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19th Conference of the Asian Pacific Association for the Study of the Liver

Poster Exhibition

Poster Exhibition – Autoimmune Hepatitis and Cholestatic Liver Disease
Poster Session, Hall 5B

PE001

Aspartate Aminotransferase to Alanine Aminotransferase Ratio (AAR) for Predicting Histology and Prognosis in Patients with Primary Biliary Cirrhosis

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Background: The aspartate aminotransferase to alanine aminotransferase ratio (AAR) has been used for fibrosis assessment in chronic hepatitis. But its predictive values for disease severity and prognosis in primary biliary cirrhosis (PBC) have seldom been investigated.
Methods: Ninety-two consecutive PBC patients in Taiwan were retrospectively evaluated to validate the AAR for assessing the severity of liver reserve, the degrees of hepatic fibrosis and predicting outcomes.
Result: AAR showed significant correlations to Mayo score, MELD score and Child-Pugh score ($r^2 = 0.156$, $P < 0.001$; $r^2 = 0.084$, $P = 0.005$; $r^2 = 0.142$, $P < 0.001$, respectively) for all patients. Among 46 patients who underwent liver biopsy, 35 were in early stage fibrosis and the remaining 11 were in advanced fibrosis. AAR was significantly higher in patients with advanced fibrosis than those with early fibrosis (mean ± standard deviation; 1.40 ± 0.44 vs. 0.98 ± 0.65, $p = 0.001$). The AAR yielded the highest area under the receiver operating curve (AUROC) of 0.847 than Mayo score, MELD score and Child-Pugh score in predicting advanced fibrosis. During a median follow-up of 44.5 months, 24 patients expired and 68 patients were alive. Patients with an AAR of 1 or less had significantly better prognosis than their counterparts ($P = 0.043$).
Conclusion: AAR is a simple and reliable marker to assess liver function and hepatic fibrosis as well as to predict outcomes in PBC patients.

PE002

Immunosuppresive Therapy in Autoimmune Hepatitis in Hong Kong Chinese: 10-Year Follow-up of a Cohort

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Background: Autoimmune hepatitis (AIH) is uncommon and immunosuppression with corticosteroids or in combination with azathioprine is the mainstay of treatment. Most literature reviews of AIH were based on western studies and data in the Chinese population was scarce.
Aim: The aim of the study is to analyse the clinical characteristics and treatment of AIH in Hong Kong Chinese.
Methods: All patients diagnosed as AIH between January 1996 and May 2008 in a regional hospital in Hong Kong were retrospectively reviewed and treatment outcomes were evaluated.
Results: Twenty-six patients with AIH were included in the study. The mean age at diagnosis was 56 (range 31-83 years). One third of them were associated with other autoimmune diseases; eight had cirrhosis at presentation, one of whom had hepatocellular carcinoma (HCC). All patients were treated either with prednisolone alone or in combination with azathioprine. Fourteen patients received long-term maintenance azathioprine therapy because of advanced age (>65 years), presence of cirrhosis, or concomitant autoimmune diseases. 58% achieved sustained remission over a median follow-up of 43 months after drug withdrawal. During a median follow-up of 5 years (range 1.2-10 years), there was no new development of liver cirrhosis or HCC in our cohort. None of the eight patients with known cirrhosis developed decompensated liver disease.
Conclusions: The sustained remission rate is higher in the Chinese population in contrast to the western studies. Long-term maintenance with azathioprine appears safe and should be advocated especially in patients with cirrhosis.

PE003

Cloning and Expression of 3-phosphoglycerate Dehydrogenase Gene and its Correlative Antibodies in Diagnosis of Autoimmune Hepatitis

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Objective: To evaluate whether the D-3-phosphoglycerate dehydrogenase (Phgdh) correlative antibodies is crucial for autoimmune hepatitis.
Methods: The constructed plasmid was transformed into *E. coli.* BL21 (D3). This fusion protein was purified by Ni-NTA chromatography . The enzyme linked immunosorbent assay (ELISA) with the fusion protein was established to detect the Phgdh autoantigen correlative antibodies in serum of patients with AIH (65) and patients with PBC (122) as well as chronic hepatitis B (CHB) (56), chronic hepatitis C (CHC)(117), and normals controls (60).
Results: The sequence of Phgdh autoantigen gene was the same as the sequence reported on the genebank.When analyzing the serum by ELISA , the immune reactivity to Phgdh was detected in 66.15% of patients with AIH, 21.42% of patients with PBC, 12.5% of patients with CHB, 6.83% of patients with CHC, and 3.3% of normal individuals.
Conclusion: The frequency of antibodies to Phgdh is much higher in patients with AIH than in patients with PBC, CHB, CHC and normal control. The antibodies to Phgdh may have utility in improved diagnosis of AIH. Our study presents the first description of the antibodies to Phgdh in AIH

PE004

Acute Liver Failure Caused by Autoimmune Hepatitis in Childhood

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Introduction : The major clinical form of autoimmne hepatitis (AIH) is chronic active hepatitis. Recently, acute liver failure with AIH has been reported, in which the prognosis is usually poor unless early diagnosis and intervention are made.
Case 1: A 4-year-old girl with systemic juvenile idiopathic arthritis was referred because of severe liver dysfunction [total bilirubin (TB) 13.7mg/dl, direct bilirubin (DB) 11.0mg/dl, AST 1,349IU/l, ALT 1,814IU/l, prothrombin time (PT) 51%]. Other tests revealed hypercytokinemia; ferritin 992ng/ml, soluble-interleukin-2 receptor (sIL2R) 10,100U/ml. A liver biopsy showed interface hepatitis without fibrosis, and rosette formation. Hemophagocytosis was not seen in bone marrow. Although normal IgG and negative for autoantibodies including anti-LKM-1, the diagnosis of AIH was suspected (IAIHG scoring;15). Because coagulopathy (PT 33%) and encephalopathy (grade II) developed, plasma exchange (PEx), continuous hemodiafiltration (CHDF), methylpredonisolone pulse therapy and cyclosporine (mPSL+CsA) were initiated. She survived without liver transplantation.
Case 2: An 8-year-old girl was referred because of severe liver dysfunction (TB 21.5mg/dl, DB 17.1mg/dl, AST 1,378IU/l, ALT 802IU/l, PT 27.1%) and encephalopathy (grade II). Other tests revealed hypercytokinemia; ferritin 1,975ng/ml, sIL2R 5,201U/ml, IgG 1,323mg/dl and positive for anti-nuclear antibodies (1:80). A liver biopsy showed prominent giant cell formation, interface hepatitis without fibrosis, and rosette formation. We diagnosed as acute AIH (IAIHG scoring;12), and started PEx, high-flow CHDF and mPSL+CsA. She survived without liver transplantation.
Conclusion: The early diagnosis and intervention are important. The appropriate immunosuppression and artificial liver support are effective for children with fulminant AIH.

PE005

Screening Serum Biomarker of Biliary Atresia by Two-dimensional Electrophoresis and Mass Spectrometry

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Background: Biliary atresia (BA) is one of the most common causes of neonatal cholestasis and the most frequent hepatic cause of death in early childhood. The incidence rate of BA is higher in Asian countries, occurring in approximately 1 of 8,000 (Asian Countries) to 1 of 18,000 (European countries) live births. Early identification and prompt intervention is very important. To im prove the early diagnosis, we used proteomic technology to screen serum biomarker for BA.
Methods: Two-dimensional electrophoresis (2-DE) and matrix-assisted laser desorption /ionization time-of-flight mass spectrometry (MALDI-TOF-MS) were employed to screen serum biomarkers specific to BA sera from idiopathic neonatal hepatitis. After pretreatment including albumin and immunoglobulin (IgG) depletion, sera were subjected to 2-DE and there after image analysis. The differentially expressed protein spots were identified by MALDI-TOF-MS.
Result: From optimized 2-DE gel images, thirty-four spots were differentially expressed and identified by MALDI-TOF-MS to be eight proteins. Overall, kininogen 1 variant was under expressed and alpha-1-B-glycoprotein, leucine-rich alpha-2-glycoprotein 1, 'SP40,40', A1BG protein, vitamin D-binding protein/group specific component , apolipoproteinA-Ⅳ, AQGV 3103 were over expressed in BA group com pared to idiopathic neonatal hepatitis.
Conclusion: 2-DE based serum proteome analysis can be useful in detecting protein expression alteration and new discovered biomarkers might be an aid in the diagnosis of BA, though further validation is needed.

PE006
Study of Various Autoimmune markers in Chronic Liver Diseases
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Background: A variety of autoreactive antibodies are detected in patients with chronic liver disease. This prospective, nonrandomized study was undertaken to evaluate the nature & prevalence of various autoantibodies in patients with chronic liver disease of diverse etiologies.
Methods: Study population included 53 patients (75% males), who met defined criteria for chronic liver disease. Detailed clinical, laboratory and sonographic evaluation was done. Sera were tested for ASMA, anti-LKM type1, AMA, APA, ANA, by standard methods. P<0.05 was considered significant.
Results: Among various etiologies for chronic liver disease, Hepatitis B was most common (28%), followed by alcohol (19%), autoimmune hepatitis in 15%, Hepatitis C (6%) and miscellaneous (2%). 30% of patients were labeled as cryptogenic after detailed investigations. ANA (>1/80) was positive in 100% of definite AIH, 33% of HCV related CLD but at titer of >1/40, 66.6% of HCV related CLD & 60% of probable AIH were found positive. ASMA (>1/40) was positive in 6% of HBV related CLD, 10% of alcohol related CLD, 33% of definite AIH, 40% of probable AIH, 33% of HCV related CLD but ASMA in titer of >1/80 was positive only in 33% oh definite AIH. APA was detected in 12.5% of cryptogenic CLD, 13.3% of HBV related CLD & 20% of alcohol & probable AIH related CLD each. AMA was detected in 1% of cryptogenic, HBV, AIH (definite) & HCV related CLD each, and 2% of alcohol related CLD & 100% of PBC.
Conclusions: Apart from AIH there is high prevalence of ANA & SMA in HCV related CLD while other antibodies has low prevalence in non-AIH related CLDs. This study also suggests that prevalence of various autoantibodies should be borne in mind while considering the diagnosis of CLD especially of mixed etiology.

Poster Exhibition – Acute Liver Failure & Transplantation Poster Session, Hall 5B

PE007
Long Term Follow-up of Patients with Primary Biliary Cirrhosis after Liver Transplantation
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Background: There were few reports related to liver transplantation to treat primary biliary cirrhosis (PBC) in China, so we performed the follow-up study to make sure the efficacy of liver transplantation to treat Chinese PBC patients.
Methods: Fifteen PBC patients after liver transplantation, including one patient received re-transplantation because of primary transplant disfunction were followed up for a median time of 70 months (38-86 months). The mean Mayo risk score before liver transplantation was 8.3±2.7. The efficacy of liver transplantation to treat PBC, de novo diseases after liver transplantation, the survival and death cause were analyzed.
Results: The liver function tests as well as the symptoms of fatigue and pruritus improved significantly after liver transplantation. All patients showed improved quality of life. One patient was found *de novo* hepatitis B virus (HBV) infection 3 months after liver transplantation, and after treatment with lamivudine and adefovir, HBV replication was suppressed and HBsAg conversion was reached. Two patients developed de novo autoimmune hepatitis (AIH), including one died from variceal bleeding at 52 months after liver transplantation. One patient died from colon cancer at 38 months after transplantation. No PBC recurrence was found during the follow-up. The overall 1-year, 2-year and 5-year survivals were 100%, 100% and 86.7%, respectively.
Conclusion: Liver transplantation can improve the survival of advanced-stage PBC patients. Some rare de novo diseases after liver transplantation may impact the long term survival.

PE008
Acute Liver Failure in Lithuania
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Background: Due to lack of published data about the characteristics of acute liver failure (ALF) in Central-East European countries, we conducted a prospective study to analyze the causes, outcomes, and prognostic factors of ALF in Lithuania.
Methods: A total of 28 consecutive patients admitted during period 1996-2004 to tertiary care center and fulfilled the entry criteria (presence of hepatic encephalopathy (HE) and prothrombin (INR) >1.5) were included into study.
Results: The most frequent causes of ALF were acute viral hepatitis B (21.4 %), drug-induced hepatitis (21.4%), and indeterminate hepatitis (17.9%); other etiologies included Budd-Chiari syndrome (10.7%), ischemic hepatitis (10.7%), Wilson's disease (7.1%), Amanita phalloides-induced liver damage (3.6%), acute fatty liver of pregnancy (3.6%), and malignant infiltration of the liver (3.6%). Among patients with drug-induced liver injury, only one case of acetaminophen poisoning was diagnosed. Clinical status of 9 persons corresponded to criteria for urgent liver transplantation (LT) (one LT was performed); 6 had contraindications, and 13 patients did not fulfill requirements. The patients' survival rate in these groups was 11.1%, 16.7% and 69.2%, respectively. In 27 non-transplanted patients univariate analysis revealed the grade of HE on the day of enrolment, total serum bilirubin, pH, and INR as risk factors for death from ALF. Multivariate logistic regressive analysis determined only INR >3.24 and serum pH </=7.29 as independent predictors of lethal outcome.
Conclusion: Improvement of liver donation system for urgent liver transplantation is essential requirement for amelioration of ALF patient's survival in Lithuania.

PE009
Analysis of Influential Factors of Prognosis of Patients with Acute-on-Chronic Hepatitis B Liver Failure after Lamivudine Treatment
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Objective: To study the impact of HBV DNA load change and its related factors on the prognosis of patients with acute-on-chronic liver failure (ACLF) after lamivudine treatment.
Methods: One hundred and thirty ACLF patients were treated with lamivudine and the influential factors on mortality of patients were studied by univariate and multivariate analysis.

Results: The mortality (50.0%) of patients in lamivudine group with MELD score from 30 to 40 was lower than that (86.1%) of control group (χ^2=23.319, *P*=0.000). Univariate analysis showed that mortality was significantly related to age (*P*=0.005), MELD score (*P*=0.009), treatment method (*P*=0.000), pretreatment HBV DNA load (*P*=0.000), the decline of HBV DNA load during therapy (*P*=0.006) and encephalopathy (*P*=0.007). In multivariate analysis, in patients with MELD scores 30-40, treatment method (*P*=0.004), pretreatment HBV DNA load (*P*=0.009), decline of HBV DNA load during therapy (*P*=0.014) and encephalopathy (*P*=0.019) were independent predictors of mortality; for MELD scores above 40, only MELD score (*P*=0.015) was independent predictive.
Conclusions: Lamivudine treatment significantly decreases the 3 month's mortality of patients with MELD score 30-40, and a low viral load pre-treatment and quick decline of HBV DNA load are good predictors for the survival of lamivudine treatment.

PE010

Dynamic Metabonomic Analysis in a Rodent Model of Fulminant Hepatic Failure and Corroboration in a Human Pilot Study

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Background/Aims: Early identification of patients with Fulminant hepatic failure (FHF) who need a liver transplantation is very important. To construct a prediction model for early diagnosis and prognosis of FHF, we studied dynamics of metabolic profiles using a D-galactosamine/lipopolysaccharide (GalN/LPS)-treated mouse model.
Methods: BALB/c mice were used to construct FHF model and sacrificed for blood collection at 4, 5, and 6 hour after treatment, respectively. Levels of plasma metabolites were quantified using gas chromatography/time-of-flight mass spectrometry and data were processed using partial least squares discriminant analysis (PLS-DA).
Results: Distinct clustering differences were observed 5 and 6 h after treatment between survival and dead groups. At 5 h, plasma levels of some metabolites differed significantly between survival, dead and control groups. Ketogenesis and the TCA cycle were inhibited in both survival and dead groups, but in dead group, the urea cycle was also inhibited and glycolysis was elevated. PLS-DA indicated that principal component weighting was greatest for plasma levels of phosphate, β-hydroxybutyrate, urea, glucose and lactate. The Y-predicted scatter plot in PLS model assigned samples to survival or dead groups using an apriori cutoff of 0.10 with 100% sensitivity and specificity. Similar results were observed in 11 FHF patients with different outcomes.
Conclusions: The PLS model based on metabonomics analysis can be used to predict outcomes well, and plasma levels of phosphate, β-hydroxybutyrate, urea, glucose and lactate may constitute a set of markers for early diagnosis and prognosis of FHF.

PE011

Therapeutic Efficacy of L-Ornithine L-Aspartate in Patients with Acute Liver Failure: A Double-blind, Randomized, Placebo-controlled Study

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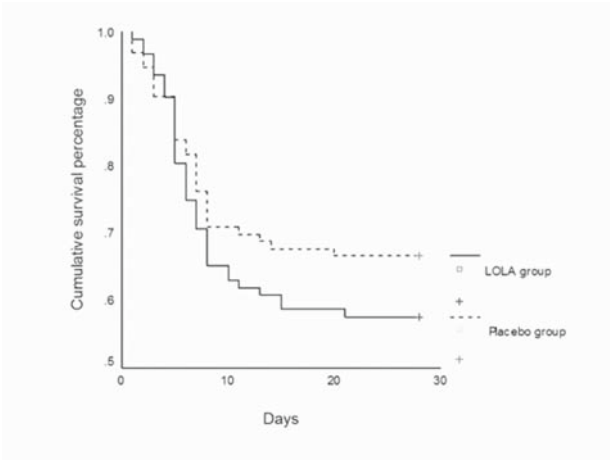
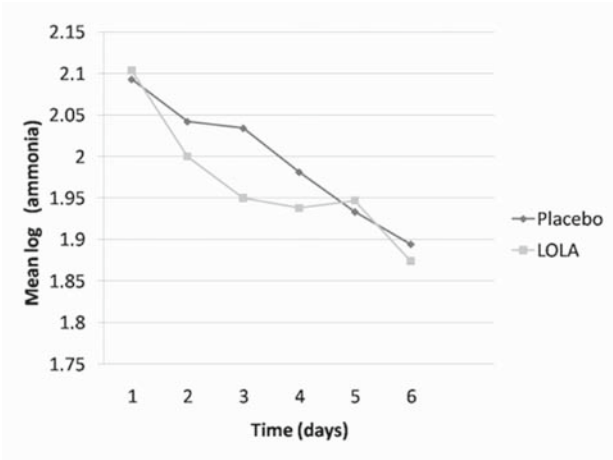
Background: In acute liver failure (ALF) high ammonia correlates with mortality and complications. Ornithine-Aspartate (OA) reduces ammonia by increasing hepatic and peripheral disposal. Present study evaluated efficacy of OA in ALF.
Methods: Placebo controlled and blinded study. 201 patients randomized to placebo or OA infusion (30 g/d for 3 days), between January 2005-October 2007. Arterial ammonia measured for 6 days. Primary end point was improvement in survival. CONSORT guidelines followed.
Results: LOLA did not improve survival (Mortality:33.3% in placebo and 42.4% in OA arm; RR of death:1.27; 95% CI: 0.88- 1.85; p=0.204). By multivariate analysis, ammonia levels were independent predictor of survival. Ammonia levels remained similar in both groups at all time points(p=0.492, by GEE analysis) . No difference in encephalopathy improvement (p=0.418), consciousness recovery time (p=0.347), or complications like seizures (p=0.058) and renal failure (p=0.615) found.
Conclusions: OA infusion did not lower ammonia levels or improve survival.





PE012

Association between Polymorphisms in the Interleukin-10 Gene Promoter and Hepatitis B-related Acute Liver Failure

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Background: The association of genetic polymorphisms of *IL-10* with the susceptibility to HBV infection and hepatitis B-related diseases has been recently emphasized. We aimed to determine the association between polymorphisms in the *IL-10* promoter and development of ALF.
Methods: In a hospital-based case-control cohort composed of 345 hepatitis B-related ALF patients and 367 asymptomatic HBV carriers, three common *IL-10* promoter polymorphisms were analyzed using the polymerase chain reaction-restriction fragment length polymorphism assay or tetra-primer amplification refractory mutation system-polymerase chain reaction. Functional analyses were conducted to verify the biological significances of the associated genetic variations.
Results: The allele frequencies of *IL-10* -592C and -819C were significantly higher in hepatitis B-related ALF patients than in asymptomatic HBV carriers. Logistic regression analysis with adjustment for age, sex, and alcohol consumption indicated that the polymorphisms of A-592C and T-819C were associated with susceptibility to hepatitis B-related ALF in the Chinese Population (dominant model; odds ratio=2.07; P<0.001). Functional analyses showed that the A-592C polymorphism alters the binding affinity of nuclear proteins and regulates *IL-10* expression. The *IL-10* gene transcription and protein production were observed to increase in LPS-stimulated peripheral blood mononuclear cells with the susceptible genotypes.
Conclusion: The A-592C and T-819C polymorphisms of the

IL-10 promoter are associated with the susceptibility to hepatitis B-related ALF in the Chinese population. *IL-10* A-592C may be a regulatory polymorphism that affects gene regulation.

PE013

The Efficacy of Entecavir Treatment for Chronic Hepatitis B Patients with Acute Liver Failure

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Background: Aim of this study is to evaluate the efficacy of entecavir (ETV) treatment in chronic hepatitis B (CHB) patients with acute liver failure.
Methods: In the treatment group, 84 CHB patients with acute liver failure were treated with ETV (0.5mg daily) and received routine supportive therapy. This group was compared to 99 patients in the control group who received supportive therapy only. All patients were divided into early, middle and late stage acute liver failure based on severity of their disease. The survival rates were determined after 180 days of therapy.
Results: At baseline, patient disease profile was similar between the treatment group and control group; except viral load was significantly higher in the treatment group (4.98 $\log_{10}$ versus 3.94 $\log_{10}$ copies/mL). In early-stage liver failure, 31/49 patients survived in the treatment group as compared with 23/58 patients in the control group (63.27% versus 39.66%; P=0.015). In middle-stage liver failure, 17/27 patients in the treatment group and 13/37 patients in the control group survived (62.96% versus 35.14%; P=0.028). In late-stage liver failure, 4/8 patients in the treatment group and 1/4 patients in the control group survived (50% versus 25%; P=0.408). At Week 4, the HBV DNA reduction in the treatment group was -3.95 $\log_{10}$ copies/mL compared to -1.78 $\log_{10}$ copies/mL for the control group (P=0.001).
Conclusions: Antiviral therapy with ETV significantly improves survival rate in CHB patients with acute liver failure, especially when antiviral treatment is initiated earlier.

PE014

Liver Dysfunction in Acute Pancreatitis: Features of Treatment

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The liver damage is an important prognostic sign of severe acute pancreatitis (SAP). Among many pathogenic factors, the changes of vasoactive substances, participation of inflammatory mediators as well as ROS (reactive oxygen species), endotoxin, etc. may play important roles in its progression. The mechanisms of liver dysfunction and its treatment are still not fully studied.
Plasma levels of IL-1β, TNF-α, myeloperoxidase (MPO), aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), lactate dehydrogenase (LDH were measured in 45 patients (21 – with severe and 24 – with mild pancreatitis). The patients with SAP divided into two groups: one received the quercetin by continuous regional arterial infusion through truncus coeliacus (CRAI group – 11 patients) and the other received standart therapy by intravenous infusion (non-CRAI group).
Liver dysfunction was noted only in patients with severe pancreatitis that accompanied by increased levels of LDH and ALAT. The clear correlation between proinflammatory mediators' concentration and enzymes (LDH, ALAT, and MPO) activity was observed. Quercetin prevented the rise in bilirubin concentration and significantly reduced the increase in transaminase activities. Quercetin has beneficial effects on liver function by enhancing antioxidant enzyme activity and decreasing the prooxidant effect. The liver function significantly improves after removing of pancreatic fluid collections and infusions of ademetionine (Geptral) – 800 mg/daily.
CRAI of a quercetin reduce liver dysfunction in patients with SAP, that significantly ameliorates the results of treatment. The evacuation of fluid collections and applying of glutathione precursors are necessary for liver dysfunction treatment in acute pancreatitis.

PE015

Effect of Splenic Artery Ligation on Hypersplenism Post Liver Transplantation for Hepatitis C Cirrhosis

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Background: The efficacy of pegylated interferon plus ribavirin for HCV re-infection following liver transplantation is poor because of severe cytopaenia leading to treatment dose reduction and/or cessation. Splenic artery ligation (SAL) has been performed at transplantation in HCV cirrhosis patients since 2005 to improve tolerability of post-transplant anti-viral therapy. This retrospective analysis evaluates the effect of SAL on hypersplenism.
Methods: Between January 2005 and August 2008, 26 patients were transplanted for HCV cirrhosis. Twelve did not have SAL performed (Group A) and 14 did (Group B). Haemoglobin, platelet and absolute neutrophil counts (ANC) were collected at pre-transplantation, 1, 2, 4 and 24 weeks post-transplant. Nonparametric methods were used to analyse results between time points (Wilcoxon matched pairs) and between the two groups (Mann-Whitney).
Results: In both groups, ANC and platelets numbers at 1 week, 2 weeks and 4 weeks were higher than pre-transplant ($p<0.0001$). Mean ANC increase from baseline at 2 weeks post-transplant was higher in patients in Group B than Group A ($p=0.067$), but not at 4 weeks ($p=0.43$) or 24 weeks post-transplant ($p=0.15$). Mean platelet increase was similar in patients in both groups.
Conclusion: Hypersplenism resolves within one month post-transplantation. Additional benefit of SAL appears limited to the first few weeks post-transplant, whereas subsequent benefit on anti-viral treatment adherence seems unclear.

PE016

A Prospective Study of the Rate of Fibrosis Progression in Recurrent Hepatitis C Post-liver Transplantation

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Background: Chronic hepatitis C (HCV) has become the leading indication for liver transplantation. Re-infection is universal and may lead to recurrent cirrhosis and graft loss. Factors linked with rapid progression include genotype, donor age and over-immunosuppression. We assessed the rate of fibrosis progression and factors associated with severe recurrence.
Method: Patients transplanted for end-stage HCV underwent annual liver biopsies, reviewed by a single Histopathologist and scored using the Metavir system. Multivariate analysis was performed to determine association between rate of fibrosis progression and host, donor, viral factors, and immunosuppression. Graft and patient survival were determined by Kaplan-Meier method.
Results: Between 1998 and 2007, HCV was the indication for transplantation in 61/252 primary transplants (24%). 38% were genotype 1, 48% genotype 2/3, and 14% unknown. Five-year patient survival was 87%; five-year graft survival was 82%. After median follow-up of 3 years, 14 developed advanced recurrent HCV – 2 cholestatic hepatitis, 12 cirrhosis. Of these, 8 developed graft failure, of whom 5 died and 2 were re-transplanted (subsequently died). Independent factors associated with severe recurrence were genotype 1 and administration of pulse steroids for acute rejection.
Conclusion: Recurrent HCV leads to accelerated fibrosis progression; with 20% developing cirrhosis and 12% HCV-related graft failure by 5 years post-transplant. The decreasing donor supply may prevent re-transplantation for recurrent hepatitis C. New strategies are needed to improve long-term outcomes, including avoidance of adjuvant immunosuppression and use of peri-operative molecular anti-viral prophylaxis.

PE017

Antioxidative and Hepatoprotective Effect of CGX, an Herbal Medicine, against Toxic Acute Injury in Mice

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Background/aims: CGX, a traditional Korean medicine has been used for various liver diseases. In this study, we investigated the protective effect of CGX and its mechanisms in CCl_4 induced acute liver injury.
Methods: The ICR mice were randomly divided into five groups. The mice were administered with distilled water for naive and control group and CGX (50 or 100 mg/kg) for 3 consecutive days. The mice were injected with 10 mg/kg of 0.2% CCl_4 After 18 h of CCl_4 treatment, the mice were sacrificed and alanine transaminase (ALT), aspartate transaminase (AST) in serum, gene expression and antioxidant enzyme in liver tissue were determined.
Results: Administration of CCl_4 induced severe liver injury in mice, as evidenced by a dramatic elevation in serum levels of ALT, and AST and by typical histopathological changes. Furthermore, CCl_4 increased oxidative stress, increasing the malondialdehyde (MDA) concentration and dramatically reducing superoxide dismutase (SOD) and catalase activity, and reduced glutathione (GSH) content in liver tissues. However, pretreatment with CGX significantly attenuated CCl_4-induced hepatotoxicity, reducing serum ALT, AST, and histopathological findings, and hepatic MDA concentrations, as compared to the CCl_4-treated mice, and restored GSH. In addition, pretreatment with CGX inhibited the CCl_4-induced gene expression of iNOS and TNF- but did not affect expression or bioactivity of SOD in liver tissues.
Conclusions: CGX has hepatoprotective effects against acute injury caused by CCl_4 in mice, and that these effects are primarily due to its antioxidative properties, associated with the GSH system.

PE018

Protective Effect of Morin on Acute Liver Damage by Carbon Tetrachloride (CCl4) in Rat

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Background: It has been suggested that in most cases hepatocellular injury is not due to the damaging agent itself but to the inflammatory cells that have been attacked by the stressed hepatocytes The importance of inflammatory cytokines as hepatotrophic factors is demonstrated by the evidence that circulating levels of TNF-α and IL-1β are increased in rats that develop liver damage. The aim of this study was to investigate possible anti-inflammatory effects of morin on CCl_4-induced acute hepatotoxicity in rats.
Methods: Rats received a single dose of CCl_4 (150 μl/100 g 1:1 in corn oil). Morin treatment (20 mg/kg) was given at 48, 24, and 2 h before CCl_4 administration.
Result: CCl_4 challenge elevated serum alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP) levels, but these effects were prevented by the pretreatment of rats with morin. To identify the mechanism of protective activity of morin in CCl_4-induced hepatotoxicity in rats, we investigated expressions of tumor necrosis factor alpha (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), and inducible nitric oxide (iNOS). The expressions of TNF-α, IL-1β, IL-6, and iNOS were increased by CCl_4 treatment and increased expressions of those were decreased by morin.
Conclusion: These findings suggest that morin prevents acute liver damage by inhibiting production of TNF-α, IL-1β, IL-6, and iNOS.

PE019

Hepatocyte Cell Death in ACLF: Mechanism and Significance – An Immunohistochemical Study.

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Background: Acute on chronic liver failure (ACLF) is defined as acute hepatic insult complicated within 4 weeks by ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease.
Caspases play an essential role in apoptosis. COX-2 is an inducible immediate early gene responsible for the release of prostaglandins during inflammatory response.
We studied the immunohistochemical expression of COX-2 and caspase-1 in liver tissue to assess their role in pathophysiology and in predicting outcome of ACLF.
Method: A retrospective analysis of 50 liver biopsies with clinical diagnosis of ACLF was undertaken. Patients were divided into two groups A and D based on clinical outcome (Alive/Died respectively). Immunohistochemical analysis for COX-2 and caspase was performed on 39 and 36 cases respectively and scored from 0-8 as per intensity and distribution. Score 6-8 indicated high intensity with focal to diffuse distribution, and was considered significant.
Results: Etiology of acute liver failure was viral or alcoholic. Increased expression of Caspase was observed in 10/21 cases in group D and none of the cases in group A(n=15) (p=0.001). Increased expression of Cox-2 was observed in 4/21 cases in group D and none of the cases in group A (n=18) (p=0.052).
Conclusion: Increased immunoreactivity of caspase in liver biopsies of patients of ACLF may indicate worse prognosis and its important role in the pathophysiology of ACLF. Immunostaining for caspase is useful for assessment of prognosis and possibility of anti-apoptotic and anti-fibrotic therapies in future.

PE020

Heterotypic Interactions in the Preservation of Morphology and Functionality of Porcine Hepatocytes by Bone Marrow Mesenchymal Stem Cells in vitro

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Background: Temporary replacement of specific liver functions with extracorporeal bioartificial liver has been hampered by rapid de-differentiation of porcine hepatocytes in vitro. Co-cultivation of hepatocytes with non-parenchymal cells may be beneficial for optimizing cell functions via mimicry of physiological microenvironment consisting of endogenous matrix proteins and soluble factors. However, the underlying mechanisms remain to be elucidated.
Methods: A randomly distributed co-culture system composed of porcine hepatocytes and bone marrow mesenchymal stem cells was generated, and the morphological and functional changes of varying degrees of heterotypic interactions were characterized. Furthermore, contributions of extracellular matrix and soluble factors within this co-culture were evaluated.
Results: A rapid attachment and self-organization of three-dimensional hepatocyte spheroids were encouraged. Studies on hepatocyte viability showed a metabolically active, viable cell population in all co-culture configurations with occurrence of few dead cells. The maximal induction of albumin production, urea synthesis and cytochrome P4503A1 activities was achieved at seeding ratio of 2:1. Immunocytochemical detection of various extracellular matrix confirmed that a high level of matrix proteins synthesis within distinct cells was involved in hepatocyte homeostasis. Data from semi-permeable membrane cultures excluding direct cell physical contact suggested that interleukin-6 was one of the key stimulators in hepatic functional enhancement.
Conclusion: These results demonstrate for the first time both cell-matrix and soluble factors have synergic effects on the preservation of hepatic morphology and functionality in the co-culture of porcine hepatocytes with mesenchymal stem cells in vitro, which could represent a promising tool for tissue engineering, cell biology, and bioartificial liver devices.

