ULTRASONOGRAPHIC IMAGING OF THE LIVER

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In Veterinary Practice, liver disorders can be frustrating to diagnose. Although in the dog, it is uncommon for a patient to have normal clinical pathology values in the presence of significant liver disease, enzymology and other clinical pathology tests rarely indicate the type of liver pathology present. In addition, even liver "specific" enzymes such as alanine amino transferase can be increased in non-primary hepatic disease and care must be taken in interpreting slight or even moderate increase. This underscores the need for much focus on the tests that may be utilised in the diagnosis of liver disease and the non-hepatic causes for changes in these tests that the clinician should be aware of when interpreting clinical pathology results (Meyer and Harvey, 1998). Assessing the small animal patients with suspected primary heptobiliary disease is rarely a simple process because no single diagnostic test currently available has perfect sensitivity and specificity (Hess and Bunch, 2000). Radiography had demonstrated limitations with reduced abdominal contrast in presence of ascitic fluid (Cockett, 1986) and liver may appear normal even in severe diseased condition (Biller *et al*., 1992). Ultrasound is complementary to the abdominal radiograph and provides a more detailed examination of the inner structure of the liver and surrounding organs. Nyland *et al*. (1995) reported that hepatic ultrasonography was an extremely useful procedure for recognition and characterization of many types of disorders involving the liver. Salvekar *et al*. (2010) reported that ultrasonography is a valuable tool for correct diagnosis of liver disease in dogs with altered echotexture of liver parenchyma visualized confirmed various liver diseases like hepatic abscess, cyst, fatty liver, cirrhosis and hepatic neoplasia and also suggested that best results were obtained by combination of both clinico-pathological and ultrasonographic evaluation for correct diagnosis.When seeking advice from a veterinarian, pet owners expect accurate diagnosis and definitive therapy of the problem. In very few cases, the diagnosis can be made by history and physical examination alone, but in most cases the veterinarian has to utilize diagnostic tests to arrive at the diagnosis. The challenge for the veterinarian is to choose the most appropriate diagnostic test to arrive at the most accurate diagnosis (Meyer and Twedt, 2000).

The World Small Animal Veterinary Association's Liver Standardization Group recently categorized canine and feline hepatic disease into four main groups: parenchymal disease, neoplastic disease, biliary disorders, and vascular disorders (Rothuizen, 2006). The details of ultrasonographic imaging of the liver in each category are provided in this article.

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Hepatic Ultrasonography In Small Animals- A Chrono Logical View

The first papers concerning the use of ultrasound to examine the abdominal organs of the dog and cat were published in 1981 (Cartee, 1981 and Nyland *et al.*, 1981). Since then ultrasonography has become an essential imaging tool for identifying abnormalities of the liver parenchyma, biliary tract and vascular system. Initially papers described the positioning of the transducer, the topographical anatomy of the canine liver, the normal ultrasonographic appearance of the liver and cases of hepatic neoplasia, cirrhosis and cholelithiasis. In 1985 ultrasound-guided liver biopsy was described (Hager *et al.*, 1985), but most of the publications concerned methodology and the ultrasonographic appearance of liver diseases such as chronic hepatitis and cirrhosis. In 1987 the ultrasonographic diagnosis of portosystemic shunts was reported by Wrigley *et al.* (1987). In 1989 Kantrowitz *et al.* described the measurement of portal blood flow velocity by means of pulsed Doppler (Kantrowitz *et al.*, 1989). Since 1990 the evolution of ultrasound machines and the wide availability of duplex Doppler allowed better description of the vascular anatomy of the liver (Carlisle *et al.*, 1992). In those years the ultrasonographic diagnosis of portosystemic shunts replaced portography (Lamb, 1996). At the same time, the diffusion of ultrasound-guided liver biopsy increased the knowledge of hepatic pathology (Biller *et al.*, 1992). The first report concerning the use of an ultrasound contrast medium was published in 2000 (Bahr *et al.*, 2000), but most of the papers on contrast media have appeared since 2003, when specific software was developed to improve their use.

