# “Lola Lacks Good Choices”

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**Introduction:**

Toxic mushrooms can be subdivided into multiple categories, including hepatotoxic, neurotoxic, gastroenterotoxic, nephrotoxic, and muscarinic mushrooms.[4] The majority of confirmed mushroom poisoning cases in dogs are caused by hepatotoxic mushrooms that contain toxic cyclopeptides.[2] Cyclopeptide-containing mushrooms contain amatoxins, phallotoxins, and virotoxins, with amatoxins being of most concern. Amatoxins consists of approximately 9 different toxins, with α-amanitin considered to be the most hepatotoxic. Amatoxin-containing mushrooms involve a selective group of mushroom genera: Amanita, Galerina, Lepiota, and Cortinarius.[3] Of all the amatoxin containing mushrooms, *Amanita phalloides* is considered the most toxic worldwide and is nicknamed the "death cap" due to ingestion most frequently resulting in death.[4] The IV lethal dose ($LD_{50}$) of α-amanitin in dogs is 0.1 milligrams per kilogram of body weight. The median lethal oral dose ($LD_{50}$) of methyl-gamma-amanitin is 0.5 milligrams per kilogram of body weight in dogs. An average *Amanita spp*. mushroom contains 4 milligrams per gram of amatoxin. This means that ingestion of 30 grams (approximately one ounce) is enough to be lethal to any size dog. All amatoxins are thermally stable and are not inactivated by boiling, cooking, drying, steaming, or freezing.

Acute liver failure occurs when hepatocellular damage becomes so extensive that hepatic synthesis, excretion, and regulation is compromised. Secondary complications from acute liver failure involve hepatic encephalopathy, coagulopathies, hypoglycemia, hyperbilirubinemia, and hypoalbuminemia.[1,3,4] Hepatotoxic mushroom ingestion most commonly causes acute liver failure by way of delayed hepatocellular necrosis and ultimately multiorgan failure.[5] Quick decontamination and identification of ingestion is the best management strategy to improve survival. Aggressive therapy immediately to support the failing liver is the mainstay of treatment

in these patients. Unfortunately, even with aggressive treatment the prognosis for ingestion of hepatotoxic mushrooms is poor in veterinary medicine.[1,2,4]

**History and Presentation:**

Lola is an approximately 4-month-old intact female Boxer who was presented to the MSU-CVM Emergency Service on November 29, 2020, for vomiting and seizures following ingestion of mushrooms on 11/28/20 from her backyard. Lola's owners reported that she vomited mushroom pieces the evening of 11/28/20, but did well throughout the night. The morning of presentation Lola would only eat a very small amount of food and she continued to vomit mushroom pieces. She became increasingly lethargic and her owners brought her to her primary care veterinarian where she received 200mLs of subcutaneous fluids and an injection of maropitant at approximately 2:30 PM. While visiting her rDVM, Lola's owners noticed that she had begun twitching her head and body. Later that afternoon she would try to bite anyone and anything that would go near her and would have bouts of screaming. Around 5:00 PM Lola became increasingly dull and started having seizures while at home. Lola's seizures were described as her being laterally recumbent, stiffening of her entire body, shaking, and voiding urine. She was immediately brought to the MSU-CVM Emergency Service for further evaluation. Prior to this event, Lola was an apparently happy and healthy puppy. Her puppy vaccines were up to date, though it was unknown which vaccines she had received at the time of presentation. Lola also had one bout of diarrhea the day of presentation.

On presentation to the MSU-CVM, Lola was laterally recumbent and dull. She had an elevated heart rate of 149 beats per minute and an elevated respiratory rate of 54 breaths per minute, with shallow breathing and an increased respiratory effort. Lola was hypothermic with a temperature of 98.8 degrees Fahrenheit, and her extremities were cold to the touch. Her mucous

membranes were pink with a capillary refill time of approximately two seconds. Remnants of blood-tinged saliva was noticed in her oral cavity. Cardiothoracic auscultation revealed no murmurs, arrythmias, crackles, or wheezes. She had bounding femoral pulses and an intact dazzle and palpebral reflex bilaterally. Her pupils were ventrally deviated with elevation of her third eyelids, making accurate assessment of her pupil sizes very difficult. Lola had a body condition score of 3/9, with decreased muscle mass. The remainder of her physical exam was unremarkable.