PE021

Clinical and Histological Efficacy of Prolonged Combination Therapy with Low Dose of Pegylated Interferon Alpha and Ribavirin of Recurrent Hepatitis C after Liver Transplantation

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Background: Treatment of recurrent hepatitis C in liver transplant is controversial. The aim of our study is to evaluate the clinical and histological efficacy of prolonged combination therapy with low dose of pegylated interferon (PEG-IFN) alpha and ribavirin of recurrent hepatitis C after liver transplantation.

Methods: Fifteen patients transplanted for hepatitis C, median age 56 years, 87% living related donor, 80% genotype 1, and median pretreatment HCV-RNA 2850 KIU/mL were treated 3-12 months after transplantation. Patients received initiated as PEG-IFN alpha 2b (1.0 μg/kg/week) and reduced to 0.5 μg/kg/week when neutrophils dropped below 1000/μL or platelets below 50000/μL. Ribavirin was initially given at 400 mg/day (↪ 60 kg) or 600 mg/day (≧60kg), decreased 200 mg when hemoglobin dropped below 10 mg/dL, and reduced given at 200 mg/day below 8.5 mg/dL. Median overall treatment duration was 34 months.
Result: Treatment was discontinued in 4 (27%) patients. Virological response defined as HCV-RNA negativity by qualitative PCR was seen 7 (47%) (SVR in one). Six patients (40%) were biochemical responders with normalization of ALT. Sequential liver biopsies were available in 10 patients. Fibrosis score decreased in 2 (20%) and remained stable in 8 (80%). Activity score decreased in 6 (60%) and remained stable in 4 (40%). No worsening of fibrosis or activity score was observed.
Conclusion: Prolonged combination therapy with low dose of PEG-IFN and ribavirin in hepatitis C after liver transplantation is effective, well tolerated and leads to an improvement in histological outcome.

PE022

Dendritic Cell Abnormality Actively Involved in the Pathogenesis of Acute-on-Chronic Hepatitis B Liver Failure

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Background/Aims: Functionally impaired dendritic cells (DCs) play important roles in suppressing host immune responses and facilitating viral persistence in chronic hepatitis B virus (HBV) infection. However, little is known regarding the status of intrahepatic DCs in HBV infection.
Methods: Based on availability, 11 recipient liver samples were obtained from acute-on-chronic hepatitis B liver failure (ACHBLF) patients who had undergone liver transplantation. The frequencies, phenotypes, and functions of intrahepatic DC subsets were analyzed.
Results: Both plasmacytoid dendritic cells (pDCs) and myeloid dendritic cells (mDCs) extensively infiltrated the liver of the ACHBLF patients and expressed mature phenotypes therein. In particular, activated hepatic pDCs produced interferon (IFN)-a, which subsequently induced interleukin (IL)-12 and IL-10 production via toll-like receptor-9 ligation in liver-infiltrating lymphocytes cultured in vitro. However, blockade of IFN-a production significantly reduced the cytokine production of the LILs. Further, a significantly low frequency of peripheral pDCs and highly reduced IFN-a production were observed in a large cohort of the ACHBLF patients, particularly in the non-survivors.Moreover, a persistently upregulated expression of hepatic IFN-a-associated genes was observed in the ACHBLF patients during disease progression.
Conclusions: Activated pDCs accumulated in large numbers in the liver of the ACHBLF patients and regulated local immune responses in chronic HBV infection.

PE023

Characterization of Circulating and Liver-infiltrating Immunologically-competent Cells in Patients with Hepatitis B-related Acute-on-chronic Liver Failure

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Background and Aims: The immunological alterations in patients with acute-on-chronic liver failure (ACLF) in relation to chronic hepatitis B virus (HBV) infection remain incompletely understood. This study attempts to characterize the feature of immunologically competent cells (ICCs) in hepatitis B-related ACLF patients.
Methods: Circulating ICCs were examined in ACLF patients (n = 75), as well as in patients with chronic hepatitis B (CHB, n = 31), CHB-related liver cirrhosis (LC, n = 36), and normal controls (NC, n = 30). Intrahepatic ICCs in some patients were further analyzed via immunohistochemical and flow cytometric analyses.
Results: Total lymphocytes, $CD4^+$ T cells, $CD8^+$ T cells, and NK cells in circulation were numerically lower in the ACLF and LC groups compared to the CHB and NC groups. Importantly, the number of these cells was significantly lower in non-surviving ACLF patients compared with surviving ACLF patients. In comparison to NC, ACLF patients displayed a significantly higher ratio of liver-infiltrating $CD4^+$ T-cell frequency than its circulating counterpart, suggesting that compartmentalization of the ICCs from the peripheral blood into the liver may partly account for the altered distribution of the ICCs in ACLF. Immunohistochemical analysis showed that intrahepatic $CD4^+$ T cells, $CD8^+$ T cells, and $CD56^+$ cells were significantly higher in the ACLF group compared with the other three groups, indicating a strong cellular immune response-mediated liver injury in ACLF.
Conclusions: The abnormal prevalence of circulating and intrahepatic ICCs possibly acts as an important factor that may drive the progression of hepatitis B-related ACLF.

PE024

Therapeutic Effect of Small Dose of Dexamethasone Zusanli (S36) Dcupoint Injection on the Early Stage of Liver Failure

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Objective: To observe the clinic effect of small dose of dexamethasone Zusanli (S36) acupoint injection on the early stage of liver failure.
Methods: Fifty-four cases were randomly divided into control and treatment group. Patients in control group were treated with routine medical treatment, i.e.general supporting therapy and anti-virus therapy with nucleoside analogue. Patients in treatment group were treated with injection of small dose of dexamethasone (2-5mg) into Zusanli (S36) plus routine medical treatment once a day for 1-2 weeks. The total effective rate, the incidence of complication, the amelioration time of clinical symptoms, the time of icterus decline, the falling of TBil and the rising of PTA of every day and HBV-DNA were analyzed.
Results: The incidence of complication, infection and hemorrhage, has no difference between treatment and control group. The total effective rate in treatment and control group was 75% and 40% respectively, with significant difference between two groups (P<0.05); the amelioration time of clinical symptoms, the time of icterus decline, the falling range of TBil and the rising range of PTA was 3.0±0.9d, 21.2±4.0 d, 8.48±2.75 μmol/L/d and 1.17±0.32%/d, respectively in treatment group, while 6.8±1.3d, 29.3±6.8 d, 4.92±1.87 μmol/L/d and 0.83±0.21%/d , respectively in control group, with significant difference between two groups (P<0.05). The change of HBV-DNA showed no difference between two groups (P>0.05)
Conclusion: Small dose of dexamethasone Zusanli (S36) acupoint injection has a better therapeutic effect on the early stage of liver failure compared to routine therpy.

PE025

Monitoring of Human Cytomegalovirus Infection in Liver and Bone Marrow Transplant Recipients

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Background: Human cytomegalovirus (HCMV) infection is a common complication of transplant recipients. Sensitive, specific and timely diagnostic tests for detection of HCMV infection remain essential for the success of therapy.
Methods: We compared the results among HCMV pp65, immediate early (IE) antigenemia assay, anti-HCMV IgM by enzyme linked immunosorbent assay (ELISA) and gBn genotype by real-time Polymerase Chain Reaction (PCR) in liver and bone marrow transplant recipients in China. And we evaluated the role of IE in monitoring HCMV infection.
Result: 911(67.8%) and 917(68.2%) positive samples by pp65 and IE antigenemia assay in 1344 samples were detected, respectively. The coincidence was 85.1%(p=0.724). There was no statistical difference in

mean first checkout time between pp65 and IE antigenemia assay (p=0.769). The level of pp65 and IE antigenemia had a significant correlation (r =0.828). Moreover, 150 (11.2%) positive samples were detected by PCR.The distribution of gB genotypes was as follows: gBn1, 60% of patients; gBn2, 13.3%; gBn1 and gBn3 mixed infection, 26.7%,gBn4 and other mixed infection were not found. The level of CMV gB DNA detected and the number of CMV positive pp65 cells correlated well (r=0.641).In addition, the positive rate of anti-HCMV IgM was 11.1%, which was significantly different from IE and pp65 antigenemia assay (p<0.05).
Conclusion: We suggested that HCMV antibody by ELISA and gBn genotype by PCR did not suit to monitor HCMV infection independently in transplant recipients, IE antigenemia assay could replace pp65 antigenemia assay in monitoring HCMV active infection and early detection of HCMV infection.

PE026

Frequency and Severity of Organ Failure at Admission Predicts Mortality in Acute-on-Chronic Liver Failure (ACLF) patients: A Prospective study

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Background: short-term prognosis of acute-on-chronic liver disease(ACLF) patients is influenced by degree of hepatic insufficiency and by dysfunction of extra-hepatic organ systems. We aimed to assess frequency and severity of organ failure at admission on 3-month mortality.
Methods: Consecutive patients ofACLF defined as per theAPASL criteria(Acute hepatic insult manifesting as jaundice and coagulopathy, complicated within 4-weeks by ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease)were included.They were further categorized based on the number and type of organ failure at admission(neurological: encephalopathy ≥2; respiratory: PaO2/fiO2 <300; circulatory: MAP <70 mmHg; renal: Creatinine ≥1.5; coagulation: Platelets $<130\times10^3$; peritoneal: presence of clinical ascites).All patients received standard of care without liver transplantation.The endpoint was death within 3 months.
Results: 82 patients of ACLF(mean age37±12, males76%) were included.The etiologies of cirrhosis were alcohol(37%), viral(40%), cryptogenic(20%), others(3%).The etiologies of acute event were alcoholic hepatitis(29%), reactivation of viral hepatitis(37%), acute viral hepatitis(15%), drugs(2%),and unknown and others(17%).At admission the meanMELD and SOFA scores were30±8 and7±3,respectively.By 3-months,55 of 82(67%) patients had died.The mortality rate correlated with the number of organs failed at admission (2-organ failure 36%, 3-organs failure68%, 4-organs failure82%, and multiorgan failure 100%;P<0.01).Both on uni- and multivariate analysis, the following types of organs significantly predicted mortality: neurological failure, renal failure and coagulation failure.
Conclusion: The 3-month mortality rate of patients of ACLF is 67%and mortality rate linearly correlates with the number of organs failure at admission.Neurological failure, renal failure and severe coagulopathy independently predicted mortality.

PE027

Acute Liver Failure in Rats with Hepatic Encephalopathy Serotonin Impact Study

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Purposes: Inquiries of 5-hydroxytryptamine (5-HT) to the influence of hepatic encephalopathy (HE) of acute liver failures (ALF) on big rat.
Methods: Sprague-Dawley big rates (80) were divided into four groups randomly and averagely: group A acted as control, while group B, C and D were used as observation of ALF. The group B, C and D were using 5% thioacetamide (TAA) in gastric lavage for creation ALF HE animal models. Group B was added by 5- HT teceptor blocking agent Cyproheptadine 10 mg/ Kg, while group C added 20 mgs/ Kg. Each group was tested by livers function, 5-HT, ammonemia ,endotoxin、brain pit magnetism resonance and brain organize histopathology by stages.
Result: Group B, C and D were obviously higher than normal matched control($t \geq 3.9$, P<0.01).The death rate in group B and C were both lower than group D ($X^2 \geq 0.63$, P<0.05) .The assay value in 72-hour of 5- HT in group D was higher than this 48-hour group.(T=6.1, P<0.01). The electricity lens checking of groups B and C showed the nerve cell swells, having the marrow kind small figure fashion, whereas in group D, a brain organize nerve cell contract, chromatin hyperplasia marrow scabbard edema denaturalization were obvious, part contain layering break crack.
Conclusion: The assay value of 5- HT was being abnormity hoist at ALF HE. The pathologic harm of brain organizations were lighter after applied 5- HT teceptor blocking agent, the death rate lowers.

PE028

Clinical Profile of Acute Liver Failure in Pregnancy

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Background: Unlike western countries, where acetaminophen poisoning and idiosyncratic drug reactions are common causes of Acute liver failure (ALF), in India, viral hepatitis account for majority. Objective of our study was to examine etiology, clinical and biochemical profile of ALF in pregnancy and to study maternal and fetal outcome.
Methods: 45 pregnant ALF patients were included consecutively after excluding chronic liver disease. 30 non pregnant female ALF patients (in reproductive-age group) were taken as controls. Detailed clinical, laboratory and sonographic evaluation was done. We compared etiology, clinical profile and complications between two groups.
Results: Viral hepatitis (76%) was the leading cause of ALF. HEV infection (60%) was common etiology in pregnant while no such predilection was seen in non pregnant patients. Ecclampsia, drugs, and acute fatty liver of pregnancy were rare. Most patients had ALF onset in III trimester (63%). Pregnant patients had more hyperacute presentation (74%) and severe encephalopathy (83%). Pregnant patients had significantly higher alkaline phosphatase, and lower serum proteins, blood glucose, serum calcium and deranged renal parameters (p<0.05). Complications like cerebral edema (45%), renal failure (32%) and hemorrhage (31%) were more common in pregnant group. Mortality was comparable in pregnant (60%) and non pregnant (56%) patients. In the group of pregnant ALF patients affected by HEV, there was significantly higher fetal loss in nonsurvivors as compared to survivors. Fetal outcome was poor with fetal loss (63%), prematurity (46%) and neonatal asphyxia (30%).
Conclusion: Hepatotropic viral infections are important cause of ALF in our region. ALF is more likely to occur in late pregnancy with more severe complications. Fetal survival is extremely poor in pregnant ALF.

PE029

Sustained and High Expression of hHGF in Mice Following Repeated Hydrodynamic Injections of Naked Plasmid

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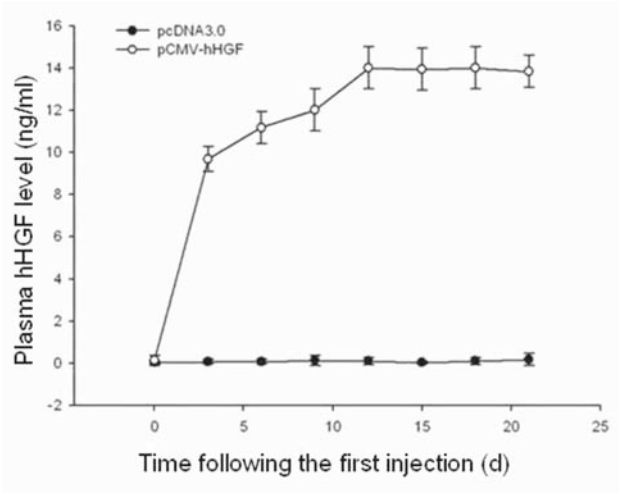
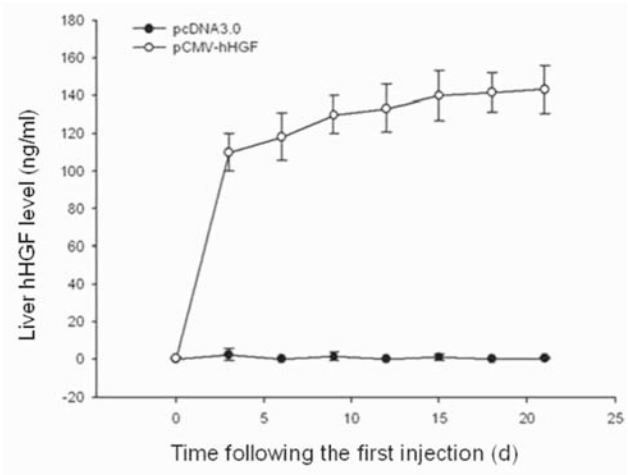
Objective: To construct human HGF expression vector (pCMV-hHGF) and characterize sustained expression of pMD-hHGF in vivo by repeated hydrodynamic injections.
Methods: Total RNA was extracted from human liver, cDNA was obtained by reverse transcription, hHGF cDNA was amplified and cloned into pMD18-T vector and the sequence were ensured by retriction endonucleases and sequencing assay. hHGF gene was dissected from pMD-hHGF and recloned into pcDNA3.0. pCMV-hHGF was analyzed by restriction endonucleases to ensure the orientation. After the plasmid was transfected into mouse livers by repeated hydrodynamic injections, we collected plasma and livers of mouse at the different time point, and then detected the expression of hHGF by ELISA.
Results: A 2187bp gene fragment was obtained and coloned into pMD18-T vector, and the sequence was correct. hHGF gene was subcloned into pcDNA3.0 vector, and then restriction endonucleases assays showed the correct orientation. At the different time point post the first hydrodynamic injection, the expression of hHGF could be detected by ELISA.

Conclusion: hHGF expression vector (pCMV-hHGF) has been successfully constructed and repeated hydrodynamic injections can promote sustained and high expression of hHGF in vivo.





PE030

Changes of Major Vessels and Spleen on CT after Splenic Artery Embolization in Recipients of Liver Transplantation

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Background: Splenic artery embolization (SAE) is performed to increase hepatic arterial flow or to decrease portal venous flow in recipients of liver transplantation (LT). Thus, the purpose of this study was to estimate SAE effect on the basis of changes in caliber of related vessels and splenic volume on pre-SAE and serial post-SAE CT scans in LT recipients.
Methods: Between 2003 and 2007, among 73 LT recipients who underwent SAE and serial follow-up CT, 43 with no compounding factor that may obscure SAE effect were included in this study. They underwent CT before and after (1week, 1month, and 1year) SAE. A radiologist retrospectively measured diameters of CA, CHA, SA, SV and splenic volume on serial CT scans. Their diameters and splenic volume on each CT were compared with those on the prior and pre-SAE CT. The difference was compared using repeated-measures ANOVA tests.
Results: CAs decreased between 1week and 1month after SAE ($P<.05$), but were stable before 1week and after 1 month. CHAs increased within 1week ($P<.05$) but decreased between 1week and 1month ($P<.05$) and remained stable after 1month. Compared with pre-SAE CT, CHAs were larger for 1month after SAE. SAs continuously decreased for 1year ($P<.05$). SVs decreased for 1 month ($P<.05$) and remained stable after 1 month. Compared with pre-SAE CT, SAs and SVs were smaller from 1week after SAE and on. Splenic volume continuously decreased for 1year except a period between 1week and 1month.
Conclusion: The increase of hepatic arterial flow persists for 1month after SAE, but returns to baseline thereafter. The decrease of portal flow may lasts for at least 1year after SAE.

Poster Exhibition – Cholangioca and Other Liver Neoplasm
Poster Session, Hall 5B

PE031

Obvious Difference of the Survivals, treated by radiofrequency ablation (RFA): Colon and Gastric Metastatic Cancers

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Background: Now, RFA has becoming an important practice of HCC therapy. In this study, we evaluated whether RFA therapy for metastatic liver tumor has a beneficial effect on patients' survival.
Methods: Forty six patients were treated by RFA for metastatic liver tumor from July 2001 through February 2008 in our hospital, of the 46, 33 patients were metastasis either form colon or stomach cancer. These 33 patients were analyzed in this investigation. Cumulative survival rate from initial RFA therapy was calculated by Kaplan-Meier method. Predictive factors for survival were identified using Cox proportional hazard regression model.
Results: The mean age of the 33 patients were 64.6 (range, 40-79). The mean size of the tumor is 28mm (range,8-70mm) and the numbers of tumor foci are 2.7 nodules↖ range,1↛ 18. The survival rates of patients treated by RFA were 49.5% at 3 years and 31.8% at 5 years in colon cancer, 15.6% at 3 years and 15.6% at 5 years in gastric cancer. In this series of 33 patients, primary cancer: colon (P=0.002 odds ratio 0.132 95%CI 0.037-0.473), younger patients (≤64) (P=0.041 odds ratio 0.312 95%CI 0.102-0.955) and multiagent chemotherapy (P=0.012 odds ratio 0.223 95% CI 0.069-0.723) were significantly correlated with better survival.
Conclusion: The survival of patients treated by RFA for metastatic colon cancers had better survival than those of gastric cancers. In addition, good indication of RFA is for metastatic colon cancers, younger patients and has to be treated by multiagent chemotherapies.

PE032

Utility of Contrast Enhanced Ultrasonography with Sonazoid in Radiofrequency Ablation (RFA) for Liver metastasis

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Background & Aims: Contrast enhanced ultrasonography (CEUS) with Sonazoid is effective for liver metastasis because enhance defect in Kupffer imaging is well delineated. The aim of this study is to investigate the detection ability of CEUS and the utility of Sonazoid in RFA for metastasis liver tumors.
Material & Methods: From January 2007 to December 2007, a total of 346 liver metastatic nodules in 87 patients (62 colon cancer, 13 breast cancer, 3 gastric cancer, 3 islet cell tumor, and 6 others) admitted to receive RFA were studied. The detection ability of liver metastasis was compared between CEUS and conventional US using enhanced CT as reference standard. The mean numbers of treatment session of RFA were compared between patient treated with CEUS assistance and historical controls matched for size and number of tumors.
Results: The detection rate was 78.6% with conventional US and 96.4% with CEUS (P=0.0004). 83 nodules in 25 patients were not detected by conventional US and detected after injection of Sonazoid. In addition, 12 nodules in 2 patients were detected not by CT but only by CEUS. The mean number of session was 1.5±0.5 as compared to 2.0±1.0 in the historical controls (P<0.001).
Conclusions: CEUS with Sonazoid is useful for detection of liver metastasis. Sonazoid is an excellent supportive agent in RFA of liver metastasis.

PE033

Development of Spontaneous Bacterial Peritonitis after Extended Hepatic Resection in a Patient without Liver Cirrhosis

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Introduction: The spontaneous bacterial peritonitis (SBP) after hepatic resection has not been reported yet in a patient without underlying liver cirrhosis, although the secondary bacterial peritonitis due to abdominal abscess is relatively common. As we experienced the first case of SBP after hepatic resection in a patient without evidence of underlying liver cirrhosis and the patient recovered well after the antibiotics treatment alone, we report this case.

Case description: A 61-year old male patient without underlying liver disease was diagnosed as stage IIIc Klatskin tumor. Right trisectionectomy with caudate lobectomy of the liver was done without acute complication. From the postoperative 18th day to the 28th day, the patient gained weight by 4.1 kg as ascites developed and showed evidence of hepatic insufficiency with prolonged prothrombin time and jaundice. CT scan, taken at the postoperative 28th day when fever occurred, showed only ascites without evidence of bowel perforation or abscess. On ascitic fluid analysis, the serum-ascites albumin gradient was 2.3 g/dL indicating newly developed portal hypertension and polymorphonuclear leukocyte (PMN) count of ascites was 1,156/mm^3. As clinical, laboratory and image findings were compatible with SBP, we started empirical antibiotics, cefotaxime, without additional intervention. Follow-up analysis of ascites at 48 hours after antibiotics treatment showed markedly decreased ascitic PMN count to 108/mm^3 and fever, leukocytosis, C-reactive protein also improved after the use of antibiotics. The patient lost weight by 4.8 kg. After two weeks' administration of cefotaxime, the patient recovered well, and was discharged without any problem.

PE034

Prognostic Factors of the Patients with Unresectable Hepatic Metastasis from Colorectal CancerTtreated by

Y. Koike[1], H. Yoshida[2], S. Shiina[2], E. Goto[2], T. Okamoto[1], T. Hamada[1], T. Murayama[1], K. Takagi[1], K. Watanabe[1], S. Matsubara[1], T. Kawase[1], M. Omata[2]
[1] Kanto Chuo Hospital, [2] Tokyo University Hospital, Tokyo, Japan

Background: The liver is the most common site of metastases from colorectal cancer. This study was conducted to clarify the prognostic factors of the patients with unresectable liver meatstases of colorectal cancer treated by percutaneous radiofrequency ablation (RFA).

Methods: From 2002 to 2008, 102 patients with unresectable liver metastases from colorectal cancer were treated by RFA, regardless of extent of hepatic metastases or extrahepatic lesions. At the initial ablation, the mean number and size of hepatic tumor foci were 6.2 7.6and 49 34 mm , respectively. More than 50% of the patients were complicated with extrahepatic metastases, and nonresponders to previous chemotherapy.Survival rates were calculated by Kapran Meier Methods. Prognostic factors of the patients were evaluated by multivariate Cox proportional hazard model.

Results: There were no procedure-related mortality. Thirteen complications (3.9%) of 4 live abscess, 2 hemoothorax, 2 intra-abdominal bleeding, and 5 others were observed. 1-, 2- and 3-year survival rates were 71%, 46% and 21%, respectively. Previous chemotherapy was significant and tumor number (more than 5), presence of extrahepatic metastases, and tumor size (more than 50mm) were marginally significant prognostic factors by multivariate analysis. When the risk grades were determined according to the number of prognostic factors, the survival rates of the patients depended.on the risk grade.

Conclusion: RFA may safely improve the prognosis of patients with unresectable liver metastases from colorectal cancer. Previous chemotherapy was the most important prognostic factor. The earlier introduction of RFA, the better may be prognosis of the patients.

PE035

Whole Genome-Wide Chromosomal Aberrations in Rare Variants of Liver Fluke-Associated Intrahepatic Cholangiocarcinoma Cell Line Based on High Resolution Microarray Comparative Genomic Hybridization Analysis

S. Dachrut[1], S. Banthaisong[1], M. Sripa[1], A. Paeyao[2], . Ho[3], S.A. Lee[3], C. Kosinski[3], M.A. Patil[3], J. Zhang[4], B. Sripa[1], X. Chen[3], C. Pairojkul[1]
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Background/aims: Carcinogenesis of intrahepatic cholangiocarcinoma (ICC)-associated liver fluke infection accumulated genetic and epigenetic alterations. Cholangiocarcinoma cell line (KKU-M213) is adenosquamous carcinoma which rare variants and not commonly found in ICC. However, interactions of liver fluke-associated ICC proceed to genetic alterations in adenosquamous carcinoma that have been not elucidated.

Objectives: To analyze the whole genome-wide genetic alterations in KKU-M213 using microarray comparative genomic hybridization. Methods: DNA of KKU-M213 and matched-sex reference were differentially labeled with fluorescence dries (Cy3 and Cy5) and mixed together with cot-1 DNA. The mixture was hybridized on array with spotting 2,464 human bacterial artificial chromosomal (BAC) clones in triplicate and mapped these directly onto human genome sequence. The genetic alterations were classified the DNA copy-number variations according to the intensities of $\log_2$ ratio (Cy3/Cy5) as DNA copy-number loss/gain and deletion/amplification.

Results: the whole genomic alterations in KKU-M213, which revealed a variety of chromosomal aberrations with a part and/or entire chromosomal gain and loss. Chromosomal amplifications were detected on 4q13.1, 4q21.1, 4q21.2, 5p tel, and 5p15.3, whereas homozygous deletions were detected on 1q23, 1q25, 1q31, 1q32-41, 1q32.2, 1q41, 1q43, 5q15-5q21, 8p22-8p23, 9p24, 10q11.2, 10q11.2-10q2.1, 10q11.2, 10q21.1 and 20q13.3.

Conclusions: The whole genome-wide genetic alterations were characterized which previously not defined in adenosquamous carcinoma. This recent advance tool is usefulness for discovering novel cancer-related gene (oncogene/tumor suppressor gene) and substitutes in *in vivo* experiment for functional testing of candidate gene involving liver fluke-associated ICC carcinogenesis.

Acknowledgements: This work was supported by Faculty of Medicine, KKU, Thailand (Grant No. I51117).

PE036

Whole Genome-Wide Chromosomal Aberrations in Rare Variants of Liver Fluke-Associated Intrahepatic Cholangiocarcinoma Cell Line Based on High Resolution Microarray Comparative Genomic Hybridization Analysis

S. Dachrut[1], S. Banthaisong[1], M. Sripa[1], A. Paeyao[2], C. Ho[3], S.A. Lee[3], C. Kosinski[3], M.A. Patil[3], J. Zhang[4], B. Sripa[1], X. Chen[3], C. Pairojkul[1]
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Objectives: To analyze the whole genome-wide genetic alterations in KKU-M213 using microarray comparative genomic hybridization. Methods: DNA of KKU-M213 and matched-sex reference were differentially labeled with fluorescence dries (Cy3 and Cy5) and mixed together with cot-1 DNA. The mixture was hybridized on array with spotting 2,464 human bacterial

artificial chromosomal (BAC) clones in triplicate and mapped these directly onto human genome sequence. The genetic alterations were classified the DNA copy-number variations according to the intensities of $\log_2$ ratio (Cy3/Cy5) as DNA copy-number loss/gain and deletion/amplification.
Results: the whole genomic alterations in KKU-M213, which revealed a variety of chromosomal aberrations with a part and/or entire chromosomal gain and loss. Chromosomal amplifications were detected on 4q13.1, 4q21.1, 4q21.2, 5p tel, and 5p15.3, whereas homozygous deletions were detected on 1q23, 1q25, 1q31, 1q32-41, 1q32.2, 1q41, 1q43, 5q15-5q21, 8p22-8p23, 9p24, 10q11.2, 10q11.2-10q2.1, 10q11.2, 10q21.1 and 20q13.3.
Conclusions: The whole genome-wide genetic alterations were characterized which previously not defined in adenosquamous carcinoma. This recent advance tool is usefulness for discovering novel cancer-related gene (oncogene/tumor suppressor gene) and substitutes in *in vivo* experiment for functional testing of candidate gene involving liver fluke-associated ICC carcinogenesis.
Acknowledgements: This work was supported by Faculty of Medicine, KKU, Thailand (Grant No. I51117).

PE037
Comparative Study of Arterial Chemoinfusion Therapy through an Implanted Port System for Patients with Intrahepatic Cholangiocarcinoma
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Background/Aims: We studied the clinical efficacy of arterial chemoinfusion therapy through an implanted port system for patients with intrahepatic cholangiocarcinoma (ICC). Thirty patients with unresectable ICC or intrahepatic recurrence of ICC after surgery were studied. Comparison was made between patients who received arterial chemoinfusion therapy through an implanted port system with adriacin and lecithin-added lipiodol emulsion in 5 patients and 5-fluorouracil (5-FU) in 7 patients. Eighteen patients were treated without port system.
Results: Disease was stable in 5 patients with adriacin and lecithin-added lipiodol emulsion and in 3 patients with 5-FU. Disease was progressed in 4 patients with 5-FU. The mean survival period was 20.8 months in patients with adriacin and lecithin-added lipiodol emulsion, 9.3 months in patients with 5-FU, and 10.5 months in patients without port system (p=0.02, p=0.04).
Conclusion: Arterial chemoinfusion therapy through an implanted port system is useful for patients with intrahepatic recurrence of ICC after surgery.

Poster Exhibition – Cholelithiasis & Biliary Tract Disease
Poster Session, Hall 5B

PE038
Dietary Factors Alter Epithelial Cells in Mice with Acute Cholelithiasis
S. Kaur[1], T. Kaur[1]
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Background: A number of dietary factors have been involved in the pathogenesis of cholelithiasis. Cholesterol overfeeding is the primary means of inducing supersaturated bile and cholesterol gallstones in animal models.Aim of the study was to investigate the rate of epithelial cell death and proliferation in gallbladder during gallstones formation.
Methods: Balb/c mice was divided into two groups control in this group animals were fed normal chow diet, High fat diet group in this group (2% cholesterol,0.5% sodium cholate, 5% butter fat and 15% coconut oil) mixed with chow diet was fed to the mice for 4 weeks. Cell apoptosis and proliferation was assayed in gallbladder epithelial cells. Histological analysis of gallbladder sections were done with hematoxylin and eosin staning.
Results: Mice fed high fat diet had apoptotic as well as necrotic epithelial cells. Rate of proliferation was enhanced after 24 and 48 hrs in mice fed high fat diet group as compared to the control group. The histopathological section of control gallbladder has normal morphology whereas gallbladder wall thickness was markedly increased; epithelial cells appeared more elongated in mice fed high fat diet.
Conclusion: Results obtain show that high fat diet markedly induced biliary epithelial cell proliferation and biliary epithelial cell apoptosis. It has been determined that when there is an injurious stimulus that leads to apoptosis, it is later followed by reparative proliferation and when there is no injurious stimulus, apoptosis occurs late in the course as part of remodeling.

