Guidelines on the use of Liver Biopsy in Clinical Practice

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These revised guidelines were drawn up for the British Society of Gastroenterology and the British Association for the Study of the Liver by Professor James Neuberger, Dr Allister Grant, Professor Chris Day and Dr Sushma Saxseena. Within the boundaries of current literature we have attempted where possible to make the guidelines "evidence based".

1. INTRODUCTION

Erlich is credited with the first liver aspiration in 1883 and subsequently the first percutaneous liver biopsy for diagnostic purposes was reported in 1923 (Bingel 1923). The technique has been modified since then, and over the last 50 years it has become a central investigation of hepatic disease. The low mortality (0.01%-0.17%) and the relatively low morbidity of this procedure have meant that liver biopsy has become widely used (Sherlock 1997).

Advances in medical technology and especially in imaging, together with advances in drug therapy have greatly influenced the diagnosis and management of hepatic disease and as a consequence the indications for liver biopsy are changing. In 1991 the British Society of Gastroenterology, together with the Royal College of Physicians of London undertook a nation-wide audit of percutaneous liver biopsy in 189 health districts (Gilmore, Burroughs et al. 1995). It is clear from this audit and from reviewing the literature that there continue to be significant differences in clinical practice with respect to liver biopsy across the UK, and a lack of standardised protocols between institutions. These guidelines examine the evidence regarding the use of and techniques for liver biopsy in adults and are intended to inform those in the UK who are considering whether a liver biopsy is appropriate in the management of the patient.

2. FORMULATION OF GUIDELINES

2.1. **Validity and Grading of Recommendations**

The guidelines have been produced to conform to the North of England Evidence Based Guidelines Development Project (Eccles, Clapp et al.1996) (Grimshaw, Eccles et al. 1995).

2.1.1 **Categories of Evidence**

The strength of evidence used to formulate these guidelines was graded according to the following system:

Ia: Evidence obtained from meta-analysis of randomised controlled trials

Ib: Evidence obtained from at least one randomised-controlled trial

IIa: Evidence obtained from at least one well designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study

III: Evidence obtained from well designed non-experimental descriptive studies such as comparative studies, correlation studies and case studies

IV: Evidence obtained from expert committee reports or opinions or clinical experiences of respected authorities.

The evidence category is indicated in parenthesis after the citations in the reference section at the end of the document.

2.1.2. **Grading of Recommendations**
The strength of each recommendation is dependent on the category of the evidence supporting it, and is graded according to the following system:

A: Requires at least one randomised-controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation (evidence categories Ia, Ib)

B: Requires the availability of clinical studies without randomisation on the topic of recommendation (evidence categories IIa, IIb, III)

C: Requires evidence from expert committee reports or opinions or clinical experience of respected authorities, in the absence of directly applicable clinical studies of good quality (evidence category IV)

2.2. **Scheduled Review of Guidelines**
As methods of diagnosis and tissue sampling change new evidence will come to light and the content and evidence base for these guidelines should be frequently reviewed.

3. METHODS OF LIVER BIOPSY

3.1. **Percutaneous Liver Biopsy**
Percutaneous liver biopsy may be classified according to the site of entry of the biopsy needle, whether the biopsy is performed in a *blind or guided* manner, or whether the biopsy track is *plugged* after the procedure.

3.1.1. **Transthoracic (Transparietal) and Subcostal Liver Biopsy**
For both these approaches the patient lies supine. The borders of the liver are usually defined by percussion or visualised by ultrasound. In most instances the intercostal space in the mid-axillary line just cephalad to the costal margin is then infiltrated with local anaesthetic, and a small incision is made through the dermis. The biopsy needle is then advanced into the intercostal space. The patient then holds their breath in expiration. The subsequent procedure for taking the biopsy then varies according to whether the biopsy needle is of the aspiration or cutting type.

If the patient has an enlarged liver extending below the costal margin then the site of entry of the biopsy needle may be subcostal. Complications are slightly more frequent with the transthoracic (4.1%) than the subcostal route (2.7%) (Perrault, McGill et al. 1978).

After the biopsy procedure the patient then lies supine for a period of time and regular observation of pulse and blood pressure are made in order to detect complications early (see section 7.10.).

3.1.2. **Blind and Guided Liver Biopsies**
A blind liver biopsy is one, which is taken as, described in section 3.1.1 without imaging of the liver immediately prior to taking the biopsy.

A guided biopsy is defined as a liver biopsy that is undertaken during real time imaging of the liver by ultrasound, CT or MRI. Guided biopsies have the theoretical advantage that the biopsy will be taken where there is thicker hepatic parenchyma, and is more likely to avoid the puncture of adjacent organs, and should allow the accurate biopsy of focal hepatic lesions where appropriate.

There is lack of agreement whether previous identification of the optimal site for liver biopsy by ultrasound examination counts as 'blind' or 'ultrasound guided'.

3.1.3. Plugged Liver Biopsy
Plugged liver biopsy is a modification of the percutaneous approach which was first described in 1984 (Riley, Irving et al.1984) (Tobin and Gilmore.1989). It has been advocated as an alternative method for obtaining liver tissue in patients with impaired coagulation where transjugular biopsy is not available.

In this technique a biopsy is taken with a Tru-cut needle in the conventional manner (section 3.1.2) but only the obturator containing the specimen is removed leaving the outer cutting sheath within the liver substance. A plastic cannula is then inserted down the sheath and while the breath is still held in expiration, gelatin is injected as the sheath is withdrawn. The procedure is safe and well tolerated (Fandrich 1996).

3.2. **Transvenous (Transjugular) Liver Biopsy**
Disorders of coagulation occur commonly in patients with liver disease and conventional practice in these circumstances where there is significant disturbance of clotting is to avoid percutaneous liver biopsy because of the risk of bleeding although the magnitude of this risk has not been defined in comparative studies. One study (Sawyerr 1993) suggested that, compared with plugged percutaneous liver biopsies, transjugular biopsy specimens were smaller (average 12 compared with 6mm in length) but was associated with an increased risk of bleeding (3.5% versus 0% for transjugular approach, not significantly different).

3.2.1.Transjugular liver biopsy was first described in 1964 (Dotter 1964). It is performed in a vascular catheterisation laboratory with video-fluoroscopy equipment and cardiac

monitoring because of the risk of cardiac arrhythmias as the catheter passes through the right atrium. The internal jugular vein is cannulated on the right side (usually) and a sheath inserted via a Seldinger technique. A 45cm long catheter is then guided under flouoroscopic control through the right side of the heart to the inferior vena cava. The catheter is then loaded with the transvenous biopsy needle and advanced into the hepatic veins and position checked by injection of contrast medium. The needle is then advanced rapidly 1-2cm past the tip of the catheter with the patient holding their breath and the liver tissue is retained in the needle by aspiration on a syringe attached to the other end of the needle whilst it is inside the liver. Specimens taken by the transjugular route tend to be shorter than those taken by the percutaneous route but are usually adequate for diagnostic purposes (Chau et al, 2002, Corr 1992).

