Cholecystitis may be much more common than many people realize. Dogs that have evidence of antibiotic responsive hepatobiliary tract disease may have a bacterial cholecystitis. Typically, both the ALT and SAP are increased, and icterus is common. Most dogs with cholecystitis do not have discernable gall stones. Many (maybe most) gall stones found in dogs and cats are clinically insignificant and only serve to confuse veterinarians. Ultrasound findings in dogs with bacterial cholecystitis are non-specific: finding "sludge" in the gall bladder can also occur in clinically normal dogs. However, aspirating bile via percutaneous puncture with a 22-25 gauge needle may be very helpful. Rarely, such aspiration technique will cause a vagal response that will cause extreme bradycardia; however, if this happens all that is usually needed is an injection of a parasympatholytic such as glycopyrrolate. Finding WBCs and/or bacteria in the bile seems to be very specific, but we are not really sure how sensitive this test is for cholecystitis. Therapy usually involves chronic (i.e., > 6-8 weeks) antibiotic therapy. If I cannot culture bacteria, I prefer to use a combination of amoxicillin and enrofloxacin. If that approach is unsuccessful, then cholecystectomy is usually the next step. Do not do a cholecystotomy or an incisional biopsy of gall bladder wall; dehiscence appears to be a major cause of morbidity and mortality after such surgery. Rather, remove the entire gall bladder and submit it for histopathology and microbiology. Be sure that you do not ligate or transect the common bile duct, or you may kill the dogs. Remember that cholecystectomy may be required to cure a patient with cholecystitis.

Emphysematous cholecystitis is classically associated with diabetes mellitus, but it probably occurs just as often in non-diabetic animals. This is diagnosed radiographically. Treatment with antibiotics that are effective against gas-producing anaerobic bacteria (e.g., penicillin, metronidazole, chloramphenicol, or clindamycin) is usually successful.

Spontaneous rupture of the gall bladder is usually due to a necrotizing cholecystitis associated with bacterial infection or mucoele (see below). Animals with septic cholecystitis and spontaneous rupture are usually icteric and present as having an acute abdomen. Cure requires cholecystectomy and aggressive antibacterial therapy. This disease seems to be uncommon, but can be life-threatening. Ultrasound is one of the best tools to detect this disease. It is important to remember that you should never take biopsies of the gall bladder. If you are going to do anything to the gall bladder, then you either a) squeeze it to see if it empties, b) aspirate it to obtain bile for cytology and culture, or c) remove it. Just make sure that when you remove the gall bladder, you do not ligate or obstruct the common bile duct.

Sometimes excessive mucus is secreted into the gall bladder and becomes so thick and inspisated that it essentially becomes a solid mass. This is referred to as a biliary mucocele. When the contents develop the consistency of thick jell-O and occlude the common bile duct,
EHBO occurs. Diagnosis is by ultrasound. You are not looking for gravity-dependent sludge; rather, you are looking for a “stellate” appearance to the gall bladder. Cholecystectomy appears to be the only appropriate therapy. Many of these patients have necrosis of the wall of the gall bladder and will eventually rupture causing peritonitis. Prognosis is good, as long as you do surgery before the gall bladder ruptures there are no post-surgical complications such as pancreatitis. A couple of very controversial points are what constitutes the ultrasonographic diagnosis of an immature biliary mucocoele, and whether gall bladders with non-gravity dependent “sludge” need to be removed or not. Some animals with “immature” mucocoeles seemingly resolve if treated with choleretics such as ursodeoxycholic acid.

Gall stones, as mentioned are usually there simply to distract the veterinarian. I am not saying that they never cause disease. I am saying that they are usually innocent of causing disease. If you find gall stones, you should first look elsewhere for the cause of the patient’s illness. If you can find nothing else that seems likely to be responsible for causing hepatobiliary tract disease in the patient, only then should you allow yourself to focus on the gall stones. Of course, if there are bacteria in the bile, then the gall stones are likely to be very important and should be removed so as to prevent recrudescence of the infection.

BIOPSY
There are basically four techniques for obtaining hepatic biopsies: a) fine needle aspiration for cytology, b) core needle (e.g., a Tru-Cut used with ultrasound or during laparoscopy), c) clam shell forceps (usually used at laparoscopy), and d) wedge (obtained surgically).