PE039
Success Rate of ERCP for Identification and Stenting in Obstructive Jaundice Caused by Malignancy in Cipto Mangunkusumo Hospital October 2004 — July 2008
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Background: Obstructive jaundice can be caused by malignancy. The treatment can be drainage by biliary stenting. In advanced malignant jaundice, the stent placement is often difficult.
Objective: To evaluate the success rate of malignant obstructive jaundice evaluation of ERCP and success rate of stent placement.
Methods: Retrospective study based on data of ERCP from October 2004 until July 2008.
Results: We evaluated 139 patients who has done ERCP examination, 131 (94,2 %) patients have clinical diagnosis of obstructive jaundice. There were 73 (55,7%) male and 58 (44,3%) female, age range 20 – 84 (median age was 51).
There were no malignancy in 66 (50,4 %) patients; malignancy in 48 (36,6%) patients and 17 (13%) patients need further evaluation.. From 114 patients, 57 (50 %) patients attempted to have stent placement, 50 (43,9 %) patients do not and 7 (6,1 %) patients have no data.
We done descriptive study on 57 patients attempted to have stent placement, 32 (56,1 %) patients succeed in stent placement whereas 25 (43,9 %) failed. Malignancy was showed to be a factor of stent failure (malignancy: 23 fail and 10 success (30,3 %) vs non malignancy: 2 fail and 22 success (91,7%)).
Conclusion: ERCP can identify the cause of obstructive jaundice in 87 % patients. The success rate of stent placement was 56,1 %. The success rate of biliary stenting in malignant obstructive jaundice was 30,3 % whereas in non-malignant cases was 91,7 %. Papillary carcinoma was the most frequent cause of malignant obstructive jaundice.

PE040
Cystobiliary Fistula in Hepatic Hydatid Disease: Diagnostic and Therapeutic Challenge
A. Shawky[1], O. El-Abd [1], M. Salama[1], F. Ismail[2], M. Taher[2]
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Background: In Hydatid disease of the liver cystobiliary fisula (CBF) constitutes an entity characterized by the occurrence of a life-threatening cholangitis with increased morbidity.
Aim: To study the different diagnostic and therapeutic aspects of cystobiliary fistula in hydatid disease of the liver.
Patients and Methods: Fourteen patients with complicated cysts were divided into 2 groups; group A: nine patients presented with cholangitis, and group B: five patients had history of jaundice. In all patients, the diagnosis of CBF was confirmed by ERC (Endoscopic Retrograde Cholangiography). Preoperative endoscopic sphincterotomy (ES) was done in group A with retrieval of hydatid daughter cysts. Seven patients (subgroup A1) were subsequently submitted to surgery entailing endocystectomy in 5 and hepatic resection in two. The remaining 2 patients in group A (subgroup A2), were managed by endoscopic therapy only. Patients of group B (n=5), were not submitted to preoperative ES and were subsequently managed by hepatic resection in one patient and endocystectomy in four.
Results: There was no mortality in the studied group. Postoperative bile leak occurred in four cases in group B. In contrast, none of the patients who were submitted to preoperative ES (subgroup A1) had bile leak. All patients received albendazole treatment.
Conclusion: ERC is important in confirming the diagnosis of CBF. Also, therapeutic ERC has a place in the treatment algorithm of CBF as it was found to be a safe and a reliable therapeutic alternative especially in high risk patients for surgery.

PE041

Contrast-Free Air Cholangiography Assisted Unilateral Plastic Stenting in Malignant Hilar Biliary Obstruction: A New Method

V. Singh[1], G. Singh [1], G.R. Verma[1], V. Gupta[1], S. Ghosh[1], R. Gupta[1], R. Kapoor[1], N. Sharma[1], A. Bhalla [1], S.K. Mahi[1]

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Background: Endoscopic palliation in malignant hilar biliary obstruction requires ERCP. However, contrast injection leads to cholangitis. Recently, contrast-free metal stenting with or without MRCP has shown encouraging results. However, MRCP and metal stents are costly. There have been no reports on the use of air cholangiography in these patients.
Methods: We prospectively studied the role of air cholangiogaphy assisted unilateral plastic stenting in these patients.
Results: Ten patients with unresectable malignant hilar biliary obstruction were studied. Air cholangiography detected type II obstruction in 8 and type I in 2 patients which is similar to MRCP. All patients underwent unilateral plastic stenting. A successful endoscopic drainange was achieved in 100% patients. Cholanngitis occurred in none and there was no 30-day mortality. No major complications were observed.
Conclusion: Air cohlangiography assisted plastic stenting in these patients is a safe and effective method of palliation. However, it requires a larger study.

PE042

An Unusual Case of IgG4-related Sclerosing Cholangitis of the Peripheral Bile Duct with no Pancreatic Lesion

H. Ryuzaki[1], T. Yamamoto[1], S. Masuoka[1], S. Kobayashi[1], K. Oyama[1], S. Ohshiro[1], Y. Hiroi[1], C. Matsuoka[1], M. Ogawa[1], N. Okano[1], K. Nakai[1], S. Amaki[1], N. Tanaka[1], M. Moriyama[1], Y. Katsura[2], M. Sugitani[2]

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Introduction: A description of IgG4-related sclerosing cholangitis (IgG4-SC) without pancreatic lesion has recently been reported. In addition to imaging, diagnosis relies on findings of elevated serum IgG4 and immunodetection of invading IgG4-positive cells. Here we report a case of IgG4-SC with only slight common bile duct abnormalities and normal pancreatic findings.
Case Study: A 65-year-old man suffering from cephalalgia, general malaise and muscle ache was admitted to our hospital. His blood examinations on admission revealed eosinophilia, mild anemia, liver dysfunction and an IgG level of 2820 mg/dl (IgG4 374 mg/dl). Although ERCP did not reveal typical stenosis or irregularities of the bile duct wall, visualization of peripheral bile ducts was slightly impaired. Echography revealed thickening of the intrahepatic bile duct and gallbladder walls as well as adenopathy. Due to a gradual increase in pleural effusion and a progression of anemia, oxygenation was begun on the seventh day of illness. Based on the combination of eosinophilia, elevated serum IgG4 levels, image findings and a negative result for helminth, IgG4-SC was suspected. Liver biopsy was performed on the ninth day of illness and steroid therapy was initiated, after which symptoms and laboratory findings improved. The IgG4-positive plasmocytic infiltrate present around the portal region at the time of biopsy disappeared within eight months of treatment.
Summary: This case displayed two unusual features that are not generally observed with IgG4-SC: complications due to hemolytic anemia, and destruction of the peripheral bile duct with little damage to the common bile duct.

PE043

A Case of Relapsing IgG4-related Sclerosing Sialadenitis and Autoimmune Pancreatitis Associated with CA19-9 Elevations at Exacerbation

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[1] *Division of Gastroenterology and Hepatology, Department of Medicine, Nihon University School of Medicine,* [2] *Department of Pathology, Nihon University School of Medicine, Tokyo, Japan*

Introduction: Various systemic diseases have been reported to be associated with IgG4. Although steroids are effective in the treatment of IgG4-related diseases, there are some reports on relapses with their treatment, and cases are often difficult to differentiate from malignant diseases. We encountered a case of autoimmune pancreatitis with sclerosing cholangitis (AIP-SC), in whom CA19-9 was elevated with episodes of exacerbation and an elevated serum IgG4 concentration. IgG4 staining was also useful for the diagnosis.
Case Study: An 81-year-old woman noticed tumors beneath the bilateral jaw and was found to have an elevated level of CA19-9 (304) seven years previously. Her left submandibular gland was removed and diagnosed as sclerosing sialadenitis. Four years previously, she was diagnosed as having diabetes mellitus complicated by a recurrence of CA19-9 (419) elevation and liver dysfunction. Cholangiocarcinoma was suspected based on ERCP, but was not confirmed by histologic findings of bile duct biopsy. Elevated IgG4 and other test results established the diagnosis of AIP-SC, so steroid therapy was initiated, after which symptoms and laboratory findings improved. This recurrence of CA19-9 elevation (634) was diagnosed as a relapse of AIP-SC based on an increased IgG4 level and histologic findings.
Summary: Some papers have reported that IgG4-positive cells are found in liver tissue in this disease, but such cells were not detected in the liver specimens in our case. This might be because intra-liver sites may have differed in the degree of morbidity, and long-term steroid therapy might have suppressed inflammation in the liver tissue.

PE044

Pathophysiological Conditions in Cholelithiasis Formation in North Indian Population.

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Background: Cholelithiasis, a gallstone disease is major cause of morbidity affecting millions of people throughout the world. Aim of the present study was to investigate the predisposing factors that lead to the formation of gallstones.
Methods: The study was carried out on gallstones, bile and serum of patients. Gallstones and bile were divided into three groups' cholesterol, pigmented and mixed gallstones. Blood of the patients was divided into two groups with gallstones and without gallstones patients. Trace elements and various biochemical estimations were carried out. Clinical history of the gallstones patients was recorded from the hospital records.
Results: Trace elements analysis in bile and gallstones showed that calcium is the main element in all the three types of stones. Iron was the main element in mixed gallstones. In pigmented gallstones magnesium and zinc were the major trace elements. Liver function tests and lipid peroxidation levels in sera were significantly increase whereas, antioxidant enzymes concentrations in sera were significantly decreased in patients with gallstones. Clinical history of the gallstones revealed the cases had jaundice, diabetes mellitus and estrogen replacement therapy respectively.
Conclusion: Results suggest that trace elements in gallstones and bile as well as clinical history of patients with chronic cholelithiasis could be the underlying factor in the pathogenesis of gallstones. The concentration of products derived from the free radicals reactions increases with degree of inflammation. Such a condition increases risk of bile saturation which would further contribute to the progress of gallstones formation.

PE045

Gallbladder Diseases among HIV/AIDS Patients in Ciptomangunkusumo Hospital, Jakarta

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[1] *Faculty of Medicine University of Indonesia, Jakarta*

Background and Aims: Diseases of the biliary tree and gallbladder are being described with increasing frequency among patients with the acquired immunodeficiency syndrome (AIDS).Therefore there is a need to do a research about the risk factors of gallbladder diseases in HIV/AIDS patients. So it can be useful to clinicians to predict the possibility of a patient having gallbladder disease and consider the options of further plans. The aim of this study was to find the prevalence and varieties of gallbladder diseases in HIV/AIDS patients.
Methods: A cross sectional study was performed in patients with HIV/AIDS who visited Ciptomangunkusumo Hospital, Jakarta. The risk factors (route of

transmision,CD4,ARV,hepatitis) and clinical presentations were studied.Ultrasonography examinations were performed to detect gallbladder annormalities.
Results: 68 patients with HIV/AIDS match the study criteria. There were gallbladder abnormalities in 22 (32.4%) subjects, which 19 (27.9%) had acalculous cholecystitis and 3 (4.4%) had cholecystitis with cholelithiasis. On bivariate analysis, there was a significant association between abdominal pain, jaundice and the use of ARV to gallbladder abnormalities (p = 0.000; 0.000; 0.004; 0.012). However, there was no association between age, sex, transmision route of HIV, hepatitis and CD4 to gallbladder abnormalities.
Conclusion: HIV/AIDS patients are susceptible to opportunistic gallbladder infection. Acalculous cholecystitis is the most frequently encountered gallbladder abnormalities of HIV/AIDS patients in this study.

PE046
Prevalence and Related Factors for Gallbladder Polyps: A Hospital-based, Cross-sectional Study
S.W. Lai[1], H.C. Lai[1], K.F. Liao[1], C.S. Liu[1], T. Lin[1], C.C. Lin[1]
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Background: The aim of this study was to assess the related factors for gallbladder polyps.
Methods: This was a hospital-based, cross-sectional study. We retrospectively analyzed the medical records of all the subjects undergoing health examination at one medical center located at Taichung city in Taiwan from 2000 to 2004. Excluding subjects with cholecystectomy, totally, 5481 subjects (3070 men and 2411 women, mean age 49.2 12.3 years) were enrolled in this study. Odds ratio (OR) and 95% confidence interval (CI) were expressed by using a multivariate logistic regression analysis.
Results: Ultrasonographic findings revealed a normal gallbladder in 4920 subjects (89.8%), polyps in 265 subjects (4.8%), stones in 278 subjects (5.1%), mixed stones/polyps in 18 subjects (0.3%). The overall prevalence of gallbladder polyps was 5.1% [(265+18)/5481], with significantly higher in men than in women (7.0% vs 2.9%, P <0.001). After controlling for the other covariates, multivariate logistic regression analysis showed that the independent related factors for gallbladder polyps were male gender (OR=2.24, 95%CI=1.66-3.01), HBsAg positive (OR=1.46, 95% CI=1.08-1.97), and cigarette smoking (OR=1.32, 95% CI=1.00-1.72). With age 20-39 as a comparison, age 40-64 was also a related factor (OR=1.55, 95% CI =1.12-2.15). There was no evidence of a correlation between gallbladder polyps and clinical parameters, such as obesity, lipid profiles, hepatitis C virus infection, liver function tests and alcohol use. Conclusions: Male gender, HBsAg positive, cigarette smoking, and age 40-64 are the related factors for gallbladder polyps, respectively.

Poster Exhibition – HBV
Poster Session, Hall 5B

PE047
The Follow-Up Ymdd Variants in Lamivudine-Resistant Patients after Long-Term Stopping Therapy
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Background: Among the approved nucleos(t)ide analogues therapies for chronic hepatitis B, lamivudine was used widely, sometime inappropriate in practice due to high safe and low price but lamivudine is associated with the highest rate of drug resistance.
Objectives: the aim of the study was to determine the YMDD variants after long-term stopping treatment in lamivudine-resistant patients using more sensitive technique.
Methods: 16 blood samples from lamivudine resistant patients were collected after long- term stopping therapy. The YMDD variants are detected using technique PCR Restriction Fragment Length Polymorphism (PCR-RFLP) at HCMC University Medical Center
Results: After stopping lamivudine treatment 25 months (6-72 months) YMDD mutants were detected in 14 (87,5%) of 16 patients. Among them 13 (92.9%) had the most important M204V/I mutant, 1(7 1%) had accompanying L180M mutant. It means that once drug resistant mutants have been selected, they are archived for the long time even if treatment is stopped. Many of patients have the features characterized for the patients in immune tolerance phase (young age, HbeAg positive, normal ALT). The treatment of this group is not strongly recommended due to low efficacy and high risk of drug resistance.
Conclusion: The most important M204V/I mutant was still detected with significant portion of the virus population after long-term stopping therapy in lamivudine resistant patients. The options of retreatment for this patients when necessary are limited due to cross-resistance. The management of chronic hepatitis B should be followed strickly the recommendations of specialized association to avoid this problem.

PE048
Increased Liver Stiffness Measurement by Transient Elastography in Severe Acute Exacerbation of Chronic Hepatitis B
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Background/Aim: Whether liver stiffness measurement (LSM) using transient elastography is reliable to assess liver fibrosis in the settings of severe acute exacerbation of chronic hepatitis B (CHB) is uncertain.
Methods: We prospectively recruited consecutive patients with severe acute exacerbation of CHB (alanine aminotransferase or ALT >10x upper limit of normal). The relationship of ALT levels and LSM were serially assessed and liver biopsy was performed after ALT normalization.
Results: Eleven patients (10 male, median age 43 years) were followed up for 25 weeks; 9 patients received anti-viral therapy. Overall, LSM was positively correlated with ALT levels (r=0.67, P<0.001). At initial presentation, the median serum ALT and LSM was 1136 (581–2210) IU/l and 26.3 (11.1–33.3) kPa. A progressive reduction in LSM was observed during subsequent visits in parallel with the reduction of ALT levels. Even after the normalization of ALT at week 12, LSM of 9 patients continued to drop at week 25. At the last visit, the median ALT was 27 (11–52) IU/l and LSM was 7.7 (4.7–10.8) kPa. Among the 5 patients who had liver biopsy performed at week 25, 4 patients had F2 fibrosis (LSM 5.7–8.1 kPa) and 1 patient had F3 fibrosis (LSM 8.6 kPa).
Conclusions: LSM using transient elastography may misdiagnose liver cirrhosis in patients suffering from severe acute exacerbation of chronic hepatitis B. LSM should be assessed after normalization of ALT levels in order to accurately assess the degree of fibrosis.

PE049
Seroepidemiology of Hepatitis B and Hepatitis C virus Infection in People Receiving Health Checkups—A Hospital-based Study
H.C. Lai[1], S.W. Lai[1], K.F. Liao[1], C.S. Liu[1], T. Lin[1], C.C. Lin[1]
[1] *China Medical University Hospital, Taichung, Taiwan*

Background: In 2007, chronic liver disease was the seventh leading cause of death in Taiwan. Hepatitis B and hepatitis C are two major causes of chronic liver disease in Taiwan. The purpose was to investigate the seroepidemiology of hepatitis B surface antigen (HBsAg) and hepatitis C virus (HCV) antibody in Taiwan.
Method: This was a hospital-based cross-sectional study. We analyzed viral hepatitis data from 2695 subjects who received health checkups at one medical center in Taichung from 2003 to 2004. All subjects were divided into three age groups, including 20-39, 40-64 and 65. This study emphasized the prevalence of HBsAg and HCV antibody by gender and age. The statistical analysis was performed by t test and ^{2}.
Result: There were 1526 men (56.6%) and 1169 women (43.4%). The mean age was 49.2 (standard deviation 12.2, range 20-84). The overall prevalence of HBsAg was 14.7%, with statistically significant difference(SSD) between gender (17.4% for men vs 11.2% for women, p <0.001). The prevalence of HBsAg was decreased with age in men, with SSD (p <0.001), and also decreased in women, without SSD (p =0.08). The overall prevalence of HCV antibody was 5.2%, without SSD between gender (4.8% for men vs 5.7% for women, p =0.272). The prevalence of HCV antibody was increased with age both in men and in women, with SSD (p <0.001).
Conclusion: We hope this study can provide the epidemiological data for further studies of hepatitis B and hepatitis C virus infection in Taiwan.

PE050

The Relationships between the SNP of E-selectin and Disease Progression in a HBV-infected Chinese Population

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E-selectin is revealed to facilitate leukocyte adhension to the endothelium and migration into inflamed tissue in inflammatory diseases. Chronic hepatitis B virus infection is regarded as a chronic inflammatory process. To examine the possible involvement of E-selectin in the etiology of chronic HBV infection, we analyzed two polymorphisms of E-selectin and determined the plasma souble E-selectin levels in patients with chronic HBV infection and controls. The frequency of C allele of the A561C polymorphism was significantly increased in patients with LC campared with controls. No significant positive association was observed between the G98T polymorphism and chronic HBV infection. But in patients with LC, divided according to the Child-Pugh classification, the frequency of T allele was of significant difference between Child'class A and class B plus C. Plasma Levels of soluble E-selectin were significantly increased in patients with chronic hepatitis and liver cirrhosiscompared with controls. In the liver cirrhosis group, levels of sE-selectin were significantly decreased from Child' class A to class C. In each group, patients with C allele of the A561C polymorphism showed higher soluble E-selectin levels than those with A allele. This is the first report describing the association between E-selectin polymorphisms and HBV-related hepatic fibrosis. Our data showed the A561C polymorphism of E-selectin gene is associated with disease progression in patients with HBV infection and controls the expression of plasma soluble levels, the G98T polymorphism may be related to fibrotic severity in patients with liver cirhosis.

PE051

Treatment of Chronic Hepatitis B (CHB) Patients with Normal Alanine Aminotransferase Level Using Nucleoside Analogues:
A Preliminary Study with Results at 1 Year

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Background: Chronic hepatitis B (CHB) patients with high serum HBV-DNA and normal serum alanine aminotransferase (ALT) levels might be considered for treatment if histopathological findings show fibrosis stage 2 or more. However, to our knowledge there is no recommendation with regard to the therapeutic agents for this group of patients.
Objective: This study was aimed to evaluate the efficacy of nucleoside analogues (entecavir or telbivudine) in treating chronic hepatitis B patients with high serum HBV-DNA and normal serum ALT levels.
Patients and method: This was an open-label study in CHB patients with high level serum HBV-DNA levels between January 2007 and October 2008. Patients were included if they showed normal serum alanine aminotransferase (ALT) level at two measurements within a 3-month interval and had fibrosis stage $\geq$ 2 on liver biopsy specimens. Patients were treated with entecavir 0.5 mg/day or telbivudine 600 mg/day. The primary endpoint was the reduction or undetectable of serum HBV-DNA at 24 week and 48 week of treatment, while the secondary endpoint was hepatitis B e antigen (HBeAg) seroconversion.
Results: During a 2-year period, 37 CHB patients with high level serum HBV-DNA with normal ALT two times with 3 months interval underwent a liver biopsy. Twenty-eight (75.7%) of 37 pts showed fibrosis stage $\geq$ 2 on histological findings (Metavir score). Twelve of these 28 patients received nucleoside analogues, 7 (58.3%) of them were men. Patients' median age was 42 (range: 24-52) years. There were 5 patients with stage-2, 6 patients with stage-3 and 1 patient with stage-4 fibrosis. Eleven (91.7%) patients had genotype B virus. At baseline, the mean serum ALT level was 32 $\pm$ 11.8 U/L and mean HBV-DNA level was 2.48 x 10^6 IU/mL, ranging from 1.23 x 10^3 to 2.4 x 10^7 IU/mL. Six patients received entecavir and the other six received telbivudine therapy. Undetectable HBV-DNA was achieved by 9 (75.0%) patients at week-24 and 2 (16.7%) patients at week-48 of treatment. One patient who had the highest HBV-DNA level had viral load reduction to 1.6 x 10^4 IU/mL at week-48 of treatment. Two out of 5 patients with positive HBeAg achieved HBeAg seroconversion at week-48 of treatment.
Conclusion: This preliminary study has shown that nucleoside analogues might be considered in the treatment for chronic hepatitis B patients with high serum HBV-DNA and normal serum aminotransferases levels.

PE052

Down-regulation of PD-1 Expression on Lymphocytes in Chronic Hepatitis B Patients with Pegylated Interferon α-2b Treatment

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Background: The dysfunction of T cells may represent a mechanism of hepatitis B virus (HBV) persistence. Programmed death-1 (PD-1) and its ligands, PD-L1/PD-L2, are new members of CD28/B7 family, as co-stimulatory molecules expressing on T cells and Antigen Present Cells (APCs). Their engaging can downregulate the T cells function, including proliferation, cytokines secretion and cytotoxicity. In periphery blood, PD-1 was upreguated on virus specific-T cells, leading to the impairment of T cells. Blocking the PD-1/PD-L can improve the function of T cells.
Methods and Patients: 21 patients with chronic hepatitis B (CHB) were treated by pegylated IFN α-2b (PegIntron from Schering-Plough, once a week, 0.5 or 1 g/kg/weight). The periphery blood were taken at 0 weeks, 4 weeks, 8 weeks, and 12 weeks. Periphery blood mononuclear cells (PBMC) were isolated from fresh heparinized blood by Ficoll-Hypaque (density: 1.077g/L) density gradient centrifugation. Then the cells were incubated with APC-conjugated anti-PD-1 antibodies. The PD-1 expression on lymphocytes was detected by flow cytometry (FCM).
Results: The PD-1 expression on lymphocytes at 0 weeks was 14.47±5.8%, at 4 weeks was 9.68±3.75%, at 8 weeks was 6.95±2.39%, at 12 weeks was 6.08±1.31% (p<0.05).
Conclusion: Treatment with IFN α-2b can downregulate the PD-1 expression on lymphocytes and may partially restore the function of T cells.

PE053

Entecavir Therapy in Hepatitis B Related Acute-on-Chronic Liver Failure

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To investigate the effects of nucleoside analogs therapy in hepatitis B related acute-on-chronic liver failure, we treated 55 HBV related acute-on-chronic liver failure patients with entecavir. as control, the remaining 74 were not treated with nucleoside analogues. Results show the survival rate of entecavir therapy group has no
significantly difference with none-treated group (P>0.05). Although entecavir greatly reduced HBV replication during different therapy times (P<0.001), the MELD score and liver function (ALT, albumin, bilirubin, prothrombin time) had no significant changes (P>0.05). Further more, we analyzed the MELD score and liver function in different HBV-DNA level patients .No significantly difference was observed (P>0.05). There is no significant correlation between HBV-DNA level and MELD score in different
therapy times (P>0.05).The HBV-DNA level between patients with over 3 months and less than 3 months survival patients showed no significant difference either (P>0.05). However, MELD score and some parameters of liver function (albumin, bilirubin, prothrombin time) showed significant difference (P<0.05). These results suggest HBV-DNA loading may not be a direct factor to increased liver injury and suppression of HBV replication may not reduce the severity of liver failure in HBV related acute-on-chronic hepatitis.

PE054

Outcomes of Entecavir (ETV) Therapy in Chronic Hepatitis B Patients with No or Suboptimal Response with Adefovir (ADV)

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Background: Before the availability of ETV, it was common to use ADV for treatment of chronic hepatitis B patients. Primary nonresponse and suboptimal response is a common problem with ADV treatment.

METHODS: We wanted to study the outcomes of Entacavir therapy in this subset of patients. Study was conducted between April 2007 to April 2008. We enrolled 30 CHB patients who had Non response to 12-24 weeks of 10 mg ADV therapy. Non response and suboptimal response was defined as non dimunition of at least one log of HBVDNA from baseline after 12 weeks of therapy and Persistence of 3 log10 after 24 weeks of therapy respectively.They were switched to 1mg entacavir before breakfast daily for at least 12 months.They had serial ALT CBC and HBVDNA measured every 12 weeks.
Results: Out of 30 patients 20 male and 10 were female. Only 8 patients were HBeAg(+).Mean HBVDNA level prior to ADV exposure was 6.5 log copies/ml.Mean duration of exposure to ADV was 26 weeks.5 patients lost to F/U.We did intention to treat analysis. 15 out 30 (50%) patient has, undetectable level of HBVDNA after 12 weeks of therapy labelled as group 1.6 out of 30 (20%) had HBVDNA level reduced by a mean of 3 log 10 copies/ml labelled as group 2.on week 24 treatment analysis all 15 patients from group 1 was HBVDNA undetectable, 2 additional patients from group 2 had undetectable HBVDNA. Conclusion: Entacavir therapy results in rapid suppression of HBVDNA levels in majority of patients with primary nonresponse or partial non response to ADV therapy.

PE055

Association of HBV Genetic Variability with Response to Lamivudine Therapy in Chronic Hepatitis B Patients with Serum ALT Over 5 Times Upper Limit of Normal

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Background: Except for serum ALT level, baseline factors predictive of therapeutic response to lamivudine in patients with HBeAg-positive chronic hepatitis B remain largely unknown. We thus studied the influence of pre-therapy viral factors on end-of-treatment responses to lamivudine therapy.
Methods: A total of 116 treatment-naïve HBeAg carriers who had pre-therapy serum ALT level> 5xULN and received lamivudine for 18 months reimbursed by the National Health Insurance were prospectively enrolled. HBeAg seroclearance and combined HBeAg seroclearance, ALT normalization as well as undetectable HBV DNA at the end of therapy were defined as primary and secondary endpoint, respectively. The pre-therapy viral factors including viral load, genotype, precore stop codon (PC)/ basal core promoter (BCP) status, and pre-S deletion were determined to correlate with therapeutic endpoints.
Results: The frequency of patients with detectable PC mutation (G1896A), BCP mutation (A1762T/G1764A), and pre-S deletion at baseline was 22.4%, 21.6%, and 12.1%, respectively. After completing 18-month lamivudine therapy, overall HBeAg seroclearance rate was 56.0%. Patients with HBeAg seroclearance had a higher prevalence of baseline PC mutation than those without (30.8% vs, 11.8%, P= .015). By multivariate analysis, the odds ratio of patients with PC mutation to develop HBeAg seroclearance was 3.33 (P= .024). In addition, the presence of PC mutation also correlated with the combined response.
Conclusions: For HBeAg-positive chronic hepatitis B patients with serum ALT> 5xULN, PC mutation could predict a higher HBeAg seroclearance rate at the end of 18-month lamivudine therapy.

PE056

The Efficacy of Adefovir Dipivoxil against All Patterns of Lamivudine Resistant Hepatitis B

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Background: Our aim was to evaluate the efficacy of adefovir dipivoxil (ADV) and determine patient-dependent or laboratoroy variables that are predictive of HBeAg loss and IVR for hepatitis B patients resistant to lamiduvine. Also we evaluated the activity of ADV against all patterns of lamivudine-resistant HBV.
Method: 179 HBV-infected patients with lamivudine resitance received ADV for ≥6 months. Quantitative HBV DNA, HBeAg/anti HBeAg, ALT was checked every 3-6months. The HBV polymerase of 161 patients were sequenced for baseline samples to determine the presence of lamivudine resistance mutations.
Result: There is no significant difference in all patterens of HBV mutation about HBV DNA reduction at 24W, 48W, 72W. There is no significant difference in all patterens of HBV mutation about ALT normalization at 24W, 48W, 72W.
Conclusion: Adefovir dipivoxil demonstrated similar potent anti-HBV efficacy regardless of the different patterns of lamivudine-resistant HBV mutations.

PE057

Cirrhosis Hepatitis B Virus Related Patients Treated with Molecular Adsorbent Recircuating System

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Background: Hepatitis B (HBV)-related end-stage liver disease is one of the most common indication for liver transplantation (LT). A number of patients dying while on the waiting list or removed because of being too ill is progressively increasing. We valued the possibility to improve the Model End-stage Liver Disease (MELD) of patients awaiting liver transplantation using a albumin dialysis: Molecular Adsorbent Recirculating System (MARS).
Methods: We treated 34 patients (19 male and 15 female) with a mean age 49.5. Inclusion criteria: serum bilirubine > 15mg/dl, MELD ≥ 25, INR > 2.1, Encephalopathy Grade ≥ II. All patients were treated with MARS mean 9±2.5 hr cycles and mean 9 treatments (range 3-15). All patients received standard medical treatment in addition to MARS dialysis. The patient survival was valued at six months.
Results: We obtained a significant change of cytokines levels as Interlukine 6 ($p< 0.02$) and Tumor Necrosis Factor alfa ($p<0.01$) in association with an improvement of kidney, hepatic and hemodynamic parameters. At the end of MARS treatments we observed a significant reduction of MELD score ($p<0.003$). The results of MELD show a rebound effect between the end of treatment and the follow up at six months without returning at starting values ($p<0.005$). Twenty patients lived and 14 dead for clinical complications.
Conclusion: The improved MELD score with MARS gave patients on LT waiting list more time of survival, thus allowing them more opportunity for liver transplantation.

PE058

Entecavir for Treatment of Lamivudine-refractory Patients Chronic Hepatitis B

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Lamivudine treatment is associated with frequent development of resistant hepatitis B virus. This incidence especially is higher in longer time of treatment and loss of treatment benefit. Entercavir is a new antiviral agent shown its high efficacy even in cases of mutations with Lamivudine resistance. In this study, we evaluate the efficacy, the safety of Entercavir in treatment of Lamivudine-refractory patients chronic hepatitis B.
Sixty chronic hepatitis B patients with evidence of Lamivudine resistance were randomly divided into two groups in proportion of 3:1. Group I (n=45) used Entecavir 1mg/day, group II (n=15) used Lamivudine 100mg/day. Treatment time was 48 weeks. Histology, ALT, HBVDNA were evaluated in the end of the treatment. Age, sex, ALT, HBVDNA, genotype, HBeAg were analyzed to evaluate their influences to the treatment.
The results have showed HBVDNA<2000 copies/mL in Entecavir group 37.78% vs. 0% Lamivudine group ($p<0.01$). HBVDNA negative in Entecavir group was 17.77% and incidence of seroconversion of HBeAg was 8.82%. ALT was normal in Entecavir group 77.77% vs. 26.66% in Lamivudine group ($p<0.001$).Histologic improvement in Entecavir group was 37.77% vs.6.66% in Lamivudine group ($p<0.05$). Patients with HBeAg negative, genotype B, low viral load were shown better results.
Entecavir was shown to be efficacious in treatment for chronic hepatitis B patients experienced with Lamivudine resistance. Entercavir is safe, with almost no side effects. Factors such as HBeAg negative, genotype B, low viral load seems to be better in response to treatment. Recurrence or mutation of Entecavir resistance should be studied further in future.