3.2.2. Transfemoral: sometimes a transjugular approach is not possible and a transfemoral route may be used instead (Munk 1999).

3.3. **Laparoscopic Liver Biopsy**
This technique is well established and its use varies widely between centres. In the U.K. it is often used for biopsying lesions found fortuitously at routine laparoscopic surgery. It has also been used in centres where access to transjugular liver biopsy is not available, for patients with abnormal clotting parameters, and also in patients who have a combination of a focal liver lesion and a coagulopathy where a histological diagnosis is essential in the management of that patient. Some U.S. centres are performing laparoscopic liver biopsy on an out patient basis (Lightdale and Das 1997) and in some Japanese centres more than 50% of liver biopsies are performed laparoscopically (Sue, Caldwell et al 1996).

The complications in laparoscopic liver biopsy include those of the laparoscopy itself.

4. COMPLICATIONS

The indications for, and methods of liver biopsy have changed over the last few years (Lebrec 1996) with the advent of new imaging techniques and the development of new indications for biopsy e.g. liver transplantation (H¸bscher 1985.). All invasive procedures have a mortality rate associated with them, and consequently the benefits of obtaining liver for histology should always be weighed against the possible morbidity and mortality of the procedure.

4.1. **Mortality and Morbidity**

4.1.1. **Mortality**
The reported mortality from percutaneous liver biopsy varies considerably. This is partly due to the fact that most of the larger series reporting liver biopsy complications have been retrospective (Piccinino, Sagnelli et al. 1986)(Lebrec, Goldfarb et al. 1982).

The overall mortality rate in the 3 months after liver biopsy has been reported to be as high as 19% (Gilmore, Burroughs et al 1995). Most of these deaths are the result of hepatic malignancy and advanced liver failure and very few are due solely to the liver biopsy. The overall mortality rate also varies according to the centre in which the liver biopsies are being performed, for example, in the Mayo Clinic the mortality from fatal haemorrhage after percutaneous biopsy was 0.11% (McGill, Rakela et al. 1990), whilst in an audit of UK district general hospital liver biopsy the death rate was between 0.13% and 0.33% (Gilmore, Burroughs et al. 1995).

4.1.2. **Causes of Mortality**
The main cause of mortality after percutaneous liver biopsy is intraperitoneal haemorrhage as demonstrated in a retrospective Italian study of 68000 percutaneous liver biopsies in which all 6 patients who died did so from intraperitoneal haemorrhage (Piccinino, Sagnelli et al. 1986). Three of these patients had a laparotomy, and all had either cirrhosis or malignant disease, both of which are risk factors for bleeding (McGill, Rakela et al. 1990, Ewe 1981). Other serious complications responded to treatment; puncture of viscera was never followed by serious clinical complications. Other series have shown however that puncture of the gallbladder followed by biliary peritonitis is a recognised cause of death (Gilmore, Burroughs et al. 1995).

As the main source of mortality after percutaneous liver biopsy is haemorrhage, it is reasonable to assume that improvements in mortality rates can be made if the clinician comprehends the risk factors for bleeding, recognises bleeding promptly and aggressively resuscitates the patient. Patients with suspected biliary peritonitis should have an early laparotomy. It has also been suggested that patients who bleed significantly (i.e. patients who have a fall of >2g/dL Hb or become haemodynamically unstable) should be considered for either laparotomy; or therapeutic angiography if the bleeding does not stop with transfusion alone (Gilmore, Burroughs et al. 1995) although angiography is likely to be of benefit only if there is bleeding from a major vessel.

4.2. **Morbidity**

4.2.1 **Percutaneous liver biopsy**
The overall morbidity from percutaneous liver biopsy is difficult to ascertain as the majority of the studies are retrospective and therefore symptoms such as post biopsy pain requiring simple analgesia are not recorded. Although many groups have studied complications there is no consensus about the division into major and minor symptoms and whether complications such as asymptomatic post biopsy intrahepatic haematoma should be included in the figures. A morbidity rate of 5.9% for patients suffering minor complications after liver biopsy has been reported (Perrault, Mcgill et al. 1978).

Pain is probably the commonest complication of liver biopsy occurring in up to 30% (Gilmore, Burroughs et al. 1995, Forssell, Bronkowsky et al.1981) with moderate and severe pain occurring in 3% and 1.5% respectively (Perrault, McGill et al. 1978). Hypotension and vasovagal

episodes are common accompaniments to pain, occurring in approximately 3% of liver biopsies (Perrault, McGill et al. 1978), and vasovagal episodes occasionally require the administration of atropine.

Significant haemorrhage (indicated by a drop in haemoglobin of >2g/dL) occurs in 0.35% -0.5% of all procedures (McGill, Rakela et al. 1990), Knauer 1978). Subclinical bleeding however occurs in a much higher percentage of patients with up to 23% of patients having intrahepatic or subcapsular haematomas detectable by ultrasound at 24hrs post biopsy (Minuk, Sutherland et al. 1987). In general these haematomas are small and not associated with significant haemodynamic compromise. Haemobilia occurs in a 0.05% of patients and patients present with biliary pain, jaundice and melaena, and arterial embolisation may rarely be required.

Puncture of other viscera occur infrequently with an incidence of between 0.01% and 0.1% (Piccinino, Sagnelli et al. 1986). The puncture of lung, colon, kidney and gallbladder together with pneumothorax, pleural effusion, and subcutaneous emphysema are well-recognised complications, which rarely require intervention (Stotland 1996).

Other recognised complications include sepsis, reaction to the anaesthetic, breakage of the biopsy needle (Lazar 1978), and intrahepatic arteriovenous fistulae (Okuda, Musha et al. 1987).

4.2.2. **Transjugular liver biopsy**
The reported complications from transjugular liver biopsy range from 1.3-20% and the mortality up to 0.5%. A true comparison with percutaneous biopsy is not appropriate since the methods are complimentary rather than alternatives and because numbers of patients in the transjugular series is small.

Complications include neck heamatoma, puncture of the neck and/or intra-thoracic arteries, transient Horner's syndrome, transient dysphonia, pneumothorax, cardiac arrthymias, fever and infection, perforation of the liver capsule which may be associated with haemorrhage,, fistula from hepatic artery to either portal vein or biliary radicles.