Today the liver ultrasonography of the dog and cat was the synthesis of these 25 years of history. The technological improvement of ultrasound machines had certainly conditioned either the diagnostic accuracy of this diagnostic technique, or our skill in small animal clinic. Now we were able to consider diseases such as cholecystitis or cholangitis in the differential diagnosis of jaundice, or we could make an early (sometimes serendipitous) diagnosis of a hepatic mass by examinating the liver of a dog with biochemical abnormalities and no specific symptomatology. Abdominal ultrasonography is routinely being used to identify hepatic parenchymal changes. Evaluation of the canine liver required a multi-faceted approach. This was because accurate assessment for liver disease requires consideration of both liver anatomy and liver function. Anatomic information needed includes gross evaluation of hepatic lobar architecture, histology, vascular anatomy and estimated portal vein blood pressure. A complete examination of the liver includes the evaluation of the parenchyma, portal and hepatic veins and the biliary system.

Ultrasonographic Anatomy Of Liver, Procedure And Probe Selection

The animal was placed in supine position with one assistant securing the rear legs while another one assisted to maintain the required positioning by restraint of the front legs and head. The area between xiphisternum and the umbilicus, extending several centimeters on each side of the umbilicus was shaved. A liberal quantity of acoustic gel was applied for effective sound transmission. The liver was imaged using 3.5 MHz or 5.0 MHz transducer. The selection of frequency was based on the body size of the animal i.e. lower frequency transducer was selected for bigger body size. Canine liver were imaged as per the procedure mentioned by Barr (1990) and Nyland and Mattoon (1995). The transducer was placed directly under the sternum with firm but gentle pressure. In this position, the transducer was placed in the midline and angled craniodorsally to image a transverse section of

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the liver. The head of the transducer was then rotated through 90° to image a longitudinal section of the liver in the midline. The image was oriented with the cranial portion of the animal to the viewer's left on sagittal scans and the right side of the animal to the viewer's left on sagittal scans and the right side of the animal to the viewer's left on transverse scan. To visualize all parts of the liver, multiple sweeps through the organ were made by directing the beam dorsally and ventrally in the sagittal plane and to the right or left in the transverse plane. Intercostal views at 11th or 12th intercostal space were used to supplement visualization of peripheral parts of the liver and viewing the major abdominal vessels. During the sweeps, ultrasonograms were evaluated for information on liver size, shape, contour and internal architecture including alternations in echogenicity (focal or diffuse), intensity (an / hypo / normal / hyper echoic pattern), hepatic vessels and to that of the surrounding organs as well as to the presence or absence of free peritoneal fluid. The ultrasonograms obtained were recorded.

Right transverse oblique and left transverse oblique positions of the transducer were used to examine the gall bladder and biliary system. Transducer position for the right oblique was on the right side, approximately 6 to 8 centimeters cranial to the xiphoid and 4 to 5 centimeters dorsal to the sternum. The transducer was angled towards the midline between costal cartilages to produce a transverse oblique scan through the gall bladder. Placing the transducer in a similar position on the left side of the animal produced the left oblique position. Attention was paid to the ultrasonographic appearance of the gall bladder size, shape, wall and contents

The structures observed in the liver on ultrasound examination were the gall bladder, seen as a round or oval anechoic structure towards the midline, the CVC, the portal veins and the hepatic veins. With the transducer placed immediately caudal to the xiphoid process and directed cranially, the portal vein and the gall bladder were visualized. These two structures served as important land marks for further examination (Nyland and Park, 1983 and Mwanza *et al.*, 1996). By rotating the transducer into a transverse position and slightly caudal to the gall bladder neck, some hepatic veins were observed. The right and left branches of the portal vein were not clearly visualized in the same scan as their branching does not occurred at the same place. The intrahepatic branches of the portal vein were differentiated from the hepatic veins by their echogenic walls (Mwanza *et al.*, 1996). Through the 11th or 12th right intercostal space, the portal vein and the CVC were easily visualized in transverse scans. From the left side, hepatic veins were recognized near the diaphragm. Here the veins from the left and medial lobes of the liver joined to form the main left hepatic vein, a major trunk draining into the CVC. The portal veins became smaller as they go deeper into the parenchyma while the hepatic veins became larger as they flow towards the CVC (Nyland and Park, 1983 and Mwanza *et al.*,1996).