PE059

Comparison of HBsAg Loss Rate According to Age Difference in Children with Chronic Hepatitis B by Long-term Lamivudine Therapy

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Backgrounds: By analyzing the characteristics of children with chronic hepatitis B who have lost HBsAg by long-term lamivudine treatment, the selection of target patients could be relevantly predictable in the treatment of chronic hepatitis B in children.
Methods: A total of 75 HBeAg positive children (< 18 y-o) were recruited who have visited Kyungpook National University Hospital from Mar. 30, 1999 to May 8, 2008. They were treated with lamivudine for at least 6 months. HBeAg seroconversion occurred during lamivudine treatment in 49 out of 75 children. They were divided into HBsAg clearance and non-clearance group. Parameters influencing treatment results were analyzed according to HBsAg loss.
Result: Thirteen out of the 49 (26.5%) patients with HBeAg seroconversion were classified as HBsAg clearance group, while 36 (73.5%) as non-clearance group after lamivudine treatment. Twenty five of 49 patients with HBeAg seroconversion were under 6 years old, in 10 (10/25, 40%) of whom HBsAg loss occurred as well. Twenty four of 49 patients were over 6 years old, in 3 (3/24, 12.5%) HBsAg loss occurred, that showed significantly difference (p-value= 0.029, OR: 4.667, CI: 1.094-19.902) compared to younger group. Age was significantly lower in HBsAg clearance group (5.1±4.3 years) than non-clearance group (8.2±5.0 years) (p=0.043), but no difference was observed in other parameters. Anti-HBs appeared in 12 patients.
Conclusion: In the treatment of HBeAg positive chronic hepatitis B with lamivudine, age was significantly lower in HBsAg clearance group than non-clearance group.

PE060

Intrahepatic Expression of PD-1, PD-L1 and PD-L2 in Chronic Hepatitis B Patients

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Background: Dysfunction of T cells may represent a mechanism of hepatitis B virus (HBV) persistence. Programmed death-1 (PD-1) and its ligands, PD-L1/PD-L2, are members of CD28/B7 family, was reported to transfer inhibitory signal, leading to the dysfunction of T cell.
Methods: Immunohistochemical analysis of tissue samples from 56 patients with chronic hepatitis B (CHB), 12 acute hepatitis B (AHB) patients and 10 health controls was performed.
Results: PD-1 was positively expressed on lymphocytes infiltrating the portal area.PD-L1 expression was the same as PD-1,also expressed in interlobular.PD-L2 expressed on kupffer cells and dendritic cells.PD-1-,PD-L1-,and PD-L2-positive cells express index of CHB patients were much more than that of health controls and AHB patients($p <$ 0.05).Between groups in CHB,the expression rate increase with the disease progression ($p < 0.05$).
Conclusion: Overexpression of PD-1 and PD-L within liver might be involved in inhibiting the immune response and be a mechanism of chronicity in HBV infection.

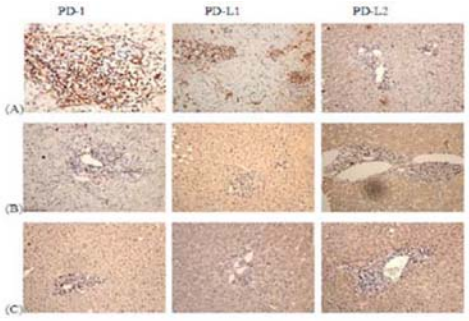

Fig.1 The expression of PD-1, PD-L1, and PD-L2 in liver tissues of CHB(A), AHB patients(B), and health controls(C)(×200). PD-1 was positively expressed on lymphocytes infiltrating the portal area predominantly and also on inflammatory cells infiltrating necrosis area in interlobular. PD-L1 expression was more extensive, apart from the area said above, also expressed on hepatocytes and sinusoidal endothelial cells, especially the area surrounding the portal area. PD-L2 mostly expressed on kupffer cells and DCs in portal area as well as interlobular. In healthy controls a few PD-1-, PD-L1- and PD-L2-positive cells were observed.

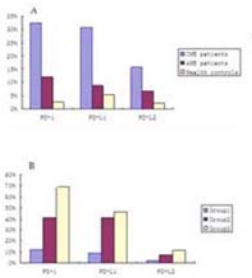

Fig.2 Comparison of PD-1, PD-L1, and PD-L2 expression between and within groups.
A. Upregulation of PD-1, PD-L1, and PD-L2 expression in CHB patients (n=56, M/F 38/18, age median 35), compared with health controls and AHB patients (n=12, M/F 11/1, age median 40.The PD-1-positive cells express index was 32.35%±20.56% in CHB patients, more than 2.68%±2.37% in health controls and also 12%±9.6% in AHB patients. PD-L1-positive cells express index of CHB patients was 30.68%±27.07%, much more than that of health controls (3.26%±5.62%), and that of AHB patients (8.7%±7.4%), $p<0.05$. The frequency of PD-L2-positive cells in CHB patients was much higher (6.57%±7.23%) than that in AHB patients (1.7%±0.2%,) and health controls (2.68%±2.35%),$p<0.05$ ($p<0.05$)
B. Between groups in CHB, the positive cells index increase with the disease progression. ($p<0.05$). The group was classified according to Ishak HAI Scoring system. Grading, group 1: scored 1–5 (n=21,M/F 14/7, age median 31); group 2: scored 6–10 (n=18,M/F 13/5, age median 30); group 3: scored >10 (n=17,M/F 12/5, age median 40). From group 1 to group 3, the positive cells index was: PD-1, 12.04%±9.96% (group 1), 21.31%±24.39% (group 2), 69.01%±18.50% (group 3); PD-L1, 8.67%±6.90% (group 1), 41.25%±28.92% (group 2), 46.68%±23.19 (group 3); PD-L2, 2.13%±2.70% (group 1), 7.4%±7.29% (group 2), 11.17%±7.90% (group 3).

PE061

Relation of HBV S Gene Mutation and HBV DNA Level in Patients with Concurrent HBsAg and HBsAb

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Background: Hepatitis B viral mutants can emerge in patients as a result of selection pressure from either immune response or treatment options. Mutations of HBsAg allow mutant virus to propagate in the presence of a neutralizing immune response, while wild-type virus in reduced to undetectable levels.
Methods: 58 chronic hepatitis B patients with both positive for HBsAg and HBsAb were studied.Serological markers of HBV were detected by ELISA and microparticle enzyme immunoassay. HBV DNA levels were determined by fluorescent quantitative PCR, S gene fragments were directly sequenced, liver function was analyzed by automatic biochemistry analyzer AU400. Correlation test was conducted to evaluate their dependablity.
Results: The level of HBsAg and HBsAb was 254.4±68.3 S/N and 39.4±38.1 mIU, respectively. HBV DNA was detectable in 46 patients. Fifty-one mutations of S gene were detected in 38 patients, and the relating amino acid substitution was at the sites of 36, 39, 47, 63, 77, 89, 90, 115, 126, 129, 139 and 154. Eight (15.7%) out of 51 mutations were located at the "a" determinant region in 14 patients, while no mutation was found at the sites of 124, 137 and 147. However, the mutation did not affect HBV replication. HBV DNA was positive correlated with HBeAg.
Conclusions: Change in HBsAg antigenicity due to S gene resulted in concurrent HBsAg and HBsAb. The existence of HBsAb did not affect HBV replication. The damage of liver failure in those patients was slight.

PE062

Immune Clearance State of HBV Infection: Time to Redefine?

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Background: HBV infection is common in Bangladesh. We often encounter young patients incidentally detected with HBeAg negative chronic hepatitis B (CHB) in our clinical practice. However the characteristics of these patients is yet to be studied in this country. The aim of this study was to study the characteristics of young Bangladeshis incidentally detected with HBeAg negative CHB.

Methods: We did percutaneous liver biopsies of 36 CHB patients aged between 8 to 20 years. They were all HBeAg negative with persistently normal or raised serum ALT values. We did pre-core mutation (PCM) study in 4 patients who were randomly selected.

Results: 56% patients had significant necro-inflammation (HAI-NI >3), while significant fibrosis (HAI-F ≥2) was seen in 17.6%. Serum ALT (cut off 42 U/L) was raised in 38.2%, while high HBV DNA load (>10^5 copies/ml) was observed only in 26.5%. PCM was negative in all 4.

Conclusion: Although CHB patients between 10-20 years of age are supposed to be in immune clearance phase, which is characterized by low HBV DNA and HBeAg positivity, the study shows that HBeAg negative CHB is an entity that can also be seen in this age group and a significant percentage of such patients may have considerable hepatic involvement. This challenges our current concept about immune clearance state of HBV infection, although much larger study is needed to draw any specific conclusion.

PE063

Comparison between HBeAg Positive and HBeAg Negative Chronic Hepatitis B in Young Bangladeshis: Experience from a Tertiary Centre

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Background: HBV infection is common in Bangladesh, but characteristics of young patients incidentally detected with chronic hepatitis B is yet to be studied in this country.

Methods: We did percutaneous liver biopsies of 88 CHB patients aged between 8 to 20 years.

Results: Significant necro-inflammation (HAI-NI >3) was seen in 79.6% patients with HBeAg positive and 56% patients with HBeAg negative CHB, while significant fibrosis (HAI-F ≥2) was seen in 20.3% and 17.6% patients in these two groups respectively. Serum ALT (cut off 42 U/L) was raised in 37% HBeAg positive and 38.2% HBeAg negative patients, while in these two groups 87% and 26.5% patients respectively had high HBV DNA load (>10^5 copies/ml).

Conclusion: HBeAg negative CHB is an entity that can also be seen in young population. A significant percentage of both HBeAg positive and negative patients may have considerable hepatic involvement.

PE064

Profile of HBeAg +ve Chronic HBV Infection in Bangladesh

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Background: Inactive HBV carriers constitute the major reservoir of HBV. Present management guidelines provide inadequate treatment modalities. They are recommended for regular check-up; treatment is only recommended when patients exhibit evidence of liver damage. This is due to lack of information about their extent of liver damage. Aim of this study was to assess extent of liver damage in HBeAg +ve patients, unaware of their infection.

Methods: In this retrospective study, records of 206 HBeAg +ve CHB patients from our pool of 561 CHB patients were reviewed. They were tested for HBsAg, HBeAg, HBV DNA, anti-HCV and serum ALT. All underwent per-cutaneous liver biopsy.

Results: 78.2% (161/206) patients were males and 21.8% (45/206) females. They were between 8-45 years of age. ALT was raised >2times UNL in 17% (35/206). 92.2% (190/206) patients had high HBV DNA (≥10^5 copies/ml), while low HBV DNA (<10^5 copies/ml) was seen in 7.8% (16/206). In high HBV DNA group, significant necro-inflemmation (HAI-NI ≥7) was seen in 48.9% (93/190) and significant fibrosis (HAI-NI ≥3) in 24.7% (47/190). Figures were 37.5% (6/16) and 31.3% (5/16) respectively in low viral load group. None tested positive for HCV infection.

Conclusion: Study indicates that machinery should be developed to characterize undetected HBV carriers in developing countries by conducting multi-center clinical studies. We have shown that considerable number of patients, unaware of their HBV infection, suffer from progressive liver damage. The overall strategy of management of chronic HBV infection should also be revisited.

PE065

High Viral Load Does Not Necessarily Represent Significant Liver Damage in Patients with Chronic HBV Infection in Bangladesh

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Background: In general, it is assumed that patients with chronic hepatitis B virus (HBV) infection with high viral load exhibit increased liver damages. Treatment guidelines also emphasize on reducing viral load. These observations were mainly accumulated from developed countries. >80% chronic HBV carriers live in the developing nations, but little is known about relationship between HBV viral load and extent of liver damage in these countries. In this study, we addressed this issue.

Methods: In this retrospective study we reviewed records of 306 CHB patients from our pool of 561 patients. All had high HBV DNA (≥10^5 copies/ml). 62.1% (190/306) were HBeAg +ve and 37.9% (116/306) HBeAg -ve. They were alsotested for anti-HCV and serum ALT. All underwent per-cutaneous liver biopsy.

Results: 51.1% (97/190) HBeAg +ve patients with high HBV DNA had non-significant hepatic necro-inflammation (HAI-NI <7); this figure was 53.4% (62/116) in HBeAg -ve patients. Non-significant hepatic fibrosis (HAI-F <3) was observed in 75.2% (143/190) and 69.8% (81/116) in HBeAg +ve and -ve patients respectively. None tested positive for HCV.

Conclusion: Correlation doew not exist between viral load and liver damage in CHB in Bangladesh. Many with both HBeAg +ve and -ve CHB with high HBV DNA do not have significant hepatic necro-inflammation and fibrosis. Further study may be needed to find out influence of other factors on liver damages in CHB in Bangladesh. Most of these patients have not been characterized and treatment modalities have not been defined for them.

PE066

Hepatitis B Virus Basal Core Promoter Mutation and DNA Load Correlate with Expression of Hepatitis B Core Antigen in Chronic Hepatitis B Patients

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Background/Aims: Expression of intrahepatic hepatitis B core antigen (HBcAg) is related to the immunopathogenesis of hepatitis B virus (HBV) infection. The role of HBV genotype and basal core promoter (BCP) mutation in expression of HBcAg was investigated.

Methods: Seventy HBeAg-positive chronic hepatitis patients (genotype B in 52 and C in 18; BCP T1762/A1764 mutation in 16) were enrolled. Clinical, virologic and histologic features were compared with regard to localization and expression of intrahepatic HBcAg. The effects of HBV genotype and BCP T1762/A1764 mutation on the expression of HBcAg were further evaluated by *in vitro* assays.

Results: Cytoplasmic, mixed cytoplasmic/nuclear, and nuclear localization of intrahepatic HBcAg were found in 38 (56.7%), 25 (37.3%) and 4 (6.0%), respectively. Fifty-eight (80.6%) of these patients expressed a high level of HBcAg. In multivariate analysis, cytoplasmic localization of HBcAg correlated only with low serum viral load (P=0.045) and BCP mutation (P=0.04). High expression level of HBcAg also correlated with high serum viral load (P=0.015) and BCP wild-type sequence (P=0.037). *In vitro* assays supported that HBV BCP mutant had lower subcellular expression of HBcAg compared with BCP wild-type strain.

Conclusions: HBV BCP mutation and viral load but not genotype contributes to the expression of intrahepatic HBcAg.

PE067

Clinical and Virological Characteristics of Hepatitis B Virus Genotype E: Key Mutation in Seroconversion, and Similarity of Regularatory Sequence to Genotype D

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Hepatitis B virus (HBV) genotypes show distinct geographical distributions and virological and clinical differences. In some of genotypes, specific substitutions and mutations have been described in association with hepatitis B e (HBe) protein expression and viral replication. In this study, genetic characteristics of HBV genotype E (HBV/E) were investigated using clinical samples obtained from 12 Hepatitis B e antigen (HBeAg)-positive, and 11 anti-HBe-positive asymptomatic carriers (ASCs) in West-Africa. Full-genome analysis of isolated HBV strains revealed strong association between precore (PC) mutation and HBeAg to anti-HBe seroconversion. ! Furthermore, using 53 partial genome sequences, correlation among HBeAg/anti-HBe status, viral load and key mutations were analyzed. The data showed that PC mutation is associated with HBeAg seroconversion and enhanced viral replication efficiency. Comparison between HBV/E and HBV/D strains reveals these two genotypes to have an identical sequence in their core-promoter-upstream and basic core promoter (CURS/BCP) regions. It has been known from the previous phylogenetic studies, that HBV/D and HBV/E cluster together in trees reconstructed on X and preCore/Core ORFs. In addition, this study, demonstrates that in spite of the high sequence similarity of CURS/BCP region, the seroconversion-related mutation patterns are different between HBV/E and HBV/D in ASC. Further studies are needed to clarify the clinical significance of the regulatory sequence similarity between HBV/E and HBV/D.

PE068

A Comparative Evaluation of Adefovir and Lamivudine in Patients of Chronic Hepatitis B, Correlation with HBV Viral Kinetics, Hepatic Necro-Inflammation and Fibrosis

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Background: Chronic hepatitis B(CHB) is an important cause of morbidity and mortality.

Methods: Pilot study involving 30 patients of CHB, were equally randomized to receive either Adefovir or Lamivudine for 6 months. Quantification of serum and hepatic HBV DNA levels by Real time PCR and liver biopsy done at start and end of 6 months.

Results: After 6 months there was significant and comparable reduction in Serum and hepatic HBV DNA viral load and liver biopsy showed significant reductions in HAI scores in both the groups. Serum ALT which was elevated to 2 or more times normalized in both the groups. In the Adefovir group 2 patients became HBeAg negative and 2 patients who were HbeAg negative at the start of therapy remained so. In the Lamivudine group one patient became HBeAc negative and 2 patients who were negative at the start of therapy remained so. In the Adefovir group 4 patients became HBV DNA (qualitative test) and in the Lamivudine group 2 patients became HBV DNA negative. There was strong correlation between serum and hepatic HBV DNA levels both before and after the completion of therapy.

Conclusion: Both the drugs bring about biochemical, histological and serological improvement with significant reduction in viral load in serum liver after 6 months without complete clearance of virus. There was not enough evidence to show therapeutic advantage of one drug over the other. The serum and hepatic HBV DNA levels correlate well with eachother before and after treatment.

PE069

Virological Response to Treatment with Pegylated Interferon alfa-2a of Chronic Hepatitis B in Children

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Aim: Assessing efficacy and safety of treatment of chronic hepatitis B in children with pegylated IFN.

Materials and Methods: 13 children (9 boys and 4 girls) aged 11–17 years with CHB treated with PEG-IFN alfa-2a, 100 μg/m^2/week during 48 weeks, 5 HBeAg-positive and 8 HBeAg-negative children, 4 previously treated with recombinant interferon. No child had liver disease greater than grade 2, stage 2. Serum HBV DNA was quantified at baseline, TW 4, ("RVR") TW 24, TW 48 (ETR) and W 72 (SVR) with RT PCR method (Roche TaqMan). ALT activity, haematology and adverse events were monitored.

Results: After 4 weeks treatment median HBV DNA level decreased from $7.8x10^3$ IU/mL at baseline to $1.43x10^2$ IU/mL ($p<0.01$). "RVR" -undetectable HBV DNA at TW4 was observed in 6/13 children and associated with lower pretreatment ALT levels <25 IU and pretreatment viral load <750 IU/mL. All children with "RVR" were HBeAg-negative pretreatment. At TW 24 and TW 48 seven children including all with "RVR" had undetectable HBV DNA. 5 children achieved SVR (undetectable serum HBV DNA in W 72), among them 3 with "RVR". In 2/6 children with "RVR" HBsAg disappearance was observed since TW 48. Leukopenia was reported in 7 children, thrombocytopenia in 3. No adverse events were observed following dose modifications.

Conclusions:

1. PEG-IFNalfa-2a is a good therapeutic option for children with CHB, in particular with HBeAg-negative CHB
2. Low pretreatment viral load and "RVR" seem to be predictive factors of efficient therapy.

PE070

Study on the Probability of HBV Infection among the Public Service Places

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Objective: It is useful data for hepatitis B control by investigating the sanitizing modes among appliances used in the public service places (PSP) and HBsAg among appliances and practitioners worked in those places.

Methods: 63 beauty parlors, barber shops and bathing centers selected by stratified randomization sampling, 682 workers were investigated in questionnaire. The HBsAg in appliances of PSP and employee was detected by RIA.

Results: The rate of HBsAg among appliances of PSP was 2.13%. The rate of HBsAg in large-, medium- and small-sized appliances was 0.63%, 2.67% and 3.70%. The rate of HBsAg has different($\chi2=6.68$, $P<0.05$). The rate of HBsAg among appliances of beauty parlors, barbering shops and footbath inns was 2.97%, 0.61% and 3.42%. Different appliances had different rate of HBsAg, such as the rate of acne needle and the forceps was 5.13% and 4.17%. The positive of HBsAg amongworkers in PSP was 7.13%. The rate of HBsAg among workers in large-, medium- and small-sized PSP was 7.34%, 8.33% and 2.94%. The rate of HBsAg among workers in beauty parlors, barbering shops, footbath inns and bathing centers was 9.01%, 6.37%, 4.35% and 7.29%. The HBsAg rate among workers was different in different works, the rate was higher in tattoo workers (13.33%), pedicures workers (12.68%), Massagists (8.03%).

Conclusions: It is important to enhance the sanitizing management in PSP and improve workers KAP) of HepB. And we should promote health education to enhance the knowledge of Hepatitis B control and build up supervision consciousness.

PE071

Effective Inhibition of HBV DNA Integration by shRNA Targeting Ku70 and Ku80

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Background: Integration of hepatitis B virus (HBV) DNA into host chromosomes is often found in chronic liver disease and hepatocellular carcinoma, which is likely an early event of HBV-related carcinogenesis. However, the molecular mechanism of integration remains unclear. Here we describe a potential mechanism of HBV integration and identify that Ku70 and Ku80, the gatekeepers of non-homologous end-joining (NHEJ) repair pathway, can serve as targets for anti-hepatitis virus integration.
Methods: Using I-Sce I endonuclease-based system, we induced a DNA double-strand break (DSB) in human hepatoma cell line HuH-7. The cells were then incubated with serum from patients with chronic HBV infection. PCR amplification and direct sequencing were used to detect the inserted sequence in the site of DSB. Finally, we employed TaqMan-based real-time PCR assay to quantify the integrated HBV DNA and evaluate the effects of shRNA on HBV integration.
Result: When HuH-7 were exposed to viral serum and incubated for several days, HBV DNA was detected in integrated form at the exact site of DNA damage. Furthermore, small interference RNA (siRNA) targeted against gatekeeper genes for NHEJ can down-regulate NHEJ repair and even the frequency of HBV integration.
Conclusion: Thus, this project provided us with the first direct evidence that DNA double-strand breaks are potential targets for HBV integration. The study has also shown that shRNAs targeted against gatekeeper genes for NHEJ can regulate the frequency of HBV integration.

PE072

Screening of Proteins Binding to HBsAg Protein from Human Pancreas cDNA Library by Yeast Two-hybrid

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Objective: To screen proteins of human pancreas cDNA library interacting with HBsAg protein. Methods: The library was amplifed, purified and evaluated, and then the puried library plasmids were transformed into yeast strain Y187. The reconstructed plasmid pGBKT7- HBsAg was transformed into yeast strain AH109 and screened on the nutrient deficiency medium SD/-Trp. The transformed AH109 mated with Y187 containing the library plasmid. The diploid yeast cells were plated on nutrient deficiency medium SD/-Trp/-Leu/-His/-Ade and SD/-Trp/-Leu/-His/-Ade containing X-α-gal for selecting. The plasmids in diploid yeast cells were extracted and electrotransformed into *E.coli* DH5α. The plasmids in DH5α were extracted, sequenced and analyzed by bioinformatic methods.
Results: Sixteen proteins interacting with HBsAg were founded.
Conclusions: These results show that HBsAg protein may be related with metabolism of glucose and lipid.

PE073

Comparison of the Sensitivity and Specificity of the Elecsys® HBsAg II Assay with other Available Assays in China for Detection of HBsAg

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Background/aims: Diagnosis and screening for HBsAg in China demands tests with high sensitivity levels. We compared the technical and clinical performance of HBsAg screening assays available in China.
Methods: The Elecsys® HBsAg II assay was compared with the Architect® and AxSYM® HBsAg assays and a national Chinese ELISA using pre-selected samples, including recombinant mutants and routine clinical samples.
Results: Elecsys® HBsAg II was the most sensitive assay for detecting positive results in seroconversion samples: up to 14 days earlier, up to 11 days earlier and up to 22 days earlier than the Architect® and AxSYM® assays and Chinese ELISA, respectively. Sensitivity was 100% for Elecsys® HBsAg II with routine samples, compared with 99.1%, 98.9%, and 95.2%, respectively. Elecsys® detected all 13 recombinant mutant samples (Table). All assays had similar specificity.
Conclusion: The high sensitivity and specificity of Elecsys® HBsAg II allows early detection of HBV infection and mutant recognition.

	Number of recombinant mutants detected (n=13)
Elecsys® HBsAg II assay	13
Architect® HBsAg assay	13
AxSYM® HbsAg assay	10
National Chinese ELISA	3

PE074

PEGASYS but not Adefovir Results in Significant Decline in HBsAg in Chinese Patients with HBeAg-positive Disease Harbouring Lamivudine-Resistant YMDD Mutations

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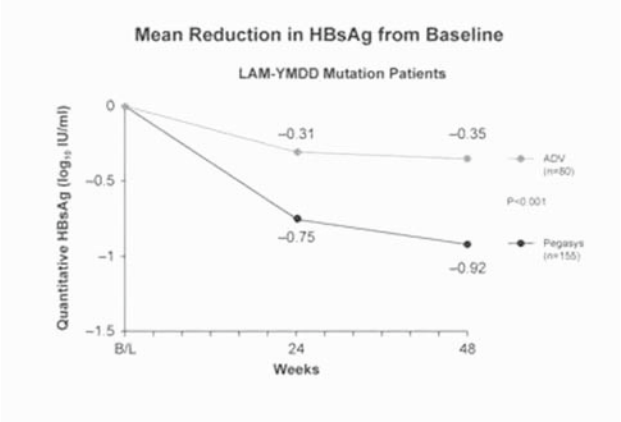
Background/aims: We compared PEGASYS vs adefovir in Chinese patients with lamivudine-resistant YMDD mutants.
Methods: 235 patients were randomised 2:1 to receive PEGASYS (180µg qw) for 48 weeks or adefovir (10mg qd) for 72 weeks. All patients continued lamivudine (100mg qd) for the first twelve weeks.
Results: Baseline demographics for the PEGASYS- and ADV-treated patients were comparable. Interim analysis (week 48) showed higher rates of HBeAg loss (14.2% vs 5%) and seroconversion (9% vs 2.5%; P=0.033) in PEGASYS-treated patients. HBsAg decline was significantly greater in PEGASYS-treated patients (Figure). 4% of PEGASYS-treated patients had cleared HBsAg by week 48 vs none treated with adefovir. A high rate of HBsAg clearance (42.9%) was observed in PEGASYS-treated patients who had achieved HBeAg seroconversion.
Conclusion: PEGASYS can induce significant on-treatment HBsAg decline in Chinese patients with lamivudine resistance with frequent HBsAg clearance in those with HBeAg seroconversion.



PE075

Effective Strategies in Controling Hepatitis B Prevalence among Dezful Blood Donors (3 years experiance)

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Hepatitis B is one of the major diseases of mankind that kills about one million persons each year in the world. Accoring to primary study about 3% of Iranian population is chronic HBV carriers. Among Iranian cirrhotics, 70-84% has evidence of exposure to HBV and 51-56% is carriers. Because increase demand of blood transfusion, high blood dependent patients and long term window period of HBV infection, any controlling HBV infection program in blood donors can enhance the blood safety and public health.

In this descriptive study included all the blood donors that referred to Dezful blood transfusion center during 2005-2008. All the blood donors screened for HBs Ag by using Enzyme immuno assay and repeatedly reactive (R.R) samples confirmed by HBC-Ab or confirmatory (neutralization) tests. The data analyzed by using SPSS 11.5.

We found that in the first year 1.052 % were repeatedly reactive and 1.045 % confirmed. The results for other years as the followed: 0.782 %(R.R) and 0.770 % confirmed and in the last 0.725 % (R.R) and 0.700 % confirmed. The repeated blood donors increase in this period (42.11 %, 50.15 % and 51.68 % respectively).

According our study, although the prevalence was higher than other region in our province, the HBV prevalence showed good decrease after stablishment strategies such as of repeated blood donor recruitment , improvement the donor selection and other educational programs . Good following up those strategies to enhance the blood safety recommended.

PE076

miRNAs Regulate the Replication and Gene Expression of Hepatitis B Virus

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MicroRNAs (miRNAs) are single–stranded noncoding RNAs of 18 to 25 nucleotides that play critical roles in a wide spectrum of biological processes. We investigated whether the miRNAs-silencing machinery influences HBV replication or antigen expression. On the basis of ELISA and MTT, the effect of 328 miRNAs on the HBsAg expression and cell proliferation was examined. Three microRNAs efficiently inhibited HBsAg expression without significant effect on the proliferation of HepG2 2.2.15 cells compared to LacZ control. Subsequently, bioinformatics analysis were used to predict targets for the three miRNAs, and the prediction results were conformed by cDNA microarray analysis. The target region in HBV genome and the 3'UTR region of one cellular gene were identified by fluorescent reporter assay, semi-quantitative RT-PCR and western blot. The results demontrated that miRNA may play an important role in replication and gene expression of HBV.

PE077

High Rates of Positive Viral Hepatitis Serology in Patients Attending a City Hospital Challenge Healthcare Providers

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Background: Community based studies in Vietnam show a very high hepatitis B (HBV) prevalence of 10-20%. Hepatitis C (HCV) prevalence is reported at 1% in rural areas and estimated to be higher in cities. Results recorded in a hospital during a campaign on occasion of World Digestive Health Day on Viral Hepatitis May 29, 2007 are reported.

Methods: HBsAg, anti-HBc and anti-HCV serology was done during the campaign in 354 unselected Vietnamese patients coming to the hospital. In addition, we also recruited two cohorts of HBsAg positive (n=397) and anti-HCV positive (n=228) consecutive patients from May to August 2007.

Results: 1) Serology in 354 patients: mean age 37 years, 45.5% male, HBsAg positive 26% (n=92), anti-HBc positive 41.5% (n=147), anti-HCV positive 6.5% (n=23).

2) HBsAg positive cohort with 57.2% men. HBeAg was determined in 66% (262/397) cases: HBeAg positive in 29% (n=76), HBeAg negative in 71% (n=186). HBV-DNA was detectable in 97.3% HBeAg positive and in 64.8% HBeAg negative.

3) Anti-HCV positive cohort with 47.4% men: genotype was done in 57.4% of cohort (131/228) with a distribution of 68.2% genotype 1 12.9% genotype 2, 18.1% genotype 6.

Conclusions: In this patient population the prevalence of HBsAg positive and anti-HCV were much higher than reported in community studies. Genotypes 1 and 6 accounted for most of HCV. These very high rates of viral hepatitis in a hospital setting challenge to healthcare providers in terms of patient management as well as caregiver's prevention.

PE078

Cost-effectiveness Analysis of Anti-viral Treatment Strategies Based on the Roadmap Model in Chronic Hepatitis B Virus (HBV) Infection

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Aim: We aimed to evaluate the cost-effectiveness of telbivudine versus entecavir with reference to lamivudine by roadmap model.

Methods: Decision analysis model was used to study the incremental cost-effectiveness ratios (ICER), i.e. the additional cost (in USD) required to achieve undetectable HBV DNA or HBeAg seroconversion for a patient at 2 years in America and Hong Kong. Entecavir was used as a continuous monotherapy. Lamivudine and telbivudine would be shifted to entecavir if HBV DNA was detectable at month 6 and continued otherwise with drug resistance treated by add-on adefovir. Weighted event rates based on previous reports were estimated for analysis.

Results: Telbivudine was generally cheaper than entecavir to achieve an incremental case of undetectable HBV DNA from lamivudine at 2 years. Entecavir was least effective and most costly for HBeAg seroconversion.

Conclusions: Telbivudine is a cost-effective alternative to entecavir particularly when its cost is low in Hong Kong.

	Lamivudine for 2 yrs (USD/patients)	ICER from Lamivudine to Telbivudine (USD)	ICER from Lamivudine to Entecavir (USD)
America			
Undetectable HBV DNA			
HBeAg positive	$16,885	$70,816	$228,293
HBeAg negative	$13,956	$34,846	$34,584
HBeAg seroconversion	$40,572	$72,206	-$81,490*
Hong Kong			
Undetectable HBV DNA			
HBeAg positive	$4,891	$5,412	$57,170
HBeAg negative	$4,125	$2,360	$8,658
HBeAg seroconversion	$11,753	$5,707	-$20,407*

* Negative ICER means that Entecavir is costly and less effective

PE079

Proteomics Identification of Glucose Regulated Protein 78 as an Endogenous Antiviral Factor in Hepatitis B Virus-transfected HepG2 Cells

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Hepatitis B virus (HBV) infection is a global public health problem, which plays a crucial role in the pathogenesis of chronic hepatitis, cirrhosis and hepatocellular carcinoma. Although considerable progress has been made, the pathogenesis of HBV infection is still elusive. There's an urgent need to elucidate the mechanisms of HBV-host interactions, to discover novel biomarkers for diagnosis and prognosis and to develop therapeutic targets for anti-HBV treatment. Herein, we applied a two-dimensional gel electrophoresis and MALDI-TOF/MS based comparative proteomics approach to globally analyze the host response to HBV by using an inducible HBV-producing cell line HepAD38. Of the 23 differentially expressed proteins identified, glucose regulated protein 78 (GRP78) was one of the most striking proteins elevated by HBV replication, which was confirmed by real-time PCR and western blotting. Knockdown of GRP78 expression by RNA interference resulted in a significant increase of both intracellular and extracellular HBV virions in HBV-transfected HepG2 cells. Reversely, GRP78 overexpression led to HBV suppression. The expression levels of hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) were determined by enzyme linked immunosorbent assay (ELISA). Immunofluoresce further revealed a positive correlation between the expression levels of GRP78 and HBsAg in both HBV-transfected HepG2 cells and HBV-infected human liver tissues. Altogether, these data demonstrate for the first time that GRP78 is an endogenous anti-viral factor in HBV-transfected HepG2 cells and may serve as a potential prognostic indicator of viral status in anti-HBV therapies.

