

AMERICAN ASSOCIATION FOR
THE STUDY OF LIVER DISEASES



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Liver Biopsy

Major trends in liver biopsy in
France : results of a nationwide
2009 survey

- **Background :**
Indications for liver biopsy (LB) in diffuse parenchymal liver diseases (PLD) have been modified due to the development of non invasive evaluation of liver fibrosis.
- **Aims:**
 - 1) to evaluate the number of LB performed in 2009 for PLD
 - 2) to compare practices and indications for LB for PLD in 2009 with those of 1997
- **Patients and Methods:**

A pre-established questionnaire was sent to French hepato-gastroenterologists working in primary, academic or private structures.

Data recorded were: number of LB for PLD, indications for LB, route of LB, mode of hospitalisation, ultrasound guidance and complications.

- **Results:**

107 centers participated in the study (they were 89 in 1997)
8581 LB were performed versus (vs.) 16000 in 1997 of which

Conclusions:

- 1) a marked diminution of total number of LB 8581 VS 16000
- 2) a relative increase in the transjugular route 22.4% VS 9%
- 3) development of US use
- 4) an increase in ambulatory LB 45% VS 27%
- 5) a marked diminution of LB for HCV whereas NAFLD increased.
- 6) Severe complications remain not exceptional but frequency is significantly reduced by US

A quality assessment/quality
improvement study of liver biopsy
specimen adequacy in routine
clinical practice

- **Background:**

A recent AASLD position paper updated several guidelines pertaining to percutaneous liver biopsy (Hepatology 2009;49:1017-44).

- **Aim:**

To assess the quality of percutaneous liver biopsy specimen size and specimen adequacy in a community-based practice setting before and after implementation of a quality improvement (QI) protocol.

- **Methods:**

We conducted a retrospective review of percutaneous liver biopsy procedures and pathology reports from 2011.

Subsequently, clinicians who performed liver biopsy were educated regarding AASLD liver biopsy guidelines, with an emphasis on recommendations regarding adequate specimen size (i.e. length \geq 3 cm).

As part of the QI protocol, these guidelines were reinforced through regular feedback and by having operators photograph the biopsy specimen next to a mm-scale ruler immediately after the procedure.

Cutting or suction needles were used according to operator preference, except when cirrhosis was suspected, in which case cutting needles were used.

- **Results:**

Compared to baseline patients (N=100), liver biopsy specimens from post-intervention patients (N=51) were:

significantly longer (specimen length 37.8 ± 1.2 mm vs. 20.5 ± 1.1 mm)

contained more portal tracts per specimen (12.5 ± 0.9 vs. 4.7 ± 0.8).

the incidence of inadequate biopsy specimens was significantly decreased (0% vs.13%).

The number of needle passes was greater among post-intervention patients (1.9 ± 0.9) vs. baseline patients (1.5 ± 0.7).

There were no significant complications among baseline or post-intervention patients.

- **Conclusions:**

This community-based quality assessment/quality improvement study of percutaneous liver biopsy revealed a substantial incidence (13%) of specimen inadequacy, which was subsequently eliminated through an evidence-based quality improvement initiative.

A randomized, double-blind,
controlled trial comparing coaxial
technique and conventional
repeated punctures for liver biopsy



Adjustable coaxial Temno® (ACT) biopsy device

The adjustable coaxial Temno (ACT) biopsy device combines the quality and reliability of the Temno brand with innovative, patented technology. The ACT device lets you manipulate the sample notch size from 9 to 19 mm for precise control with small lesions and peace of mind in vascular areas. A coaxial introducer needle is included. For use in kidney, liver and lung biopsies.



- **Background and aims:**

Main complications of liver biopsy are pain and hemorrhage increased with the number of punctures.

Coaxial biopsy technique has advantage of only one puncture using a catheter into liver. We evaluated the efficacy and safety of this technique by comparing incidence and severity of adverse events.