Ultrasonography In Parenchy Mal Disease

Non-neoplastic canine parenchymal diseases include steroid-induced hepatopathy, hepatic lipidosis, amyloidosis, acute and chronic hepatitis, cirrhosis, necrosis (eg, toxic insult, ischemia, immune mediated), abscessation, granulomas and metabolic storage diseases.

Parenchymal abnormalities of the liver may be diffuse, focal or multifocal. Ultrasound is sensitive at detecting focal and multifocal disease but can be poor at detecting diffuse changes. Therefore, a definitive diagnosis should be based on a minimum combination of ultrasound features, blood test results, and tissue sampling results (Voros *et al.*, 1991). An enlarged liver is a subjective finding and may be generalized or focal. Generalized causes may be due to steroid hepatopathy, lipidosis,

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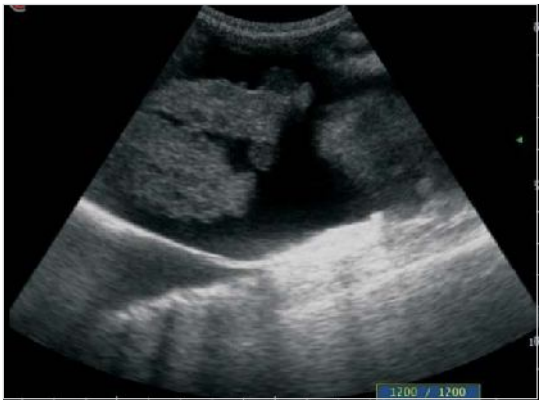
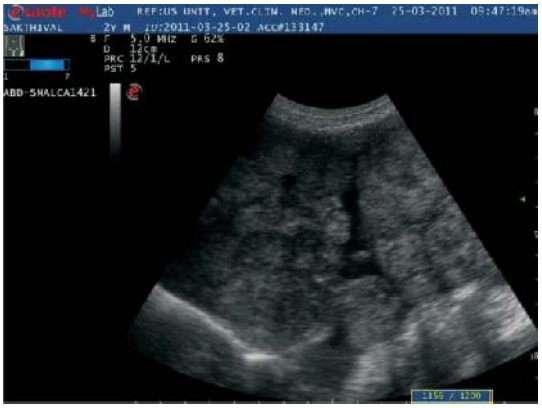
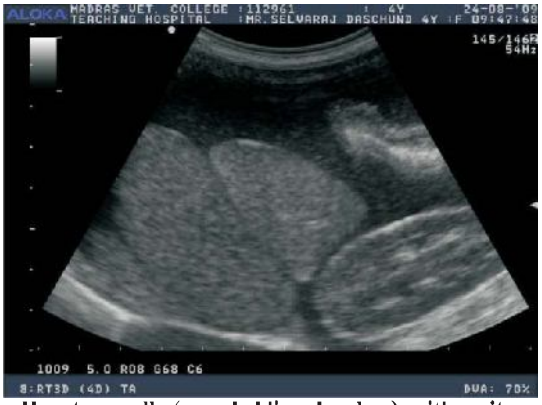




Diffuse Liver Tumour

Liver Cirrhosis



Hepatomegally (rounded liver borders) with ascites

amyloidosis, diabetes, hepatitis, congestion, neoplasia (eg, lymphoma, histiocytic sarcoma, mast cell tumor) and hepatocellular carcinoma (HCC). Focal or lobar enlargement may be due to primary or metastatic disease or by cysts, hematomas, abscesses, granulomas, lobar torsion or thrombosis. Whereas in portosystemic shunts (PSSs), cirrhosis or fibrosis, the liver is typically small and the stomach appears closer to the diaphragm than usual.