An electrocardiogram (ECG) revealed a sinus tachycardia. Pulse oximetry revealed an SpO2 of 100% at room air, and her blood glucose was too low to read on the glucometer. A venous blood gas panel was performed immediately upon arrival and revealed a decreased PO2 of 42.03 mmHg (45-65), severely elevated blood lactate of 14.6 Mmol/L. (0.5-2.5), metabolic acidosis of 7.076 (pH 7.35-7.46), and a moderate to severe hypoglycemia of 27 Mg/dL (64-112). Serum chemistry revealed a mild hyponatremia of 142.6 mmol/L (143-153), mild hypokalemia of 3.21mmol/L (3.7-5.9), a severely elevated ALT of 2145 U/L (10-90), mildly elevated ALP of 346 U/L (11-140), and a moderate hypoproteinemia 4.2 of g/dL (5.5-8.0) characterized by a mild hypoalbuminemia 2.2 g/dL (2.5-3.9). Serum chemistry also revealed a moderate hyperphosphatemia of 7.4 mg/dL (2.5-5.0), a moderate hyperbilirubinemia of 1.3 mg/dL (0.2-0.6), and a severely elevated creatinine kinase of 808 U/L (50-30). A non-invasive blood pressure revealed a low systolic blood pressure of 70 mmHg. AFAST revealed scant fluid in the diaphragmatic/hepatic and hepatic/renal quadrants. TFAST revealed no free fluid. Parvo antigen ELISA was negative.

Due to her history of mushroom ingestion and having elevated liver enzymes, hypoglycemia, hyperlactatemia, hypoalbuminemia, and many more clinical signs, Lola's

presumptive working diagnosis was hepatotoxicity or acute liver failure secondary to hepatotoxic mushroom ingestion. Additional problems of hypotension, dehydration, scant abdominal fluid, and increased respiratory effort remained.

**Diagnostic Approach and Considerations:**

With Lola's presumptive diagnosis of acute liver failure, it was essential to perform further diagnostics to determine the extent of hepatic damage. The liver plays an important role in the production of proteins, synthesis of coagulation factors, regulation of blood glucose, and detoxification of blood by metabolizing ammonia and lactate[1]. Due to the large role of the liver and the inability to utilize a single test to evaluate dynamic liver function, blood work (particularly, monitoring of liver enzymes and markers of liver dysfunction, including glucose, cholesterol, bilirubin, and albumin), imaging, coagulation assays, and tissue sampling may need to be combined to assess hepatic function and the degree of hepatic damage[1,2]. In acute hepatic necrosis the hepatic leakage enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are typically the first values increased on blood work. This is usually followed by hyperbilirubinemia, prolonged prothrombin time, and hypoglycemia[1].

As previously discussed, Lola's initial serum chemistry on presentation (11/29/20) revealed a severely elevated ALT, moderately elevated ALP, and a moderate hyperbilirubinemia. On 11/30/20 a complete blood count, serum chemistry, coagulation profile, ISTAT, and ammonia level were performed. Complete blood count revealed a mild neutrophilia of 13,480 /ul (3100-11800), with an increase in banded neutrophils of 426 /ul (0-400) and a severe lymphopenia of 238 /ul (1100-4800). Coagulation profile revealed a severely prolonged PT of 116.1 seconds (5.0-12.0) and a severely prolonged PTT of 52.8 seconds (10-20). Serum chemistry revealed a mild hypokalemia of 3.13 Mmol/L (3.70-5.90), moderate hypoglycemia of

30 mg/dL (75-125), severely elevated ALT of 6170 U/L (10-90), severely elevated ALP of 930 U/L (11-140), moderate hyperbilirubinemia of 3.4 mg/dL (0.2-0.6), mild hypoproteinemia of 4.6 g/dL (5.5-8.0), mild hypoalbuminemia of 2.4 g/dL (2.5-3.9), moderate hyperphosphatemia of 7.4 mg/dL (2.5-5.0), and severely elevated creatinine kinase of 1061 U/L (50-300).Baselineammonia levels were within normal limits. I-STAT revealed a decreased PO2 of 34 mmHg (85-100), mild hypokalemia of 3.2 Mmol/L (3.4-4.9), moderate hypoglycemia of 25 mg/dL (60-115), and metabolic acidosis characterized as a pH of 7.186 (7.35-7.45) and a HCO3 of 14.4 (15-23).