- **Methods:**

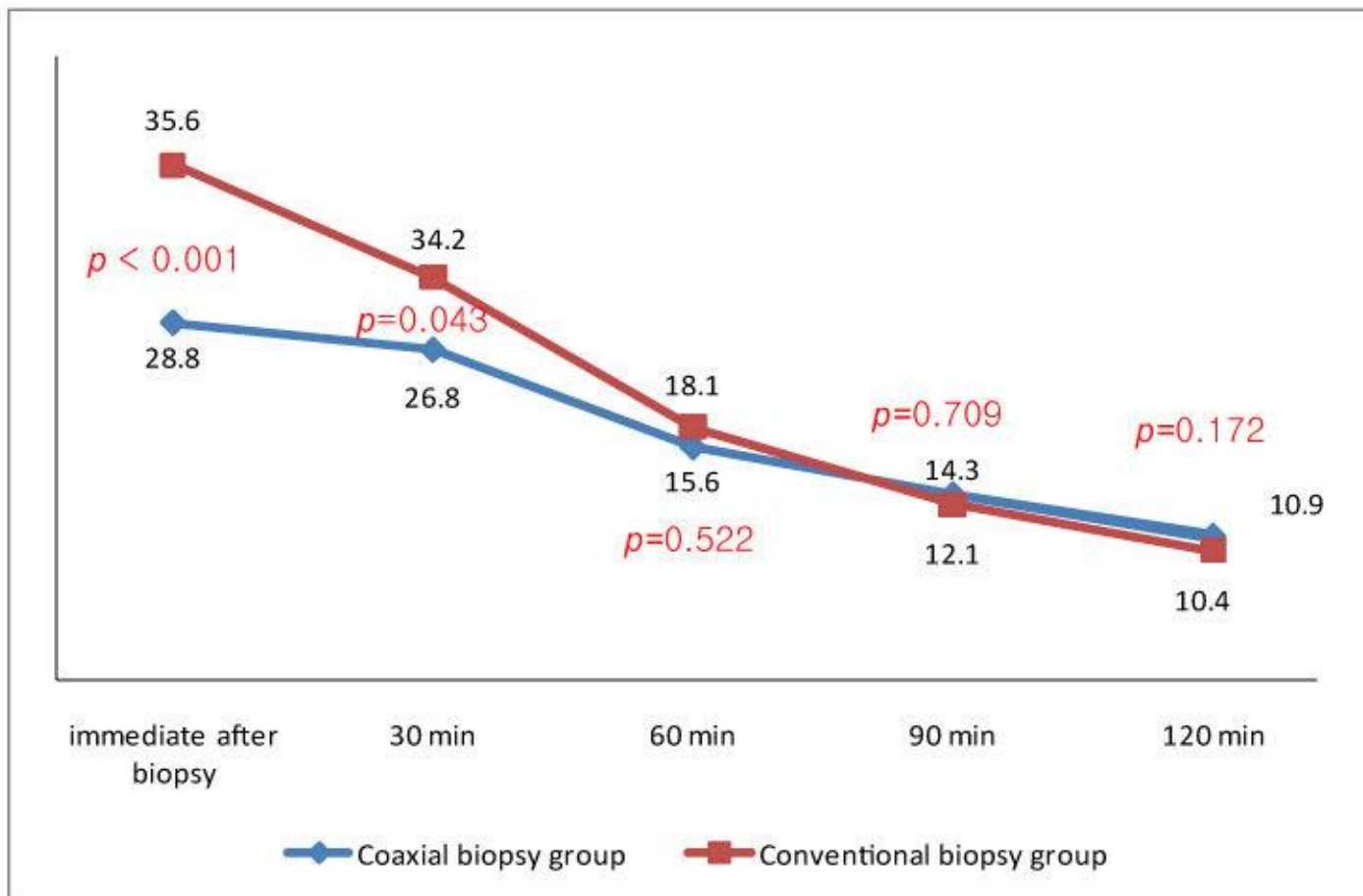
We enrolled 425 consecutive patients, undergoing percutaneous liver biopsy.

Patients were randomized into coaxial biopsy group or conventional biopsy group.

Biopsies were performed using 16 gauge automated biopsy needle under ultrasound guidance.

Pain was assessed every 30 minutes using a visual analogue scale (VAS) with vital sign monitoring.

● Degree of post-procedure pain by VAS



Complication rate in relation to the number of biopsy passes in percutaneous liver biopsy.