Diffuse Parenchymal Disease

Diffuse parenchymal disease generally affects all lobes and may appear normal, isoechoic or hyperechoic. A large group of hepatic diseases exists that can lead to infiltration of the liver without disruption of the architecture, making disease difficult to detect (Voros *et al.*,1991). Cholangiohepatitis, diffuse prenodular (early) metastatic carcinoma or sarcoma, round-cell neoplasia (eg, lymphoma, mast cell disease, histiocytic sarcoma), patchy or diffuse fatty infiltration, vacuolar hepatopathy, storage diseases (eg, amyloidosis, copper), toxic hepatopathy and early degenerative changes associated with micronodular hyperplasia and fibrosis are the diseases involved with diffuse parenchymal changes. The overall accuracy of ultrasound as the sole criterion for discriminating among the categories of diffuse liver disease is less than 40% in dogs and less than 60% in cats, hence biochemical or hematologic added with the ultrasonography will improve the diagnosis. However, a definite diagnosis can be achieved only with hepatic biopsy which is considered as a gold standard technique (Feeney *et al.*, 2008).

There are no specific sonographic findings in acute hepatitis and are variable because of many different etiologic factors that cause hepatic inflammation. The most common

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sonographic finding in hepatitis is probably hepatomegaly. Hepatomegaly is difficult to diagnose objectively with sonography. The so-called "starry night liver" pattern (Kurtz *et al.*, 1980 and Zwicble, 1995) increased periportal echoes coupled with decreased parenchymal echogenicity is not useful clinically.

Vacuolar changes in the liver associated with lipidosis and steroid hepatopathy usually cause hepatomegaly in conjunction with diffuse hyperecho genicity and rounded borders. Similar findings are also reported with hepatocutaneous syndrome in dogs (Beatty *et al.*, 2002). Mast cell disease affecting the liver may appear sonographically normal or diffusely hyperechoic. Nodular hyperplasia appeared as a homogenous or a diffuse mixed mass lesion with either increased or decreased echogenicity (Nyland, 1984). Barr (1991) observed a diffuse, heterogenous disturbance in the normal even echotexture, irregularity of the margins of the liver lobes with free fluid and multiple tortuous blood vessels in the prehepatic region in cirrhosis while Banerjee (2003) found that in chronic hepatitis, the liver was bright with irregular border and histopathology revealed nodular hyperplasia and extensive fibrosis.

Focal Parenchymal Disease

Focal or multifocal changes in the liver parenchyma are easier to identify ultrasonographically than diffuse changes (Nyman 2004). Hypoechoic, hyperechoic, and anechoic lesions are easy to identify because they contrast better with the surrounding parenchyma. The cystic lesions are the easiest to detect, even when extremely small. Anechoic cavitary structures in the liver can be attributable to necrosis, neoplasms or cysts.

Cyst

Cystic structures generally have sharply defined borders, can be round or

Sonographic findings that can be seen with diffuse hepatic parenchymal diseases (Gaschen, 2009)

Disease	Ultrasound Findings				
	Normal	Enlarged	Hyperechoic	Hypoechoic	Mixed Echogenicity
Acute hepatitis	✓	✓	-	✓	-
Chronic hepatitis	-	-	✓	-	-
Lipidosis	✓	✓	✓	-	
Steroid hepatopathy	✓	✓	✓	-	✓
Other vacuolar disease		✓	✓	-	-
Amyloidosis	✓	✓	-	✓	✓
Copper storage disease	✓	-	-	-	-
Toxic insult	✓	-	✓	-	-
Micronodular hyperplasia	✓	-	-	-	-
Fibrosis and cirrhosis	✓	-	✓	-	✓
Metastatic carcinoma	✓	✓	-	-	✓
Small round-cell neoplasia					
Lymphoma	✓	✓	✓	✓	✓
Mast cell	✓	✓	✓	-	-
Histiocytic sarcoma	✓	✓	✓	-	-
Drug administration					
Phenobarbital	✓	✓	✓	-	-
Superficial necrolytic dermatitis	-	✓	-	-	✓
Congestion	-	✓	-	✓	-