Abdominal radiographs taken on 11/30/20 revealed decreased serosal detail with the inability to differentiate peritoneal effusion from a normal variant due to Lola's young age. Abdominal ultrasound revealed a hyperechoic and enlarged liver, mild peritoneal effusion, and thickened pyloric and colonic walls. Fine needle aspirates of the liver during abdominal ultrasound were not obtained due to prolongation of her clotting factors and risk for hemorrhage. With Lola's increased respiratory effort, thoracic radiographs were also obtained and revealed an unstructured interstitial to coalescing alveolar pulmonary pattern in the caudal subsegment of the left cranial lung lobe. This is most likely attributed to aspiration pneumonia from multiple episodes of vomiting and regurgitation.

On 12/1/20 a coagulation profile and venous blood gas analysis (NOVA) were performed. Coagulation profile revealed an improved, but prolonged PT of 88.8 seconds (5-12) and PTT of 65.8 seconds (10-20). NOVA revealed a metabolic acidosis of 7.25 (7.35-7.45), low hematocrit of 33% (35-50), low BUN of 6 Mg/dL (10-26), a severe hyperlactatemia of 5.5 Mmol/L (0.6-2.9), mild hypercalcemia of 1.41 Mmol/L (1.12-1.40), and moderate hypoglycemia of 47 Mg/dL (60-115).

On 12/2/20 a complete blood count, neurochemistry, and ammonia level were performed. Ammonia profile revealed a severe hyperammonemia of 468 umol/L (0-95). Complete blood count revealed a moderate leukocytosis of 20.38 $10^3$/ul (4-12.20), a low red cell count of 3.08 $10^6$/ul (5.60-7.90), a mildly low hemoglobin concentration of 6.9 g/dL (11-19.7), a low hematocrit of 21.4% (35.2-55.7), and mildly low PCV of 21% (34-60). There was also a moderate to severe mature neutrophilia of 17,119.2 /ul (3100-11800). Serum chemistry revealed a mild hypernatremia of 162 Mmol/L (143-153), mild hypokalemia of 3.23 Mmol/L (3.70-5.90), moderate hyperchloridemia of 140 Mmol/L (106-122), a decreased BUN of 5 Mg/dL (8-24), severely elevated ALT of 5305 U/L (10-90), severely elevated of ALP 1866 U/L (11-140), severe hyperbilirubinemia of 5.8 mg/dL (0.2-0.6), a moderately low total protein of 3.5 g/dL (5.5-8.0), a mild hypoalbuminemia of 1.8 g/dL (2.5-3.9), mild hypoglobulinemia of 1.7 g/dL (2.1-4.3), mild hypocholesterolemia of 120 mg/dL (140-360), and a mildly increased creatinine kinase of 442 U/L (50-300).

On 12/3/20 a small animal liver panel, repeat coagulation panel, repeat ammonia profile, blood gas analysis, and pneumonia thorax recheck radiographs were performed. Coagulation profile revealed further improvement, but continued prolongation of PT of 29.9 seconds (5-12) and PTT of 28.7 seconds (10-20). Ammonia profile revealed a severe hyperammonemia of 157 umol/L (0-95). Small animal liver panel revealed a severe hyperglycemia of 296 Mg/dL (75-125), moderately low BUN of 6 Mg/dL (8-24), severely elevated ALT of 3245 U/L (10-90) and ALP of 2001 U/L (11-140), moderate hypoproteinemia 3.9 g/dL (5.5-8), mild hypoalbuminemia of 1.8 g/dL (2.5-3.9), severe hyperbilirubinemia 8.0 Mg/dL (0.2-0.6), and mild hypocholesterolemia 131 Mg/dL (140-360). Pneumonia thorax recheck radiographs revealed an alveolar pulmonary pattern within the cranial and caudal subsegments of the left cranial lung

lobe and the left caudal lung lobe, with a leftward mediastinal shift. The previously found diffuse unstructured interstitial pulmonary pattern in the right hemithorax had improved.

