practices.

Characterizing Hepatic Lipidosis

Using liver biopsy specimens, a retrospective study identified 31 confirmed cases of hepatic lipidosis in llamas and alpacas submitted to Oregon State University Veterinary Diagnostic Laboratory. This study revealed a predominately middle aged, pregnant or lactating female population to be affected.¹ In contrast to other species, males accounted for 22.6% of the cases and age ranged from 5 months to 18 years. This is very different demographics of affected animals compared to the disease process seen in cattle, sheep and goats. In these cases there were no significant associations with any infectious, parasitic, or toxic causative agent. A number of case reports on hepatic lipidosis in camelids were in association with tick paralysis.

The most common factor documented in histories from these affected camelids was recent significant loss of appetite or severe weight loss. This period of not eating or weight loss varied from a couple of days to several weeks. The whole spectrum of body condition scores (thin to obese) were represented in the affected group of animals. In some cases, there were other medical problems, such as diarrhea, evident around the time the condition developed. In other cases, there were changes in social or environmental conditions such as uncharacteristic hot weather or movement of animals in or out of

certain pastures or pens. Some llamas were reported to be clinically normal less than 24 hours before being found ill or dead.

Examination of blood values for the affected animals showed that most had elevations in enzymes that indicate liver disease. These are not, however, specific for hepatic lipidosis and may be increased with any cause of liver disease. Biochemical measures associated with negative energy balance (nonesterified fatty acids [NEFA]), liver dysfunction (bile acids, sorbitol dehydrogenase [SDH], gamma-glutamyl transferase [GGT]), and muscle damage (creatinine kinase [CK], aspartate transaminase [AST]) were consistently elevated. Elevated concentrations of blood lipids (lipemia) and ketones (ketonemia, measured as beta-hydroxybutyrate [BHB]) were not consistently associated with hepatic lipidosis in this retrospective study population compared to other literature reports. Low total protein, but not low blood urea nitrogen, was also a common clinical finding in affected animals. These data suggest similarities in the pathogenesis of hepatic lipidosis in camelids to other species and not just ruminants.

Diagnostic Indicators

Since a history of recent anorexia or weight loss was the most common factor in the naturally-occurring cases of camelid hepatic lipidosis, a feed-restriction model was used in an attempt to mimic this condition.² Blood samples and liver biopsies were obtained regularly throughout the study to determine physiologic response and potential onset of disease. Feed restriction ended when there was any indication in blood work, biopsy, or clinical signs of the onset of hepatic lipidosis.

To induce metabolic changes consistent with hepatic lipidosis, mature grass forage (< 8% crude protein) was fed at a rate of 0.25% of body weight. Most

camelids will eat between 1.2 and 1.5% of body weight at maintenance. Fifty percent (5 of 10) of the llamas developed hepatic lipidosis to some degree based on histologic (liver biopsy) evaluation. No animals became depressed or recumbent. All llamas in the study on average lost over 15% of body weight. Llamas that developed hepatic lipidosis tended to have greater body weight loss in the first week and younger crias (less than 7 weeks) if they were lactating.

Blood tests showed expected increases in liver enzymes in those that developed hepatic lipidosis, but not in those that simply lost weight. This is important in telling us that our blood indicators of liver disease (bile acids, AST, GGT, and SDH) are relatively specific in llamas. All llamas had elevated concentrations of NEFA indicating negative energy balance and fat mobilization. There was no significant difference in NEFA concentration between affected and unaffected animals; however, mean NEFA concentration was maintained above 1 mEq/L in affected animals. Llamas with hepatic lipidosis had significantly higher mean BHB concentrations (10.24 mg/dl) than did non-affected llamas (0.92 mg/dl), indicating abnormal liver fat metabolism. This is a curious finding as camelids are not particularly ketogenic given their naturally high blood glucose concentration. Case reports are mixed as to whether or not ketosis was present in affected animals. Even with elevated ketones, the concentration in affected llamas is not nearly as high as commonly observed in ketotic cows, sheep, and goats. This is an important point as most veterinarians working with farm animals would not consider the BHB concentrations in the affected animals to be of concern and might miss the diagnosis. Definitive diagnosis of hepatic lipidosis is only accomplished by microscopic or analytical measurement of fat content of liver biopsy specimens,

though some key diagnostic blood parameters are useful supportive findings (Table 1).

Disease Mechanisms

Further research at Oregon State University on the unique aspects of glucose metabolism in llamas and alpacas might help explain their propensity for this disease. Unlike other ruminant animals, llamas and alpacas maintain higher blood glucose concentration (85-100 mg/dl), similar to that of nonruminant animals. Given the type of diet consumed by llamas and alpacas, this ability to maintain and greatly increase blood glucose concentrations when stressed was a puzzle. Research suggests llamas and alpacas become “insulin resistant” as they age, somewhat similar to becoming a diabetic.^{3,4} Insulin is a key metabolic regulator not only for blood glucose, but also fat mobilization. With insulin resistance, body cells will not utilize glucose efficiently while fat cells can more readily mobilize stored fat for use as an alternative energy source. This metabolic scenario would result in more rapid fat mobilization during periods of negative energy balance. Further research is needed to better understand underlying metabolic issues in normal and hepatic lipidosis affected animals and the potential role of insulin.