PE080

Predictor of Response to Adefovir Dipivoxil Long-Term Treatment in Lamivudine-Resistant HBeAg-Positive Chronic Hepatitis B Patients

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Background/Aims: To evaluate the predictors of response to long-term treatment of adefovir dipivoxil (ADV) in patients with emerging lamivudine (LAM)-resistant hepatitis B e antigen (HBeAg)-positive chronic hepatitis B (CHB) patients.

Methods: One-hundred-thirty-four LAM-resistant HBeAg-positive CHB patients were treated with ADV for a median of 28.0 months (range, 18 – 54 months), following LAM therapy for a median of 25.5 months (range, 5 – 66 months). 65 patients (48.5%) were switched from LAM to ADV monotherapy, 43 (32.1%) were switched to ADV with 1 month of LAM overlap therapy, and 26 (19.4%) were switched to ADV with 3 months of LAM overlap therapy. The influence of baseline parameters on treatment response to ADV in patients with LAM-resistant HBeAg positive CHB was analyzed.

Result: During the follow-up period, 28 (20.9%) of 134 patients achieved complete response, defined as normalization of ALT level, negative HBV DNA by a Digene hybrid capture assay and achievement of HBeAg loss. Sixteen (11.9%) patients achieved HBeAg seroconversion. Twenty-eight (20.9%) patients developed ADV-related mutations during ADV treatment. In multivariate analysis, virological response at 3 months (OR=9.70, 95% CI: 32.63-35.78, p=0.001), defined as serum HBV DNA levels less than 5 $\log_{10}$ copies/mL or a reduction in serum HBV DNA levels greater than 2 $\log_{10}$ copies/mL after 3 months of ADV therapy, independently predicted complete response.

Conclusions: Virological response at 3 months was the strongest predictor of ADV response in LAM-resistant HBeAg-positive CHB patients.

PE081

Role of HBV DNA Level and Genotype/ Subgenotype in Severe Liver Diseases

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Background/Aims: To explore the effects of HBV DNA level，HBV genotype/subgenotype on the pathogenesis of severe liver diseases in Chongqing.

Methods HBV DNA level was analyzed in patients with severe liver diseases in retrospect,and HBV genotype/subgenotype，HBV DNA level，and HBeAg were determined in patients with hepatocellular carcinoma (HCC,n=78), Liver cirrhosis(LC, n=58),chronic hepatitis B(CHB, n=20) and acute on chronic liver failure(ACLF, n=42).

Results HBV level from high to low with CHB were LC, ACLF and HCC in turn($P<0.05$). HBV genotype was mainly genotype B.The rate of genotype B and C were 51.3% and 47.4%respectively in HCC patients, 60.3% and 39.7% in LC patients, 55% and 40% in CHB patients, 55% and 40%in ACLF patients. The percentage of genotype B/C in ACLF patients was higher in compared with other groups. But the distribution of HBV genotype among groups was not statistically different($P>0.05$).Subgenotypes of genotype B were almost Ba but one. Subgenotypes of genotype C were mainly Ce in Chongqing area, and there was no statistical difference among the 4 groups ($P>0.05$).

Conclusion: HBV DNA level seems not to be a determining factor at end point of severe liver disease. Both genotype B and C of HBV can lead to severe liver diseases, and there are more mixed infections by different genotypes in ACLF.

PE082

The Efficacy of Switching to Entecavir (ETV) Monotherapy in Japanese Lamivudine (LVD)-Experienced Patients.

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Background: This study aims to determine the efficacy of switching to 0.5mg ETV daily in chronic hepatitis B (CHB) patients previously treated with LVD.

Method: Retrospective analysis of CHB patients (n=134) previously on 100mg LVD daily and switched to 0.5mg ETV daily.

Results: LVD-experienced patients were divided into three groups based on HBV viral load at time of switching to ETV (<2.6 $\log_{10}$ copies/mL; 2.6–5.0 $\log_{10}$ copies/mL and >5.0 $\log_{10}$ copies/mL). Detection of LVD-resistant virus at the time of switching was higher in the group with HBV DNA 2.6 $\log_{10}$ copies/mL (76% in both 2.6–5.0 and >5.0 $\log_{10}$ copies/mL groups versus 23% in <2.6$\log_{10}$ copies/mL group) and was higher in patients treated with LVD for 3 years (52% versus 24% for patients on <1 year of LVD). A year after switching to 0.5mg ETV daily, HBV DNA undetectable rates were 100% (42/42), 94% (17/18) and 43% (6/14) for <2.6, 2.6–5.0 and >5.0 $\log_{10}$ copies/mL groups, respectively. ALT normalization occurred in more than 90% patients at the end of the first year of switching to ETV for all three patient groups. Only one patient in the 2.6–5.0 $\log_{10}$ copies/mL group, who had LVD-resistant mutants at the time of switching, developed ETV resistance during follow-up.

Conclusion: Switching from LVD to ETV maintains or improves viral suppression and ALT normalization, especially in patients with viral load <5.0 $\log_{10}$ copies/mL.

PE083

HBsAg Decline in Patients Treated with PEGASYS and its Association with Post-treatment Response in HBeAg-positive Chronic Hepatitis B

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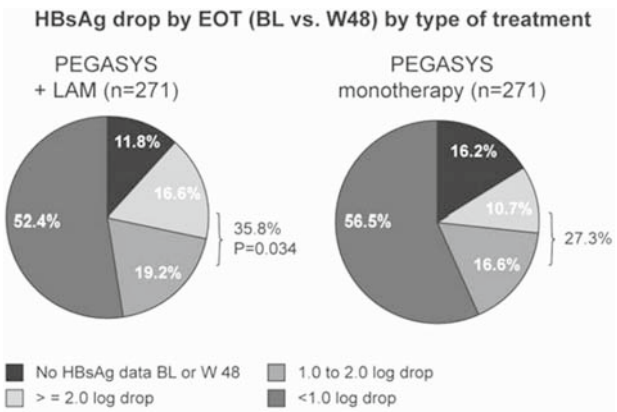
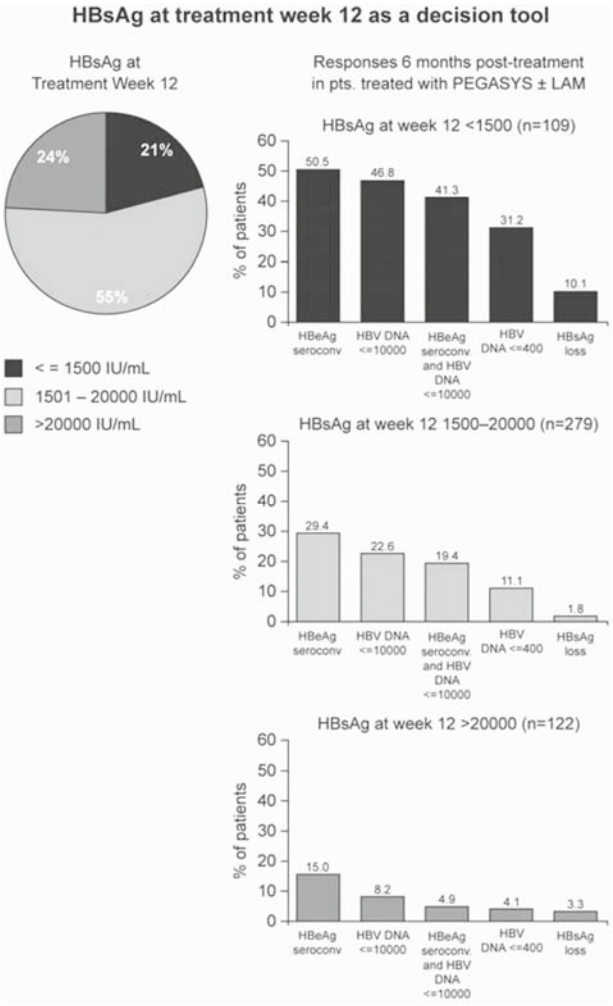
Background/aims: We investigated the association between on-treatment HBsAg decline and sustained response in patients treated with PEGASYS±lamivudine.

Methods: HBsAg levels were measured retrospectively pre-treatment and at weeks 12, 24, 48 and 72 using the Abbott Architect HBsAg assay in sera from 542 patients (83% Asian) treated with PEGASYS alone (180µg qw; n=271) or combined with lamivudine (100mg qd; n=271) alone for 48 weeks as part of a large multinational trial. Response was measured 6 months post treatment.

Results: More patients treated with combination therapy had >1 log decline in HBsAg from baseline to week 48 (Figure). HBsAg level <1500 IU/mL at week 12 was associated with higher rates of response to PEGASYS±lamivudine 6 months post treatment (Figure). Data comparing HBsAg and HBV DNA as on-treatment predictors of response will be presented.

Conclusion: On-treatment HBsAg monitoring may be useful for predicting response in patients treated with PEGASYS.





PE084

Rosiglitazone Suppresses the Replication of Hepatitis B Virus in HepG2 Cells

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Background/aim: Chronic hepatitis B patients are clinically treated with nucleot(s)ide analogues and IFN-α. Nucleot(s)ide analogues have problems including drug resistance in continuous treatment, and IFN-α has disadvantages of limited effectiveness and side effects. Therefore, novel antiviral drugs are still needed. In this study, the suppressive effect to the replication of HBV was examined in vitro by using bezafibrate and rosiglitazone, which are ligands of peroxisome proliferator activated receptor (PPAR) α and γ, respectively.!

Methods: The cytotoxicity of bezafibrate and rosiglitazone to HepG2 cells was examined with MTS assay, and the concentration of 50% cytotoxicity (CC50) was calculated. HepG2 cells were transiently transfected with the plasmid containing 1.3-fold HBV genome of a genotype B strain. After 24 hours of transfection, rosiglitazone and bezafibrate was added to the cells. Using the medium at day 3 after the addition of drugs, HBV DNA was quantified with real-time PCR.!

Results: The CC50 of bezafibrate and rosiglitazone in HepG2 cells were 250 µM and 150 µM, respectively. The amount of HBV-DNA in the medium was decreased when the density of bezafibrate was over 200 µM, but the density demonstrated considerable cytotoxicity. In contrast, rosiglitazone of 5 µM, which showed no cytotoxicit, decreased the amount of HBV DNA. The 50% effective concentration (EC50) was calculated to be 9.8 µM. !

Conclusions: In this study, it was suggested that the replication of HBV was inhibited by rosiglitazone of the density without cytotoxicity. The mechanism is uncertain and being investigated now.

PE085

Serum Hepatitis B Virus DNA Level at 24-week is a Reliable Predictor of the Efficacy of 2-year Lamivudine Treatment

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Background: The objective of this study was to evaluate the early virologic response for prediction of achievement of HBeAg seroconversion and hepatitis B virus (HBV) DNA negativity after two years of lamivudine treatment in chronic hepatitis B (CHB) patients.
Methods: In this *retrospective* study, adult patients with chronic hepatitis B (255 *HBeAg*-positive and 122 *HBeAg*-negative) were treated with lamivudine (100 mg/day), and followed-up up to 72 months. Response and resistance to the treatment were assessed during the treatments with lamivudine.
Results: It was found that gender, age, baseline levels of ALT and HBV DNA, serum HBV DNA at week 24 (P =0.019 , OR = 0.442) were closely related to the achievement of HBeAg seroconversion, undetectable HBV DNA level and emergence of drug resistance after 2 years of lamivudine treatment. HBeAg positive patients with baseline serum HBV DNA in 10^6-10^8copies/ml and serum HBV DNA $\leq 10^3$copies/ml at week 24 showed high response rate of ALT normalization rate (91.7%), undetectable HBV DNA rate (84.5%), HBeAg seroconversion rate (55.2%), as well as low drug resistance rate (25.4%) after 2 years of treatment. Similarly, HBeAg negative patients with serum HBV DNA $\leq 10^3$copies/ml at week 24 could achieve high 2-year response rate of ALT normalization rate (72.41%), undetectable HBV DNA rate (82.3%), and low drug resistance rate (15.5%).
Conclusion: Serum HBV DNA $\leq 10^3$ copies/ml at 24-week provide the best prediction of 2-year lamivudine treatment response.

PE086

HBsAg Clearance Continues to Increase after end of Treatment with PEGASYS ± Lamivudine: 5-year Follow-up Study in Patients with HBeAg-negative Disease

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Background/aims: Unlike oral antivirals, a finite course of (peg)interferon can induce sustained post-treatment response in patients with chronic hepatitis B (CHB), with increasing rates of HBsAg clearance observed in patients who respond during post-treatment follow-up. HBsAg clearance is considered to be the closest outcome to a cure, being associated with improved histological outcome, reduced incidence of HCC and increased survival.
Methods: In a randomised multinational study, patients (HBeAg-negative) received 180µg PEGASYS+placebo (n=177); 180µg PEGASYS+100mg lamivudine (n=179); or 100mg lamivudine (n=181) for 48 weeks, and were assessed 6 months post-treatment. From this initial study, 230 of those who had received PEGASYS±lamivudine and 85 patients who had received lamivudine monotherapy participated in a long-term observational study to investigate post-treatment response. HBsAg clearance at yearly post-treatment follow-up visits up to 5 years post-treatment was analysed.
Results: HBsAg clearance in patients treated with PEGASYS±lamivudine increased post-treatment (3% at 1 year to 6%, 8%, 11% and 12.2% at years 2, 3, 4 and 5). At year 5, 28 PEGASYS-treated patients (12.2%) had cleared HBsAg compared with 3 (3.5%) of lamivudine-treated patients (P=0.022). 16/28 PEGASYS-treated patients had anti-HBsAg (HBsAg seroconversion). Detailed analysis of the 5-year follow-up data will be presented.
Conclusion: The ability of a finite course of PEGASYS to induce sustained response with increasing HBsAg clearance rates in responders during post-treatment follow-up supports its use as first-line therapy in HBeAg-negative patients with CHB.

PE087

Use of the Elecsys® HBsAg II Assay for Simple and Accurate Quantification of HBsAg Levels in Sera of Patients Infected with HBV

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Background/aims: Recent studies suggest that quantification of HBsAg levels early during treatment can be used to predict post-treatment response to PEGASYS. Elecsys® HBsAg II (Roche) is a sensitive assay for the detection of HBsAg. This assay can be used for the quantification of HBsAg levels using a simple dilution algorithm. We compared results obtained using the Elecsys® HBsAg II method with those of a commonly used quantification assay.
Methods: HBsAg levels obtained using the Elecsys® HBsAg II assay were compared with those obtained using the Abbott Architect® HBsAg assay for a total of 40 samples from patients infected with HBV genotypes A (n=8), C (n=1), D (n=29) and F (n=2). Samples were diluted 1:100 in diluent provided by the manufacturer. Samples with HBsAg levels >250 IU/mL were retested at a final dilution of 1:1000. Samples with HBsAg levels <0.05 IU/mL were retested undiluted.
Results: Overall, HBsAg levels measured with the two assays correlated well (R^2=0.9718) over a wide range (3–3x10^5 IU/mL). Discrepancies in HBsAg levels >±20% were reported for a minority of the samples (n=15), mainly distributed evenly above and below the ideal line (n=11). In the four low titre (range 3–9x10^3 IU/mL) samples with greatest discrepancy Elecsys® underestimated values (in two cases by >50%).
Conclusion: The Elecsys® HBsAg II assay provides a simple and reliable means for determining HBsAg levels. This simple assay format could be used to provide useful information during on-treatment monitoring of HBsAg levels in patients with chronic hepatitis B undergoing therapy.

PE088

Distribution of Hepatitis B Virus Genotypes among Patients with Chronic Infection in Japan Shifting toward an Increase of Genotype A

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Background: Acute hepatitis B virus (HBV) infection has been increasing through promiscuous sexual contacts, and HBV genotype A (HBV/A) was frequent in patients with acute hepatitis B (AHB) in Japan. To compare the geographic distribution of HBV genotypes in patients with chronic hepatitis B (CHB) in Japan between 2005-2006 and 2000-2001, with a special regard to changes in the proportion of HBV/A.
Methods: A cohort study was performed to survey changes in genotypes of CHB patients at 16 hospitals from all over Japan. Furthermore, we have investigated clinical characteristics of each genotype and examined genomic characteristics of HBV/A isolates by molecular evolutionary analyses.
Results: Of the 1271 patients, 3.5%, 14.1% and 82.3% were infected with HBV/A, B and C, respectively. In comparison with our previous survey during 2000-2001, HBV/A was twice as frequent (3.5% vs. 1.7%, P = .02). The mean age was lower in the patients with HBV/A than B or C. Based on phylogenetic analyses of 11 full-length genomes and 29 preS2/S sequences from patients, HBV/A isolates would have been imported from Europe/the United States, as well as the Philippines/India. They clustered with HBV/A from AHB patients and infiltrated all over Japan already.

Conclusions: HBV/A has been increasing in CHB patients in Japan as the consequence of AHB, spreading in the younger generation through promiscuous sexual contacts, thrust by an inclination of HBV/A to induce chronic hepatitis. The spread of HBV/A infection in Japan should be prevented by universal vaccination programs.

PE089

Attitudes and Practices among People with Hepatitis B Attending a Tertiary Hospital Hepatology Clinic in Malaysia

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Objectives: This study examined the attitudes and practices of people with hepatitis B with regard to their daily living, lifestyle and prevention.
Methods: 483 hepatitis B patients attending the hepatology clinic at the University of Malaya Medical Center (UMMC), Kuala Lumpur were interviewed.
Results: Respondents had a mean age of 46.3 (SD=14.7) years and the mean duration from time of diagnosis was 12.2 years (SD= 8.8) years.
53.8% were worried about their diagnosis and 17.4% could not enjoy their daily activities since diagnosis. Almost half (47.2%) were embarrassed to reveal their diagnosis to the public but most of them (93.6%) will inform their family. 22.6% believed that people with hepatitis B would die in a short time, while 33.5% were against hepatitis B patients working in a food industry. Only 6.4% reported being discriminated due to Hepatitis B. With respect to lifestyle changes after diagnosis, 57.3% made healthier food choices, 46.6% increased their exercise, 27.1% reduced alcohol intake, and 16.1% stopped smoking. For prevention, 97.7% no longer shared personal items, 50.3% did not share dining utensils, and 97.7% did not engage in blood donation. Most of them (91.7%) encouraged their immediate family members to undergo screening for hepatitis B.
Conclusion: The findings highlight the stigma and misconceptions that exist among the hepatitis B patients.Patient and public education about hepatitis B and its prevention are essential to increase awareness and demystify the disease.

PE090

Chronic Viral Hepatitis in Patients on Renal Replacement Therapy

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Introduction: Chronic viral hepatitis is common in end-stage renal disease (ESRD), from endemic hepatitis B (CHB) and nosocomial hepatitis C (CHC). Reduced outcomes post-renal transplant were reported thus CHB and CHC cirrhosis became contraindications to listing. However, these predated effective anti-viral therapies. We reviewed outcomes of patients with chronic viral hepatitis following assessment for renal transplantation.
Methods: Prospective database of ESRD patients with viral hepatitis referred for renal transplantation was reviewed.
Results: 110 patients were assessed. 23 patients underwent kidney transplantation. Two were cirrhotic and had liver/kidney transplantation; both died within 6 months. 21 were non-cirrhotics, of whom 20 are alive. 14/20 have functioning allografts; predictors were normal ALT and low viral load. Of the 87 non-transplanted, 31 had cirrhosis; 17/31 received anti-virals. Mortality was 35% – 7 liver-related (3 hepatoma,1 bacterial peritonitis,3 sepsis –5 inactive cirrhosis); 4 non-liver related (2 cerebral,1 haemorrhage,1 renal –3 inactive cirrhosis). 12/20 surviving cirrhotics received anti-virals. In non-transplanted non-cirrhotics, mortality was 18%; 80% of survivors had inactive disease. 23 CHB patients received Lamivudine; 11 Adefovir (Lamivudine resistance). 11 CHC patients received IFN-based therapy.
Conclusion: Excellent outcomes are achieved in ESRD patients with CHB/CHC post-renal transplant, in absence of cirrhosis. Normal ALT/non-detectable viral load can predict graft function. However, cirrhosis is associated with high mortality on dialysis whereas non-cirrhotics with inactive disease do well. The role of kidney transplantation in cirrhotics with suppressed viral replication needs to be reassessed.

PE091

The Truncated HBc149 Interferes with Replication of Hepatitis B Virus

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Hepatitis B virus (HBV) capsids play an important role in production of progeny virus and other elements of the virus life cycle. Misdirection of capsid assembly and formation of aberrant particles may be an effective approach to interfere with virus replication. HBV capsids can be assembled in vivo and vitro from the dimeric HBV core protein (HBcAg). The interaction of single and dimeric HBcAg with some truncated HBcAg is verified in vitro. The truncated HBcAg consists of the first 149 amino acids and lacks the C-terminal, 34-residue RNA-binding domain. Method: we transiently transfected hepG2.2.15 with pcDNA3.1HBc149 by Fugene6.after 48 and 96h, HBVDNA, HBeAg and HBsAg in culture supernatant were detected and cell subjected to Southern blot and Immunofluorescence analysis. Result: The level of HBsAg and HBeAg had gentle change, we found that HBVDNA decreased at 96h after transfection($10^3 \sim 10^4$copies/ml↓P<0.01) ,but replication intermediates obviously decreased from 48h. Some positive signal of HBcAg located around the nuclear and conglomerated in cytoplasm compared to the control. Conclusion: The truncated HBc149 can inhibit replication of hepatitis B virus. Misdirection of capsid assembly and formation of aberrant particles could be an important cause.

PE092

Interruption of Perinatal Transmission of Hepatitis B Virus (HBV) With a Recombiant Yeast

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Objective: To assess the long-term efficacy of recombinant yeast derived hepatitis B vaccine in infant s born to HBsAg and HBeAg carrier mother.
Methods: A total of 273 neonates born to HbsAg, HBeAg both positive mothers were vaccinated with 5 ,5 ,5μg doses of recombinant yeast derived hepatitis B vaccine by 0 ,1 , and 6 months schedule. They were all followed for 129 years after the primary vaccination.
Results: Twelve infant s (6.63 %) become HBsAg positively conversed in 9 year after primary vaccination ,and the positive rate of HBsAg in 1-9 year was 0.72 %-6.8 % ,17.18 % of child in no/ lowly respond become HBsAg positively. At the ninth year, the positive rates of anti-HBs were 60 % above. Anti-HBs positive rates and immunity level were higher at 3-5 year old by repetition immunity than others.
Conclusion: The recombinant yeast derived hepatitis B vaccine have good immunogenecity and long-term protective efficacy to HBV interruption of perinatal transmission , a booster dose seems necessary in aged 3-4 years to the mother with HBsAg and HBeAg.It is high risk tobecome HBsAg positively in the baby of norespones to hepatitis B vaccine.

PE093

CHB Patient Group-initiated Programme to Improve Awareness, Adherence and Treatment Outcomes in Asia Pacific

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Background: Worldwide, over 400 million people live with chronic hepatitis B (CHB); 300 million in Asia Pacific. Regional survey data from 1,500 patients in 10 countries showed a lack of knowledge and understanding of CHB, its severity and impact on quality of life. This initiative aims to coordinate patient groups in the region and devise programmes to improve knowledge and healthcare outcomes.
Methods: The patient groups met in Hong Kong in May 2008 and identified common needs to: (1) improve educational resources; (2) raise awareness; (3) increase diagnostic yield; and (4) enhance treatment compliance through education about the need for sustained viral suppression to reduce long-term complications.
Results: A patient engagement programme was developed for people with newly diagnosed or known CHB. The programme comprises:

- Detailed information about CHB
- A health-tracking tool for self-monitoring of blood tests and treatment progress
- Detailed information for carers/family
- A patient-physician communications video (including role-play)

- Mobile phone text messages providing advice and compliance/appointment reminders

Conclusion: This programme was developed to address the needs of patients and clinicians. Improved knowledge and long-term support, particularly for patients on antiviral medication, is expected to improve quality of life. The programme encourages clinicians and patients to develop enduring therapeutic partnerships to promote optimal outcomes.

Acknowledgement: The CHB patient group meetings and the patient engagement programme are supported by an unrestricted educational grant from GlaxoSmithKline.

PE094

Serum HBV RNA Level Reflects the Potency of Nucleos(t)ide Analogue

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Background and aims: Serum HBV RNA is detectable in patients treated with lamivudine (LMV) or entecavir (ETV) (Hatakeyama, 2007 and Huang, 2008). The aim of this study was to determine the clinical significance of serum HBV RNA levels in patients treated with nucleos(t)ide analogues of different potency.

Methods: Serum HBV RNA was serially determined in 20 patients treated with nucleos(t)ide analogues for 48 to 52 weeks (9 with adefovir (ADV), 5 with LMV, and 6 with ETV). Serum HBV RNA was quantified by reverse transcription of HBV nucleic acid extract with subsequent real-time PCR.

Results: HBV RNA was detectable in 11 patients as follows: 2 of 9 in ADV (22%), 3 of 5 in LMV (60%), and 6 of 6 in ETV (100%) ($p = 0.002$). Mean log serum HBVDNA levels at baseline were 10.1 ± 0.6 for ADV, 6.6 ± 2.0 for LMV, and 9.5 ± 0.9 for ETV, which were comparable between less potent ADV and most potent ETV ($p = 0.14$). During antiviral therapy, peak log HBV RNA level of patients with ETV was significantly higher than that of those with ADV or LMV (3.2 ± 0.9 vs. 1.3 ± 0.2 or 1.3 ± 0.4, $p = 0.024$).

Conclusions: Serum HBV RNA levels may reflect the potency of nucleos(t)ide analogues. Further studies are needed to confirm the clinical significance of serum HBV RNA level.

Acknowledgments: This study was partly supported by Japanese Society of Gastroenterology 2007 Research Fellowship Program Award.

PE095

Hepatitis B Virus PreS2 Protein Upregulates Human Telomerase Reverse Transcriptase via a Novel PreS2 Responsive-Region in Hepatitis B Virus Related Hepatocellular Carcinoma

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Background: Hepatocellular carcinoma (HCC) is the third leading cause of cancer death with an estimate of more than 500 000 incidences in the year 2000. 53% of HCC cases in the world are related to Chronic Hepatitis B Virus (HBV), 100% of HBV related HCC show high telomerase activity. Our earlier studies show that preS2 gene expression can enhance the growth rate, malignant tendency and telomerase activity of HepG2 cells via up-regulating human telomerase reverse transcriptase (hTERT).

Methods: Antisense oligonucleotide blocking assay in HBV-integrated HepG2.2.15 cells and RT-PCR in clinical samples were used to confirm the preS2-mediated hTERT upregulation.

Truncated or mutate constructions, co-transfection, Dual-luciferase reporter assay and EMSA were used to study the mechanism of preS2-mediated hTERT upregulation.

Results:

1. Blocking preS2 expression reduces hTERT mRNA expression, telomerase activity and tumorigenicity of HepG2.2.15.
2. PreS2 translocates into the nucleus and transactivates hTERT promoter in immortal liver cell line LO2, HCC cell lines and COS-7.
3. A 65-bp region located between -371 and -306 bp upstream of the translational start site (TSS) was responsible for the transactivation but not c-myc.
4. A novel HBV preS2 protein responsive-region (PRR) which locates between –349 and –329 bp upstream of the TSS in the hTERT promoter was identified.
5. PreS2-positive HCC samples has higher hTERT mRNA level and stronger binding activity to the PRR element.

Conclusions: HBV preS2 protein upregulates hTERT via the PRR element to involve HCC development.

PE096

Clevudine with or without Vaccine Demonstrates Potent Antiviral Activity in the Naive HBeAg-positive Chronic Hepatitis B Patients.

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Background: In the phase III clinical trials, clevudine 30mg for 6 months showed potent antiviral activity along with a marked post-treatment antiviral effect. The objective of this study is to compare the anti-HBV activity of combination of clevudine and vaccine over clevudine alone in chronic hepatitis B (CHB) patients in a randomised way.

Methods: The patients are received clevudine for 24 weeks and then combination of clevudine and vaccine for another 24 weeks or clevudine alone for 48 weeks. Eligible patients were treatment-naïve HBeAg(+) CHB patients with HBV DNA levels≥500,000 copies/mL. The primary endpoint is the proportion of patients with HBeAg loss. Preliminary results are presented here.

Results: Thirty-one patients have completed week 24 visits and from them, 15 patients (11 in clevudine alone and 4 in combination group) have completed week 36 visits. At week 24, 26% of patients had HBeAg loss. At week 36, 46% in clevudine alone and 25% in combination group (3 months on combination after clevudine monotherapy) had HBeAg loss. At week 24, 63% of patients had negative HBV DNA by Amplicor PCR (<300 copies/mL). At week 36, all of patients in both groups had negative HBV DNA by PCR and 73% in clevudine alone and 80% in combination group had normal ALT.

Conclusion: Clevudine demonstrated good serologic response as well as significant viral suppression and ALT normalization. With this data, we conclude that combination therapy of clevudine and vaccine for short period does not show the superiority over clevudine alone.

PE097

The Reasonable Number of Clones for Hepatitis B Virus Quasispecies Analysis

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Background/Aims: To determine the reasonable number of clones for HBV quasispecies analysis.

Methods: 16 chronic hepatitis B patients were enrolled，with HBVDNA levels range from 4~10 log copies/ml. HBVDNA was extracted. HBV reverse transcriptase (RT) gene encompassing the overlapping surface（S）gene was amplified by polymerase chain reaction, then cloned and sequenced. Ten positive clones for each sample were sequenced in the first group, and then additional ten positive clones were sequenced in other groups until up to thirty clones. The characteristics of HBV quasispecies including Shannon entropy and genetic distance were calculated.

Results: The Shannon entropy and genetic distance of 10 clones group was higher than those of 20 and 30 clones group, either in RT gene or in S gene ($p<0.01$). While the Shannon entropy and genetic distance of 20 clones group showed on difference with those of 30 clones group, neither in RT

gene nor in S gene (p>0.05). The number of different quasispecies detected in 30 clones group was higher than that of 20 and 10 clones group (p<0.01). The Shannon entropy and genetic distance in three different clones group had no correlation with HBV DNA levels (p>0.05).
Conclusion: Although the number of different quasispecies detected was increased with the augmentation of clone number, the quasispecies characteristic didn't changed significantly when the clone number more than 20. The information contained in 20 clones per sample could well represent the quasispecies characteristics. The clone number was not necessary modulated according to different HBV DNA levels.

PE098

A1762T and G1764A Mutations of Hepatitis B Virus, Associated with Increased Risk of Hepatocellular Carcinoma, Reduce the Enhancer II/basal Core Promoter Activity

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Background: Recent studies reported that basal core promoter mutation (A1762T and G1764A) was associated with more aggressive progression of liver disease from inactive carrier to active hepatitis, and eventually to liver cirrhosis and HCC. But the effect of the double mutations on the activity of enhancer II/basal core promoter is still uncertain.
Objectives: To evaluate the influence of nt1762 A/T and nt1764 G/A mutations on HBV enhancer II/basal core promoter activity.
Methods: The PCR fragments of HBV enhancer II/basal core promoter (nt1601 to nt1815) from the serum-derived genotype B HBV DNAs of one HBV carrier aged 66 and one HBV related hepatocellular carcinoma patient aged 26 were introduced into the pGL3-Basic-Vector from Promega via restriction sites of Xho I and Hind III. The nt1762 A to T and T to A, the nt1764 G to A and A to G mutations were carried out by GeneTailor Site-Directed Mutagenesis System from Invitrogen. The promoter activity was evaluated by comparing firefly luciferase measurement with Renilla luciferase as the internal control using the Dual-Luciferase Reporter Assay System from Promega.
Results: The luciferase reporter assay results indicated that the 1762 T to A combined with 1764 A to G mutations increase (P<0.001) while the 1762 A to T combined with 1764 G to A mutations decrease (P<0.05) the HBV enhancer II/basal core promoter activity significantly.
Conclusions: Associated with increased risk of hepatocellular carcinoma, A1762T and G1764A double mutations of hepatitis B virus reduce the enhancer II/basal core promoter activity.