Fine needle aspiration (FNA) can be done on dogs or cats. A 25 to 23 gauge needle is advanced into the liver either blindly or with ultrasound guidance. As long as the needle goes straight into the liver and straight out, there is minimal risk of hemorrhage, even if other organs are punctured. If the animal is a clinical bleeder, has a prolonged mucosal bleeding time, or has a platelet count < 20,000/ul, then one must consider whether the possible benefits outweigh the risks of this procedure. The main advantages of FNA are a) it is easy and b) it is relatively safe. If the animal is tractable, anesthesia or sedation are not necessary. The main disadvantages of FNA are a) it does not reveal architecture of the liver (i.e., it will not reveal whether regeneration nodules or atrophy are present) and b) it commonly misses important disease (e.g., it will not reveal fibrosis and it typically misses many infiltrative diseases, even when they are extensive). A good example of the latter occurs in cats with possible hepatic lipidosis. Simply finding hepatocytes with vacuoles, while diagnostic for lipidosis, does not eliminate other hepatic disease (e.g., cholangiohepatitis or lymphosarcoma) and does not necessarily ensure that the lipidosis is severe enough to cause the clinical signs seen in the patient.

Fine needle aspiration is very appropriate for discrete masses because it is likely that if lymphoma or carcinoma is present, it will be detected. In like manner, finding organisms (e.g., histoplasmosis) is diagnostic. If the cytologic diagnosis is definitive for such infectious or neoplastic disease, then further biopsy techniques (e.g., laparoscopy) can be canceled. However, if the FNA is not definitive for one of these diseases, then biopsy with laparoscopy is performed. You can almost never eliminate a diagnosis (even lymphosarcoma) because it was not found with a fine needle aspirate FNA can be very specific, but it is not sensitive. Fine needle aspirates only “count” if they are positive for cells that cannot be considered normal under any circumstance (e.g., neoplastic cells, Histoplasma capsulatum). Therefore, FNA is reasonable
and appropriate as a first line diagnostic in animals with obviously focal lesions that could be malignant. You can do it in patients with diffuse disease, but never eliminate disease based upon a negative fine needle aspirate.

Core needle biopsy is usually performed with a Tru-Cut (or one of its modifications such as the Monopty or Biopyt) or a Menghini or a Vim-Silverman needle. While these needles can be used blindly, they are usually used in conjunction with ultrasonography or laparoscopy. It is preferable to use these needles with such guidance because the possibility of complications is substantially more with this procedure than with a fine needle aspiration (e.g., you can puncture the posterior vena cava or gall bladder with a 25 gauge needle and probably have no complications; the same cannot be said about taking a 14 gauge core out of the same organs). As before, you need to have serious justification for performing this procedure on animals that are clinically bleeding, have a prolonged mucosal bleeding time or those with platelet counts < 20,000/ul. The advantages of core needle biopsy are a) you can often obtain a piece of tissue large enough to determine some of the architecture, b) you can sometimes diagnose infiltrative diseases that were previously missed by fine needle aspiration, and c) it is a relatively safe technique. The main disadvantages are a) it is very easy to obtain samples that are too small, too fragmented, or too few to be diagnostic, b) this technique can easily miss a lot of important histologic changes and can easily miss significant disease, and c) in inexperienced hands, you can go through the liver and biopsy organs that you do not want to biopsy (e.g., the diaphragm, heart, intestines). This technique tends to be potentially specific, but it is still somewhat insensitive. Tru cut biopsies are more sensitive than fine needle aspirates, but they are still substantially less sensitive than laparoscopic biopsies or surgical biopsies. Furthermore, there are many ways of doing this technique wrong and obtaining useless samples of liver. You need to take at least 2 and preferable 3 adequate sized samples with such a needle. It is best if they are from different lobes of the liver. It is very important that each sample is at least 15 mm and preferably 20 mm long. You need a sample this long in order to have sufficient tissue to reliably find many abnormalities such as bridging fibrosis, which is necessary for diagnosing cirrhosis. Finally, you should always use the largest gauge needle that can safely be used in the patient. A 16 gauge needle is probably the smallest size that should be used, even in cats. Small gauge needles can easily miss "spotty" lesions whereas larger gauge needles are more likely to fine lesions. Contrary to what is said, these needles can usually be re-used many times. However, once they become excessively dull, they will not obtain samples of the length desired and must be discarded. Laparoscopy is a clearly superior technique for hepatic biopsy and should be done in preference to ultrasound guided samples. However, if you decide that you will do ultrasound-guided Tru-cut biopsies anyway, you want at least 2 and preferably 3 cores, each 20 mm long, from the largest gauge instrument that you can safely use in a particular patient. If possible, use a needle that obtains a 14 gauge core.