- **Background:**

Percutaneous liver biopsy (PLB) remains the gold standard to assess liver fibrosis. The length of a PLB should ideally be ≥ 25 mm for accurate fibrosis assessment with Metavir. Consequently, more than one biopsy pass may be needed. We aimed to determine whether the complication rate is affected by the number of biopsy passes.
- **Methods:**

A retrospective cohort was created enrolling all PLB performed at the Erasmus MC University Medical Center in the Netherlands between January 2005 and October 2011. All biopsies were performed according to guidelines, by experienced hepatologists using abdominal ultrasound and 14-Gauge Tru-cut needle. *Complications were categorized into:* mild (event requiring hospitalization ≤ 2 days, and/or no intervention) and severe complications (event requiring hospitalization ≥ 3 days, and/or intervention).

- **Results:**

We analyzed 1382 PLB obtained from 1170

Complications were mild in 4.0% were severe in 1.6%

Patients with a high number of biopsy passes, female sex, platelet count $\leq 120 \times 10^9/L$, and/or INR ≥ 1.4 are at risk for overall complications

Patients with a non-viral diagnosis, female sex, and/or INR ≥ 1.4 are at risk for severe complications.

- **Conclusions:**

PLB is a relatively safe invasive procedure to assess liver fibrosis

Clinical, Pathologic and Gene
Expression Association with Percent
Collagen Measured by Computer
Assisted Morphometry in Patient
Chronic Hepatitis-C

- Methods:

Liver biopsies of 102 Chronic Hep-C patients were stained with either H&E or sirius red by standard histochemical methods.

- For 35 CH-C patients Peripheral Blood Monocyte Counts (PBMCs) were collected prior to initiation of treatment.

- **Results:**

There were significant correlations between % collagen and METAVIR, as well as MHA1 fibrosis score.

A relatively weak but statistically significant correlation was detected between % collagen and APRI score.

Multivariate regression analysis indicated that lower level of LGALS9 and higher level of PRKRA expression were both independently associated with increasing % collagen.

Ariadne pathway analysis indicates the possibility of a direct positive or negative role for LGALS9 and PRKRA in the process of fibrogenesis.

- **Conclusions:**

There is also gene expression profiles associated with increasing collagen as a more sensitive measure of hepatic fibrosis.

CPA using Sirius red stained liver biopsies is more accurate than trichrome staining and reliably predicts the development of hepatocellular carcinoma

- 250 patients with chronic Hepatitis C.
- Results:
- 59 patients had advanced fibrosis (Metavir F3-4). Correlation between CPAt (Trichrome) and CPA (Sirius Red) was 0.7. Mean CPAs was higher than mean CPAt by 3.6%.
- Using stratified analysis, significant differences between CPAs and CPAt were only found in Metavir F0 to F3. Both CPAs and CPAt were well correlated with Metavir and Ishak.

- 36 patients with advanced fibrosis had surveillance for HCC. Multivariate analysis found that only CPAs correlated with HCC. The area under ROC curve (AUROC) of CPAs was 0.95. It was higher than that of CPAt, Ishak, Metavir and Hepascore.

A cut-off point of CPAs>20% had a sensitivity of 100% and specificity of 93.3%.

- **Conclusion:**

CPA determined with Sirius red staining was more sensitive and accurate for quantifying hepatic collagen than Masson's trichrome staining, especially in the early stages of liver fibrosis.

CPAs was highly predictive of the appearance of HCC with higher AUROC scores than staging with either the Ishak or Metavir systems or Hepascore.

Digital image analysis of collagen for chronic Hepatitis B patients. Should we follow the treatment guidelines?

- **Background**

Chronic HBeAg-negative patients with slightly elevated HBV DNA and ALT levels should be considered for liver biopsy and treated if there is moderate/severe inflammation and/or at least moderate fibrosis on biopsy according to AASLD and EASL practice guidelines. The 'moderate fibrosis' cutoff has not been defined using Ishak (or any staging system), which are in any case descriptive categories and not quantitative measurements of collagen.

- **Aims**

To define the best cutoff value of collagen in liver biopsies for CHB patients HbeAg(-) requiring treatment.

- **Methods**
Consecutive liver biopsies between 2000-2010 from treatment naive HBeAg(-) patients, with HBV DNA <20,000 IU/mL and ALT <2ULN(upper limit of normal) were evaluated retrospectively using both Ishak system and stained with Sirius red for digital image analysis(DIA) expressed as collagen proportionate area(CPA). 84 patients
- **Median CPA for:**

stage 1	3%	(2-6)
stage 2	4%	(2-10)
stage 3	6%	(3-11)
stage 4	9%	(6-12)
stage 5	10%	(8-13)

CPA of 5% correlated with stage ≥3 with 80% sensitivity and 84% specificity.