PE099

Progressive Fibrosis in Chronic Hepatitis B Patients with Serum Alanine Aminotransferase Less than 2 Times Upper Limit of Normal

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Background/Aims: A substantial proportion of chronic hepatitis B (CHB) patients with mildly elevated alanine aminotransferase (ALT) have significant fibrosis. We evaluated the factors associated with significant fibrosis and clinical outcomes in these patients.
Methods: One hundred five CHB patients with ALT less than two times the upper limit of normal underwent liver biopsy. Multiple clinical, biochemical and virologic variables were evaluated to determine the predictors of significant fibrosis and progressive liver disease.
Results: There were 27 patients in the low normal ALT group, 21 in the high normal ALT group, 37 in the low elevated ALT group, and 20 in the high elevated ALT group. Fifty eight patients (55.2%) had significant fibrosis (≥ stage 3) and 35 (21.0%) had significant inflammation (≥ grade 3). The age, platelet count and grade of inflammation were factors associated with significant fibrosis. Progressive liver disease was observed in 23 (27.4%) of the 84 followed-up patients. The stage of fibrosis, ALT group and antiviral therapy were significant predictive factors for progressive liver disease.
Conclusion: Liver biopsies should be recommended in patients over 35 years with mildly elevated ALT levels, and antiviral therapy should be considered in patients with significant fibrosis to prevent progressive liver disease.

PE100

Analysis of Hepatitis B Virus Drug-resistant Mutations for 2,000 Patients with Chronic Hepatitis B Virus in China

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Background: Four nucleos(t)ide analogues (NAs) are currently approved for the treatment of HBV infection in China. However, long-term benefits are limited by the emergence of drug-resistant viruses.
Methods: Patients accepted the examination based on physician's instruction. HBV reverse transcriptase gene was amplified from serum *via* nested PCR and sequenced directly.
Results: Well-recognized drug-resistant mutations were detected in 567 of 2,000 patients. In patients receiving NA monotherapy, corresponding drug-resistant mutations were detected in 214/381 for lamivudine (LAM), 35/333 receiving adefovir (ADV), 0/57 for entecavir (ETV), and 9/17 for telbivudine (L-dT). The mutations were detected in 272/615 patients receiving 31 kinds of sequential/combined usages of the 4 NAs. M204I (32%), M204V+L180M V173L (32%), and M204I+L180M (21%) were identified as major mutant patterns of LAM monotherapy. N236T A181 substitution was the dominant ADV-resistant mutation. T184 substitution was the dominant ETV-resistant mutation always accompanied with LAM-resistant mutation. L-dT-resistant mutation was M204I L180M exclusively. ADV-resistant mutation was frequently seen in LAM–resistant patients receiving ADV sequential therapy rather than those receiving ADV add-on therapy. Controversial LAM/ADV-resistant mutations including A181T, V214A, Q215S and I233V were detected in some patients singly or with the well-recognized drug-resistant mutations. Interestingly, the drug-resistant mutations were also observed in a few of patients naïve to NAs.
Conclusions: The exploration of HBV drug-resistant mutation profile in large clinical samples furthers our understanding of HBV drug-resistant status in China with implications for administrating anti-HBV therapy more reasonably.

PE101

Circulating Toll-like Receptor (TLR) 2, TLR4 and CD4+CD25+CD127low/- regulatory T Cells Correlate with Hepatitis B Virus Infection

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Background: TLRs play a crucial role in sensing and initiating innate antiviral response and Tregs actively suppress immune response, contributing to viral persistence and chronic tissue damage. In this study, we determined TLR2 and 4 expression and Treg frequency, as well as their function in the effect of HBV infection.
Methods: TLR2 and TLR4 expression on monocytes and circulating $CD4^+CD25^+CD127^{low/-}$ Tregs were determined by flow cytometry in 16 AHB, 42 CHB, 22 AsC and 20 NC. Spearman correlation was performed to investigate associated variables on Treg or TLRs. PBMCs were stimulated with HBeAg or HBcAg and the TLRs profile was examined.
Result: TLR2 expressions were up-regulated in CHB and AsC, while TLR4 were increasingly expressed in AHB and AsC. Treg frequency in CHB was significantly higher than that in NC. In CHB, the increased TLR2 negatively correlated with HBV DNA loads and Treg frequency negatively correlated with TLR4 expressions. TLR2 was up-regulated after HBeAg stimulation in both NC and CHB.
Conclusion: Increased Tregs may be associated with CHB and there might be possible interactions between HBeAg, TLR signaling and the innate immune response, which may partially explain the mechanism of HBV infection induced immuno-tolerance.

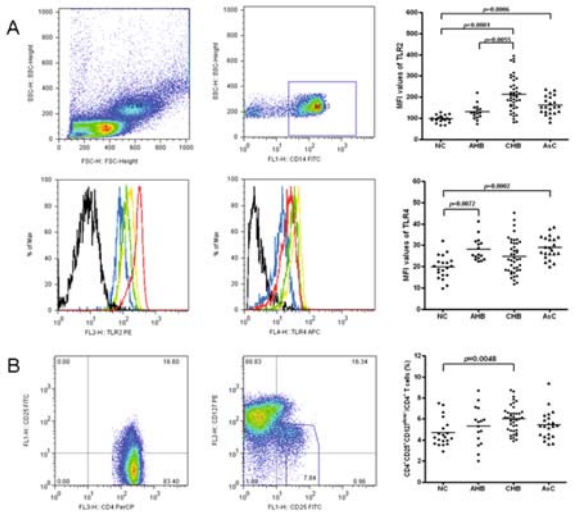

Fig.1 (A) Typical TLR profiles and expressions on CD14+ peripheral blood monocytes in control subjects and patients with HBV infection. (B) Frequency of circulating CD4+CD25+CD127low/- Tregs in various subjects.

PE102

Antiviral Efficacy of Adefovir Dipiroxil in Treatment of Patients with Chronic Hepatitis B among Different Genotypes

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Objective: To study clinical efficacy of adefovir dipiroxil in treatment of patients with chronic hepatitis B among different genotypes.

Methods: 55 patients with chronic hepatitis B of HBeAg positive received adefovir dipiroxil therapy at 10mg once daily for 48 weeks including 36 male and 19 female. Age was (34±8.25). The course of disease was (6.7±1.35). HBV-DNA was quantitatively determined by polymerase chain reaction (PCR) technique, and HBV genotype was determined by PCR microwave gene chip technique. Antiviral efficacy was assessed using measuring the following scales: the ALT normalization rate, HBV-DNA negative conversion rate and the HBeAg/anti-HBe seroconversion rate.

Results: Among 55 serum specimen, HBV genotype distribution was 38 genotype C, 14 genotype B, and 3 genotype non-B or C respectively. In genotype B, ALT normalization rate was 78.57%(11 cases), HBV-DNA negative conversion rate was 35.71%(5 cases) and the HBeAg/anti-HBe seroconversion rate was 14.28%(2 cases). In genotype C, ALT normalization rate was 76.31% (29 cases), HBV-DNA negative conversion rate was 47.37%(18 cases) and the HBeAg/anti-HBe seroconversion rate was 18.42%(7 cases). The efficacy of adefovir dipiroxil showed no significant differences between genotype B and C in the treatment of chronic hepatitis B （P>0.05）.

Conclusion: Adefovir dipiroxil is an effective antiviral drug. HBV genotype is irrelevant to the antiviral efficacy of adefovir dipiroxil in treatment of patients with chronic hepatitis B.

PE103

The Effect of Anti-HBV Drugs on Albumin and Bilirubin Levels, and Platelet Count

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Background/Aim: We assessed the efficacy of anti-HBV drugs on the liver function.

Methods: Patients with HBV-related disease followed at our center between 2005 and 2007 were enrolled. Lamivudine (100mg), lamivudine (100mg) +adefovir (10mg), or entecavir (0.5mg) was administered to the patients with detectable HBV DNA and elevated ALT. Liver function (ALT, ALB, and T.Bil) and platelet count were observed. ALT, ALB, T.Bil, and platelet count of treated group at pretreatment, year 1, and year 2 were compared with untreated group.

Results: Eighty six patients with positive HBsAg were enrolled between Jan 2005 and Dec 2007. Seven patients (2 acute infection, 1 overlap infection with HCV, 7 lost of follow up) were excluded. In total 76 patients were followed up for a median follow up of 26 (range 2-39) months. Of 76 patients, 32 received anti-viral treatment. Twenty one patients were treated with lamivudine, 4 with lamivudine+adefovir, and 7 with entecavir. The mean of levels of pre-treatment–year1–year2 were ALT:129-37-43 (U/L), ALB:4.0-4.4-4.4 (g/dl), T.Bil:1.0-0.8-0.7 (mg/dl), and Plt:14.3-15.4-16.0 ($x10^4$mcl) respectively. Markers of untreated group (n=44) (at baseline–year1–year2) were ALT:33–40–35 (U/L), ALB:4.4– 4.4–4.4 (g/dl), T. Bil:0.8–0.8–0.9 (mg/dl), and Plt:18.7–18.0–18.5 ($x10^4$mcl) respectively. Although all of four markers in treated group were significantly worse than untreated group at baseline, all of four markers did not showed significant difference from untreated group at year2.

Conclusion: Treatment with anti-HBV drugs showed the efficacy not only transaminase levels, but also on albumin, bilirubin, and platelet count improvement–improvement of "hepatic reserve" which is valuable for prevention of cirrhosis.

PE104

Nucleotide Analogues can Satisfactory Inhibit HBV Replication of HBeAg-negative Chronic Hepatitis B Patients with ALT＜2×ULN

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Background: Currently, HBeAg-negative chronic hepatitis B(CHB) is increasing. But there are still controversial on the treatment of HBeAg-negative CHB with ALT＜2×ULN. We have investigated the clinical efficacy of nucleotide analogues(NAs) in the treatment of HBeAg-negative CHB with ALT＜2×ULN.

Methods: The data of patients who were treated by NAs for more than 2 years and with ALT 1～2×ULN (n=87) , ALT≤1×ULN(n=43) and ALT≥2×ULN(n=88) were collected, and 12W and 24W virologic response, 48W and 96W complete response, virologic breakthrough and clinical resistance were analyzed.

Results: Compared with the base line, HBV DNA level in all three groups were significantly decreased (P＜0.01), and there was no significant difference between ALT 1～2×ULN group and ALT≥2×ULN group. The viral load was significant decreased in ALT≤1×ULN group at 12W, 24W and 36W (P<0.05). Virologic response at 12W and 24W，complete response at 48W and 96W was 71.3%, 82.8% , 82.8% and 86.2% respectively in ALT 1～2×ULN group and was 51.2%, 60.5%, 65.1% and 74.4% respectively in ALT≤1×ULN group. There was no significant difference between ALT 1～2×ULN group and ALT≥2×ULN group. Virologic response at 12W and 24W and complete response at 48W were significant decreased (P<0.05) in ALT≤1×ULN group. There was no significant difference among the three groups in virologic breakthrough and clinical resistance.

Conclusion: HBV replication can be satisfactory inhibited by NAs in HBeAg-negative CHB patients with ALT＜2×ULN, which suggests that in these patients the indication of ALT is different from HBeAg-positive patients.

PE105

Quantitative HBeAg Assay as a Predictive Factor of HBeAg Seroconversion Induced by PEG-IFNα-2a Therapy to HBeAg-positive Chronic Hepatitis B

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Background: To find predictive factor for HBeAg seroconversion in the treatment of HBeAg-positive chronic hepatitis B (CHB) by PEG-IFNα-2a.

Methods: HBeAg-positive CHB patients were given PEG-IFNα-2a treatment for 48 weeks. Clinical data were collected every 3 months. Receiver Operator Characteristic (ROC) curve was employed to calculate positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity.

Results: Sixty-five patients completed PEG-IFNα-2a therapy. Among them, 17 (26.15%) were found HBeAg seroconversion and 19 (29.23%) were found HBeAg loss at cessation of therapy. None of age, gender, ALT level and HBV DNA load at baseline had relationship with HBeAg seroconversion. HBeAg level of baseline was correlated to HBeAg seroconversion, with *P* value as 0.003 (Table 1). According to ROC curve, supposed AUC as 0.705 and *P* value as 0.042, the PPV, NPV, sensitivity and specificity of HBeAg level as 61 at 12 week were 0.361, 0.862, 0.765 and 0.521, respectively. Supposed AUC as 0.828 and *P* value as 0.001, the PPV, NPV, sensitivity and specificity of HBeAg level as 15 at 24 week were 0.452, 0.912, 0.824 and 0.646, respectively. The HBeAg level (s/co) and decreased degree (percentage) at 12 week and 24 week were significant related to HBeAg seroconversion (Table 2).
Conclusion： HBeAg level at baseline and at 12th and 24th week and its decreased degree (percentage) during the treatment course could be used as predictive factor for HBeAg seroconversion.

PE106
Effect of Hepatitis B Immunoglobulin on Interruption of HBV Intrauterine Infection
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Background: It is well documented that perinatal transmission is the major cause of chronic HBV infection in China. The aim of this study was to evaluate the efficacy of interruption of HBV intrauterine infection with hepatitis B immunoglobulin (HBIG) in pregnant women with HBeAg positive.
Methods:: A prospective randomized controlled trial was adopted. Each subject in the trial group (28 cases) was given 200 IU HBIG intramuscularly every 4 weeks from 28-week of gestation, while each subject in the control group (24 cases) received placebo in the same way. The cord blood of newborns were collected for detecting HBsAg, HBeAg and HBV-DNA.
Results: For newborns, HBeAg positive rate in trial group was 21.4%(6/28).HBeAg positive rate in control group was 79.2%(19/24). There was significant difference in HBeAg positive rate of newborns between the two groups($P < 0.01$, RR = 0.27). HBV-DNA positive rate in trial group was 25%(7/28). HBV-DNA positive rate in control group was 83.3%(20/24). There was significant difference in HBV-DNA positive rate of newborns between the two groups($P < 0.01$, RR = 0.30). HBV-DNA load of 7 cases of newborns in trial group was lower than that of their mothers($T = 28, P = 0.02$). There was no significant difference in HBV-DNA load between women and their newborns after delivery in control group ($T = 81.5, P > 0.1$).
Conclusion: It is effective and safe to prevent HBV intrauterine infection with HBIG from the 28(th) wk in pregnant women with HBeAg positive.

PE107
Retrospective Analysis of Chronic Hepatitis B in Yunnan Province - From 2003 -2007
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Background/Aims: To comprehend the recent five years epidemiological and clinical features of the chronic hepatitis B patients in Yunnan province.
Methods: Retrospective analysis 11909 cases of HBV infected patients medical history of chronic hepatitis B patients whom experienced diagnosis and/or treatment in hospital during 2003 to 2007. 9985 cases of them are outpatients, 1924 cases are inpatients. All of the cases were determined serum HBV DNA and HBsAg, anti-HBs, HBeAg, anti-HBe, anti-HBc.903 cases were detected pre-core G1896A mutate.
Results: The ratio of the HBeAg-negative patients and HBeAg-positive patients cases are 63.89% and 36.11% respectively. From 2003 to 2007, the percentage of HBeAg-negative patients are 57.22%, 62.41%, 64.45%, 66.67% and 65.80% respectively. The cirrhosis and HCC ratio in HBeAg-negative patients significant higher than HBeAg-positive patients (30.4% vs 21.7%; 6.6 %vs 2.8%; p), especially, the cirrhosis and HCC cases obviously more in both HBeAg and anti-HBe patients are negative than HBeAg-negative but anti-HBe positive patients (.36.7% vs 26.7%; 7.9%vs5.5%, p).The prevalence of pre-core G1896A mutate have no significant difference regardless of HBV serum marker status or the state of illness.
Conclusion: Recent 5 years the HBeAg-nagative chronic hepatitis B patients are gradually increasing in Yunnan province. While the HBeAg disappear but no anti-HBe serum transfer, and the virus still active replication - It may be a crucial phase determined the diseases outcome, which should be pay more attention by physicians. The clinical significant of pre-core G1896A mutate remain unknow.

PE108
Efficacy of Interferon for Chronic Hepatitis B Patients with Normal or Paranormal ALT
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Background: We reported Interferon treatment for 4 cases with normal or paranormal ALT but in which liver histologic exam showed G2-4 and/or S3-4.
Methods: 4 patients were male with an average age of 28 years.Mean ALT was 46.7 IU/L and HBV DNA level was 3~5 log10copies/ml. Two patients were HBeAg positive; one patient was both negative for HBeAg and anti-HBe and one patient was anti-HBe positive. Liver biopsy showed G2~G4 and S3~S4 respectively. 3 patients were treated with IFN-alpha, Liver biopsy was repeated after 1 year.Only one patient had received combination therapy with IFN and adefovir after 10 months treated IFN monotherapy and liver biopsy was taken after 1.5 years.
Results: All patients got normal ALT after 1 year treatment. HBV DNA was undetectable in 3 patients. 2 patients with initial positive HBeAg cleared. But 3 patients still were anti-HBeAg negative.Liver biopsy showed change fromG4 S3-4 to G2 S2-3 in 1 patient; fromG2 S3 to G3 S4 in 1 patient and no change in the other 2 patients.
Conclusions: Though ALT and HBV DNA improved after 1 year treatment, histological improvement is not satisfying. 1 patient's improvement in liver histology may be due to seroconversion before treatment and adding Adefovir after 10 months of interferon therapy. After 8 months of combination therapy we did liver biopsy again. The other 3 patients were HBeAg negative, but HBeAb were also negative, liver biopsy was taken 1 year later without combination of nucleoside analogs.

PE109
Evaluation of Long Term Efficacy of Hepatitis B Vaccination
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Objective: To evaluate the long term effectiveness of preventive HBV infection and to monitor the incidence of hepatitis B in children to see possible impact on the program of Long An that was launched in 1986.
Methods: (1) Set up a surveillance systemof hepatitis ,to evaluate the possible impact on incidence of hepatitis B. (2) To serologically evaluate the effect of the program, a stratified random sampling of 1000 subjects in 1987 birth cohorts was recruited for long term follow up at the age 1-20 years. (3) Cross-sectional seroepidemiolgical survey was carried out in the county in 1985 before the program and 20 years later. HBsAg , anti-HBs and anti-HBc were tested by RIA.
Results: The average coverage of hepatitis B vaccine was 89. 1 %. At 20 years after vaccination, the seropositivity for HBsAg in population of 1-20 years has decreased from 16. 0 % to 2. 3 %, the annual effectiveness was 89. 7 %. HBV accumulated infection rate was 3. 5 %, protective rate was 96. 2 %. The incidence of acute hepatitis B was 1. 60 per 100,000 in population aged 1 - 20 years , it decreased by 91.3 % as compared with the incidence of 18.38 per 100,000 in same age group in 1985 - 1987.
Conclusion: Mass hepatitis B vaccination program in Long An County has proved to be effective in control of HBV chronic infection and incidence of acute hepatitis B.

PE110

Comparison of Real-time PCR with the COBAS Amplicor Test for Detection of Hepatitis B Virus DNA in Serum Samples

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Aim: To compare the clinical performance of a real-time PCR assay with the COBAS Amplicor Hepatitis B Virus (HBV) Monitor test for quantitation of HBV DNA in serum samples.

Methods: 151 Serum samples from 47 chronic hepatitis B patients with positive HBeAg who received lamivudine therapy were analyzed in parallel by the real-time PCR HBV kit and COBAS Amplicor HBV Monitor. The performance and linearity were evaluated and compared.

Results: Monitor was more sensitive than real-time PCR (paired χ^2, P=0.005) (Table 1). The HBV DNA levels measured by the real-time PCR correlated very well with those obtained with the Monitor test (r=0.842，P<0.001), but no linear correlation was found of the samples below 3 $\log_{10}$ copies/mL tested by real-time PCR (r=0.139，P=0.266) (Figure 1).

Conclusion: The real-time PCR assay is less sensitive than Monitor for quantitation of HBV DNA levels.

Table 1 Performance of real-time PCR for HBV DNA quantitation compared to COBAS Amplicor Monitor

	Amplicor COBAS			
LightCycler	+	−	total	P
+	88	0	88	0.005
−	57	6	63	
total	145	6	151	

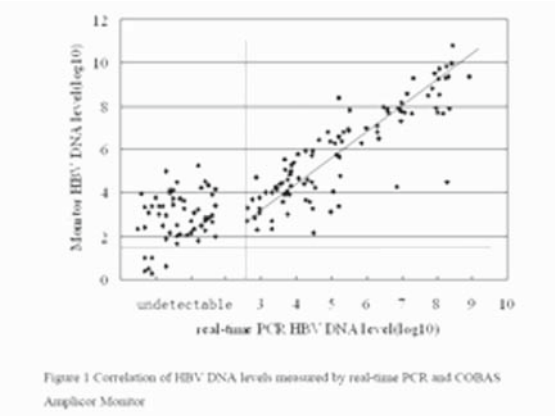

Figure 1 Correlation of HBV DNA levels measured by real-time PCR and COBAS Amplicor Monitor

PE111

Evolution of Hepatitis B Viral Quasispecies during HBeAg Sseroconversion

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Background and Aims: Although the evolution of viral quasispecies may be related to the pathological condition of disease, little is known about this in hepatitis B virus (HBV), especially during HBeAg seroconversion.

Methods: Nucleotide sequences of HBV precore/core genes from 5 time points were analyzed in four cohorts of chronic hepatitis B, interferon-induced seroconverters (IS, N=9), interferon non-responders (IN, N=9), spontaneous seroconverters (SS, N=9) and non-seroconverters (SN, N=9), followed during 60 months on average. Only patients with genotype C were used. Viral diversity was then estimated after nucleotide genetic distance was assessed and phylogenetic trees were constructed.

Results: Analysis of 1800 nucleotide sequences showed that the nucleotide genetic distance of seroconverters (IS and SS; $9x10^{-3}$ substitutions/site and $8.5x10^{-3}$ subsititutions/site, respectively) was similar to that of non-seroconverters (IN and SN; both $7x10^{-3}$ substitutions/site) before seroconversion. Compared to that of nonseroconverters (IN and SN; $6.5x10^{-3}$ substitutions/site and $7.5x10^{-3}$ substitutions/site, respectively) the viral diversity of seroconverters (IS and SS; $13x10^{-3}$ substitutions/site and $12x10^{-3}$ substitutions/site, respectively) was significantly higher after seroconversion ($p<0.05$) and it was higher after seroconversion in seroconverters compared with that berore seroconversion ($p<0.05$) while it almost didn't change in non-seroconverters irrespective seroconversion. Phylogenetic trees also showed that complex trees appeared in secoconverters and relatively simple in nonseroconverters.

Conclusions: The distinctly higher viral diversity after seroconversion in HBeAg seroconverters could be related to increased HBV-specific T-cell responses and escape mutant which arise from stronger selective pressure caused by host immune activity.

PE112

Adefovir Dipivoxil 10mg (ADV) Resistance at 5 yrs in Chinese HBeAg+ve Chronic Hepatitis B (CHB)

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Background: Long term ADV provides clinical and histological improvement in CHB, but may lead to emergence of treatment associated resistant mutations. We report on ADV resistance data from Chinese HBeAg positive subjects treated for 5 years.

Methods: 480 HBeAg positive CHB subjects were randomized in an initial 52 weeks controlled ADV study (with a 12 weeks placebo period in half of patients) and then offered open label ADV treatment for a further 208 weeks. A total of 474, 456, 443, 421 and 390 subjects completed the 1st, 2nd, 3rd,4th and 5th yr, respectively. At the end of each year samples were analysed from those subjects with protocol-defined HBV DNA breakthrough for the rtN236T or rtA181V ADV mutations associated with resistance. Sera from subjects with breakthrough were analysed at all subsequent yearly timepoints whenever possible.

Results: At the end of the 1st yr, none of the 45 subjects with HBV DNA breakthrough had either mutation. Sera were available for analysis from 137, 199, 228 and 187 subjects with viral breakthrough at the end of the 2nd, 3rd, 4th and 5th yr, respectively, with new mutations identified in 6, 20, 24 and 20 subjects at the same timepoints. Of the cumulative 70 subjects at the 5th yr analysis 31 had rtN236T, 29 had rtA181V, and 10 had both mutations.

Conclusion: Treatment with ADV in Chinese HBeAg positive CHB subjects for up to 5yrs resulted in a cumulative rate of 14.6% (70/480) ADV resistance-associated mutations with HBV DNA breakthrough.

PE113

Rapid Virologic Response Predicting End-of-treatment Virologic Response and HBeAg Seroconversion in Naive Chronic Hepatitis B Patients with Adefovir Dipivoxil Treated

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Background and aims: To evaluate the predictive significance of rapid virologic response (RVR) for achieving an end-of-treatment virologic response (ER) or HBeAg seroconvertion and the predicting indicator of nonresponse (NR).

Methods: 205 patients with chronic hepatitis B were treated with ADV and prospectively observed to 48 weeks. We assessed the values of virus load reduction at weeks 4, 8, and 12 weeks to predict the ER and HBeAg seroconversion. The association between less reduction of viral load at 12 and 24 weeks and nonresponse was also analyzed.

Results: After 48 weeks of therapy, serum HBV DNA levels decreased with a median 4.07±2.47 log10 copies/mL. Twenty-three(11.2%) of patients had ER. Twenty-six (12.7%) patients achieved HBeAg seroconversion. HBV DNA <4 log 10 copies/mL at week 4 predict both ER and HBeAg seroconversion. HBV DNA> 4log10 copies/mL at 4 weeks but decline to <4log10 copies/mL at 12 weeks or 24 weeks both can predict ER and HBeAg seroconversion. Less than 2 log 10 HBV DNA reductions at 24 weeks might predict NR.
Conclusions: The virologic response within 4 weeks could be useful for prediction of ER and HBeAg seroconversion of adefovir therapy. Failing to EVR might not predict NR.

PE114

Risk Fctors of Aefovir Rsistance in Lamivudine-resistant Chronic Hepatitis B Patients with Genotype C

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Background: Adefovir (ADV) is considered as a first-line therapeutic agent against lamivudine (LAM)-resistant chronic hepatitis B (CHB). Notwithstanding, it might induce subsequent ADV resistance. We assessed the predictors of ADV resistance in LAM-resistant CHB patients particularly with genotype C.
Methods: This retrospective cohort study included the patients treated with ADV for LAM resistance between October 2005 and March 2008 at Seoul National University Hospital, Seoul, Korea. The incidence and the predictive factors of ADV resistance were evaluated by Kaplan-Meier and Cox regression analysis.
Result: A total of 233 patients were included: in 40 patients, ADV was added on LAM (add-on therapy), and in 193 patients, LAM was switched to ADV (switch therapy). During 16.5 months of follow-up, 25 patients developed ADV resistance (rtA181V and/or rtN236T) and all had undergone switch therapy. The cumulative probability of ADV resistance at the 24th month was 17.5%. Although add-on therapy induced no ADV resistance, it failed to show significant superiority over switch therapy (P=0.220). In multivariable analysis, female (odds ratio [OR], 2.75; 95% confidence interval [CI], 1.22–6.17; P=0.014), liver cirrhosis (OR, 2.39; 95% CI, 1.07–5.33; P=0.033), and age >45 yr (OR, 3.31; 95% CI, 1.14–9.66; P=0.028) were independent risk factors of ADV resistance.
Conclusion: ADV add-on therapy developed no ADV resistance during the observation period. Therefore, add-on therapy is recommended to LAM-resistant CHB patients with genotype C who have any risk factors for development of ADV resistance: female, liver cirrhosis, and age >45 yr.

PE115

Five Years of Continuous Entecavir (ETV) for Nucleoside-naïve HBeAg (+) Chronic Hepatitis B (CHB): Results from Study ETV-901.

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Background: In study ETV-022, ETV demonstrated superior virologic, histologic and biochemical benefit compared to lamivudine (LVD). This study (ETV-022/-901) presents efficacy and safety results for patients who received 5 years continuous ETV treatment.
Methods: The study evaluates ETV-treated nucleoside-naïve HBeAg (+) patients who completed ETV-022 and enrolled into ETV-901 with a treatment gap ≤35 days. The proportion of patients with HBV DNA <300copies/mL, ALT normalization, HBeAg loss or HBeAg seroconversion was evaluated at Week 240.
Results: Of 146 ETV-treated patients enrolled in ETV-901, 98 met criteria for inclusion into 5 year ETV treatment analyses. The proportion of patients achieving efficacy endpoints through 5 years of ETV therapy is presented the table.
Conclusions: The majority of patients experienced durable serum HBV DNA suppression (94%) and ALT normalization (80%) after 5 years ETV therapy.

End point	Week 240*
HBV DNA < 300 copies/mL (n%)	88/94 (94)
ALT ≤1 x ULN (n%)	78/98 (80)
HBeAg loss** (n%)	39/95 (41)
HBeAg seroconversion** (n%)	16/95 (17)

**Denominator represent patients with available samples; **Numbers/proportions represent additional patients achieving HBeAg loss or HBeAg seroconversion during treatment in ETV-901; Serology tests were performed by local laboratories*

PE116

Diagnostic and Prognostic Significance of Hepatitis B Core IgM in Patients with Acute Hepatitis B and Chronic Hepatitis B Flare.

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Background: AHB and CHBF can be difficult to be differentiated clinically at presentation as patients usually have similar clinical manifestations.HBcIgM can be positive in both groups.
Objectives: To determine the accuracy of HBcIgM in diagnosing AHB and the correlation between HBcIgM and liver inflammation (ALT), bilirubin & biosynthetic functions (albumin,PT).
Methods: A retrospective cross-sectional study involving patients with HBcIgM positivity between June 2006-December 2007, satisfying the definition for AHB and CHBF,and fulfilling the exclusion criteria was performed. HBcIgM test were done by using Microparticle Enzyme Immunoassay (MEIA) and results were expressed as an Index value.HBcIgM positivity was defined as Index value of >1.00
Results: 74 patients were positive for HBcIgM and 60 fulfilled the criteria(33 AHB, 27 CHBF).HBcIgM was significantly higher in AHB compared with CHBF(median 3.46 vs 1.70;p <000.5).The HBcIgM arbitary Index value of ≥2.76 was highly sensitive(97%) and specific(85%) in diagnosing AHB with high accuracy(AUROC 0.964;95% CI:0.925-1.003;p<0.0005).Among patients in both groups, there was a weak, but significant negative correlation between HBcIgM and PT above control(r = -0.309,p =0.016).However, among patients with CHBF,the negative correlation between HBcIgM and PT above control was moderately strong(r = -0.557,p =0.003).There was also a weak, but significant positive correlation between HBcIgM and albumin in with CHBF(r = +0.434,p =0.024).
Conclusion: HBcIgM index value is very useful in differentiating AHB from CHBF.The role of HBcIgM to prognosticate patients with AHB or CHBF needs further exploration.
Abbreviations:
HBcIgM-hepatitis B core IgM antibody
AHB-acute hepatitis B,CHBF-chronic hepatitis B flare
ALT-alanine transaminase,PT-prothrombin time

PE117

Detection of Emerging Drug Resistance Mutations Associated with Major Approved HBV Antivirals Using a Novel Line Probe Assay (LiPA).

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Background/Aims: An increasing number of antiviral drugs are being used to treat chronic hepatitis B virus (HBV)-infected patients. However, induced viral escape mutants – some potentially cross-resistant – lead to viral non-responsiveness and treatment failure. Effective treatment strategies must therefore take possible drug resistance (DR) into account with respect to monitoring and selection of alternative drugs. We evaluated the use of an updated INNO-LiPA HBV DR v2+v3 reverse hybridization assay versus sequence analysis to detect resistance mutations.

Methods: 273 clinical samples (from untreated HBV patients or treated with different antivirals; HBV genotypes A-H) were tested for mutations with the LiPA assay and sequencing. For LiPA, samples were extracted with the QIAamp® DNA blood mini kit (Qiagen), and then tested on the LiPA strips. Sequencing-derived reference data were subjected to phylogenetic analysis (Kodon version 3.10 Applied Maths, Neighbour joining, with Kimura-2 parameter). Sequential samples from 9 patients were evaluated as well.
Results: Quasi-perfect concordance (> 99.6%) was obtained between the two assays for the samples tested. No indeterminate results were observed. For one sample, LiPA provided additional information (wild-type/mutant mix), whereas sequencing showed only wild type. For sequential samples, LiPA was clearly able to detect emerging treatment-resistance mutations associated with viral breakthrough.
Conclusions: LiPA accurately detects the complex quasispecies nature of HBV and can help unravel the dynamics of emerging HBV resistance during treatment with different antiviral drugs. Like its predecessor, it is useful for the monitoring and early detection of drug resistance.