Laparoscopic biopsy utilizing clam shell (i.e., “double spoon”) biopsy forceps has several advantages. First, laparoscopy allows one to visualize lesion which cannot be detected by imaging techniques. Secondly, laparoscopy also typically produces relatively large, high quality tissue samples from multiple liver lobes (as opposed to ultrasound generally allowing one to biopsy the left lateral liver lobe only). Done correctly, laparoscopy is an excellent way to obtain superb hepatic tissue samples for histopathology. You can explore the abdomen, examine most of the liver, find lesions that were missed by ultrasound, and then take multiple biopsies from at least 2 or 3 different hepatic lobes. Laparoscopy costs the client more and takes more time to do
than ultrasound guided biopsies; therefore, you have to decide if you want a less insensitive technique that is less expensive (i.e., ultrasound), or a more expensive technique that you can have much more faith in (i.e., laparoscopy). The best approach is probably to first perform ultrasonography, at which time you can do a fine needle aspirate of any masses to be sure that there is not an obvious lymphoma or carcinoma. The next step is to perform laparoscopy to examine the liver and obtain optimal biopsy samples. This approach is more expensive, but offers a substantially greater likelihood of finding the cause of the hepatic disease, especially when it is not uniformly distributed throughout the liver. Despite the technique being so safe, clients must always be warned that some patients with hepatic disease (even those with chronic, apparently "stable" hepatic disease) may acutely decompensate and die after any form of hepatic biopsy.

Coagulation function should be checked prior to any biopsy procedure. There seems to be poor correlation between which animals have prolonged clotting times (e.g., PT, PTT) and which ones will bleed excessively after hepatic biopsy. A mild to moderately increased PT and/or PTT is not necessarily a good reason to avoid hepatic biopsy. Major prolongations of clotting times (e.g., > 3 times normal) usually correlate with severe bleeding, but these animals are typically found by mucosal bleeding time. Additionally, the clotting times will not detect patients with vonWillebrand’s disease. I prefer the buccal mucosal bleeding time (coupled with a platelet count) as the screening procedure to detect patients that may bleed excessively from hepatic biopsy as opposed to any of the clotting times. In general, I only worry if the animal is significantly thrombocytopenic (< 30,000/ul), is bleeding spontaneously or excessively after venipuncture or other procedures, or consistently has a prolonged buccal mucosal bleeding time (i.e., > 5 min). If the mucosal bleeding time is well within normal, then laparoscopy can usually be done even with platelet counts of 50,000/ul. If there seems to be clinically significant bleeding, you might still be able to perform laparoscopy, but you should have electrocautery and be ready to give a fresh whole blood transfusion, plus surgery if necessary. Some clinicians will automatically give most patients with significant hepatic disease subcutaneous injections of vitamin K₁ prior to any biopsy procedure. While administering Vitamin K₁ usually is not necessary, every once in a while you find a patient for whom it makes a major difference in clotting; therefore, it is reasonable. Regardless of how you biopsy the liver, always watch the patient closely for 3-4 hours after the biopsy procedure to see if there is any evidence of hypovolemia suggesting significant hemorrhage. Remember, the PCV will not necessarily change during acute hemorrhage.

Bleeding is seldom a problem with laparoscopy, but dogs with obvious portal hypertension may have excessive bleeding if the spleen is punctured with the Veress needle or trocar. If bleeding occurs, administration of blood is usually sufficient unless there is a concurrent coagulopathy.

Hepatic lobular collapse looks much like cirrhosis when viewed grossly, laparoscopically, or by ultrasound. However, there is no fibrosis, just loss of hepatocytes. Therefore, there is no need to use potentially dangerous drugs (e.g., azathioprine, colchicine) or even prednisolone. This disease can be associated with dermatohepatopathy, which sometimes responds to amino acid infusions. However, we have also seen improvement with more conservative management aimed as protecting the hepatocytes.

Noncirrhotic portal hypertension closely mimics cirrhosis in its clinical appearance, but is easily distinguished from cirrhosis by biopsy. This disease in particular is an important reason
why you need to biopsy the liver of dogs with “obvious” cirrhosis; they might have a very different disease. Noncirrhotic portal hypertension generally has a much better prognosis than cirrhosis. It is now believed that this disease might be a manifestation of portal vein hypoplasia (discussed under congenital portosystemic shunts and microvascular dysplasia). The dog can have a small liver, polyuria-polydipsia, acquired portosystemic shunting, massive ascites, and still have a much better prognosis than seen in animals with cirrhosis. Animals with noncirrhotic portal hypertension often respond well to conservative, symptomatic and supportive therapy to alleviate ascites. They may be successfully controlled for months or years. It is sometimes important to combine diuretic therapy with low salt diets so as to enhance the effectiveness of the diuretic therapy. If the patient stops eating, it becomes very important to monitor serum potassium and magnesium concentrations.