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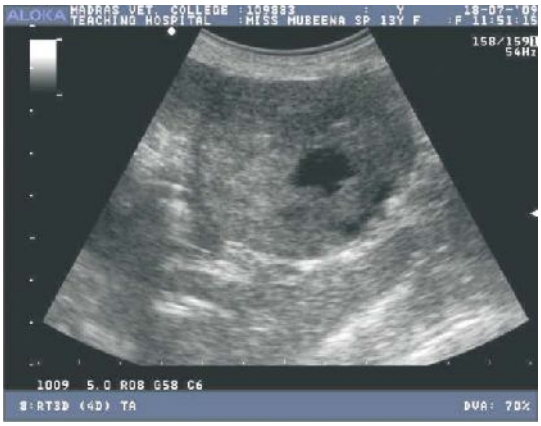
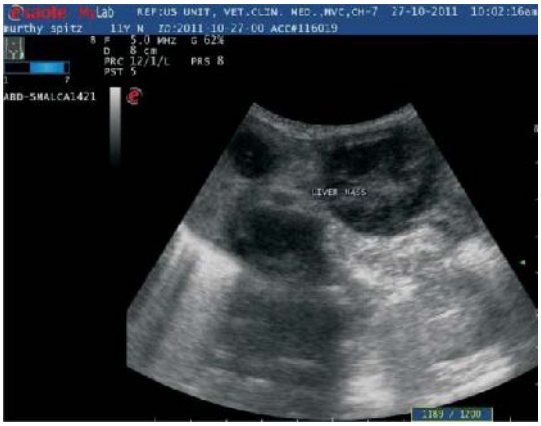


Hepatic Abscess



Multifocal Hepatic Mass

irregular in shape, and may even contain hyperechoic septa. Acoustic enhancement is typically identified in the far field, distal to the cyst (Barr, 1991).

Abscess

Hepatic abscessation occurs rarely in small animals and may appear similar to a primary tumor, granuloma, or hematoma because of its highly variable sonographic (d'Anjou, 2008) features. Abscess result due to bacterial infections that reach the liver by means of the portal vein or umbilical vein, ascending by means of the bile system or by direct penetration of the liver and may also occur secondarily to necrosis of hepatic neoplasms. On ultrasonography the hepatic abscesses may be round to irregular in shape with a hypoechoic central region.

Granuloma

Granulomatous causes of focal hepatic disease in dogs may be either infectious (mycobacterial) or non infectious (foreign material). Ultrasonographically granulomas in dogs appear as multifocal hyperechoic and well-marginated parenchymal lesions.

Liver lobe torsion

This is a rare entity in the dog and it leads to congestion and necrosis of the affected lobe or lobes (Scheck, 2007). Ultrasonographi cally the affected lobe appears hypoechoic and color Doppler shows reduced or no blood flow within the lobe.

Ultrasonography In Neoplastic Disease

Neoplastic disorders in dogs and cats are categorized as hepatocellular (nodular hyperplasia, adenoma and HCC), cholangiocellular (biliary adenoma, biliary carcinoma and mixed), hepatic carcinoids, primary vascular and mesenchymal (hemangiosarcoma and myelolipoma), hematopoietic (lymphoma and histiocytic sarcoma), and metastatic (Charles *et al.*, 2006). The ultrasonographic appearance of the neoplastic diseases may be diffuse, focal or multifocal.

Ultrasonographic evaluation of hepatic masses consisted of quantification and localization of the masses, characterization of their echogenicity, identification of their distribution (solitary or diffuse) and observing for evidence of cystic or vascular components. However, the ultrasonographic appearance of benign lesions such as nodular hyperplasia and many malignant lesions may appear similar in dogs and is difficult to differentiate (Voros *et al.*, 1991) which can only be achieved by histopathology. The ultrasonographic appearances of hepatic lesions were often nonspecific, some studies had attempted to characterize ultrasonography findings which were most consistent with liver cancer. Some

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lesions identified ultrasonographically within visceral organs may take on a halo effect and were called target lesions because of a hypoechoic rim surrounding an isoechoic to hyperechoic center and these target lesions were associated with malignancy (Hemangiosarcoma, HCC, carcinoma, insulinomas, bile duct carcinoma, lymphoma and histiocytic sarcoma), with a positive predictive value of 74% for a focal lesion and 81% for multiple lesions however benign causes of target lesions are also recorded which include nodular hyperplasia, pyogranulomatous hepatitis, chronic active hepatitis and cirrhosis (Cuccovillo and Lamb, 2002). Nodular hyperplasia was found to be present as a solitary finding or as multiple lesions and suspected that the presence of nodular hyperplasia might not be detected in many animals because the echogenecity of the lesion were not distinct (Center, 1996).