PE118

Application of Mass Spectrometric Analysis to Detect Precore A1896 and Basal Core Promoter T1762/A1764 Gene Mutations in Type B Viral Chronic Liver Diseases and Their Clinical Significance in Genotype C.

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Precore (PC, G1896A) and basal core promoter (BCP, A1762T and G1764A) mutations of HBV are important for predicting the risk of hepatocellular carcinoma (HCC). We developed a new mass spectrometry-based assay using restriction fragment mass polymorphism (RFMP) to detect A1896 and T1762/A1764 mutations, and applied it to analyze their clinical significance in type B liver diseases (N=336), including 35 HCCs, 118 liver cirrhosis (LC), 157 chronic hepatitis B (CHB), and 25 HBsAg-positive with low level viremia (inactive HBsAg carrer, IHC). We devided patients into 4 major groups according to the presence of wild (W) or mutant (M) genes in BCP/PC regions; W/W, W/M, M/W and M/M gene types. Each proportion was 9.5%, 3.6%, 41.4% and 23.5%, respectively. Mixed infection (X) was also found as minority; 4 W/X, 28 M/X, 15 X/W, 4 X/M and 13 X/X. Disease distributions (HCC, LC, CHB and IHC) in each group were as follows; [W/W (n=32)] 3.1%-6.3%-90.6%-0; [W/M (n=12)] 0-16.7%-58.3%-25%; [M/W (n=139)] 9.4%-42.5%-46%-2.2%; [M/M (n=79)] 11.4%-45.5%-20.1%-13.9%. These results suggest that, in Korea where only genotype C has been identified, BCP dual mutation is predominant (>73.2%), while BCP wild alone is only 13.1%. Especially, A1896 mutation alone without BCP mutation (W/M type) is uncommon, while BCP mutation alone without A1896 mutation (M/W type) is most common. It might be suggested that prognosis of wild type in BCP and PC region (W/W type) is much better than that of M/W or M/M types.

PE119

Long-Term Entecavir (ETV) Therapy Results in Reversal of Fibrosis/Cirrhosis and Continued Histologic Improvement in Patients with HBeAg(+) and (-) Chronic Hepatitis B (CHB): Results from Studies ETV-022, -027 and -901.

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Background: ETV resulted in improved liver histology compared to LVD at 1 year. Histologic data for patients on ETV for a median of 6 years is evaluated.
Methods: ETV-treated patients completing ETV-022 or ETV-027 received ETV (1.0mg daily) in ETV-901. Primary endpoints included ≥2-point decrease in Knodell necroinflammatory score, no worsening of Knodell fibrosis score and improvement in Ishak fibrosis score (IFS) (≥1-point decrease) vs. baseline. Secondary endpoints included proportions with HBV DNA<300 copies/mL, ALT normalization, and IFS normalization in patients with advanced fibrosis/cirrhosis.
Results: ETV treatment led to significant histological improvements and improved IFS in 96% (55/57) and 88% (50/57) of patients respectively. Of 10 patients with baseline fibrosis/cirrhosis (IFS≥4), all demonstrated ≥1-point improvement in IFS (median change of -3).
Conclusions: Long-term ETV therapy in nucleoside-naïve CHB patients results in durable virologic suppression, continued histologic improvement and regression of fibrosis/cirrhosis.

ETV long-term histology cohort (n = 63)		
	Biopsy At Week 48 (n = 62)	Biopsy at median time 6 years (n = 57)
Histologic improvement, (n%)	46 (74)	55 (96)
Improvement in Ishak fibrosis score (≥ 1-point decrease), (n%)	19 (31)	50 (88)
Improvement in Ishak fibrosis score (≥ 2-point decrease), (n%)	4 (6)	25 (44)
Mean change from baseline in Knodell Necroinflammatory score	–3.4	–6.4
Mean change from baseline in Ishak fibrosis score	–0.2	–1.5
Knodell HAI ≤ 3 in patients with baseline HAI ≥ 4, (n%)	14/60 (23)	41/55 (75)
HBV DNA < 300 copies/mL, (n%)	44/63 (70)	63/63 (100)
ALT ≤ 1 x ULN, (n%)	41/63 (65)	54/63 (86)

PE120

Entecavir Therapy for Chronic Hepatitis B: Improved Virologic, Biochemical, and Serologic Responses through 1-Year

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Background/Aims: Entecavir is a potent inhibitor of HBV DNA polymerase, which has been shown to be safe and effective for the treatment of chronic hepatitis B (CHB) patients. The aim of this study was to evaluate the virologic, biochemical, and serologic responses of entecavir through 1 year in CHB patients.
Methods: From 2007 May to 2008 October, we reviewed 82 patients (mean age 46±12 years, male:female=57:25) who were diagnosed as CHB patients (HBeAg (+) 64). Forty-seven patients (57.3%) had been treated with 0.5 mg of entecavir and 35 (42.7%) with 1 mg of entecavir, respectively. Mean follow-up period was 25±17 weeks. HBV DNA was quantified by bDNA assay with a lower limit of detection of 141,500 copies/mL.
Results: Median HBV DNA levels before therapy was 7.64 $\log_{10}$ copies/mL and the median decreases from baseline in HBV DNA were -4.19, -4.31, -5.09, -5.31, and -5.59 $\log_{10}$ copies/mL at 4 (n=39, p<0.001), 12 (n=62, p<0.001), 24 (n=42, p<0.001), 36 (n=22, p<0.001), and 52 (n=15, p =0.053) weeks of follow-up, respectively. At baseline, overall median ALT was 106 IU/L and the proportions of patients with normal ALT were 13%, 48%, 56%, 71%, 67%, and 69% at baseline (n=82), 4 (n=42), 12 (n=63), 24 (n=44), 36 (n=24), and 52 weeks (n=16) after entecavir therapy, respectively. Thirteen cases (15.9%) of HBeAg seroconversion were noted.
Conclusions: Entecavir 0.5 mg or 1.0 mg once daily therapy demonstrated early viral suppression and significant biochemical and serologic improvement in patients with CHB through 1-year.

PE121

Risk of Hepatocellular Carcinoma in Patients with Chronic Hepatitis B Virus Infection

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Background: Hepatitis B virus (HBV) infection is a major risk factor for the progression of liver diseases. Because its clinical course varies, it is difficult to detect the predictive factor for the prognosis of patients with HBV infection. The aim of the present study was to determine the risk factors for the occurrence of HCC.!
Methods:! A total of 620 patients who tested positive for hepatitis B surface antigen and were referred to Chiba University Hospital between February 1985 and March 2008 were included in the study, and their following characteristics were analyzed: age, gender, the status of HBeAg, ALT, HBV-DNA level, and PLT.!
Result: HCC was detected in 30 cases during the follow-up period (5.4 ± 5.1 years). Multivariate analysis revealed that age [compared with young patients: odds ratio (OR) = 1.07, 95% confidence interval (CI) = 1.03–1.11] and PLT level (compared with patients with low PLT level: OR = 0.99, 95% CI = 0.98–0.99) were the predictive factors for HCC occurrence. In patients with age more than 35 years, the HBV-DNA level (compared with <5.0 log copies/ml: OR = 3.29, 95% CI = 1.40–11.5) and PLT level (OR = 0.99, 95% CI = 0.98–0.99) were the predictive factors for HCC occurrence.
Conclusion: Advanced age and low PLT level were the risk factors for HCC occurrence in patients with HBV infection irrespective of the PLT level at baseline. In patients with age more than 35 years, viral load was also a risk factor for HCC.

PE122

Hepatitis B Virus Inhibit the Activity of Mitogen Activated Protein Kinase p38 (MAPK p38) in Peripheral Blood Mononuclear Cells (PBMCs)

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Background/Aims: To explore what role of MAPK p38 signal transduction play in HBV infection and host immune response.
Methods: Through detect the activity of MAPK p38 in PBMCs of chronic HBV infection patients by quantitative ELISA, compare the baseline level and after stimulate by lipopolysaccharide(LPS)the activities of MAPK p38 changes.
Results: Before treated by LPS, the total MAPK p38 level of PBMCs have no significant difference among the healthy control group, different stage groups with HBV infection, however, after treated with LPS, The phosphorylated MAPK p38 (pTpY180/182) in healthy control group are significant elevate than HBV infected groups(120.0±52 vs 80.2±84.8, $p<0.05$). In the two groups which HBsAg, HBV DNA are positive, alanine aminotransferase elevate than normal and HBsAg positive, but HBV DNA lower under the detect limited level, after treated by LPS the pTpY180/182 although lower than healthy control yet, but significant elevated than themselves before treated by LPS(86.6±38.6 vs117.8±21.3, 63.3±24.7 vs 93.1±21.8; $p<0.05$).Otherwise, in the group of both HBsAg and HBV DNA are positive, but ALT is normal, before and after treated by LPS, the level of pTpY180/182 have no significant difference.
Conclusion: MAPK p38 is a important signal transduction pathway which involving in inflammation and immune response, especially, MAPK p38 activated up-regulate the IFN-gamma mRNA. According to the result shown, we propose a hypothesis, HBV infection and virus active replication inhibit the MAPK p38 activated, consequent on host immunotolerance and HBV persistence, thus, MAPK p38 may be as a potential therapeutic target to break immnotolerance and establish host anti-viral states.

PE123

Multiple Sites for Evaluation of the Performance of the Elecsys® HBsAg II Assay

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Background/aims: Hepatitis B virus (HBV) surface antigen (HBsAg) is one of the most important markers for diagnosis of acute and HBV infection. High sensitivity of HBsAg assays can reduce the diagnostic window during course of disease. In addition, the presence of HBV mutants may be affected by the performance of the HBsAg kit. Therefore, the technical performance of the Elecsys® HBsAg II assay was explored, using samples (including recombinant mutants), at multiple sites in three countries.
Methods: Nine HBsAg screening centers in Thailand, Korea and Singapore compared the sensitivity of Elecsys® HBsAg II assay with that of their routine testing procedure – Abbott Architect® (7 centers), Abbott AxSym® (1 center) and Bayer Advia® Centaur HBsAg assays (1 center) using preselected seroconversion panels (n=5), recombinant HBV mutant panels (n=13) and routine clinical practice samples (n=1,863).
Results: The sensitivity of Elecsys® in seroconversion samples was equivalent to the Architect® assay, but more sensitive than the AxSym® and Advia® Centaur assays (26 vs 23 and 24 vs 18 positive bleeds, respectively). There was concordance between the Elecsys® and Architect assay results with respect to potentially cross-reactive samples (99.74%). The Elecsys® and Architect® assays detected all recombinant mutant samples, whilst AxSym® and Advia® Centaur failed to detect three and nine samples, respectively.
Conclusion: Elecsys® HBsAg II assay was not only highly sensitive and specific when compared with established HBsAg screening assays, but also reliably detected HBsAg mutants. Therefore, this attractive assay is suitable for HBV diagnosis and assessing safety of blood products.

PE124

Adefovir in Monotherapy or in Combination with Lamivudine for Treatment of Lamivudine-resistant Chronic Hepatitis B

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Background: Recent studies have shown a higher rate of adefovir-resistant mutation in lamivudine-resistant chronic hepatitis B (CHB) patients treated with switch-to therapy than those treated with add-on therapy. We compared the clinical efficacy of adefovir monothrapy and lamivudine-adefovir combination therapy in lamivudine-resistant CHB.
Methods: A prospective cohort study was performed in 49 patients with lamivudine-adefovir combination therapy and 77 patients with adefovir monotherapy for lamivudine-resistant CHB over 18 months.
Result: Biochemical response was achieved in 41 patients (83.7%) treated with combination therapy and in 77 patients (92.8%) treated with monotherapy ($p=0.101$). Virologic response was observed in 19 patients (38.8%) in combination therapy and in 26 patients (31.3%) in monotherapy ($p=0.383$) and treatment periods for virologic response was significantly shorter in patients with combination therapy than in monotherapy (8.9±4.8 months vs. 13.9±5.0 month, $p=0.001$). Cumulative rate of virologic response was significant higher in patients with combination therapy than monotherapy ($p=0.033$). HBeAg loss was found in 6 patients (16.2%) in combination therapy and 17 patients (20.5%) in monotherapy ($p=0.485$). Biochemical breakthrough was found in 17 patients (20.5%) with monotherapy significantly more frequent than 3 patients (6.1%) with combination therapy ($p=0.026$). Genotypic resistance to adefovir was developed in 1 patient (2.0%) in combination therapy and 9 patients (10.8%) in monotherapy
Conclusion: To achieve a complete virological response and reduce the risk of adefovir-resistant mutants in lamivudine-resistant CHB patients, adefovir in combination with lamivudine is preferable.

PE125

Factors Associated with Antiviral Effect of Adefovir Depivoxil in Lamivudine-resistant Chronic Hepatitis B

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Background/Aims: Adefovir dipivoxil (ADV) effectively inhibits both wild-type and lamivudine (LAM)-resistat chonic hepatitis B virus (CHB) replication. The aims of this study were to determine the factorts associated with antiviral effect of ADV in LAM-resistant CHB.
Methods: One hundred-eighteen LAM-resistant CHB patient (74.6% HBeAg-positive) were treated with ADV plus LAM (n=96) or ADV monotherapy (n=22) for a mean of 33.0 months. Restriction-fragment mass polymorphism analysis was used for detection YMDD and ADV mutants.
Results: Fifty-eight patients (49.2%) achieved complete response(CR) defined as HBV-DNA levels <2000 copies/ml and ALT normalization. Twenty-eight patients (23.7%) achieved initial vilologic response(IVR) defined as HBV-DNA levels $<10^4$ copies/ml within the first 6 month of treatment. 47 (53.4%) of 88 HBeAg-positive patients exhibited HBeAg loss and 31% seroconverted to anti-HBe Ab. Five (4.23%) patients developed ADV-related mutations. Factors associated with IVR were pretreatment level of ALT (P=0.00), AST (P=0.00), pretreatment HBV DNA level (P=0.03), HBeAg negativity (P=0.01) and HBeAb positivity (P=0.00). Factors associated with CR were IVR (P=0.00), HBeAb positivity (P=0.01), pretreatment level of ALT (P=0.01), AST (P=0.02) and y-Glutamyl Transferase (P=0.04). Age, sex, presence of liver cirrhosis, pretreatment HBV DNA level and the type of YMDD mutants were not related to an CR during ADV treatment.
Conclusions: ADV therapy achieved CR in more than 49% of LAM-resistant CHB. Factors associated with CR were IVR, HBeAb positive status, high base line ALT, AST, GGT levels.

PE126

Kinetics Study of Hepatitis B Virus with Entecavir Therapy in Chronic HBV Infection

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Objectives: To study a kinetics of hepatitis B virus during 12-week and 24-week of treatment with enticavir (ENT); To compare the detecting results of HBVDNA levels from different detection reagents.
Methods: Thirty-seven cases of chronic HBV infections were selected randomly, treated with daily dose of ENT 0.5-1.0mg (0.5mg for nucleoside-naïve patients, 1.0mg for lamivuding-refractory patients). Evaluation indexes: Serum HBVDNA, HBV serological markers, and liver function tests. HBVDNA levels were measured by PCR assay, using both domestic reagents and Roche Cobas Amplicor,. The lower limits of measure level of HBVDNA were 1000 copies/ml and 300 copies/ml, respectively.
Results: Mean baseline of HBVDNA was 5.24log10copies/ml for detection using domestic reagents and 5.70log10copies/ml for that using Roche Cobas Amplicor, (P>0.05). The ratios of cases with undetectable (<1000 copies/ml) HBVDNA at week-12 and week-24 were 46.2% and 72.9%, respectively. The ratios of cases with undetectable (<300 copies/ml) HBVDNA at week-24 were 54.5%. Among the cases whose HBVDNA were lower than 1000 copies/ml(using domestic reagents), the ratio of HBVDNA lower than 300 copies/ml(using Roche Cobas Amplicor) was 94.7%.
Conclusions: ENT can suppress HBV DNA rapidly no matter the patients with ALT elevation or not. There is a concordance on HBVDNA levels detection between domestic reagents and Roche Cobas Amplicor.

PE127

Study on the Effect of Quantity of HBV cccDNA, tDNA in the Hepatocytes and HbsAb in the Serum in Chronic Hepatitis B Patients by Nucleoside Analogue Antiviral Therpay

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Background：The study on the effect of nucleoside analogue therapy on the quantity of hepatocellular cccDNA and tDNA and sera HBV DNA, HBsAg to probe reliable marks for evaluation of therapy endpoint.
Methods：The quantity of hepatocellular cccDNA and tDNA and sera HBVDNA were assayed by FQ-PCR, and sera HBsAg by ELISA in 4 CHB patients over 2 years nucleoside analogue therapy satisfied the China criteria of therapy endpoint (therapy group)and 12 CHB patients without antiviral therapy and sera HBVDNA$<10^3$ copies/ml(control group).
Results: The quantity of hepatocellular cccDNA, tDNA and sera HBVDNA, HBsAg in therapy group were lower than that of control group,but low level hepatocellular cccDNA in therapy group could be detected.
Conclusion: Long term nucleoside analogue therapy may consume hepatocellular cccDNA with decreasing of hepatocellular tDNA and sera HBVDNA, HBsAg; Although the patients have satisfied the China criteria of therapy endpoint, low level of hepatocellular HBVcccDNA were detected, cessation of therapy may cause relapse.

Chart1：the HBV marks of 4 cases with nucleoside analogue antiviral therapy

item	case1	case2	case3	case4
Baseline serum HBVDNA（copys/ml）	$1.6x10^4$	$1.3x10^8$	$2.4x10^9$	$1.6x10^8$
Serum HBVDNA post therapy（copys/ml）	$<1.0x10^3$	$<1.0x10^3$	$<1.0x10^3$	$<1.0x10^3$
Baseline serum HBeAg	–	+	–	+
Serum HBeAg post therapy	–	–	–	–
Baseline serum HBsAg（mIU/ml）	53.6	271.57	8.07	252.2
Serum serum HBsAg post therapy（mIU/ml）	54.74	30.14+	0.16+	213.55
antiviral drugs	LAM /+ADV*	LAM	LAM	ADV
months of therapy	40.5*	32	51	27
months of maintain respond	21	29	50	14
months of maintain sera conversion	—	31 *	11*	13*
hepatocellular cccDNA（copys/cell）post therapy	6.19	1.34	5.61	5.14#
hepatocellular tDNA（copys/cell）post therapy	11.91	3.63	16.33	30.86

Note：*：LAM 19 months, HBVDNA rebound→LAM+ADV 2 months→ADV 20 months。
HBeAg sera conversion； # ：HbsAg loss

Chart 2：comparison on the hepatocellular cccDNA、tDNA and serum HBsAg between the of antiviral group and non-antiviral group with serum HBV DNA<1.0x103copys/ml（$\bar{x} \pm s$）

group	no	hepatocellular cccDNA（copys/cell）	hepatocellular tDNA（copys/cell）	serum HBsAg（mIU/ml）
Antiviral group	4	4.57±2.20	15.68±11.41	72.36±96.51
Non-antiviral group	11	12.13±19.07	58.44±113.58	179.07±105.35

PE128

Peptides that Lead Nuclear Entry of Nucleocapsid of Hepatitis B Virus in HepG2.2.15 Cells

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Background: The nuclear entry of nucleocapsid is a key step for the HBV life cycle and the formation of covalently closed circled DNA (cccDNA). It has been supposed that the carboxyl-terminal arginine-rich domain of the core protein contains a signal for nuclear localization (NLS). Whereas HBcAg was primarily distributed in cytoplasm and no marked cccDNA was detected in HepG2.2.15 cells.
Methods: We designed peptides containing a cell-penetrating sequence (RRRRRRR) and a nucleocapsid binding sequence (GSLLGRMKGA) with/without a classic nuclear localization sequence (PKKKRKV) and these sequences were linked by a soft linker Acp. HepG2.2.15 cells were treated with the peptides at levels of 0μM, 25μM and 50μM for 4 days.
Results: Compared with that of control cells, the results showed HBV DNA levels in culture medium decreased at least 2 log10 both in 50μM of peptide RRRRRRRAcpGSLLGRMKGA treatment group and RRRRRRRAcpGSLLGRMKGAAcpPKKKRKV treatment group; whereas HBsAg and HBeAg increased at 1.34±0.21 folds and 2.15±0.37 folds respectively. The signal strength of cytoplasmic HBcAg increased at about 2.5-fold in both groups. In RRRRRRRAcpGSLLGRMKGAAcpPKKKRKV treatment group, nuclear HBcAg increased about 3.2-fold and obvious cccDNA signal was detected by southern blot.
Conclusion: Our results implied that the NLS of core protein likely does not expose to surface of nucleocapsid in HepG2.2.15 cells, the artificial peptide containning NLS binds to the nucleocapsid and leads nuclear entry of nucleocapsids and then facilitates the formation of cccDNA. Our study presents a tool for study on cccDNA formation and nuclear entry of nucleocapsid.

PE129

Establishment of Real-time Fluorescence Quantitative PCR to Detect HBV cccDNA Based on LightCycler System

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Aims: To establish a reliable real-time fluorescence quantitative (RFQ) PCR method to quantify HBV cccDNA, basing on LightCycler system and Taqman probe.
Methods: HBV genotypes A-G were aligned to obtain a conserved sequence, crossing rcDNA gap, which was used to design cccDNA primers and Taqman-MGB probe. Also another pair of primers for quantify HBV total DNA (tDNA) was designed, utilizing the same probe. To increasing specificity, we added plasmid-safe ATP-dependent dnase (PSAD) digestion step just before cccDNA PCR amplification. A standard curve from 9 standard plasmid samples, from 2.0×10^9 to 2.0×10^1copies, was created to examine our system. 50 HBV cccDNA samples with known-amount were quantified by creating standard curve from 5 standard samples.
Results: The standard curve had clear log-phase and excellent parallelism, which means nice and equal amplification efficiency in all reaction capillarys. The slope (regression coefficient) of standard curve was -3.141, mean square error was 0.0990 and regression coefficient was -1.0. All of these key indexes measured up. In 50 tests, we got right results if the starting templates of cccDNA copies were between 10^2~10^9copies. The range was superior to commercial HBV kits. By quantifying 16 samples containing different amounts of cccDNA and rcDNA, digested or undigested, PSAD digestion would eliminate 10^7 rcDNA molecules, leaving 10^2 cccDNA molecules untouched. The test specificity was maintained up to 1:100,000 ratio of cccDNA:rcDNA.
Conclusions: The RFQ-PCR based on LightCycler system for HBV cccDNA quantification is reliable, sensitive, with high specificity and low cost.

PE130
Changes of Toll-like Receptor3 on Dendritic Cells Derived from Peripheral Blood Mononuclear Cells in Patients with Chonic Hepatitis B and Chronic Severe Hepatitis B
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Background: To study the changes of Toll-like receptor (TLR)3 on dendritic cells derived from peripheral blood mononuclear cells(MoDC) and its role in the pathogenesis of chronic hepatitis B(CHB) and chronic severe hepatitis B(CSHB).
Methods: The expressions of TLR3 on 10000 MoDC were stimulated by poly I:C, and then were determined by flow cytometry in 20 healthy controls, 28 patients with CHB and 30 patients with CSHB.The level of interferonβ（IFN-β）was determined by ELISA. The differences of expression of TLR3 on MoDC and serum IFN-β among the three groups of study subjects were determined by student-t test.The correlation between TLR3 and IFN-β were determined by linear correalation test.
Results: The values of mean fluorescence intensity(MFI) of TLR3 on MoDC of the healthy controls, patients with CHB and CSHB were 1593.00±349.65,1369.56±287.08,and 1203.96±192.40.The serum IFN-β(pg/L) of respective groups was 172.66±37.96,107.98±31.15 and 72.06±29.58. There was a gradual decrease of these values from the group of healthy controls to the group of patients with CHB and CSHB .Significant positive correlations between TLR3 and serum IFN-βwere found.
Conclusion: TLR3 may have a role in the pathogenesis of CHB and CSHB.

PE131
Entecavir Therapy for up to 48 Weeks in Chinese Patients with HBeAg-positive Chronic Hepatitis B
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Background/Aim: To evaluate the efficacy and safety of entecavir treatment in patients with HBeAg-positive chronic hepatitis B who had not previously received a nucleoside analogue.
Methods: Fifty-five patients received 48-week entecavir 0.5mg/d therapy. Serum HBV DNA load was measured with quantitative real-time-PCR. Alanine aminotransferase (ALT) activity, HBeAg, anti-HBe-antibodies, HBV DNA level in serum were evaluated at baseline, week 2, 12, 24 and 48 during therapy. Evaluation of safety and tolerance was based on clinical adverse events and laboratory analyses.
Results: HBV DNA levels declined sharply by around 3 $\log_{10}$ copies/mL during the first two weeks, with a highly significant reduction ($p<0.0001$) at week 2 and thereafter, as compared to those at baseline; 31%, 51% and 78% of the patients had undetectable serum HBV DNA levels at week 12, 24 and 48 respectively. Highly significantly decreasing serum ALT ($p<0.0001$) occurred during the first 2 weeks of the study. At week 48, ALT levels were normalized in 84% of the patients. HBeAg seroconversion (HBeAg negative, HBeAb positive) was achieved in 7.3% and 14.5% of patients by 24 and 48week. At the end of 24th and 48th weeks, complete response (ALT normalization and HBV DNA and HBeAg loss) was observed in 11% and 15%, respectively. There was no evidence of drug resistance or adverse effect in CHB patients treated for up to 48 weeks.
Conclusion: Entecavir treatment through 48 weeks was well tolerated and resulted in continued benefit for patients with HBeAg-positive chronic hepatitis B.

PE132
Single Nucleotide Polymorphisms of The MxA Gene Promoter And Sustained Treatment Response of Chronic Hepatitis B or C Patients With Interferon Treatment: A Meta-analysis
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Aim: To assess the associations of single nucleotide polymorphisms of the MxA gene promoter and sustained treatment response of chronic hepatitis B or C patients with interferon treatment by meta-analysis of individual dataset from all studies published till date.
Methods: To clarify the impact of MxA gene promoter polymorphisms on sustained treatment response of chronic hepatitis B or C patients with interferon treatment, we performed a meta-analysis of the published data from eight studies comparing the frequencies of MxA gene promoter polymorphisms at nt –88 G/G, -88 G/T, –88 T/T and nt –123 C/C, -123 C/A , -123 A/A alleles in individuals with interferon treatment. As we identified the heterogeneity between studies, summary statistical data were calculated based on a random-effect model.
Results: The sustained treatment response rate was higher in patients with the nt –88 G/T and nt –123 C/Aalleles in the MxA promoter SNP . The Meta-analyses yielded summary estimatesodds ratio (OR) were 2.07 [95%CI (1.58, 2.7), P <0.00001] and 1.9 [95%CI (1.32, 2.73), P =0.0006] of the nt –88 G/T and nt –123 C/A alleles, respectively.
Conclusion: MxA gene promoter polymorphisms at nt -88 G/T and nt -123 C/A may be useful as a marker to predict the sustained treatment response of chronic hepatitis B or C patients with interferon treatment, and further investigation regarding their real significance is warranted in a large series of patients.

PE133
Variation of Hepatitis B Virus in Patients Infected via Mother to Infant Transmission
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Background: To determine whether HBV with the same characteristics causes dissimilar mutations in different hosts.
Methods: Full-length HBV genome was amplified and linked with pMD T18 vector. Positive clones were selected by double-restriction endonuclease digestion (EcoRI and HindIII) and PCR. Twenty seven clones were randomly selected from an asymptomatic mother [at two time points: 602 (1 d) and 6022 (6 mo)] and her son [602 (S)]. BioEditor, Clustal X and MEGA

software were used to perform phylogenetic and mutational analysis. Potential immune epitopes were determined by the Stabilized Matrix Method (SMM), SMM-Align Method and Emini Surface Accessibility Prediction.
Result: All of the 27 sequences were genotype C, the inner-divergence for the mother and son was 0%-0.8%.13 specific nucleotides differed from the other pubished genotype C isolates were co-exist in the mother and her son. AA 1-11 deletion in preS1 was the dominant mutation in the mother (14/18). The 1762T/1764A double mutation existed in all clones of the mother, 3 of them were also coupled with G1896A mutation, but none were found in the son. 17 bp deletion starting at nucleotide 2330 was the major mutation (5/9) in the son, which caused seven potential HLA class I epitopes and one B cell epitope deletion, and produced a presumptive new start codon, downstream from the original one of the P gene.
Conclusion: The son was infected HBV from his mother, and discrepant mutation occurred in the mother and her son during infection.

PE134

A Randomized, Double-blind Trial of Telbivudine versus Lamivudine in Adults with Compensated Chronic Hepatitis B — 104-week Sub-study Result in Taiwan

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Background/aims: Nucleos(t)ide analogues have been recognized as an effective treatment for chronic hepatitis B. This randomized, double-blind trial compared the efficacy and safety of telbivudine and lamivudine after 104-week therapy in patients with compensated chronic hepatitis B in Taiwan.
Methods: We analyzed 114 Taiwanese patients from GLOBE trial receiving telbivudine 600mg (n=58) or lamivudine 100mg (n=56) once daily for 104 weeks. The primary efficacy endpoint was therapeutic response with serum HBV DNA <5 $\log_{10}$ copies/ml and either hepatitis B e antigen (HBeAg) loss or alanine aminotransferase (ALT) normalization.
Results: The therapeutic response at week 104 was 74.8% in telbivudine group versus 50% in lamivudine group (p=0.005). More patients with telbivudine achieved nondetectable serum HBV DNA (<300 copies/ml) (p=0.024) and ALT normalization (p=0.021) at the end of treatment. The cumulative resistant rate was significantly lower in those with telbivudine treatment (p=0.0032). The rate of HBeAg seroconversion was comparable in both groups (p=0.407). Although a lower percentage of patients in lamivudine group (83.9%) reported adverse events than those in telbivudine group (89.7%), the difference was not significant.
Conclusions: Telbivudine demonstrates a significantly greater efficacy and a lower resistant rate than lamivudine in treatment of chronic hepatitis B in Taiwan.

PE135

Tumor Necrosis Factor-α-308 Gene Promoter Polymorphism in Chronic Hepatitis B Virus Infection: Meta-analysis of 4338 Cases and 3013 Controls

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Background: Tumor necrosis factor-α (TNF-α) plays a pivotal role in the viral clearance and host immune response to HBV, and the capacity for TNF-α production in individuals is influenced by a major genetic component. The studies of TNF-α-308 gene promoter polymorphism in chronic HBV infection have reported apparently conflicting results.
Objective: To derive a more precise estimation of the relationship between the polymorphism of TNF-α-308 gene promoter and chronic HBV infection.
Method: Meta-analysis was done of 22 case-control studies in relation to TNF-α-308 gene promoter, involving a total of 4338 chronic HBV infection cases and 3013 controls. The pooled odds ratios (ORs) for the risk associated with the genotypes of GA, AA, and GA+AA (A-allele carriers) compared with the GG genotype were calculated.
Results: Overall meta-analysis indicated that -308A heterozygotes (GA) had 22% decreased risk of developing CHB with a borderline significance (OR = 0.78; 95% CI: 0.60–1.02; $P = 0.065$). For the -308A allele homozygotes (AA) and carriers (GA+AA), the pooled ORs both indicated a significantly decreased risk of CHB (OR = 0.39; 95% CI: 0.21–0.73; $P = 0.003$; and OR = 0.74; 95% CI: 0.57–0.96; $P = 0.026$, respectively) (Table 1). In the subgroup analyses by ethnicity, significantly decreased risks were associated with -308 variant genotypes (GA and AA) in Mongoloid populations in all genetic models. However, no significant associations were found in Caucasoid.
Conclusion: The meta-analysis suggests that the TNF-α-308A allele is a low-penetrant protective factor for chronic HBV infection, especially in Mongoloid.

PE136

Programmed Death-1 Expression is Associated with the Disease Status in Hepatitis B Virus Infection

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Aim: To define the potential role of PD-1/PD-Lpathway in different HBV infection status; we examined the expression of PD-1on CD8+ T cells in PBMC of patients with CHB and AEHB infection.
Methods: The PD-1 level on CD8+ T lymphocytes and the number of HBV specific CD8+ T lymphocytes in patients and healthy controls were analyzed by flow cytometry. PCR was used to measure the serum HBVDNA levels.
Results: The level of PD-1 expression on CD8+ T cells in CHB patients was higher than that in AEHB patients and healthy individuals. Compared to AEHB patients, lower frequency of HBV-specific CD8+ T cells was detected in CHB patients. There was an inverse correlation between the strength of HBV-specific CD8+ T-cell response and the level of PD-1 expression. Besides, there was a significant positive correlation between HBV viral load and the percentage of PD-1 expression on CD8+ T cells in CHB and AEHB subjects. However, PD-1 expression was not associated with ALT levels.
Conclusion: Our results confirm previous reports that HBV specific CD8+ T-cell response in the peripheral blood is more intense in patients with AEHB than in CHB with persistent viral infection. Moreover, there is a negative correlation between the level of PD-1 and the intensity of virus specific CD8+ T cell response.

