Liver Biopsies – what and why

Biochemical parameters for liver disease have significant limitations in terms of sensitivity and specificity for liver disease. A biopsy for **cytological or histopathological assessment** is usually required to definitively diagnose hepatobiliary disease, helps guide treatment decisions and provides important prognostic information. In addition to sampling focal lesions, best practice includes sampling grossly normal looking liver if indicated on blood tests or clinically indicated. The methods available are a balance between invasiveness and reliability of the samples.

Fine Needle Aspiration (FNA) of the liver

FNA are a simple and inexpensive method for investigation liver diseases by collecting cells for cytology. Cytology is appropriate where the tissue architecture is not important and in which the lesion is more-or-less diffuse in an area or the entire organ. It is suitable for investigating hepatic lipidosis and neoplasia, especially round cell neoplasia such as lymphoma, mast cell tumours, or multiple myeloma. Unfortunately, FNAs are often disappointing for other solitary neoplasia such as primary hepatic epithelial neoplasia (carcinomas) as the cells cannot be distinguished from normal hepatocytes so histological examination for the assessment of infiltration is needed. Sarcomas often exfoliate poorly, resulting in low numbers of cells for cytological evaluation.

Aspiration can also be used to sample the gall bladder (cholecytocentesis) which is especially useful in cats with cholangitis, for cytological and bacterial investigations to pin-point the diagnosis and optimise treatment. An ultrasound-guided gallbladder aspiration has low risks as long as the wall does not have significant changes visible on ultrasound.

Ultrasound-guided Transdermal Tissue Core Needle Biopsy (Tru-Cut biopsies)

This can be performed in anaesthetised patients (deep sedation is sometimes adequate) and is considered low-risk and is cheap. It retrieves very small samples for histology. It is useful for the diagnosis of hepatitis, vacuolar hepatopathy and some neoplasms, where the architectural arrangement of the diseased tissue is important and will be captured in small samples, and if intrahepatic changes are focal and not visible on the surface of the liver. Several biopsies are taken to ensure the pathologist has enough portal triads for a diagnosis – at least 3-12 are needed for histopathological interpretation and copper staining. Tru-Cut needle biopsies are contraindicated if the liver is small or there is significant ascitic fluid present. Samples can be non-diagnostic if insufficient liver samples are collected and inadequate number of portal triads are sampled, and they do not allow

appreciation of coarse architectural changes in which variability within a tumour may be missed.

Surgical Wedge Biopsies

Larger tissue samples can be obtained by laparoscopy or laparotomy but a general anaesthetic will be required with surgery or access to expensive equipment and the training to obtain the samples. The advantages are the possibility to assess the liver surface macroscopically and to obtain larger biopsy samples which allow assessment of more parameters such fibrosis, copper quantification, fluorescence in situ hybridisation (FISH) and PCR testing for infectious agents, and to obtain biopsies of other organs such as the pancreas and intestines.

Technique	Advantages	Disadvantages
Ultrasound-guided fine needle aspiration	• Minimally invasive • Sedation only required • Ideal for obtaining samples of bile from gallbladder	• Rarely helpful in the diagnosis of liver disease due to small sample size • Only useful for generalised disease – primarily lipidosis and lymphoma • Risk of gallbladder rupture if cholecytocentesis performed - rare
Ultrasound-guided Tru-Cut biopsy	• Larger sample size allowing examination of hepatic architecture • Can be used for focal disease • Can be performed under deep sedation	• Difficult in very small liver or if significant ascites present • Requires specialist equipment and skill • Biopsies are not as accurate as wedge biopsies • Biopsies are too small to allow quantitative copper estimation
Laparotomy	• Allows excellent visualisation of liver and biopsy sites •Haemorrhage easily monitored and controlled	• Requires general anaesthesia • Invasive • Visualisation of lesions within the liver parenchyma is poor unless combined with ultrasound

Technique	Advantages	Disadvantages
Laparoscopy	• Minimally invasive procedure • Others as laparotomy	• Same as laparotomy • Availability

How to prepare for liver sampling

FNA do not need any preparation and can be taken under sedation or conscious. For all other liver biopsies, bleeding tendencies need to be evaluated with haematology (confirm platelets >100,000/µl) and routine coagulation profile of prothrombin time (PT) and activated partial thromboplastin time (APTT). In high risk breeds von Willebrand factor activity and a buccal mucosal bleeding time should be evaluated. Patients will need to be anaesthetised for ultrasound-guided Tru-Cut biopsy, except under exceptional circumstances and a light general anaesthetic is often safer than a deep sedation.

As we are in a lungworm region (*Angiostrongylus vasorum*), I require that all dogs having Tru-cut biopsies are treated for lungworm within the preceding 2 weeks with a licensed product. Lungworm does not always cause abnormalities in the coagulation profile to cause coagulation issues.

Cats for cholecystocentesis do not need any coagulation prior to sampling and this can be performed under sedation or general anaesthesia.

Please make sure owners are fully informed about any biopsy procedures that are scheduled for their pet. This included what information a biopsy can hope to show and what it cannot, associated costs and that these might increase if there is a problem with the biopsy procedure or additional test on the samples are recommended, and the possibility and risks of complications. Please contact me if you need more information on this.

What to send the samples for

In addition to H&E stained sections, a panel of histochemical stains greatly enhances interpretation of the liver biopsy. The reticulin stain helps assess hepatic architecture, aids in recognition of proliferative foci and defines areas of parenchymal collapse and/or extinction. Masson's trichrome for fibrillar collagen demonstrates the amount and distribution of fibrosis, complements the reticulin stain in evaluating liver architecture and accentuates individual necrotic hepatocytes. Although hemochromatosis is rare in

dogs and cats, the Prussian blue stain for iron is useful for mapping areas of inflammation, identifying Kupffer cell iron sequestration, and aids in proper identification of various pigments (lipofuscin, hemosiderin, bile). Staining sections for copper (Rhodanine) is essential to determine the need for chelation therapy and I advise this is requested on all liver biopsy samples. Copper qualification requires frozen liver tissue (5-10g) for quantitative determination – the SRUC do this (https://www.sruc.ac.uk/business-services/veterinary-laboratory-services/veterinary-diagnostics/) for £30.

Interpretation

It is important to use a pathologist who has an active interest in liver pathology and research, currently Bridge and Cambridge Vet School pathology service are the two that I recommend.

After liver biopsies

After fine needle aspirates or cholecystocentesis, the patient should remain in the practice for a couple of hours to be monitored. After transdermal core needle biopsy (tru-cut needle biopsies), the patient should be hospitalised for the remainder of the day (minimum of 3-4 hours) to monitor for significant haemorrhage, although this is a very rare complication. I do not recommend discharge before this time. During the this time the patient should be checked regularly for signs of haemorrhage by monitoring demeanour, capillary refill time, heart rate and pulse quality. After a tru-cut needle biopsy, I leave a care sheet detailing what to monitor and what to do if there is a problem.

References

- Kemp SD, Zimmerman KL, Panciera DL, Monroe WE, Leib MS, Lanz OI. A comparison of liver sampling techniques in dogs. J Vet Intern Med. 2015 Jan;29(1):51-7. doi: 10.1111/jvim.12508. Epub 2014 Nov 24. PMID: 25417960; PMCID: PMC4858056.
- https://www.histovet.com/pdf/HIS_ChoosingRightBiopsy.pdf

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