According to this cutoff of CPA, 3 of 22 (14%) patients with Ishak stage 1 and 7 of 25 (28%) patients with Ishak stage 2 had significant fibrosis but did not receive treatment according to current guidelines.

- **Conclusion:**

CPA measurement in CHB patients has a good correlation with Ishak stage.

However, CPA evaluation capture stage 1 and 2 patients with similar collagen content to stage 3.

Use of CPA should be formally evaluated for treatment thresholds in chronic HBV patients.

The comparison of radiologic findings and histopathology for the diagnosis of hepatocellular carcinoma

- **Purpose:**

Detection and characterization of focal lesions in the liver is critical for screening patients with liver cirrhosis. The aim of this study was to investigate the sensitivity of magnetic resonance imaging (MRI) and spiral computed tomography (CT) for the diagnosis of hepatocellular carcinoma (HCC) and relation between radiologic findings and histopathology in HCC.

- **Conclusion:**

Typical early enhancement and early wash-out pattern on CT and MRI showed a significantly increased well differentiated hepatocellular carcinoma on histopathology.

Hepatocellular Carcinoma and Prognostic relevance of Mallory- Denk and intracytoplasmic hyaline bodies in hepatocellular carcinoma

Results:

In 53% of HCCs either MDBs or IHBs were present.

Both inclusion types were found in 24%, MDBs only in 21% and IHBs only in 8% of cases.

Presence of MDBs was associated with fatty change, ballooning of tumor cells and neutrophilic infiltrates ($p < 0.001$).

Patients with H

CCs with both types of inclusions had shorter overall survival as compared to patients with HCCs without inclusions or MDBs or IHBs only ($p < 0.001$). Multivariate analysis revealed tumor stage and presence of both, MDBs and IHBs as independent prognostic variables.

- **Conclusion:**

Simultaneous occurrence of MDBs and IHBs in HCC identifies a subset of patients with poor prognosis.

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- **Conclusion:**

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Fatty Liver Disease

Serial liver biopsy assessment of
phlebotomy as a therapy for non-
alcoholic steatohepatitis

- **Background:**

Unfortunately, short of sustained weight loss and management of other metabolic risk factors, there are no specific therapies for NASH.

Elevated iron indices are well described in NASH and may contribute to disease severity.

Iron reduction via phlebotomy has been suggested as a potential therapy.

However, no study to date has evaluated phlebotomy in a prospective manner on pre and post treatment liver histology.

- **Methods:**

Patients with biopsy proven NASH defined Nonalcoholic fatty liver disease Activity Score ≥ 3 plus cytological ballooning score ≥ 1 .

Phlebotomy was carried out to achieve near iron depletion (serum ferritin ≤ 50 ng/ml or Hgb 10.0 g/dL).

Repeat liver biopsy, anthropometric and biochemical measurements were performed 6 months following the end of treatment.

- **Results:**

23 patients with biopsy proven NASH completed follow up

Iron reduction resulted in a statistically significant improvement in total NAS activity score (-0.74 ± 1.83).

While no significant change was seen in the individual histological features all showed a trend towards improvement.

No adverse effects were reported.

Conclusion:

The results of this study are promising and suggest that this well tolerated therapy may have a beneficial effect on liver histology and supports a relationship between body iron and liver disease in NASH

Liver biopsy versus no liver biopsy in
patients with suspected non-
alcoholic fatty liver disease (NAFLD):
A decision analysis

- BACKGROUND:

Performing a liver biopsy in a patients with suspected NAFLD is controversial despite it being the only reliable way to diagnose and establish the severity of liver injury and fibrosis.

- AIMS:

1) To determine if performing a liver biopsy in patients with suspected NAFLD/NASH improves quality-adjusted life years and

2) Identify what areas of research are needed to better inform decision-making.

- METHODS:

- We created a Markov model to simulate disease progression in a hypothetical cohort of 50 year-old patients with elevated liver enzymes and echogenic liver on ultrasound.

- The benefit versus harm of liver biopsy was quantified over a 20-year horizon, assuming only biopsy-proven patients received pharmacologic therapy. to perform liver biopsy

- RESULTS:

Not performing a liver biopsy resulted in 18.10 quality-adjusted life years (QALYS), compared to 18.07 QALYS in the group that underwent biopsy.