Ultrasonography Of Biliary Disease

Biliary disease is divided into four main categories: biliary cystic disease, cholestasis, cholangitis and diseases of the gallbladder (eg, mucoceles, cholecystitis) (van den Ingh *et al.*, 2006)

Icterus is a typical sign with gall bladder diseases which occur due to either intrahepatic or extrahepatic cholestasis. Kurtz and Middleton (1996) were of view that the normal gall bladder wall was sonographically visible as a thin echogenic line which typically measured about 2.03 mm in thickness and this varied with transducer type and placement or angulation of the sound beam relative to the organ insonated.

Gallbladder wall thickening

Generalized gallbladder wall thickening can occur with cholecystitis, cholangiohepatitis, hepatitis, free peritoneal fluid, and hypoproteinemia, the wall may appear to have a "double" layer in these instances (d'Anjou, 2008). Various authors have described the ultrasound findings of gall bladder wall thickening in patients with ascites was highly predictive of liver cirrhosis (Brogna *et al.*, 1996; Huang *et al.*, 1989 and Georgeier and Mechkov, 1991).

Choleliths can occur, more commonly in dogs, and appear as hyperechoic structures of variable size, number and shape that produce acoustic shadowing and may be an incidental findings in older dogs while the nonmineralized material called the biliary sludge was found to appear sonographically as a gravity dependent, moderately echogenic material within the gall bladder or it mimicked a mass lesion within the lumen (Newell *et al.*, 1995). The sludge can lead to potential obstruction to the biliary tract.

Gallbladder mucoceles occur in dogs and are an important cause of icterus and obstructive disease. They are caused by cystic mucinous hyperplasia leading to increased mucin production that distends the gallbladder and can eventually cause wall necrosis and rupture. Ultrasonogra-phically the classic finding is that of a "kiwi fruit" pattern of hyperechoic striations radiating from a central point and sometimes may have stellate pattern.

Gall Bladder wall rupture

Ultrasonographic signs of rupture include loss of the gallbladder wall continuity, hyperechoic surrounding mesentery, and free peritoneal fluid and the sensitivity of ultrasonography for diagnosing gallbladder rupture is reported as 85% (Nyland *et al.*, 2002).

Cholangitis or cholangiohepatitis

The appearance on ultrasound will be hypoechoic liver parenchyma with prominent-appearing portal vascular structures (Newell *et al.*, 1998) and may include thickening of the gallbladder wall and bile duct wall and increased amounts of sludge in the gallbladder.

Ultrasonography In Vascular Disease

Venous congestion of the liver occurs

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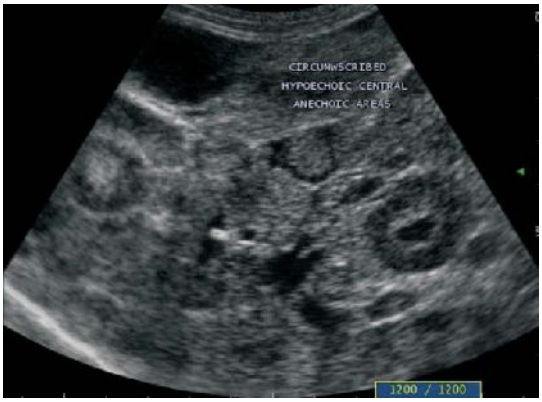

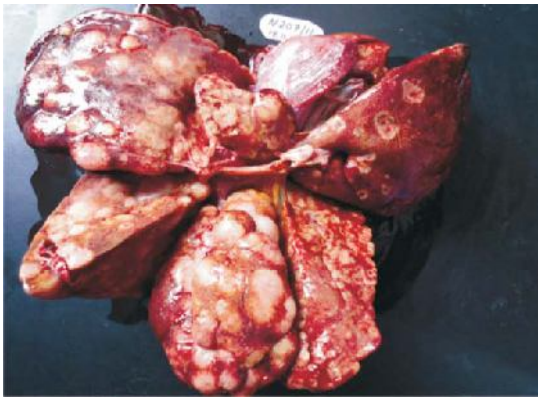

Circumscribed multifocal areas in liver parenchyma with mixed echogenicity and the gross lesions on the right indicating umbicated appearance of the liver surface (Cholangiocellular carcinoma)

secondarily to increased resistance to flow toward the right atrium by way of the vena cava. This may be attributable to a right atrial mass causing obstruction, pericardial effusion or invasion of the vena cava by a tumor. The hepatic vein is grossly dilated, as is the vena cava and the liver often becomes enlarged and diffusely hypoechoic. Ascites is usually also present.