Lobular dissecting hepatitis is another disease that mimics cirrhosis. It is a “chronic hepatitis/cirrhosis”-like disease in which there is fibrous connective tissue infiltrating between hepatocytes. It typically occurs in younger dogs, causing ascites and signs of hepatic failure. Diagnosis requires biopsy, and the prognosis is much worse than that of chronic hepatitis or non-cirrhotic portal hypertension or lobular collapse.

Hepatic neoplasia may be primary or metastatic. Lymphosarcoma and carcinomas are the main types of neoplasms found in the liver parenchyma, although hemangiosarcoma is also reasonably common. Be sure that any infiltrates do not look like hemangiosarcoma before you try a fine needle aspirate; such trauma to a hemangiosarcoma can cause the animal to die much sooner than it would have otherwise. Many animals with hepatic malignancies, either primary or metastatic, have normal ALT and SAP activities. Miliary neoplastic infiltrates may not be detectable by imaging techniques, even with very high quality ultrasonography. It is easy to not find neoplasia if you are performing a fine needle aspirate blindly or with ultrasound guidance. Laparoscopy is much more sensitive at finding miliary infiltrates and metastatic lesions.

In particular, be aware that hepatocellular carcinomas can be devastating if they rupture; they can bleed as severely as a ruptured hemangiosarcoma. Most hepatocellular carcinomas can be palliated by surgery. Even though the tumor may recur, this may not happen for over a year. Therefore, surgical removal of malignant hepatocellular carcinomas is often a reasonable approach, assuming that it is positioned so that it can be surgically removed. Size is not a concern. Benign hepatomas can often be successfully removed, despite attaining very large sizes. In fact, the larger masses might be more likely to be benign as opposed to malignant. Do not make decisions about whether or not to do surgery simply based upon the size of a mass.

Nodular hyperplasia often looks exactly like cancer on ultrasound and even on gross examination of the liver. You absolutely cannot differentiate nodular hyperplasia from tumor without cytology or histopathology. This is the main reason why you should almost never euthanatize a dog based upon a presumptive diagnosis of tumor.

Pyogranulomatous hepatitis is seen from time to time. Such inflammatory hepatic disease can be due to fungal disease (e.g., histoplasmosis), atypical mycobacteria or can be idiopathic. It will only be diagnosed by hepatic biopsy; CBC and analysis of abdominal fluid cytology will not be helpful. Some dogs with idiopathic pyogranulomatous hepatitis respond to aminoglycosides, suggesting that there is an infectious etiology. Bartonella vinsonii has been suggested to be a cause in some dogs. This hypothesis is uncertain at this time. The most important point is that it is best to start off assuming that pyogranulomatous hepatitis to be infectious in nature and treat accordingly. If and only if there is no evidence of infection on
special stains or culture of bile and hepatic tissue or serology, as well as no response to aggressive antibiotic therapy should anti-inflammatory therapy be tried.

Acute hepatic necrosis can occur for numerous reasons. Ingestion of Sago palm seeds is one of the more common causes seen at TAMU. Depending upon how much was ingested, these dogs can present with severe, acute hemorrhage due to DIC and inability to produce coagulation proteins. They are often icteric. Prognosis seems to depend upon how much was ingested; therefore, it is worth attempting to treat if the patient does not seem to be in imminent danger of dying. Treatment is supportive (see discussion on hepatosupportive therapy, above) plus directed at treating DIC. Plasma infusions are one of the best treatments of DIC; much better than simply giving heparin. However it is easy to give insufficient amounts of plasma.

Mushrooms and aflatoxins (e.g, from moldy food) are other causes of acute hepatic necrosis. Most patients ill from ingesting mushrooms do relatively well if the treatment begins relatively soon. If Amanita toxicity is likely, milk thistle is documented to be an effective therapy. Aflatoxins can be quite devastating, and there have been cases of large lots of dog food contaminated with aflatoxin, resulting in many dogs dying. Xylitol (Splenda) can be very toxic to dogs, even when all they do is eat some chewing gum with the chemic