5. INDICATIONS FOR LIVER BIOPSY

Percutaneous liver biopsy has a small but inherent risk even in the most experienced hands, and it should therefore only be performed when the benefits of knowing the histology outweigh the risks to the patient (in terms of altering treatment or disease outcome). Prospective studies have shown that the histological findings after liver biopsy altered treatment in less than one third of cases, although histology may help in establishing the diagnosis (Sorbi 2000, Skelly 2001). These benefits should be continually re-evaluated as new treatment options become available such as has occurred with the new antiviral therapies in viral hepatitis and in liver transplantation.

5.1 **Acute hepatitis**
Acute hepatitis of unknown aetiology including possible drug related hepatitis has long been an indication for percutaneous liver biopsy, but liver biopsy in typical acute viral hepatitis is usually not necessary. The usefulness of liver biopsy in chronic viral hepatitis was once hotly debated however with the advent of new antiviral therapies there is no doubt of the value of histology is assessing those patients who will benefit from treatment and their response to it.

5.2 **Hepatitis C (HCV) viral infection**
The role of liver biopsy in patients with HCV infection (as shown by HCV-RNA in peripheral blood) is uncertain. The recent guidelines from the National Institutes of Health (2002) states that 'there is a need to establish the role of liver biopsy in the therapeutic management of patients with chronic Hepatitis C'. In particular, the consensus statement suggests that the value of liver biopsy in patients with HCV infection and normal liver tests, the need for and timing of follow-up biopsies in those who have minimal fibrosis and deferred treatment, and the requirement of biopsy in those with non-genotype 1 virus, require definition. Nonetheless, biopsy at present, as with other indications, remains the only reliable method of assessing the degree of fibrosis and exclusion of other causes for liver damage.

The current EASL Consensus statement, (1999) published three years before the latest NIH guidelines. Suggest that 'it is appropriate and important to obtain a percutaneous biopsy before beginning therapy, in order to provide a base-line, to provide an opportunity to grade the severity of necro-inflammation and to stage progression of cirrhosis.

Both the British Society of Gastroenterology and the National Institute for Clinical Excellence have published guidelines on the management of those infected with HCV.

5.3 **Hepatitis B viral infection**
The decision to treat patients with chronic HBV infection will be dependant on their clinical state and the degree of viral replication. The current EASL Guidelines state that interpretation of a liver biopsy by an expert pathologist is an accepted part of the diagnosis and management of patients with HBV infection. Whilst, as with other indications, liver biopsy will help identify other cause for liver disease and can be used for grading fibrosis and inflammation. As the EASL guidelines state, these are useful mainly for clinical trials.(The EASL Jury, 2003).

5.4 **Genetic hemochromatosis**
The role of liver biopsy in the diagnosis and management of patients with genetic hemochromatosis is unclear. The guide-lines from the American Association for the Study of Liver Disease states that 'liver biopsy is useful to document the presence of cirrhosis (if not evident from radiological studies) to rule out significant iron overload when iron markers are equivocal, or to investigate other

causes of liver disease'. The conclusion is that liver biopsy is helpful in suspected hereditary hemochromatosis when documentation of hepatic iron content and the stage of fibrosis is necessary or to rule out other causes of liver disease. If qualitative iron studies indicate iron overload, then this should be confirmed by quantitative iron measurement (Tavill 2001). In contrast, the guidelines from the European Association for the Study of the Liver (EASL) 2000) recognised that liver biopsy was the gold-standard includes a liver biopsy but recognised that the emergence of biochemical and genetic testing may allow the avoidance of liver biopsy in the vast majority of cases.

We therefore recommend that liver biopsy is indicated to define or exclude the presence of cirrhosis, in those cases where biochemical and genetic testing do not give a clear diagnosis and where other causes of liver disease need to be excluded.

5.5 **Wilson's Disease**

The diagnosis of Wilson's disease is made on clinical history, estimation of serum copper and caeruloplasmin and the urinary excretion of copper before and after a challenge with d-penicillamine. Genetic tests may help in selected cases. The histological features characteristic of Wilson's Disease are not specific. Sometimes, estimation of liver copper may help contribute to the diagnosis but levels are not diagnostic.

5.6 **Infections and Pyrexia of unknown origin**

Occasionally, histological examination and culture of biopsy material can help in the diagnosis of infections such as tuberculosis.

5.7 **Primary Biliary Cirrhosis**

A persistently raised E_2-AMA strongly suggests a diagnosis of PBC (even if patients have no other signs or symptoms of PBC) (Metcalfe, Mitchison et al. 1996). Thus, in the characteristic case there is usually no need to do a liver biopsy to make the diagnosis of PBC. The presence or absence of cirrhosis is of limited prognostic significance.

5.8 **Primary Sclerosing Cholangitis (PSC)**

The diagnosis of classical primary sclerosing cholangitis (PSC) related cholestasis is usually made at endoscopic retrograde cholangiography or magnetic resonance cholangiography and diagnostic histological features in needle biopsies are often not seen. Liver histology may be needed to make the diagnosis of small duct PSC.

5.9 **Alcoholic liver disease**

The role and timing of liver biopsy in patients with suspected liver disease associated with alcohol remains uncertain. The histological diagnoses of fatty liver, fibrosis and cirrhosis cannot confidently be made without histology. Furthermore, in those with a history of alcohol excess, other factors may be the cause or contribute to the degree of liver damage. In patients with a history of alcohol excess and evidence of liver damage, a liver biopsy is helpful in determining the degree of liver damage, estimating the reversibility and defining other contributory factors.

Liver histology is needed to confirm alcoholic hepatitis since the clinical diagnosis is incorrect in up to 20%.

5.10 **Autoimmune hepatitis (AIH)**

Liver biopsy is indicated both in the diagnosis and follow-up of patients with autoimmune hepatitis. The American Association for the Study of Liver Disease Guidelines (Czaja and Freese, 2002) recommend that liver biopsy should be undertaken as part of the workup for the diagnosis of AIH. The role of liver biopsy in the monitoring of immunosuppression is less certain. Liver biopsy is recommended prior to cessation of immunosuppressive treatment is recommended in those who are in clinical and serological remission since in this situation, about half will have interface hepatitis and will relapse when immunosuppression is withdrawn (Czaja and Freese, 2002). The role of liver biopsy in those who are in clinical and biochemical remission and immunosuppression is stable, is uncertain: on-going histological inflammatory activity is likely to lead to progressive cirrhosis and this activity can be reliably excluded only on liver histology so some recommend liver biopsy every 2 years but this is uncommonly done in practice.