**Pathophysiology:**

The pathophysiology behind ingestion of amatoxin-containing mushrooms primarily involves the liver as the main target organ.[5] After ingestion, amatoxins exert toxic effects on the cells of the gastrointestinal tract during absorption. The liver then takes a direct hit of amatoxins from the gastrointestinal tract via portal venous circulation. Cells that have a high metabolic rate, such as hepatocytes, crypt cells, and proximal convoluted tubules of the kidneys are most prone to the toxic effects from amatoxins.[2] Shortly after ingestion, absorption of amatoxins into systemic circulation and distribution into the extravascular space is very rapid. Hepatocytes uptake α-amanitin via OATP1B3, which is an organic anion-transporting polypeptide.[1] Uptake of amatoxins results in selective inhibition of RNA polymerases, which are critical enzymes required for synthesis of messenger RNA. Lack of messenger RNA causes a decrease in protein synthesis and cellular-level metabolism is halted.[1, 2, 5]Apoptosis of hepatocytes and amanitin-induced insulin release are both additional effects that contribute to the pathogenesis of disease.[1]Since amatoxins inhibit both RNA polymerase II and RNA polymerase III, the regenerative capacity of the liver is halted due to the lack of protein synthesis needed to do so. The liver can no longer repair the lysis it sustains and centrilobular and periportal hepatic necrosis occur. With increasing decline of liver function, there is a chance for tubulointerstitial nephropathy to follow liver failure and precipitate a rapidly fatal syndrome known as hepatorenal syndrome.[5]

Toxicity can be divided clinically into four different phases after ingestion, although not all phases of disease will be present in every single case.[1, 2, 4] The initial phase is a latency period

where no clinical signs are present approximately 6-12 hours after ingestion. The second phase, also known as the gastrointestinal phase, occurs within 8-24 hours post ingestion. Poisoned animals will experience signs of vomiting, diarrhea, lethargy, abdominal pain, and anorexia. The third phase of disease is a false recovery phase that occurs within 12-24 hours, or even up to a few days after ingestion, during which the animal seems to have recovered from the disease. [2, 4] In the third phase, it is essential to monitor liver and kidney function, as fulminant liver failure begins to develop, and hypoglycemia can occur from the breakdown of liver glycogen stores within the liver. During the second or third phase, increases in AST, ALT, ALP, and bilirubin can also be seen.[2] Beginning in the third phase, coagulation parameters such as prolonged PT and PTT occur. The fourth and final phase of disease occurs 36 to 48 hours after ingestion, and is characterized by fulminant hepatic failure.[1,2,4] Subsequently renal and multiorgan failure can occur along with encephalopathy and coagulation disorders.[4] In this phase, affected animals are most likely to appear ataxic, icteric, lethargic, and have polyuria, polydipsia, seizures, or coma. Unfortunately, puppies or regular size dogs that ingest large amounts of amatoxins can die very rapidly of amanitin poisoning within the first 24 hours after exposure.[4]

The primary effects on the liver and the secondary complications and clinical signs of hepatotoxicity are the clinical clues to piecing together this case. As previously discussed, the liver is a main organ for synthesis, production, and regulation of important components in the body and common sequelae of elevated liver enzymes, coagulopathies, hyperbilirubinemia and icterus, hypoglycemia, and hypoalbuminemia are most seen with liver disease. Other complications of acute liver failure involve hyperammonemia and interruption of metabolization of ammonia to urea in the liver, causing secondary acute hepatic encephalopathy. Ammonia is believed to play a crucial role in the development of acute hepatic encephalopathy, with

astrocytes taking the burden of a large detoxification role[1] when a diseased liver cannot function properly. This role of astrocyte detoxification can lead to astrocyte mitochondrial damage, production of reactive oxygen species, and osmotic swelling.[1] Astrocyte swelling can cause major secondary consequences of cerebral edema and raised intracranial pressures.[6] Clinical signs of hepatic encephalopathy can range from minor mentation changes to significant excitatory neurologic dysfunction.[1] Agitation, hyperreflexia, aggression, or even seizures are common clinical signs seen. A depressed neurological state can also be present, where dull mentation or comatose is seen.[6]

Amatoxins are not metabolized by the body and are primarily excreted in the urine unchanged, with a small amount of toxins being excreted in the bile (up to 7%).[1, 2]Amanitins can be detected in the urine far before clinical signs in an animal are ever noticed, with amatoxins being excreted in the urine for several days post ingestion. The true frequency of amatoxin toxicity in small animals is difficult to confirm due to the need for identification of amatoxins in specimens from an affected animal.[1]There are challenges to establishing a confirmed diagnosis due to the limited assays in veterinary medicine for toxin detection. Liquid chromatography and mass spectrometry can be used to identify the presence of amatoxins in the serum and urine of dogs. Submission of mushroom pieces from the environment or gastric contents to a mycologist can also confirm exposure. Postmortem submission of the liver or kidneys has also been diagnostic in detecting amatoxins.[1,4]