Liver biopsy was also preferred if the death rate from biopsy was less than 0.3% or the probability of progression from compensated to decompensated cirrhosis was greater than 2%/year.

- CONCLUSIONS:

In the current clinical environment, the decision whether or not to perform a biopsy on patients with suspected NAFLD is associated with minimal difference in outcome either way.

Thus, this decision is to some extent a preference-sensitive one.

Prevalence and risk factors for
Steatosis among liver donors who
had no evidence of fatty liver on
ultrasonography: Potential
implication for pre-operative liver
biopsy

- **Background :**

The degree of steatosis of donated liver is one of decisive factors that determine graft function in recipient and recovery of remnant liver in living donor. Hence, the assessment of hepatic steatosis is a critical element to judge donor compatibility. Controversy exists whether routine pre-operative liver biopsy is necessary for potential liver donors. We evaluated the prevalence and predictors of steatosis among liver donors who had no evidence of fatty liver on ultrasonography (US-negative), the most widely used non-invasive tool to screen fatty liver.

- **Methods :**

Degree of hepatic steatosis was reviewed for 492 US-negative liver donors.

- **Results :**

The prevalence of severe, moderate, mild and no steatosis were 0.6% , 10.8% , 39.6% , and 49.0%

- **Conclusion :**

About a half of US-negative liver donors have steatosis \geq mild degree and one-tenth of them has \geq moderate degree.

USG assessment is not sufficient to exclude donors with significant steatosis especially for those with high BMI and triglyceride level, and thus, pre-operative liver biopsy should be positively considered for them.

Increased Hepatic Cytochrome P450
2E1 (CYP2E1) Activity in Children
with Biopsy-proven Nonalcoholic
Steatohepatitis (NASH)

- **Background:**

Oxidative stress and lipid peroxidation may play a role in the pathogenesis of NASH.

Hepatic CYP2E1 activity is increased in adult NASH and may contribute to increased lipid peroxidation that is evident in adults with NASH.

- **Methods:**

Hepatic CYP2E1 activity and peripheral lipid peroxidation were measured in 6 obese, nondiabetic, biopsy-proven pediatric NASH) and 7 healthy, lean controls (5M, 2F; 10-16 yrs).

Hepatic CYP2E1 activity was assessed using oral clearance of chlorzoxazone (CHZ), a valid *in-vivo* probe for CYP2E1 activity.

Serum lipid peroxidation was assessed by measuring serum level of malondialdehyde (MDA) by HPLC.

- **Results:**

Hepatic CYP2E1 activity was significantly greater in children with NASH compared to controls .

There was a trend towards higher serum MDA in children with NASH compared to controls.

Hepatic CYP2E1 activity correlated significantly with BMI, HOMA and serum MDA but there was significant interaction among these 3 variables.

- **Conclusions:**

There is increased hepatic CYP2E1 activity in children with NASH which is strongly associated with BMI, insulin resistance and lipid peroxidation.

Further studies with age- and BMI- matched obese controls are currently underway.

Histologic Predictors of
Improvement in Fibrosis in NASH:
Results from the Clinical Research
Network PIVENS Trial

- **Background:**

The primary response in the Pioglitazone v Vitamin E v Placebo for the Treatment of Nondiabetic Patients with Nonalcoholic Steatohepatitis (PIVENS) trial (NEJM 2010;18:1675) was histological and defined as: decrease in the nonalcoholic fatty liver disease activity score (NAS) ≥ 2 with at least one point contribution from hepatocellular ballooning and no worsening of fibrosis stage.

- **Aim:**

To analyze changes in the non-fibrosis histological features as predictors of improvement in fibrosis stage (≥ 1) in 96 week biopsies from all treatment arms.

- **Conclusions:**

Regardless of treatment arm, 38.5% of 221 subjects who had baseline and 96 week biopsies for evaluation following PIVENS showed improvement in fibrosis ≥ 1 .

This outcome was independently associated with improvement in the composite NAS ≥ 2 as well as Pathology Committee determined resolution of steatohepatitis.

These findings support a link between fibrosis improvement with improvement in disease activity.