5.11 **Non-alcoholic liver disease (NAFLD)**

NAFLD is found increasingly commonly. The role of liver biopsy for this indication is not clearly established. Currently, it is not possible to differentiate fatty liver from non-alcoholic steato-hepatitis (NASH) without liver histology. Liver tests do not reliably confirm or refute the diagnosis or stage the extent of liver fibrosis. As NASH (rather than steatosis) is associated with progression to cirrhosis, there is an argument for taking a liver biopsy in all cases of fatty liver.. Those with NASH would require follow-up and treatment. However, this would have major implications on resources and there is no licensed treatment for NASH. A recent working party have stated the 'strict guidelines for the use of liver biopsy do not exist' (Neuschwander and Caldwell, 2003).

5.12 **Abnormal liver tests of unknown cause**

Liver biopsy may be used in the investigation of abnormal liver enzymes but this must be taken in context, tempered by the results of other routine investigations, and take into account the patient's details. For example, the investigation of an isolated raised alkaline phosphatase will be very different in an 80 year old compared to a 25 year old. Elevations in g-glutamyl transferase (g-GT) have been shown to be a sensitive marker of alcohol misuse.

However, liver histology in those with persistently abnormal liver tests and in the absence of diagnostic imaging and serology may identify the cause of the liver test abnormalities and, in a small proportion, indicate the need for specific treatment (Skelly 2001, Sorbi 2000). Of those with an isolated rise in the gamma-GT, 11% had evidence of hepatic fibrosis (Skelly 2001).

5.13 **Focal liver lesions**
The role of percutaneous liver biopsy in the diagnosis of focal liver lesions depends largely upon the clinical picture. In most patients with malignant hepatocellular carcinoma ultrasound scanning, CT and measurement of serum a-foetoprotein will allow a diagnosis to be made. Similarly a patient with a past history of colonic resection for neoplasia who presents with a solitary lesion in the liver associated with an elevated carcinoembryonic antigen, may not require a biopsy of the lesion to make the diagnosis of a potentially resectable metastasis. Liver biopsy also carries a documented risk of seeding tumours down the biopsy track (Hamazaki, Matsubara et al. 1995). The magnitude of this risk is currently unknown. Modern imaging techniques can also help to define other types of focal hepatic lesions such as haemangiomata and focal nodular hyperplasia. Liver histology will be helpful when the nature of the lesion is unknown.

5.14 **Following liver transplantation**
The use of liver biopsy after liver transplant is increasing, and policies on histological monitoring vary between liver transplant units. Some units perform routine biopsies (Nakhleh, Schwartzenberg et al.1990). Liver biopsy is also useful in the diagnosis of invasive CMV infection and in assessing recurrent disease (Hubscher, Elias et al. 1993) (Harrison, Davies et al.1993).

Liver histology is usually necessary to determine the cause of liver test abnormalities following liver transplantation since it is not possible to differentiate, on the basis of liver tests, rejection, preservation or reperfusion injury, viral infection, drug toxicity, recurrent disease and other causes of graft damage. The use of protocol liver biopsy in those with normal liver tests following liver transplantation is uncertain but may reveal unexpected abnormalities requiring intervention (Sebagh et al, 2003, Neuberger et al, 1998, Berenguer et al, 2001).

5.15 **Research**
Using liver biopsy in the context of research is a controversial area but has undoubtedly given us invaluable information in the past in such areas as hepatitis C disease progression and the development of new drugs. In circumstances where the patient will derive no potential benefit from the procedure, and will thus only accrue the risks of that procedure, the patient should be fully aware of this and give written consent. The procedure will also need approval from the appropriate Research Ethics Committee (or equivalent).

6. CONTRAINDICATIONS

Many of the contraindications to percutaneous liver biopsy were defined by studies performed during the early years when liver biopsy was far less widely used than it is now. These studies were done before the advent of the Menghini "one second" technique and with larger diameter needles; whilst some of these contraindications appear to be common sense, many of them have been quoted as dogma in medical texts with very little evidence to support them.

6.1. **The Uncooperative Patient**
In percutaneous liver biopsy it is essential that the patient is co-operative as an untoward movement when the biopsy needle is in the hepatic parenchyma can lead to a tear of the liver and capsule and subsequent torrential bleeding. If the patient is frightened then the use of midazolam as sedation can be considered with no increased risk (Alexander and Smith 1993). If the patient remains uncooperative and the benefit of obtaining liver histology outweighs the risk to the patient then liver biopsy under general anaesthesia should be considered.

6.2. **Extrahepatic Biliary Obstruction**
Extrahepatic biliary obstruction is frequently quoted as a contraindication to liver biopsy because of the risks of biliary peritonitis, septicaemic shock and death (LoIudice, Buhac et al. 1977). However in one study, serious complications in at least 2% of patients (including biliary peritonitis) and significant complications in another 4% followed the percutaneous liver biopsy (Morris, Gallo et al. 1975). With current imaging techniques (specifically ERCP and MRI cholangiography), liver biopsies should only be performed in the context of biliary obstruction when there is doubt about the diagnosis and the benefit to the patient outweighs the risk. Under these circumstances the transjugular approach would be preferable (Rosch, Lakin et al. 1973).

6.3. **Bacterial Cholangitis**
The risk of inducing peritonitis and septic shock after liver biopsy has made cholangitis a relative contraindication. However if a liver biopsy is performed when a biliary system is infected then culture of a piece of liver can give useful bacteriological information especially in the context of investigation of TB or a PUO. Bacteraemia after percutaneous biopsy of a normal liver is a well-recognised phenomenon (McClosky, Gold et al. 1973) occurs in up to 14 % of biopsies (LeFrock, Ellis et al, 1975). These findings confirm the risks of disseminating infection at the time of liver biopsy.

6.4. **Abnormal Coagulation Indices**
There are widely divergent opinions about the values at which abnormal coagulation indices become contraindication to percutaneous liver biopsy. A number of investigators have demonstrated that the degree of bleeding from the liver puncture site (observed at laparoscopy) bears no correlation to the peripheral blood coagulation parameters mentioned below when these parameters are modestly elevated (Dillon, Simpkin et al.1994)(Gazelle, Haaga et al. 1992). Some of these investigators have postulated that this discrepancy in liver bleeding time may be due to the inherent elasticity of the biopsy track collapsing down after the core has been taken together with the high local levels of clotting factors within the hepatic parenchyma (Ewe 1981). It should however be borne in mind that during a blind percutaneous liver biopsy, the liver is not the only structure to be punctured and as the skin and subcutaneous tissues (and occasionally other organs) can bleed, peripheral indices of clotting must still be taken into consideration.