**Treatment and Management:**

When treating hepatotoxic mushroom ingestion there is no specific antidote or definitive medications labeled for treatment, despite numerous treatment options.[5] In a 1987 study, 23 Beagles were given an oral dose of the lyphilized *Amanita spp.* fungus. Intravenous

silymarin/silibinin (50 mg/kg) was administered to 11 Beagles, with treatments given 5 and 24 hours after poisoning. These treatments were mixed with intravenous infusions of 5% dextrose (100mLs) and LRS (200mLs) to prevent hypoglycemia and dehydration. The control group, which consisted of 12 Beagles that were only given dextrose and LRS, died from hemorrhagic hepatic necrosis. However, 4 of the 12 Beagles died in hepatic coma 35-54 hour after poisoning. All 11 hounds in the treatment group survived, showing less pronounced liver damage and markedly diminished hepatotoxicity. This study showed that silibinin exerts protective effects on the liver and may prevent death, if given in the early stages of intoxication. Unfortunately, intravenous silibinin is not available in the United States for treatment in veterinary medicine. Oral silibinin/silymarin, however, is available for treatment in patients capable of swallowing oral medications.[7]

If ingestion of hepatotoxic mushrooms is suspected, then decontamination of gastric contents and administration of activated charcoal is recommended to prevent further toxin absorption. Aggressive therapy should be initiated immediately, as supportive care to aid a failing liver and compensation for the lost functions of the liver is the mainstay of treatment. Intravenous fluid therapy is necessary to correct dehydration and maintain perfusion, especially in patients that are unable to accept oral fluid administration.[1,2,3] Balanced crystalloid solutions such as Plasmalyte-A or 0.9% NaCl are recommended for treatment for patients that are suffering from acute liver failure. Lactated ringer solutions would not be a desired selection, as lactate is used as a buffer in this fluid type and a functioning liver is needed for proper metabolization. Reduction of ammonia levels is key to treatment of hepatic encephalopathy that typically ensues. Minimizing precipitating factors of hepatic encephalopathy, such as inflammation, hyperammonemia, alkalosis, hyponatremia, and hypokalemia, is also part of the

treatment plan. Acute liver failure patients should have their blood glucose monitored every 2-4 hours, with dextrose supplementation given as needed. Electrolytes deficiencies, such as hypokalemia, hyponatremia, hypophosphatemia, and hypomagnesemia should also be monitored daily and replenished as needed in these patients.[1] Hyponatremia should be avoided in these patients since there is an increased risk for cerebral edema, especially if hepatic encephalopathy is suspected. In acute cases with hyponatremia and severe neurological impairment, hypertonic saline should be used to improve cerebral edema.[1]

There is limited information published on the efficacy of hepatoprotective medications and their usage against mushroom toxicity in affected animals.[3] Potential hepatoprotective medications such as silymarin, S-adenosylmethionine (SAMe), vitamin C and E, and N-acetylcysteine (NAC) are often added to the treatment regime to decreased oxidative stress of the liver.[1,3] The liver functions as a storage reservoir for vitamins A, D, E, K, and B12; therefore, supplementation with vitamin K1 is suggested for acute liver failure patients. Nutrition is also essential in acute liver failure patients, as enteral feeding would aid to support the gastrointestinal mucosa. Acute liver failure patients mainly remain in a hypermetabolic state with increased energy requirements, often causing them to be in a catabolic state. Unfortunately, skeletal muscle breakdown can lead to increased ammonia production and an increased risk for hepatic encephalopathy.[1] Patients that suffer from acute hepatic encephalopathy and severe neurological dysfunction may benefit from parenteral nutrition instead. In patients with hepatic encephalopathy, it is essential to limit their protein intake to prevent excessive ammonia production and worsening of their neurological signs.[1,3] Lactulose enemas and/or oral lactulose is used to acidify colonic contents and bind to urease-producing bacteria, reducing production of ammonia. The need for antimicrobial therapy is essential when a failing liver can no longer