Effect of probiotics (cultured
lactobacillus subtilis/streptococcus
faecium) in the treatment of
alcoholic hepatitis

- **Background:**
Gut-derived microbial lipopolysaccharide (LPS) has been known as a central role in the pathogenesis of Alcoholic Hepatitis .
- **Methods:**
Patients were randomized to receive 7 days of cultured lactobacillus subtilis/streptococcus faecium (1,500 mg/day) or placebo.
- **Results:**
117 patients (probiotics: 58 and placebo: 59)

In the probiotics group:

The mean level of AST, ALT, ALP, GGT and were improved

The number of gram negative bacteria was significantly reduced

The levels of interleukin 1 β , TNF- α , and LPS did not show difference.

Tumours

β -catenin hepatocellular adenomas (HCA) are rare but represents the most important subgroup of HCA associated with dysplasia, borderline lesion and hepatocellular carcinoma

- **Background**

In Western countries, distribution of HCA subtypes is:

1. 30% HNF1 α mutated HCA (H-HCA),
2. 45% inflammatory HCA (IHCA),
3. 15% β -catenin mutated HCA (β -cat HCA) - half of this subtype also of IHCA subtype and
4. 10% unclassified HCA (UHCA)

One of the major risks of HCA is malignant transformation in HCC (4 to 9%).

- **Aim.**

To assess HCA subtypes at risk for HCC among cases classified as HCA with dysplasia, borderline nodule and HCC with HCA.

- **Materials.**

We retrieved 30 resected HCA showing:

1. dysplasia (cytological atypia, not diagnostic for HCC),
2. borderline lesion (cytological and/or architectural foci suspicious but not diagnostic of HCC) or
3. HCA with HCC [HCC foci, HCC with HCA rim, HCC without Liver Fatty Acid Binding Protein (LFABP) expression, HCC coexisting with at least one HCA].

- **Conclusion.**

All HCA subtypes may present with dysplasia, borderline lesion or overt HCC.

In our study, β -cat HCA (with or without IHCA) represents the most important subgroup for HCC transformation and eventual death due to HCC.

Metabolic Liver Disease

Progression of Hemosiderosis in Cirrhotic Human Livers

- **Background:**

Hemosiderosis is associated with more rapid decompensation and decreased time to transplant in patients with cirrhosis. The rate of iron accumulation is unknown.

- **Results:**

Of 132 patients,

45 had an iron score of 0 both on a pre-transplant biopsy and explant;

12 patients had a score of 0 on pre-transplant biopsy and increased to an iron score of 2-4 on explant; and

49 patients had an iron score of greater than 0 (1-4) on both pre-transplant biopsy and explant.

- **Conclusion:**

Age and TIPS placement are associated with increase in iron deposition in a linear manner. After controlling for age and TIPS placement, there is no correlation between increase in hepatic iron deposition and the time interval between pre-transplant biopsy and explant.

Hepatic iron accumulation in cirrhosis has an unpredictable time course. These results may have implications for understanding the mechanisms of secondary iron overload.

Transient Elastography and
assessment of severe liver fibrosis in
C282Y homozygote HFE
hemochromatosis patients with
indication of liver biopsy (serum
ferritin > 1000 $\mu\text{g}/\text{L}$ and/or
abnormal transaminase levels)

- **Background:**

The stage of liver fibrosis is a major prognostic factor in HFE hemochromatosis.

When, at the time of diagnosis, serum ferritin (SF) levels are > 1000 µg/L and/or serum transaminase levels are increased, the risk of severe fibrosis is elevated. Then liver biopsy is required.

Transient elastography (TE) could be a valuable alternative means for assessing liver fibrosis in hemochromatosis but it has not been yet validated in such an indication.

- **Methods :**

61 consecutive untreated C282Y +/- patients who underwent liver biopsy for assessment of hepatic fibrosis according to the METAVIR scoring system, had measurement of TE (Fibroscan[®], Echosens, France) at the time of diagnosis

- **Conclusion :**

In HFE hemochromatosis, a TE threshold of 9.0 KPa allows a reliable identification of patients with severe fibrosis.

The classical SF threshold of 1000 $\mu\text{g/L}$ permitting the exclusion of severe fibrosis could be upgraded which would result in restricting the indication of TE to a subgroup of patients with SF > 1682 $\mu\text{g/L}$. Larger samples are needed to refine these results.