6.4.1. **Prothrombin Time**
Several large studies have failed to show an increased risk of bleeding associated with a prolongation of the prothrombin time of 4 seconds above control values (Ewe 1981)(McGill, Rakela et al. 1990)(Dillon, Simpson et al. 1994). The largest retrospective study of percutaneous liver biopsy to date failed to show any correlation between a prolongation of prothrombin time by 7 seconds over control values and the occurrence of haemorrhagic complications (Piccinino, Sagnelli et al. 1986). In contrast, a number of other studies however have corroborated the widely held belief that a coagulopathy predisposes the patient to haemorrhage after percutaneous liver biopsy (Mahal, Knauer et al. 1979). The 1991 BSG audit of the biopsy practice in 189 health districts in the UK demonstrated that bleeding was commoner if the INR was raised, with 3.3% of the bleeds occurring when the INR was between 1.3 and 1.5, and 7.1% occurring when the INR was >1.5 (Gilmore, Burroughs et al. 1995). This however implies that approximately 90% of the bleeds occurred in patients with INR<1.3 and reinforces the fact that having a normal INR or prothrombin time is no reassurance that the patient will not bleed after the procedure.

6.4.2. **Thrombocytopaenia**
The level at which thrombocytopaenia becomes a contraindication to percutaneous liver biopsy is uncertain from published data. One authority proposes a platelet count above 100,000/mm^3 (Menghini 1976) whilst other groups such as the Mayo Clinic regard counts as low as 56,000/mm^3 to be safe (McGill, Rakela et al. 1990). Most recognised UK texts require that the platelet count be above 80,000/mm^3 (Sherlock 1997) whilst a survey of mostly US centres showed a preference for platelet counts of above 50,000/mm^3 (Sue, Caldwell et al. 1996). One study of 87 patients found that those patients with a platelet count below 60,000/mm^3 were significantly more likely to bleed after percutaneous liver biopsy than those with platelet counts above this value (Sharma, McDonald et al. 1982). The evidence for a cut off value remains scanty and takes no account of the function of the platelets (see 6.4.3.).

The effect of thrombocytopaenia due to hypersplenism compared with thrombocytopaenia due to bone marrow failure upon bleeding has, to our knowledge, not been studied in significant detail and its effects are currently unknown.

The absolute value of the platelet count may not be crucial in determining the risk of bleeding as it is well recognised that even those patients with normal prothrombin times and platelet counts can have severely deranged bleeding times. Nevertheless for a percutaneous liver biopsy the minimum platelet count felt to be safe without the need for support is 60,000/mm^3.

6.4.3. **Platelet Function / Bleeding time (BT)**
The practice of measuring bleeding time (BT) before liver biopsy is much more common in Asia compared to the U.S. (73% V's 36%)(Sue, Caldwell et al. 1996). Our experience suggests that BT is seldom if ever measured in U.K. centres prior to liver biopsy even though the ingestion of aspirin, clopidrogel and other non-steriodal anti-inflammatory drugs or anti-platelet drugs in the week prior to invasive intervention is reported to be a recognised contraindication by several authorities (there are to our knowledge however no convincing data to support this as a contraindication to percutaneous liver biopsy).

Patients with renal impairment usually have abnormalities of platelet function. According to one small study, patients with end stage renal failure on haemodialysis are at high risk (up to 50%) of haemorrhagic complications after percutaneous liver biopsy, independent of the BT (Wolf, Weber et al.1995). This same study suggested that liver transplant recipients with a BT greater than 10 min (upper limit of normal) had a higher incidence of bleeding complications compared to those with a BT less than 10 min. The sample size however is too small to allow any firm conclusions to be drawn.

Several other factors are likely to affect platelet function with or without affecting the BT. This fact, together with the considerable variation in results obtained between different operators, makes the use of the bleeding time as a measure of risk for haemorrhage difficult to interpret. The Royal Free Hospital were able to show that within a group of cirrhotic patients, those with abnormal BT's (42%) were more likely to have significantly lower platelet counts, longer prothrombin times and higher blood urea and serum bilirubin than those with normal BT's (58%). They also demonstrated that the bilirubin concentration as well as the platelet count were independently correlated with the BT (although the correlation for the latter was weak, and the elevated serum bilirubin may well be just a surrogate marker for the severity of liver disease)(Blake, Sprengers et al.1990).

6.5. **Ascites**
Percutaneous biopsy of the liver in the presence of tense ascites is considered a contraindication in many texts. The reasons for this vary from, the high likelihood of not obtaining a biopsy specimen because of the distance between the abdominal wall and the liver to, the risk of uncontrollable bleeding into the ascites. Whilst these reasons appear sensible they are not substantiated in randomised controlled clinical trials. There is evidence however to support the fact that CT or ultrasound guided liver biopsy in the presence of ascites does not affect the complication rate (Little, Ferris et al. 1996) (Murphy, Barefield et al. 1988).

Notwithstanding these studies it seems logical that if a liver biopsy is clinically indicated in a patient with tense ascites then there are several alternatives, the most obvious being to perform a total paracentesis prior to performing the percutaneous biopsy. Other options include image-guided biopsy, transjugular liver biopsy, or laparoscopic biopsy.

6.6. **Cystic Lesions**
Modern imaging techniques can often identify benign cystic lesions of the liver as such thereby eliminating the need for biopsy in many cases. Cystic lesions within the liver may communicate with several structures including the biliary tree and therefore run the risk of biliary peritonitis after biopsy.

The cystic lesion quoted most often as a contraindication to percutaneous liver biopsy was the echinococcal cyst because of the risk of dissemination if the hydatid cysts throughout the abdomen, and the risk of anaphylaxis. Recent advances in the treatment of hydatid disease of the liver mean that this may no longer be so (Kumar and Chattopadhyay. 1992). Aspiration of hydatid cysts with 19-22 gauge needles under ultrasound guidance has been shown to be safe and can be used both diagnostically (Bret, Fond et al. 1988) and therapeutically (Felice, Pirola et al.1990) for the injection of hypertonic saline or 95% ethanol under albendazole cover.

6.7. **Amyloidosis**
The use of liver biopsy in the diagnosis of amyloid liver disease was first used in 1928 (Waldenström, 1928). Volwiler and Jones reported the first death from haemorrhage after amyloid liver biopsy. This episode together with further reports of haemorrhage after liver biopsy in patients with amyloid have lead to the dubious inclusion of amyloid liver disease in the list of contraindications to percutaneous liver biopsy (Volwiler & Jones, 1947). No large controlled trials have been performed to date which show an increased risk of haemorrhage after liver biopsy in amyloid liver disease. However in 1961 a small series of liver biopsies in amyloid liver disease were reported. One patient out of eighteen had an intraperitoneal bleed but this patient was treated conservatively (Stauffer et al. 1961). Stauffer decided that liver biopsy was a useful tool in the establishment of the diagnosis of hepatic amyloid, and certainly in the context of the investigation of hepatomegaly of uncertain aetiology this seems reasonable. However if a diagnosis of amyloidosis had already been made or is strongly suspected then one would need a good indication for performing a percutaneous liver biopsy rather than for performing a more benign procedure such as a rectal biopsy.