neutralize bacterial pathogens coming from the gastrointestinal tract, which could lead to secondary bacteremia and septicemia. Antimicrobials that cover anaerobic bacteria are chosen to minimize ammonia production/absorption. Extended coverage empirical antimicrobial usage is recommended when suspicion for infection or sepsis is high, especially if there is progressive hepatic encephalopathy, refractory hypotension, or suspicion for the presence of SIRS (systemic inflammatory response syndrome). Although acute liver failure patients may be coagulopathic, plasma therapy is not recommended solely on prolonged PT or aPTT, but may be needed for patients who experience hemorrhage or persistent hypovolemia.[1] Secondary gastrointestinal bleeding is common in acute liver failure and the usage of proton pump inhibitors would be beneficial in these patients.[1,2]

**Case Outcome:**

On the evening of presentation (11/29/20), a jugular catheter was placed and Lola was given a one liter bolus of plasmalyte + 50% dextrose (1 ml/kg) immediately. She was then continued on intravenous Plasmalyte + 5% dextrose (70 ml/kg/day) overnight. She received a lactulose retention enema and 2.2 mLs of lactulose orally every 6 hours. She was placed on Unasyn (30 mg/kg IV q8hr) and a rescue dosage of Midazolam (0.05 mg/kg) was available at all times during her hospitalization on seizure watch. Lola was placed in an oxygen kennel due to her increased respiratory effort and furthering respiratory distress from potential fluid overload. Lola's blood glucose was monitored every one to two hours and her blood lactate was monitored every four hours. Her blood glucose levels are listed in order as measured overnight: 50 mg/dL, 93 mg/dL, 143 mg/dL, 196 mg/dL, 142 mg/dL. Her blood lactate measurements are listed as taken in order overnight: 8.5 Mmol/L, 6.6 Mmol/L, and 5.2 Mmol/L. Lola was interested in eating a small amount of canned food but regurgitated brown fluid shortly after eating. Lola

remained in ICU overnight where her temperature, weight, and respiratory rate and effort were monitored, and treatments were adjusted accordingly.

On 11/30/20 Lola was transferred to the MSU-CVM internal medicine department and was dull, weak, and approximately 7% dehydrated. She had an abnormal skin turgor, tacky mucous membranes, and a capillary refill time of 3 seconds. She lacked a menace response OU, with slightly constricted pupils OU, and intact pupillary light reflexes. She had watery, dark to bloody diarrhea and vomited tan to bloody fluid. She had an increased respiratory rate and mildly increased lung sounds, with no crackles or wheezes appreciated. She could adequately oxygenate and no longer needed an oxygen cage. Lola remained on intravenous Plasmalyte fluids + 2.5% dextrose flowing through one catheter and 0.45% NaCl + 0.1 mEq/kg/hr KCl+ 5% dextrose that flowed through her second catheter. She was given multiple Plasmalyte boluses (150 mLs) and dextrose boluses (150 mLs) to combat her hypotension and hypoglycemia. Her hypotension improved with boluses, but she continued to have bloody diarrhea and vomited dark bloody fluid multiple times throughout the day. She was placed on a metoclopramide CRI (3 mg/kg/day) to help minimize vomiting and regurgitation. She was placed on ondansetron (0.5 mg/kg IV q8hr), pantoprazole (1 mg/kg IV q12hr), lactulose (3 mg/kg PO q6hr) if awake enough to swallow, Unasyn (30 mg/kg IV q8hr), maropitant (1 mg/kg IV q24hr), vitamin K1 (1 mg/kg IV once), vitamin K1 (1mg/kg SQ q12hr), N-acetylcysteine (140mg/ml IV once), N-acetylcysteine (70 mg/ml IV q6hr over 20 minutes), milk thistle (135 mg tablet PO q25) if awake enough to swallow, lactulose retention enemas (10 mL lactulose + 50 mL warm water retained for 20 minutes q6hr), Flumazenil (0.02 mg/kg IV once), flumazenil CRI (0.01 mg/kg/hr diluted with D5W), and sodium bicarbonate 8.4% (3.6 ml IV once over 20 minutes). Due to her mental decline and suspected cerebral edema and hepatic encephalopathy, Lola was given two doses of

hypertonic saline (3ml/kg IV) six hours apart. She was not offered any oral medications due to lack of swallowing and further risk for aspiration.