Distinctive pathogenic roles of iron deposition in hepatocytes and reticulo-endothelial cells for the development of chronic hepatitis C

- **Background:**

Chronic hepatitis C is frequently associated with hepatic iron overload.

Iron-induced oxidative stress promotes liver injury, the pattern of iron deposition in hepatocytes and macrophages cells would play a distinctive role.

Hepatocytes produce hepcidin, which facilitates REC iron deposition against iron overload

Macrophages evoke hepatic inflammation by cytokine production.

- **Aims**

We examined the clinical implications of the iron deposition pattern in CHC.

- **Results:**

208 patients had HC iron deposition (0/1/2/3/4: n=164/93/74/31/10) and

125 patients had REC iron deposition (0/1/2: n=247/88/37)

Serum transaminase levels and hepatic scores for stage, grade and steatosis were significantly higher in patients with REC iron than in those without REC iron.

TNF- α mRNA levels were higher in patients with mixed HC/REC iron than in those without REC iron.

Soluble TNF- α receptor levels were significantly greater in patients with REC iron than in those without REC.

- **Conclusions:**

REC iron deposition can enhance hepatic TNF- α production, thereby progressing CHC.

Although HC iron deposition can promote REC iron deposition via hepcidin synthesis, additional factors may contribute to this process.

Controversies in diagnosing and
treating Wilson disease in children -
results of an international survey

- **Introduction:**

The aim of this study is to determine consensus and variation in how pediatric hepatologists (PH) diagnose and treat Wilson disease (WD) patients.

- **Methods:**

PH, either members of AASLD Pediatric Liver Special Interest Group or ESPGHAN, were invited to participate in this web-based, international survey.

- **Results:**

Participation was 43%

The majority (64%) see 1-10 WD patients regularly

Publications by Roberts and Schilsky (Hepatology 2008) and Ferenci et al. (Liver Int. 2003) were preferentially used as guidelines (65% and 21%, respectively).

For 90%, basal 24-hr urine copper excretion > 40µg /24h indicated a need for further investigations

The definition of normal liver copper content varied:

25% interpreted 50µg/g and 56% 250µg/g as pathological

Genetic testing is performed in all patients by 48% and not at all in 13% in suspected WD cases.

- **Conclusions:**

The approach to diagnosing and treating WD in children by PH is distinctly variable.

The reasons for these differences in clinical practice are not entirely clear but likely include regional variations.

Viral Hepatitis

Natural History of HCV and HIV

Background:

It has been theorized that HIV may modify the natural history of HCV infection by accelerating fibrosis progression.

Studies have also shown that anti-viral agents lead to improved histologic liver fibrosis and inflammation in patients with HCV and HIV.

Design:

HCV and HCV-HIV patients having paired liver biopsies before and after antiviral therapy were identified using a pathology database search.

ASMA immunostaining was performed on formalin-fixed, paraffin-embedded paired liver biopsies from 17 patients with HCV and 9 with HCV/HIV.

% fibrosis was measured for each biopsy

ASMA expression in HSCs was graded (0 none, 1 focal, 2 diffuse).

Chronic hepatitis grade and stage were based on Batts and Ludwig scheme.

- **Conclusion:**

Our findings confirm that treatment with anti-viral agents regress fibrosis despite the absence of virologic response in both HCV mono and HCV-HIV co-infected patients.

The fibrosis stage and grade of inflammation both had significant correlations with the calculated percent area of fibrosis.

This demonstrates the correlation of percent area of fibrosis with a commonly used fibrosis staging system.

Evaluation of Liver And Plasma HCV
RNA Kinetics And Telaprevir Levels In
Genotype 1 HCV Patients Treated
With Telaprevir Using Serial Fine
Needle Aspirates

- **Background**

Although HCV is hepatotropic, HCV replication has largely been studied in the periphery.

- **Aims:**

We evaluated liver samples obtained by FNA to characterize the effect of TVR/Peg-IFN/RBV on viral kinetics in liver and plasma of 9 treatment-naïve and 6 prior Peg-IFN/RBV non-responders with chronic genotype-1 HCV.

- **Methods:**

FNA samples were obtained at baseline, 10h, D4, D15 and D56 after TPR initiation. Plasma and liver HCV RNA levels were quantified.

TVR was quantified using liquid chromatography/mass spectrometry.

- **Conclusions:**

Human liver TVR levels were substantially lower than predicted from preclinical models.