6.8 **Obesity**
In the obese patient, it may be difficult to identify the liver by percussion. In this situation, the biopsy should be done under ultrasound guidance.

7. THE BIOPSY PROCEDURE

7.1. **Informed Consent**
Informed consent should be obtained in writing prior to the biopsy procedure in accordance with individual hospital policies. Consent forms should contain the patients' native language wherever possible, and when this is not possible there should be access to a competent interpreter to ensure adequate understanding by the patient of both the risks and benefits of the procedure and the commands given to them during the biopsy.

7.2. **Experience of the Operator**
There are no good data to show that the grade of the person performing the percutaneous liver biopsy has any affect upon the complication rate after the biopsy. The only data available is that from the 1991 BSG audit demonstrating that the frequency of complications was slightly higher if the operator had performed less than 20 biopsies (frequency of complications was 3.2% if operator had performed <20 biopsies compared with 1.1% if the operator had performed >100 biopsies). No difference in the complication rates between gastroenterologists and general physicians was seen (Gilmore, Burroughs etal.1994). A radiologist or clinician that is experienced in venous cannulation usually performs Transjugular biopsies.

We recommend that pre-registration house officers should not perform percutaneous liver biopsies except in the context of specialised units, where liver biopsies are done frequently, and only then under close supervision.

7.3. **Sedation**
Anxious patients should be given the opportunity to have midazolam sedation for the biopsy procedure if there is no contra-indication. Sedation should be given in accordance with the British Society of Gastroenterology guidelines on the administration of sedation for endoscopy. Midazolam should be given with caution in the context of liver disease.

7.4. **Haematological Investigations**
All patients undergoing percutaneous liver biopsy should have blood grouped and serum saved, and in hospitals where cross matching is difficult, patients should have blood available.

The prothrombin time (or international normalised ratio) and platelet count should be checked prior to the biopsy (preferably within 24 hrs). With the current data it can be seen that there is no clear consensus as to the length of the prothrombin time at which the biopsy should not be performed. Consequently we feel that current advice should be followed and thus if the prothrombin time is prolonged by four seconds or more (or INR>1.4) then other strategies to improve the coagulopathy should be tried (section 7.4.1).

The level of the platelet count at which a percutaneous liver biopsy should not be done is as controversial (see 6.4.2), however there is evidence that in patients with a platelet count as low as 60,000 / mm^3 a percutaneous liver biopsy can be performed with no increase in complicated rate.

7.4.1**. Vitamin K, Fresh Frozen Plasma (FFP) and Platelet Transfusion**
Vitamin K, fresh frozen plasma and platelet support is in wide use for the correction of coagulation abnormalities prior to liver biopsy. There are however very little data about the values at which correction of these coagulopathies should be abandoned in favour of plugged or transjugular biopsy. Vitamin K is useful

but should be given parenterally and at least 12 hours prior to the biopsy, and is most effective where the disturbance in coagulation is due to biliary obstruction or malabsorbtion. The prothrombin time should be checked before doing the biopsy to ensure that clotting abnormalities are corrected. If vitamin K is ineffective, then fresh frozen plasma given immediately prior to the biopsy in a dose of 12-15 ml/kg body weight may correct the prothrombin time (Spector, Corn et al. 1966)(Contreras, Ala et al.1992). One study however, has shown that FFP corrects the prothrombin time in only 20% of cases (Gazzard, Henderson et al. 1975). Platelet transfusion prior to percutaneous liver biopsy in thrombocytopenic patients has been used widely but has been hampered by the lack of studies showing its efficacy, especially in the context of patients with liver disease who may have other associated disorders of coagulation. It has been suggested that patients should initially receive 1 unit per 10 kg body weight and the effect of this transfusion be assessed by the platelet count obtained one hour later (Consensus Conference-1987). However, post-transfusion platelet increments do not necessarily correlate with decreased risk of bleeding as platelet function may vary and it has been shown that 30% of patients receiving platelet transfusion show no improvement in in-vitro bleeding time (a measure of platelet function) (Kristensen, Eriksson, et al 1993).

Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernantant have recently been published (O'Shaughnessy et al, 2004).

7.5. *Pre*-Biopsy Ultrasound

Whether all patients about to undergo percutaneous liver biopsy should have an ultrasound is a contentious issue. Ultrasound is a safe and readily available investigation. Practice amongst gastroenterologists varies greatly, with only half the operators using ultrasound guidance (Muir 2002, Mayoral 2001, Rossi 2001). There is, both in Europe and North America, a move for more biopsies to be done by the radiologists under ultrasound guidance (Angtuaco 2002). Continental European gastroenterologists are required to be proficient in this method of imaging. However this is not current practice in the U.K.

One of the reasons for performing a pre-biopsy ultrasound is to rule out anatomical variation e.g. Chilaiditi syndrome where small bowel lies between a shrunken liver and the abdominal wall, thereby avoiding inadvertent puncture of an adjacent viscus (Dixon, Nunez et al. 1987). Ultrasound also permits the detection of focal lesions (which may or may not have been suspected) allowing for the opportunity of a targeted biopsy or fine needle aspiration at a later date under image guidance with a lower risk of haemorrhage.

Percussing for the superior and inferior borders of the liver is usually adequate for selection of the biopsy site (Qureshi, DuBose et al.1997), however in some patients where the borders of the liver are unclear (e.g. the obese or cirrhotics) ultrasound is helpful.

7.6. Ultrasound Guided Percutaneous Liver Biopsy

Ultrasound guided percutaneous liver biopsy is used extensively in the investigation of focal liver lesions, however its use in diffuse liver disease is more controversial.

It has been postulated that ultrasound guided biopsy should reduce complications. One prospective study (Riley 1999) showed that pre-biopsy ultrasound resulted in alteration of the position for biopsy in 21 of 165 patients. and abandonment of the procedure in 4. Reasons for these alterations included interposition of lung or gall bladder. In contrast, the rate of haematoma formation is unaffected by the use of ultrasound guidance (Vautier, Scott et al. 1994). Pre-biopsy imaging may reduce the number of passes and so lead to less bleeding (Stotland, Lichtenstein et al.1996)(McGill, Rakela et al. 1990).

There are a few studies comparing blind and ultra-sound guided liver biopsies. (Stotland and Lichtenstein, 1996, Papini et al 1991, Lindor et al, 1996, Farrell et al, 1999.Caturelli, Giacobbe et al 1996). These studies, often relatively small or retrospective, do suggest that ultra-sound guided liver biopsies are more efficient and associated with fewer major and minor complications than blind biopsies.