On 12/1/20, Lola's showed slight improvement in awareness and mentation while trying to walk and stand in her cage, but remained unable to track objects and people. Anisocoria was visible, with the right eye being constricted more than the left eye. She continued to lack a menace response OU and her pinpoint pupils had slightly improved. Her vomiting turned to regurgitation of bloody fluid and she continued to poop melena. She had a significant decrease in her frequency of regurgitation and defecation compared to the day before on transfer. Her hypoglycemia waxed and waned throughout the day and her hypotension remained, with the need for several Plasmalyte fluid boluses. She was given a fresh frozen plasma transfusion (8 ml/hr) to help with hypotension and continued prolongation of clotting factors. Aminocaproic acid (100 mg/kg IV q8hr) was added to her treatment regime and her potassium chloride was increased (0.15 mEq/kg/hr). All other treatments remained the same, with the fluctuation of fluid rates and boluses due to hydration assessments throughout the day. That evening, Lola had an increased respiratory rate and cardiothoracic auscultation revealed a popping sound over her left dorsal thorax. She was placed back in the oxygen cage and ceftazidime (30 mg/kg IV q6hr) was added to her treatments. Lola was able to be syringe fed oral lactulose and a small amount of water during her evening treatments, as she would lick and swallow when fluids were placed into her mouth.

On 12/2/20, Lola continued to slightly move around in her kennel, although she was still very weak. She would open her eyes and react to noises made while calling her name. She was dehydrated with a skin tent, tacky mucous membranes, and a capillary refill time of 3 seconds. Lola managed to pull out one of her catheters overnight and her hydration status declined due to

hypovolemia preventing peripheral venipuncture. She also regurgitated more due to the metoclopramide having to be given subcutaneously without having two catheters. With the need for increased fluids due to her persistent dehydration and waxing and waning hypoglycemia, a jugular catheter was placed. She was placed on 10% dextrose to combat her persistent hypoglycemia and another plasma transfusion was performed. Her mentation remained improved, with less constricted pupils OU and she continued to lack a menace response OU. Cardiothoracic auscultation revealed a 3/6 left systolic murmur and crackles bilaterally, with worsening in the left thorax. A tube check revealed placement of her jugular catheter to be deeper than suspected and her previously suspected pneumonia progressed to a diffuse unstructured interstitial pulmonary pattern. Her bloody regurgitation increased in frequency and her respiratory rate and effort were both increased. Lola was placed on nebulization treatments every 6 hours to help break down any mucus in her lungs. Her abdomen was distended after evening treatments and abdominal effusion was noted on aFAST. Abdominocentesis was performed and approximately 250mLs of fluid was removed from her abdomen, improving her respiratory effort and rate significantly. She became persistently hypothermic with the need for a bair hugger overnight.

The morning of 12/3/20, Lola began having thick, mucoid regurgitation and very harsh lung sounds bilaterally. Her mentation declined despite improvement of her ammonia levels and liver enzymes, adequate glucose supplementation, and total parenteral nutrition. She began having pinpoint pupils again and became non-responsive. She had persistent, declining hypotension despite multiple fluid boluses and hypertonic saline administration. Lola's family elected to discontinue therapy and Lola was humanely euthanized, with wishes for a full necropsy and cremation. Necropsy revealed diffuse hepatocellular degeneration and necrosis,

with severe megalocytosis and multifocal biliary hyperplasia. Multifocal renal tubular degeneration and necrosis was also present. The lungs had bronchointerstitial pneumonia from aspiration pneumonia with severe pulmonary edema present. There was cerebral and cerebellar edema with neuronal necrosis. The small intestine had mild and acute enteritis. Clinical signs were consistent with toxin exposure, especially *Amanita spp*. ingestion. Interestingly, the megalocytosis suggested chronic exposure to a different toxin, such as Sago Palms or pyrrolizidine alkaloids in the recent past, beforemushroom ingestion, which likely limited her chances of survival.

**Conclusion:**

Hepatotoxic mushroom ingestion can lead to delayed hepatocellular necrosis and ultimately multiorgan failure, especially when ingestion is not known. Rapid identification, decontamination, and aggressive supportive therapy is essential when mushroom ingestion is suspected. Unfortunately, specific antidotes to treat acute liver failure secondary to hepatotoxic mushroom ingestion do not exist in veterinary medicine. Even with multiple therapy options available and aggressive therapy, the prognosis remains poor to guarded in affected animals.

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