To summarize, camelids of a variety of ages, gender, body condition, and reproductive status are susceptible to

development of hepatic lipidosis. Conditions that place increased energy demands, such as pregnancy and lactation, increase potential risk for hepatic lipidosis. Factors such as social and environmental stressors and other disease conditions appear to also predispose camelids to loss of appetite and weight thus potentially predisposing them to accumulation of fat in the liver. Blood metabolites can be used to identify risk (NEFA for fat mobilization) and potential disease presence (elevated liver enzymes). The next column will address treatment and prevention approaches to hepatic lipidosis.

References:

¹Tornquist, S.J., R.J. Van Saun, B.B. Smith, C.K. Cebra and S.P. Snyder. Histologically-confirmed hepatic lipidosis in llamas and alpacas: 31 Cases (1991-1997). *J Am Vet Med Assoc* 1999;214(9):1368-1372.

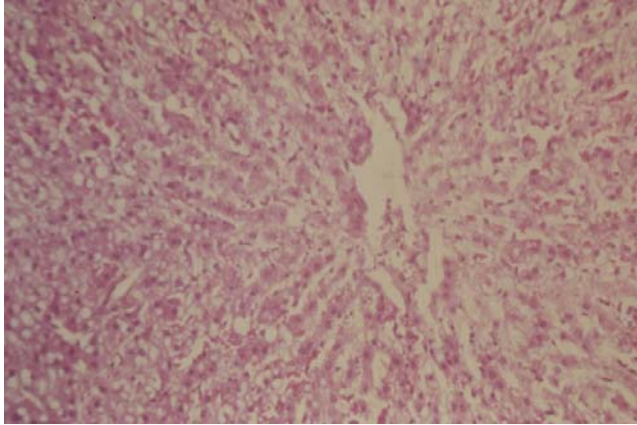
²Tornquist, SJ, Cebra, CK, Van Saun, RJ, Smith, BB. Metabolic changes and induction of hepatic lipidosis during feed restriction in llamas. *Am J Vet Res* 2001;62(7):1081-1087.

³Cebra, C.K., Tornquist, S.J., Van Saun, R.J., Smith, B.B., 2001. Glucose tolerance testing in llamas and alpacas. *Am. J. Vet. Res.* 62(5):682-686.

⁴Cebra, C.K., McKane, S.A., Tornquist, S.J., 2001. Effects of exogenous insulin on glucose tolerance in alpacas. *Am. J. Vet. Res.* 62(10):1544-1547.

Figure 1. Microscopic section of a liver biopsy from a normal llama (A) and a llama with severe fatty liver (B).

A. Normal liver cells (hepatocytes) with central biliary canal.



B. Fatty infiltration of the liver. Notice the large vacuoles in the cells that would be filled with fat. Affected livers are pale yellow in color and will float in water.

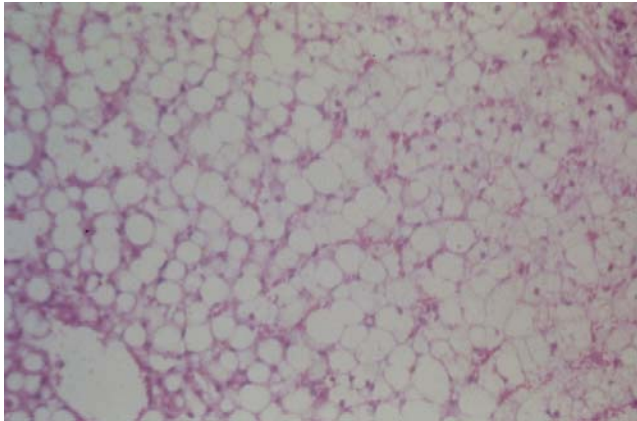


Table 1. Key blood metabolites used to help diagnose hepatic lipidosis and monitor response to therapy. The indicated alarm values are observed threshold values for llamas affected with hepatic lipidosis compared to unaffected animals. Definitive diagnosis of hepatic lipidosis is only achieved by liver biopsy.

Parameter ^a	Indicates:	Normal Range ^b	Alarm Values
NEFA	Measure of fat mobilization, increases risk for hepatic lipidosis	< 0.4 mEq/L < 0.6 mEq/L (lactating)	> 1.0 mEq/L
BHB	Measure of ketone body formation (ketosis)	0.12-0.75 mg/dl	>10 mg/dl
Bile acids	Measure of liver function, prolonged elevation following insult	1.1-22.9 mEq/L	> 30 mEq/L
GGT		16-46 IU/L	> 150 IU/L
SDH	Measure of liver function, rapid response after insult	0-22 IU/L	> 60 IU/L
AST	Measure of liver function and muscle breakdown, rapid response after insult	66-235 IU/L	> 750 IU/L

^aAbbreviations: NEFA = non-esterified fatty acids; BHB = beta-hydroxybutyrate; GGT = gamma-glutamyl transferase; SDH = sorbitol dehydrogenase; AST = aspartate transaminase.

^bLlama reference values from Oregon State University Clinical Pathology Laboratory, Corvallis, Oregon.