Nyland *et al.* (1995) opined that the distended common duct was best visualized ventral to the portal vein in a transverse view at the right 11th or 12th intercostal space, which was usually not visible in that view in normal animals. The "shot gun" or "too many tubes" sign was sometimes recognized on sagittal scan of the liver after 5-7 days of obstruction which referred to visualization of dilated intra-hepatic ducts clustered around portal vessels. Ultrasonography can identify the presence of shunt vessels whereas the accuracy of identification of PSS varies widely, and it is generally recognized that the diagnostic usefulness of ultrasonography is heavily dependent on the skill and experience of the

Nodular hepatic infiltration: causes and sonographic appearance (Gaschen, 2009)

Disease	Nodule Echogenicity						
	Hyperechoic	Hypoechoic	Anechoic	Isoechoic	Mixed	Mineralization	Target Lesions
Hematoma	Early	Late	Possible	✓	Late	Possible	-
Cysts	-	-	✓	-	✓	-	-
Granuloma	✓	-	-	-	-	Possible	-
Regenerative nodules	✓	Most common	-	✓	✓	-	Possible
Abscess	✓	✓	✓	-	✓	Possible	-
Neoplasia	✓	✓	-	✓	✓	Possible	-
Myelolipoma	✓	-	-	-	-	-	-

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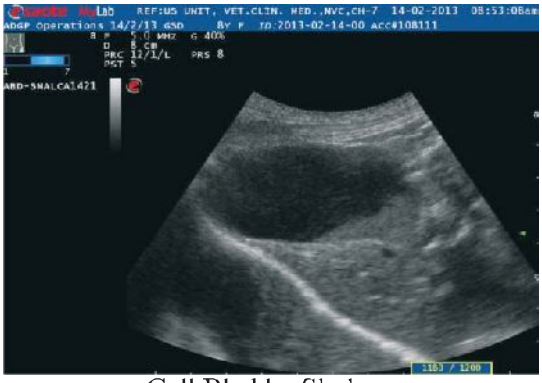
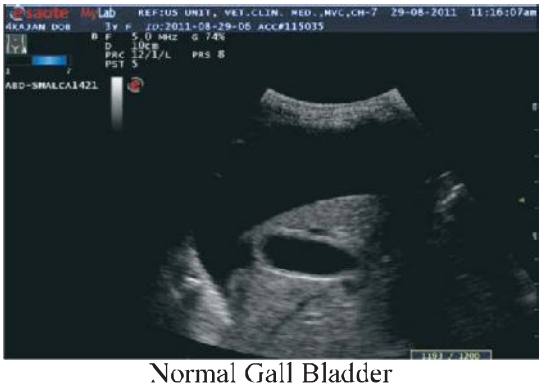
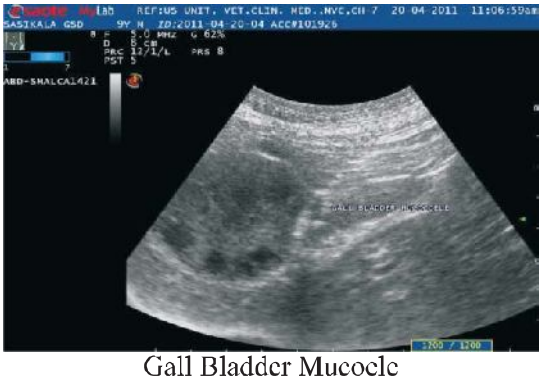