We believe that the use of guided liver biopsy or fine needle aspiration in the diagnosis of hepatic tumours is the safest method of management of these patients.

It is also useful to have a pre-biopsy ultrasound to rule out any anatomical abnormalities and in patients whom the liver cannot be easily identified for reasons such as obesity. There are training implications if UK gastroenterologists were to undertake ultrasound-guided liver biopsy (Shah 1999).

However whilst the use of ultrasound guidance in percutaneous liver biopsy for diffuse liver disease may reduce some of the complications and therefor cost and inconvenience to a small number of patients, it is not considered the standard of care in all units in the UK.

7.7. Prophylactic Antibiotics

Bacteraemia associated with liver biopsy in both structurally normal and abnormal livers have been well documented (LeFrock, Ellis, et al. 1975)(McClosky, Gold et al.1973). Therefore prophylactic antibiotics should be used in the context of valvular heart disease or when there is a previously documented bacteraemia.

Several groups have assessed the risks of septic complications for patients with choledocho-jejunostomy after liver transplantation. The conclusions of the Mayo group were that there was an increased risk (12.5%) of septic complications in these patients (Bubak, Parayko,et al.1991) whereas the Royal Free group could show no increased risk providing there was no occult biliary obstruction (Ben-Ari, Neville et al.1996). This study had too few

patients to be able to make strong recommendations, however other groups have come to the same conclusions (Galati, Monsour et al. 1994).

The current data on the use of prophylactic antibiotics is inconclusive and we feel that for patients in whom biliary sepsis is suspected it is prudent to use them.

7.8. **Type of Biopsy Needle**

The two main types of needle currently being used in the UK are the Tru-cut and the Menghini needles (Gilmore, Burroughs et al. 1995). These two needles employ different methods for sampling hepatic tissue. The former, as its name describes is a cutting needle, while the latter employs a suction technique. These needles come in varying diameters, and the type and gauge of needle that is optimal for percutaneous liver biopsy has been the subject of several studies.

The largest series to look at needle type in relation to complications describes a complication rate of 3.5/1000 for the Tru-cut needle and 1/1000 for the Menghini needle. Death, serious haemorrhagic complications, pneumothorax and biliary peritonitis all occurred more frequently with the Tru-cut needle when compared to the Menghini needle, while puncture of other viscera and sepsis were more frequent with the Menghini needle (Piccinino, Sagnelli et al.1986). Other groups have compared the older Jamshidi suction needle with the Tru-cut/ Vim Silverman cutting needles and found no difference in complication rates (Perrault, McGill et al. 1978)(McGill, Rakela et al.1990). The theoretical advantages of the Menghini suction technique were described in the original paper (Menghini. 1970), the main advantage being that the needle is only in the liver parenchyma for a "second". This allows less time for the patient to move, thereby minimising the potential for tearing the capsule.

The gauge of the biopsy needle and its effect on post biopsy bleeding has been investigated for the suction style needle. One group demonstrated that larger needles produced more bleeding after liver biopsy in anaesthetised pigs. This was statistically significant when comparing 2.1mm(14-gauge) with 1.6mm(16-gauge) needles, and also when comparing 1.6mm with 1.2mm(18-gauge) and smaller needles (Gazelle, Haaga et al.1992). Human studies of the effect of biopsy needle diameter on complications are rare, however Forssell et al, could not demonstrate any difference in the incidence of intrahepatic haematoma formation when comparing the 1.6mm modified Menghini needle with a 1.9mm Jamshidi needle.

The potential advantages of using smaller suction biopsy needles should be weighed against the disadvantages of having a smaller biopsy specimen (Rocken 2001). Specimens from the Tru-cut needles are larger and give more information about liver architecture and may thereby increase the diagnostic yield. The disadvantages of making several passes of the biopsy needle should also be borne in mind (see below).

7.9. **Number of Passes**

It has been demonstrated that taking more than one core of liver at biopsy can increase the diagnostic yield, but this may have an effect on morbidity. It has been clearly shown that making more passes increases the incidence of complications when the percutaneous biopsy is taken by either transthoracic or subcostal approaches. In one paper the increased incidence reached significance when more than three biopsies were taken (Perrault, McGill et al. 1978). This was subsequently confirmed by other studies showing that when blind percutaneous liver biopsy is undertaken, taking two specimens improves diagnostic yield with an increased number of minor complications when more than three consecutive biopsies are taken (Maharaj & Bhoora. 1992).

A large study of 9212 liver biopsies also showed that the risk of haemorrhage does not only increase with the number of passes made, but is also significantly linked to the age of the patient and the presence of malignancy (McGill, Rakela, et al. 1990). Therefore we conclude that under circumstances where the likelihood of a sampling error is high such as in some cases of macronodular cirrhosis, two biopsies could be taken. However the decision to do this for patients with advanced age or malignancy should be tempered by the increased risk of complications.

7.10. **Post Biopsy Observation**

The decision about the length of time that a patient should remain in hospital after a blind percutaneous liver biopsy is dependent on several factors. The main consideration in practical terms however is the likely time period in which complications are going to occur.

It has been shown that delayed haemorrhage can occur up to 15 days after percutaneous liver biopsy in patients who develop a coagulopathy post biopsy (Reichert, Weisenthal, et al.1983). The occurrence of delayed haemorrhage is also documented after the reinstatement of warfarin therapy several days after percutaneous liver biopsy. Clearly patients can not be kept in hospital for 2 weeks or more after liver biopsy so a compromise has to be made on the basis of current knowledge.

The first large studies addressing the issue of post-biopsy observation were stimulated by the drive to perform outpatient percutaneous liver biopsies. These papers showed that the majority of complications occurred in the first three hours after liver biopsy (Knauer. 1978) (Perrault, McGill et al. 1978), and recommended that patients should be kept in hospital for 6 hours after the procedure. A later paper described 61% of complications after liver biopsy occurring in the first 2 hours, 82% of complications occurring in the first 10 hours, and 96% of complications occurring in the first 24 hours. In this paper recounting 68,276 liver biopsies, six patients died, and all showed signs of bleeding within 6 hours of the procedure. (Piccininio, Sagnelli et al. 1986).

The position that the patient should be nursed in after the liver biopsy has not been investigated, and various centres

have differing policies including nursing the patient supine, on their right hand side or simply "flat"(Perrault, McGill et al.1978)(Douds, Joseph et al. 1995). No controlled trials have been performed to assess these different techniques. Standard percutaneous liver biopsy observations include monitoring the patient's vital signs every 15 minutes for the first 2 hours then every 30 minutes for 2 hours then hourly for the rest of the remaining period. This protocol is reasonable when one considers that 61% of complications occur in the first 2 hours.