Viral populations were similar in liver and plasma.

Interestingly, we observed an initial plateau in liver rather than a first phase rapid viral decline.

These data support a model where high and low level HCV replication sites exist in liver driven by the local host cell milieu. The high-level replication sites drive the plasma viral kinetics and the low-level liver replication sites drive the clearance needed to achieve SVR.

Misc

Hepatic Lymph Node Histology at Time of Kasai Procedure for Biliary Atresia

- Background:

Hepatic hilar lymph nodes removed during a Kasai procedure for biliary atresia (BALN) show extreme variation in size and content of reactive follicles (germinal centers, GC), a hallmark of B cell stimulation in the lymph node.

Extra-hepatic biliary remnants (EHBR) typically reveal variation from granulation tissue to active fibroplasia to dense fibrous cords, but inflammation is usually minimal.

- Hypothesis:

The size and extent of follicular development in BALN at the liver hilum adjacent to the EHBR will indicate whether a local immune response has been activated during the period before BA becomes symptomatic, and may be related to the histology of the EHBR and to outcome after the KP.

- **Results:**

BALN mean areas were larger than controls

The frequency of primary follicles / mm² was comparable in both groups.

GC were virtually absent in control LN, but not in BALN. However, 45% of BALN contained no GC (non-reactive).

We assessed 25 nonreactive vs. 31 reactive BALN with respect to

(1) histology of atresia in the EHBR (inflammation /active fibroplasia vs. inactive end-stage atresia) and

(2) successful drainage vs. need for early transplant.

The number of GC/area was significantly higher in the early transplant group

- **Conclusion:**

The hepatic hilar lymph nodes in biliary atresia are enlarged compared to age-matched controls and often contain multiple GC indicating a humoral immune response.

Absence of GC in H&E stained sections in almost half of our cases is evidence for absent B-cell response.

Absence of GC may be a predictor of successful drainage.

The Change in Etiology of Hyperbilirubinemia in Pregnancy Over the Last 35 Years

- **Background:**

The incidence of abnormal liver function tests in pregnancy has been reported to be 0.3- 3 %. Acute hepatitis B is considered to be the most common cause of jaundice during pregnancy, accounting for 40% of cases

Pregnant women who had a total bilirubin > 1.2mg/dL were identified and their medical records were reviewed.

- **Results:**

Over the 5 year study period, 440 pregnancies with hyperbilirubinemia in 430 individual patients were identified out of a total 80,848 deliveries, resulting in a prevalence of hyperbilirubinemia of 0.5% in our study cohort.

- The most common cause of hyperbilirubinemia were:

1. Gallstone related disease (22%)
2. Pre-eclampsia/eclampsia (12%) and
3. intrahepatic cholestasis of pregnancy (12%).
4. 1 patient had acute HBV
5. 0 had acute hepatitis A.

Wake up and smell the coffee

Coffee Consumption in NAFLD
Patients with Lower Insulin
Resistance is Associated with Lower
Risk of Severe Fibrosis

- **Background:**

Coffee has several reported health effects, including inverse associations with type 2 diabetes and with hepatic fibrosis in NAFLD patients (*Molloy et al. Hepatology 2012; 55(2):429*).

- **Aim:**

We explored in more detail the relationships between coffee intake and insulin resistance (IR) with respect to NAFLD histologic severity.

- **Results:**

The frequency of coffee consumption (cups/day, cpd) was as follows:

0 cpd: n=230 (29%); <1 cpd: n=219 (28%); 1 - <2 cpd: n=116 (15%); ≥ 2 cpd: n=217 (28%).

Alcohol and tobacco consumption increased with increasing coffee intake.

There was a significant inverse association between coffee intake and severity of fibrosis among patients with lower HOMA-IR but no significant association between coffee intake and severity of fibrosis among patients with higher HOMA-IR.

No significant association was found between coffee intake and severity of steatosis, lobular inflammation, ballooning or definite NASH histology.

- **Conclusions:**

Increasing coffee consumption is inversely associated with severity of fibrosis among NAFLD patients with lower HOMA-IR.

Similar analyses will be performed using longitudinal data in the NASH CRN. Given the ubiquity of coffee intake in the U.S. population, these findings warrant further investigation in patients with NAFLD.

Nov 1-5, 2013
The Liver Meeting[®] 2013
Washington, DC