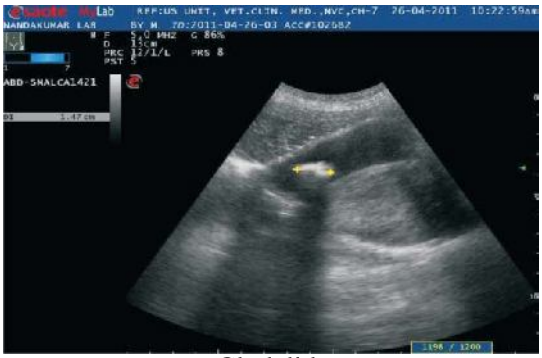
Gall Bladder Sludge



Normal Gall Bladder



Gall Bladder Mucocle



Cholelith

operator (Pratschke, 2010). Another condition is thrombosis of the portal vein which are associated with the diseases leading to coagulopathies. They are recognized ultrasonographically as intraluminal structures of moderate to high echogenicity and the absence of color Doppler signals within the lumen. Thrombosis can be focal or can extend into all branches of the portal venous system and cause acquired shunting (Gaschen, 2009).

Ultrasound Guided Interventional Techniques

Liver biopsy was required for definitive diagnosis and was indicated if the disease was chronic and / or signs were severe or progressive (Rutgers and Haywood, 1988 and Twedt, 1998). The establishment of an accurate diagnosis was dependent on two important components sampling an adequate amount of tissue and interpretation of the histology by someone well-versed in liver pathology (Meyer, 1996)

Percutaneous ultrasound-guided aspiration and biopsy of the liver have become routine in small animals. Patient preparation should include fasting for 12 hours before the ultrasound examination and tissue sampling. A coagulation profile is an important screening test before tissue core biopsy procedures, especially considering that several coagulopathies may occur with liver disease. Prothrombin time, activated thromboplastin time and a platelet count are the minimum tests that should be performed for screening purposes. Dogs should preferably be placed under general anesthesia for biopsy of the liver. Sedation (may or may not) with local anesthesia for fine-needle aspirations may be required. Diffuse lesions, the most accessible region of the liver should be sampled if aspiration. If more samples are required then core biopsy samples may be attempted. Tissue core needles with a 2-cm long sample notch

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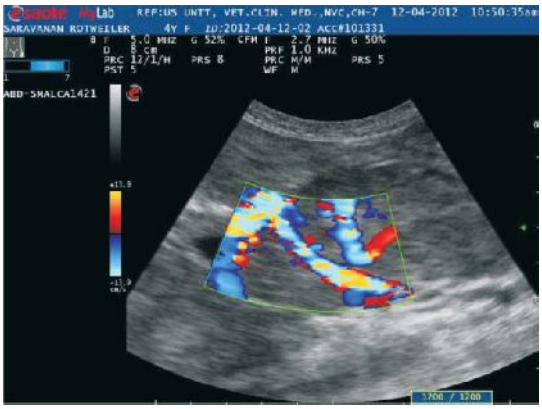

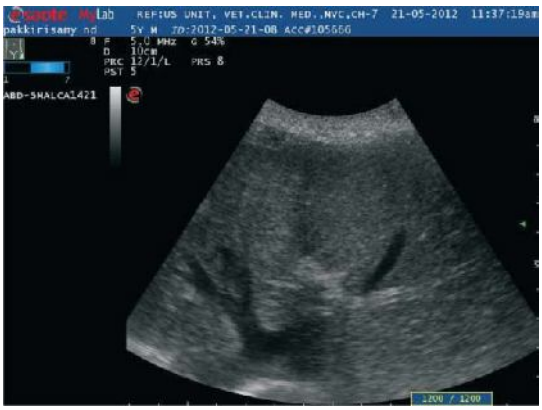

should be used and are typically 16 or 18 gauge depending on the size of the animal. Recommended are for medium- to large-sized dogs, 16-gauge needles while 18-gauge needles are best for smaller dog. Manual, semiautomatic and automatic (spring-loaded gun) can be used depending on the personal preferences of the sonographer. Fine-needle aspiration is generally performed with 20- to 22-gauge 1.5-in needles for diffuse lesions, small nodules and cystic or highly vascular structures. Complications of ultrasound-guided tissue sampling are rare however patients should be evaluated with ultrasound for the presence of free fluid.

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