8.0 TRANSJUGULAR LIVER BIOPSY

A transjugular approach to liver biopsy is indicated when there risks of a percutaneous approach is contra-indicated (such as coagulopathy, significant ascites, suspected vascular tumour, a failed percutaneous liver biopsy) or when other vascular interventions are planned (such as insertion of a transhepatic portal-systemic shunt or measurement of hepatic pressures.

Contra-indications include technical problems, such as poor vascular access, right heart thrombus or other obstructive lesions.

9. OUTPATIENT PERCUTANEOUS LIVER BIOPSY

Outpatient percutaneous liver biopsy has been performed in many U.S. centres since the early 1970's (Perrault, McGill et al 1978). In 1991 this practice had not been widely taken up in this country with only 4% of percutaneous liver biopsies being performed as day cases (Gilmore, Burroughs et al. 1995). In centres which do perform day case biopsies in this country a 91% patient satisfaction rate has been quoted, and in carefully selected populations the admission rate to hospital after day case liver biopsy is 2.2% to 3.2% (Douds, Joseph et al. 1995)(Janes & Lindor. 1993).

In 1989 the American Gastroenterological Association published a consensus statement on outpatient percutaneous liver biopsy which we feel largely applies to U.K. patients (Jacobs, Goldberg et al. 1989). They recommended that patients undergoing this procedure should have no conditions that might increase the risk of the biopsy including: encephalopathy, ascites, hepatic failure with severe jaundice or evidence of significant extrahepatic biliary obstruction, significant coagulopathies or serious diseases involving other organs such as severe congestive heart failure or advanced age. We would add that patients with a strong suspicion of malignancy should not be biopsied as an outpatient because they have a 6-10 times higher risk of haemorrhage compared to patients without cancer (McGill, Rakela et al. 1990).

The consensus statement also recommends that the place where the biopsy is performed should have easy access to a laboratory, blood bank and inpatient facilities should the need arise, and there should be staff to observe the patients for 6 hours. The patient should be hospitalised if there is any significant complication including pain requiring more than one dose of analgesic in the 4 hours post liver biopsy. The patient should also be able to return easily to the hospital where the biopsy was undertaken within 30 minutes, and should have a reliable individual to stay with on the first post-biopsy night. If the above criteria can not be met, then the patient should not be biopsied as an outpatient.

Performing percutaneous liver biopsies as an outpatient has considerable potential for cost saving and reallocation of resources (Perrault, McGill et al 1978).

10. RECOMMENDATIONS

10.1. Before performing a percutaneous liver biopsy there must be a clearly defined indication for the biopsy, and the risks to the patient should not outweigh the potential benefits.

10.2. We recommend that all patients who are about to undergo a percutaneous liver biopsy should have had some form of imaging of the liver. The interval between the imaging of the liver and the biopsy will depend on the clinical situation and the probability that there will have been any changes in the anatomy or pathology. This will allow the detection of abnormal anatomy in the area of the proposed biopsy (see section 7.5.), whilst at the same time detecting focal lesions which should be biopsied under image guidance. We recommend that, where possible, the biopsies should be done either under direct ultra-sound guidance, where the ultrasound has been used to identify the optimal site for the biopsy or where ultrasound has been previously performed. Recommendation Grade B.

10.3. The patient's platelet count and prothrombin time should be checked in the week before the percutaneous liver biopsy providing that the patients liver disease is stable.

10.3.1 If the platelet count is > 60 000/mm^3 then the biopsy can be safely performed. If the platelet count is 40 000 - 60 000/mm^3 then platelet transfusion may increase the count enough for the biopsy to be performed safely by the percutaneous route. If however platelet transfusion does not increase or the platelet count is <40 000/mm^3 then alternative biopsy methods as described in sections 3.1.3., 3.2., and 3.3. can be tried (sections 6.4. and 7.3.). Drugs that affect platelet function (such as aspirin or clopidrogel) should be discontinued (where possible) at least two days before biopsy. Recommendation Grade B.

10.3.2 If the prothrombin time is <4 seconds prolonged then percutaneous biopsy can be safely undertaken. If the prothrombin time is 4- 6 seconds prolonged then a transfusion of fresh frozen plasma may bring the prothrombin time into the desired range (sections 6.4. and 7.4.). If the PT is >6 seconds prolonged then other biopsy methods should be tried. Recommendation Grade B.

10.4. Informed consent should be obtained from all patients prior to percutaneous liver biopsy in accordance

with local hospital guidelines. The patient should also be able to understand and co-operate with instructions given by the person performing the liver biopsy (section 7.1).

10.5. Sedation with midazolam may be given for percutaneous liver biopsy in accordance with the BSG guidelines on sedation during endoscopy. Sedation should be given with caution in liver disease (section 6.1.). Recommendation Grade B.

10.6. The type of needle used for the biopsy will depend on the experience of the operator and the type of needle they are used to. Where a larger biopsy is not required the Menghini needle should be used in preference to cutting needles as this technique appears to have a lower complication rate (which may however be at the expense of the diagnostic yield). Where the operator has only experience of one style of needle they should use the technique most familiar to them. (section 7.8.). Recommendation Grade A.

10.7. The grade of the operator has not been shown adversely to affect the complication rate from percutaneous liver biopsy. We feel however that doctors who have performed less than 20 biopsies should not perform the procedure unsupervised and that house officers should not be performing percutaneous liver biopsies except in the context of a busy specialised gastrointestinal units (section 7.2.).
Recommendation Grade B.

10.8. Prophylactic antibiotics should be given to patients with valvular heart disease or those at risk of bacteraemia (section 7.7). Recommendation Grade B.

10.9. Usually one pass of the biopsy needle retrieves enough hepatic tissue for diagnostic purposes, however if there may be a sampling error (such as may occur in macronodular cirrhosis) which will result in an inappropriate diagnosis, then two passes may be made without significantly affecting complication rate (section 7.9.). Recommendation Grade B.

10.10. Post liver biopsy observation should continue for 6 hours and if at the end of this period there have been no complications then the patient may be discharged. The patient should however have a responsible person to stay with on the first post-biopsy night and should be able to return to hospital within 30 minutes should the need arise (section 7.10). Recommendation Grade B.

10.11. It is recommended that patients undergoing outpatient percutaneous biopsy should have no conditions that may increase the risk of the biopsy procedure (section 8.). Recommendation Grade B.

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These guidelines have been prepared by the British Society of Gastroenterology. They represent a consensus of best practice based on the available evidence at the time of preparation. They may not apply in all situations and should be interpreted in the light of specific clinical situations and resource availability.