PE137

Study of Chronic Hepatitis B (CHB) Patients in Malaysia: Demography and Clinical Features.

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Background: This study examined the characteristics of CHB among populations in a multi-ethnic country.
Methods: This study is a retrospective review of medical notes of CHB patients seen in outpatient clinics from 11 public hospitals between 2005–2006. Cirrhosis was defined by any of the following: histology, radiological evidence of nodular or shrunken liver, or ≥2 combinations of splenomegaly, ascites on imaging, varices by endoscopy and platelet count <100,000/μL.
Results: 3,275 patients with a mean age of 41.5±14.5 years: 65.3% were aged 20–49; majority were male (64.6%); 73.7% of patients had HBeAg(-); and anti-HCV antibodies were detected in 3.56% of patients. Cirrhosis was

observed in 10.9% of patients with a mean age of 51.8±12.9. The ethnic composition was 53.1% Chinese; 27.3% Malay; 14% indigenous Sabahans; 2.9% indigenous Sarawakians; 1.8% Indians and 0.8% others. Chinese patients were on average, older (mean 45.6±14.5 years), Indians patients had higher mean alanine transaminase and indigenous Sarawakian patients had the highest rate of cirrhosis (P<0.0001). During the study period, 20.7% of patients were on treatment and they were significantly older than those who were not on treatment (mean age 44.6 ± 14.5 vs 40.7 ± 14.3). Lamivudine was the first agent used in 86.9% of cases.
Conclusions: In Malaysia, CHB remains a public health issue and significantly afflicts males in the productive age groups and of Chinese ethnicity. The observed differences among ethnic groups could point to different disease severity which needs to be addressed in the local treatment guideline and policy.

PE138
Necroinflmmatory Activity Influences on Liver Stiffness in Addition to Fibrosis Stage in Patients with Chronic Hepatitis B
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Background/Aims: Liver stiffness measurement (LSM) has been validated for predicting fibrosis stage in patients with chronic hepatitis C. However, studies on LSM for chronic hepatitis B (CHB) are few, and the relationship between histologic findings and liver stiffness needs to be further elucidated. This study was conducted to assess the association of histologic activity on liver stiffness in addition to fibrosis in patients with CHB
Methods: Thirty three patients who had taken liver biopsy and LSM at Korea University Ansan Hospital between March 2008 and October 2008 were enrolled. Necroinflammatory activity and fibrosis stage were assessed by Metavir system. Activity, fibrosis, and the sum of both score were included for the correlation analysis with LSM
Results: Among 33 patients, 29 (87.9%) were male, and median values were as follows: age, 42 (20~54); AST, 49 IU/L (19~627); ALT, 62 IU/L (8~778); Total bilirubin, 1.03 mg/dL (0.4~2.39); LSM, 10.1 kPa (4.2~43.5). Fibrosis stages were F1 in 4 (12.1%), F2 in 9 (27.3%), F3 in 12 (36.4%), and F4 in 8 (24.2%) patients. Spearman correlation coefficient with LSM were 0.457 (p=0.008) for activity, 0.694 (p<0.001) for fibrosis stage, and 0.724 (p<0.001) for the sum of activity and fibrosis. In linear regression analysis, only the sum of activity and fibrosis remained to be significant.
Conclusions: Not only fibrosis but also activity was an important factor for determining LSM for CHB. It would be more appropriate to consider both activity and fibrosis for interpretation of LSM in patients with CHB

PE139
Establishment and Validation of a New Method for HBeAg Quantification in HBeAg Positive Chronic Hepatitis B (CHB) Using Samples from Patients Treated with Telbivudine
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Background: HBeAg seroconversion is a key goal of CHB therapy. HBeAg kinetics may predict HBeAg seroconversion during treatment. We aim to develop a robust HBeAg quantitative method as the value of HBeAg quantitation is undefined and data is limited.
Methods: We evaluated two commercially available qualitative HBeAg assays (Abbott Architect, Siemens Centaur) for their linear range and validated them against Paul-Ehrlich Institute (PEI) standards. HBeAg levels were determined from samples of untreated and telbivudine-treated CHB patients.
Results: As a pre-requisite for quantitative use, the linear range for the Architect (0.5-43 PEIU/mL) and Centaur (0.05≥5 PEIU/mL) assays were defined. Architect was selected for further investigation. HBeAg levels of 44 untreated patients (mean HBV-DNA 9.8 $\log_{10}$ copies/mL, mean ALT 166.7 IU/mL) varied from 0.4 to 1073.5 PEIU/mL (median 161.7 PEIU/mL). In 23 patients (mean HBV-DNA 9.9 $\log_{10}$ copies/mL, ALT 166 IU/mL) treated with telbivudine for 12 weeks, baseline HBeAg levels varied from 1.6 to 664 PEIU/mL (median 150.7 PEIU/mL). After 12 weeks of telbivudine treatment, median HBeAg level was 4.4 PEIU/mL, with 76% decline from baseline (median decline 95.1 PEIU/mL, range 1.4-657.6 PEIU/mL). Individual HBeAg decline from baseline varied but occurred in all patients and was not correlated to baseline or decline from baseline HBVDNA.
Conclusion: HBeAg quantitation is feasible and robust with Architect HBeAg assay. HBeAg decline occurred in all telbivudine-treated patients, and was not correlated to HBVDNA. Whether the magnitude of HBeAg decline is predictive of future HBeAg seroconversion merits further investigation.

PE140
CK Elevation During Chronic Hepatitis B (CHB) Treatment with Telbivudine: Experience from the Combined GLOBE (NV-02B-007/CLDT600A2302) and 015 (NV-02B-015) Study Clinical Safety Database.
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Background: Creatine phosphokinase (CK) is a commonly used marker of muscle damage and is elevated by many factors (e.g. exercise, injury, drugs). Normal CK levels are affected by muscle mass and elevated levels are described during the natural course of CHB. 22% of patients in the GLOBE study had pretreatment Grade 1-4 CK elevations.
Methods: We reviewed data from this combined study clinical safety database, and describe the experience of CK elevation and its relationship to adverse event reports of muscle related symptoms.
Results: The frequency of new onset of Grade 3-4 CK elevations in telbivudine-treated patients (combined database ITT population) was 1.8% (15/847), 6.3% (53/838), 3.2% (27/826) and 5.1% (40/786) from weeks 0-24, 24-52, 52-76 and 76-104 respectively. The frequency of Grade 3-4 CK elevations for all patients from week 0-104 was 12.6% (107/847).
The majority of Grade 3-4 CK elevations were asymptomatic, rarely resulted in discontinuation or interruption, spontaneously declined within 1 or 2 visits and were not associated with more frequent muscle-related adverse events. Cumulative data from this combined database showed no relationship of the degree of increased CK to acute or persistent muscle disease.
Conclusion: CK elevations are associated with HBV disease and were also common during the GLOBE and 015 trials and were not predictive of the development of muscle related symptoms. Onset of muscle-related symptoms should prompt clinical and treatment review, including concomitant medications.

PE141
HBV Replication Down-regulated the Expression of Long Form Leptin Receptor in Cell Cultures
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Backgrounds: Leptin plays a crucial role in the regulation of energy balance and body weight control by activating the long form of the leptin receptor (Ob-R_L). Epidemiologic studies showed that obesity is one of the factors associated with HBV related hepatocellular carcinoma. Methods: Huh7 cells were transiently transfected with 1.3 copies of HBV-replicon plasmid. After 48h, cells were harvested and total RNA of the cells were extracted and reverse-transcribed into cDNA. Long form and short form leptin receptor (Ob-R_L, Ob-R_S) mRNA transcription levels were assayed by Real-time PCR respectively. And mRNA transcription levels and protein expression of Ob-R_L and Ob-R_S in HepG2.2.15 cells were also detected. Results: After transfected by 1.3 copies HBV-replicon plasmid, the mRNA transcription level of Ob-R_L was inhibited significantly (**P<0.01), but the mRNA transcription level of Ob-R_S did not change, and the Ob-R_L protein expression was reduced. In HepG2.2.15 cells, the mRNA transcription level

of Ob-R_L was also significantly lower than the mRNA transcription level of Ob-R_L in HepG2 cells, while the mRNA transcription of Ob-R_S in HepG2.2.15 and HepG2 cells didn't show significant difference. Besides, the protein expression level of Ob-R_L in HepG2.2.15 was also lower than it in HepG2 cells. Conclusion: HBV replication down-regulated the expression of long form leptin receptor in cell cultures, which could in part explain the clinical observation of obesity in association with development of serious sequelae in HBV infections.

PE142

The Results of Entevavir Treatment in Patients with Chronic Hepatitis B

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Purpose: We evaluated the short and long term effectiveness of entecavir.
Patients and Methods: Those patients had received diagnosis of chronic hepatitis B. Their pretreatment transaminases, HBsAg, anti-HBs, HBeAg, anti-HBe, HBV-DNA were checked and a liver biopsy and a resistance test for Lamivudine (LAM) and Adefovir (ADV) were performed. A total of 44 patients who were taking entecavir for at least 24 weeks were included in the study.
Findings: The biochemical and virologic response were observed in 88.8 % at 3 and 6 months and in 75 % at 12 months. In 9 HBeAg positive patients who had received therapy previously, the biochemical response was observed in 88.8 % at 3 and 6 months and in 100 % at 12 months. The virologic response in 77.7 % at 3, in 88.8 % at 6, and 100 % at 12 months. Posttreatment HBeAg seroconversion did not develop. In 9 HBeAg negative patients the biochemical and the virologic responses were observed in 88.8 % at 3 months and 100 % 6 and 12 months, respectively. In 17 HBeAg negative patients had received therapy previously, the biochemical response was observed in 76.4 % at 3, in 100 % at 6 and 12 months. The virologic response in 94.1 % at 3, in 100 % at 6 and at 12 months.
Conclusion: In our study, a higher therapy-response rate was achieved, especially in HBeAg negative patients. In HBeAg positive patients biochemical and virologic response rates were high.

PE143

Association of Diabetes Mellitus and Hepatitis B Virus Infection

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Background/Summary: Patients with liver disease are known to have a higher prevalence of glucose intolerance. Preliminary studies suggest that viruses can be an additional risk factor for the development of diabetes mellitus. Individuals with type II diabetes have an increased prevalence of cirrhosis, and a proportion of patients with acute and chronic liver disease develop diabetes mellitus. There is now emerging epidemiological data to suggest that Hepatitis C virus (HCV) infection may also contribute to the development of diabetes reported to be higher than expected compared with the general population. While these investigations suggest an epidemiological association between HCV infection and diabetes, large controlled studies are required to observe association between HBV infection and diabetes. The present study was designed to study the relative proportion of Diabetes mellitus in patients suffering from hepatitis B virus (HBV) infection.
Materials and Methods: The Cross Sectional study comprised of 94 age and sex matched patients suffering from hepatitis B virus infection. HBV infection was diagnosed with hepatitis B surface antigen (BY Elisa) and Diabetes Mellitus was diagnosed according to the "American Diabetic Association Criteria". Pregnant females, patients on Corticosteroids or hydrochlorthiazide therapy, and patients simultaneously suffering from HCV infection and HBV infection were excluded from the study. The study period was from November, 2000 to September, 2002.
Results: A total of 318 patients were registered, out of which 94 cases fulfilled the inclusion criteria, 4.25% hepatitis B virus infected cases were diagnosed as diabetics.
Conclusion: This study does not suggest the presence of Association and relationship of Diabetes Mellitus and Hepatitis B virus infection.

PE144

Do Chronic Hepatitis B (CHB) Patients with Negative HBeAg and Serum HBV-DNA at or Below 4log10copies/ml Have Stable Viral level and Non-Progressive Liver Disease?

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Background: In EASL 2008, we reported significant liver disease among HBeAg negative patients with serum HBV-DNA level $\leq 4\log_{10}$copies/ml (i.e. $2.0x3\log_{10}$IU/mL) and alanine aminotransferase (ALT) <55IU/L. This reflects fluctuating nature of these levels. The aim of this retrospective study is to demonstrate the frequency of fluctuation among this group of CHB patients.
Methods: Clinical records of HBeAg negative treatment naïve CHB patients with at least one serum HBV-DNA $<4\log_{10}$copies/ml were reviewed.
Results: There were 194 (62.5% male, median age 48.0 years) CHB patients with negative HBeAg and HBV-DNA $<4\log_{10}$ copies/ml (Roche COBAS Amplicor PCR assay, LOD<300copies/ml). 32 had serial HBV-DNA measurements within 2 years; 7 of them (21.9%) had increase serum HBV-DNA level by $>1\log_{10}$ copies/ml; 2 patients had associated serum ALT elevation from normal (normal range <55 IU/L), 4 had persistent normal ALT, and one had persistently raised ALT. 5 (15.6%) had serum HBV-DNA level decrease by $>1\log_{10}$ copies/ml. Another 20 patients had HBV-DNA levels fluctuating within $1\log_{10}$ copies/ml. 159 HBeAg negative patients with single HBV-DNA measurement showing $<4\log_{10}$ copies/ml had serial serum ALT measurements within 3 years. 35 (22.0%) patients had intermittent / persistently raised ALT; while 124 (78.0%) patients had persistently normal ALT.
Conclusions: HBeAg negative CHB is common among Chinese. Serial serum HBV-DNA and ALT measurements are necessary to detect fluctuating levels and progressive liver disease that may require antiviral therapy.

PE145

Development of a Mathematical Model for Estimation of Hepatitis B Virus Infection in Various Age Groups and Determination of Country-Specific Vaccination Strategy

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Background: To determine the best vaccination strategy, a model that reflects the country-specific infection profile is needed. Methods: A model was built in order to obtain the age-specific infection frequency Q(t) for neonates(n), infants(i), children(c), and adults(a). The infected group can either become HBsAg(+) or anti-HBs(+)* based on F(t). Q(t) can be found from P(t) = [Q(t) x (1 – F(t)) x CRs + Q(t) x F(t) x (1 - CRas)], where P(t) represents the proportion of the late anti-HBs(+)** group and CRs/CRas denote natural conversion of HBsAg/anti-HBs. To test the model, cross-sectional serologic marker data in Korea were used. Because F(t), CRs, and CRas were known(F(n)=0.1, F(i)=0.5, F(c)=0.8, F(a)=0.95, CRs=0.015, CRas=0.02), in order to determine Q(t), only P(t) values were needed, which were evaluated from logistic modeling using the glm() function of S-PLUS. Results: The infection frequencies during neonate, infant, children, and adult periods in non-vaccinees were 15.4%, 33.3%, 16.6%, and 34.7%, respectively. Each group's likelihood of infection compared to adults was then: neonates 170.2 times more likely, infants 33.5 times, and children 0.9 times, making a strong case for neonatal and infantile vaccination for the studied region. Conclusions: The HBV infection model can be used for determining the most cost-effective strategy for HB vaccination in nations where longitudinal data are not available. And where longitudinal data are available, it can be used to determine the appropriate time of transition of vaccination strategy to maintain cost-effectiveness.

PE146

The Effect of Telbivudine on Peripheral Blood Regulatory T cells and Its Significance in Patients with Chronic Hepatitis B

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Objective: To investigate the effect of Telbivudine on peripheral blood regulatory T cells and its significance in patients with chronic hepatitis B.
Methods: 36 patients with HbeAg positive chronic hepatitis B were recruited and receiving telbivudine treatment for 9 months. Before and during 3 、6 、9 months of treatment , Flow cytometry was used to detect the proportion of peripheral blood Tregs; real-time PCR was used to detect the levels of HBV DNA in surum, markers of hepatitis B virus infection were detected by ELISA assay and levels of alanine aminotransferase in serum were measured.
Results: The proportion of peripheral blood Tregs in patients with CHB was significantly higher than that in healthy controls and decreased over 6 or 9 months of treatment to a level comparable to that of healthy controls. After 3 months of treatment, The rate of ALT normalization in patients which the proportion of peripheral blood Tregs was unreduced was significantly lower than that in patients which the proportion of peripheral blood Tregs was reduced ($P<0.01$). 3, 6 or 9 months of telbivudine treatment resulted in negative HbeAg in 4(11%) patients, 7(19%) patients or 9(25%) patients respectively. Within 9 months of treatment, 7 (19%) patients seroconverted from HBeAg to anti-HBe , in which the proportion of peripheral blood Tregs had decreased to a level comparable to that of healthy controls over 3 or 6 months of treatment.
Conclusion: During antiviral treatment with subsequent reduction of the viral load or ALT levels, the proportion of Tregs decreased to a level similar to that of normal healthy controls. In addition, seroconversion from HBeAg to anti-Hbe was prone to be established in patients which the proportion of Tregs decreased quickly at the early phase of antiviral treatment with Telbivudine.

PE147

Safety and Efficacy of Combination Treatment of Pegylated Interferon and Entecavir for Patients with ALT <1.5×ULN and HBV DNA >105 copies/ml

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Background: In China a part of patients with ALT <1.5×ULN and HBV DNA $>10^5$ copies/ml will advance into hepatic cirrhosis even hepatoma. So these patients should not only be monitored but also be treated. This study was made to determine the safety and efficacy of combining therapy of pegylated interferon alpha 2a (peg-IFNα-2a) and entecavir in treating naive patients with ALT <1.5×ULN and HBV DNA$>10^5$ copies/ml.
Methods: Nine patients with HBsAg positive over 6 months and ALT<1.5×ULN、HBV DNA $>10^5$ copies/ml were taken as research subjects. Before treatment,liver biopsy was used to assess histological damage. Patients were treated with peg-IFN α-2a 180μg /week for 48 weeks, and in the first 12 weeks entecavir 0.5 mg/day was applied, then it was stopped.
Results: 1 Liver biopsy showed that 7 patients had mild inflammation. 2 After 12 weeks' treatment , HBV DNA level in all patients decreased to less than 10^4 copies/ml, and after 24 weeks' treatment(12 weeks after entecavir was stopped)HBV DNA in all patients was less than 10^3 copies/ml. 3 Normal ALT was seen in all patients after 12 weeks' treatment and 24 weeks' treatment. 4 None of the patients had peripheral neuropathy with combining treatment.
Conclusions: 1. Bulk of patients with ALT <1.5×ULN and HBV DNA$>10^5$ copies/ml had mild inflammation and need treatment. 2 Combing treatment of peg-IFN and entecavir was safe and effective to this group. 3 It proved that it was safe for patients to stop treatment with entecavir after short time use.

PE148

Comparison of Abbott RealTime HBV and Roche COBAS Amplicor HBV Monitor for Monitoring Serum HBV DNA Levels in Chronic Hepatitis B Patients

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Background & Aims: Quantification of serum HBV DNA levels is important to monitor viral replication in chronic hepatitis B (CHB) patients. Both Abbott RealTime HBV and Roche COBAS Amplicor HBV Monitor are updated fully automatic commercial assays for HBV DNA quantification. The aim of this study is to compare the performance of these two assays on the HBV DNA quantification in CHB patients.
Methods: Serial serum samples from 30 CHB patients were collected at the baseline and at days 4, 7, 10 and 14 and weeks 3, 4, 8 and 12 after the commencement of therapy. Genotype was determined by sequence alignment. Abbott and Roche assays were employed for HBV DNA extraction and quantification according to the instructions of manufactories.
Results: HBV DNA quantification results of Abbott assay was significantly correlated with those of Roche assay (r=0. 972, $P<0.0001$). For genotype C, the difference in HBV DNA levels [median (range): 1.22 (-0.16-2.36) log units] measured by these two assays was significantly higher than that for genotype B [0.66 (-0.52-1.63) log units, $P<0.0001$]. Moreover, the difference in serum HBV DNA levels after 12 weeks antiviral treatment [1.18 (-0.21-1.76) log units] measured by these two assays was significantly higher than that in baseline serum HBV DNA levels [0.68 (-0.12-1.24) log units, $P<0.0001$].
Conclusion: The quantification results of Abbott RealTime HBV showed a good correlation with those of Roche COBAS Amplicor HBV. But the performances of these two assays have significant difference in the quantifications of serum HBV DNA levels in genotype C patients and in patients after 12 weeks antiviral therapy.

PE149

Perinatal Transmission Status of Hepatitis B Virus in Asymptomatic Carriers in Bangladesh: Experience from a Tertiary Centre.

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Background/Aim: To find out the mode of the transmission of HBV in asymptomatic carriers and build up awareness against the transmission of HBV.
Method: It was a prospective study in the Dept. of Medicine (IPD & OPD) and Transfusion Medicine in Rajshahi Medical College Hospital from June 2005 to July 2007. 300 asymptomatic carriers of HBV were included. HBsAg was detected incidentally during routine screening tests done for blood donation programme, foreign mission and courses abroad. All the HBsAg positive patients were confirmed by doing HBsAg (ELISA) tests after 6 months. All were positive.
Result: Among 300 asymptomatic carriers male 270 and female 30. Age between 15 to 35 yrs.Detail history & clinical examination were done at the entry. HBeAg positive only in 15 patients. ALT above 60 U/L in 17 patients, HBV-DNA (PCR) detectable in 15 patients, coarse liver echotexture in 20 patients, Oesophageal Varix small size in 02 patients. Serum Albumin, PT, AFP all were normal range. Screening of all the family members of the carriers was done. Among 300 index cases 130 (43.33%) family members most likey mother,father, brother, sister or cousin were HBsAg positive. Liver related death was present in 50 families(16.66%).
Conclusion: This study shows perinatal transmission transmission is the most important mode of transmission of HBV in asymptomatic carriers in Bangladesh. HBV transmission is preventable. Mass education is required about the transmission of HBV. Screening of HBV should be mandatory in all pregnant women. Bangladesh Government has integrated the HBV vaccination in EPI.

PE150

"Bitten Once, Shy twice" - Not True for Our Hepatitis C Infected Population and for Health Care Workers!

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Background: Guidelines suggest Hepatitis B Virus (HBV) vaccination to all Hepatitis C Virus (HCV) infected patients and healthcare workers. We attempted to find out HBV vaccination status in our HCV infected population, and healthcare workers.

Methods: Prospective survey of 100 consecutive HCV infected patients and also doctors and paramedical staff in our hospital.
Results: Major sources of viral infection in study patients (58 males; average age 40 years - range 18 to 65 yrs) were reused syringes (38 pts). Twenty had a household member infected with HCV. Twenty were co-infected with HBV. Eighty five of HCV infected patients were not vaccinated.against HBV. Twenty five of them (29%) had financial reasons and 45 patietns (52%) had lack of awareness. Out of 30 doctors, 12 and 15 did not know about their HBV and HCV status respectively, but none was known to have either of these infections. Four (13%) were not vaccinated against HBV. Out of 29 paramedical staff, 1 was HCV positive, 11 each were unaware of their HBV and HCV status, and remaining were negative for these markers. Thirteen of them (44%) were not vaccinated against HBV.
Conclusion: Thirty eight percent HCV infected patients were infected by reuse of syringes. Eighty five percent were not vaccinated against HBV, out of which 52% had no awareness about it, whereas 29% could not financially afford it. A significant number of paramedical staff and some doctors were also not vaccinated

PE151

A Clinical Study of Efficacy and Predictors in the Treatment of Hepatitis B e Antigen Positive Chronic Hepatitis B with Interferon Alpha 2b

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Background: Early prediction of efficacy could decrease unnecessary interferon exposure of patients with chronic hepatitis B.
Methods: A multi-center clinical study. Patients were injected interferon alpha 2b 5 Million IU subcutaneously every other day for 24 weeks and 24-week follow-up was followed.
Results: 53 patients (44 male) were enrolled, 27.5 ±9.1 years old. 24 hours after administration, hepatitis B virus (HBV) load decreased significantly (6.96±1.03log copies/ml, P<0.05) from baseline (8.00±0.93 log copies/ml). HBV load was 4.94±1.47 and 5.25±1.58 log copies/ml at week 24 and 48, respectively. At the two points upwards, complete response rate was 4.2%(2/48) and 7.9%(3/38), partial response rate was 35.4%(17/48) and 34.2%(13/38), respectively. At week 4 and 12, HBV DNA levels of complete responder and partial responder were lower than those of non-responder (P<0.05) at week 24. At baseline, on hour 12, day 2, 3, week 2, 4 and 12, HBV DNA levels of complete responder were lower than those of non-responder at week 48 (P<0.05). Multiple linear regression showed that baseline HBV DNA was the independent variables to predict the response at week 24 and 48.
Conclusions: Interferon alpha 2b was effective in treating patients with HBeAg positive chronic hepatitis B. It could decrease the HBV DNA level rapidly. Early HBV DNA levels were predictive to response at the end of treatment and follow-up. Baseline HBV DNA level was the independent predictor of the response at the end of treatment and follow-up.

PE152

Programmed Death 1 Up-regulation is associated with Higher Liver Inflammatory Reaction in Chronic Hepatitis B Patients in Immune Clearance Phase

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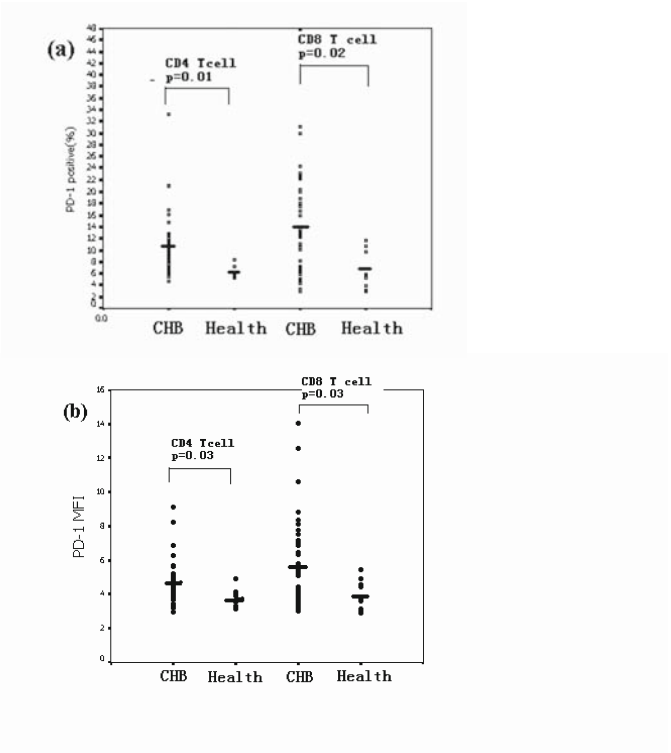
Aim: To investigate features of PD-1 expression on peripheral Tcells and PD-L1 expression in liver in chronic hepatitis B (CHB) patients in immune clearance phase.
Methods: PD-1 expression on total peripheral T cells were evaluated by using flow cytometry. Immunostaining was performed according to the EnVision ChemMate methods. The degree of PD-L1 expression was scored and assessed according to the percentage and staining intensity of positive cells.
Results: Compared to health control, the percentage of total peripheral T cells expressed PD-1 was elevated in CHB with repeatedly increasing ALT level. No specific association between the percentage of PD-1 positive and the mean fluorescence intensity（MFI）of PD-1 expression on total T cells with serum viral load were found. But ALT level was correlated with the MFI of PD-1 expression on total CD8+T cells significantly. PD-L1 is up-regulated on hepatocytes by viral infection, and high expressed in fibrosis section.
Conclusion: The MFI of PD-1 on CD8+T cells plays important role in regulating the immune-host interaction in CHB in immune clearance phase. And PD-1 expression on T cells is correlated with high immune inflammatory refection.



PE153

HBeAg Persistency is Associated with HBV-specific T-cell Response and Liver Damage in Patients with Chronic Hepatitis B

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Aim: To study the quantity, characteristic of HBV-specific T-cell and the extent of liver damage in chronic hepatitis B (CHB) patients with different HBeAg status.
Methods: 103 CHB patients were enrolled and divided into two groups according to the HBeAg status, and the liver damage index were analyzed. The frequency and Foxp3 expression of $CD4^+CD25^+$ regulatory T cells (Treg) were measured, as well as the frequency and phenotypic molecules expression of HBV-pentamer+ T-cell. HBV specific T-cell responses including cellular proliferation and IFN-γ production, with or without anti-PD-L1 and/or anti-CTLA-4 blocking, were also observed.
Results: The demographic characters, serum ALT, AST levels, the frequency and Foxp3 expression of $CD4^+CD25^+$ Treg were similar, while the serum HBV DNA levels were higher in HBeAg+ patients (P <0.05). The liver necroinflammation was comparatively more severe in HBeAg- patients (P =0.056), but the median percentage of liver cirrhosis was much higher in

HBeAg+ patients (P <0.05). The difference of HBV-specific T-cell frequency was not significant between two groups, while the expression levels of PD-1 and CTLA-4 on HBV-specific CD8 T cells were significantly higher in HBeAg+ patients (P both <0.05). Combined using of anti-PD-L1 and anti-CTLA-4 mAb significantly increased the cellular proliferation in either HBeAg+ or HBeAg- patients, but only markedly enhanced the IFN-γ production in HBeAg+ patients.
Conclusion: HBeAg persistency could probably induce higher expression of PD-1 and CTLA-4 on the HBV-specific T cells and result in T-cell impairment, high HBV DNA load and high percentage of liver cirrhosis in HBeAg+ CHB patients.

PE154
Hepatocyte Apoptosis in Patients with Chronic Hepatitis B
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Background: To investigate the relationship between hepatocyte apoptosis and the level of inducible nitric oxide synthase (iNOS) in hepatic tissue in the patients with chronic hepatitis B（CHB）.
Methods: we observed 37 cases with CHB and 10 normal controls. Transferase-mediated-UTP-biotin nick-end labling (TUNEL) technique was used to detect apoptosis cells and immunohistochemical staining were also performed to investigate the expression of inducible nitric oxide synthase (iNOS) in biopsy samples .The serum level of ALT，HBV-DNA，grading of necroinflammatory activity and staging of fibrosis were also assessed.
Results: Hepatocytes in all CHB liver tissues were positively stained by TUNEL in various degree. In contrast, control tissues did not show DNA fragmentation. A significant correlation was seen between apoptosis index (AI) and necroinflammatory grading ((r=0.404, P=0.015) and serum iNOS level （r=0.465, P=0.004）. It did not correlate with fibrosis stage and serum alanine aminotransferase level.
Conclusion: The oxidative stress.in patients with CHB may reflected the apoptosis of hepatocyte. Apoptosis involves in liver injury of CHB,but with no significant correlation to serum level of ALT.

PE155
Genotype and Mutation of the Hepatitis B Virus Polymerase RT Region in Patients with Lamivudine Resistance
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Objectives: To investigate the genotype-dependent development of lamivudine resistance in hepatitis B virus (HBV).
Methods: 215 patients with chronic hepatitis B who had been treated with lamviudine for more than 1year, and become lamviudine resistance were analysed for the HBV genotypes and cumulative rate of RT region mutant with standard DNA sequencing technology.
Results: Among the 215 patients, 60 patients were infected with HBV genotype B (HBV/B)(27.9%), and 155 with genotype C (HBV/C)(72.1%). In the HBV/B patients, 16/60(26.7%) were of subtype Ba, and 44/60(73.3%) were of of subtype Bj. The cumulative type and YMDD mutation rates in patients with genotype C were showed as L180M+M204V (67/155,43.2%) > L180M+M204I (52/155,33.5%) > M204I (36/155, 23.3%), while in patients with genotype B as L180M+M204V 36/60(60.0%) > M204I(24/60, 40.0%), none of L180M+M204I.
Conclusions: Our results indicated that in patients with lamivudine resistance, HBV genotype C (HBV/C) were higher than genotype B (HBV/B). In both genotypes the combined mutations (180+204 sites) were found more than the single 204 site, showed some significance for monitoring lamivudine resistance.

PE156
Expression of IL-35 in Peripheral Blood Mononuclear Cells in Patients with Chronic Hepatitis B
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Background & Aims: IL-35, a novel identified inhibitory cytokine specifically produced by regulatory T cells (Tregs), is an Ebi3-IL-12α heterodimer encoded by Epstein-Barr-virus-induced gene 3 (*Ebi3*) and interleukin-12 alpha (*Il12α*). The aim of the study is to determine the expression levels of IL-35 in peripheral blood mononuclear cells (PBMCs) of chronic hepatitis B (CHB) patients in different phases.
Methods: A total of 36 treatment naïve CHB patients, including 17 in immune-tolerant phase [group 1, ALT: 21 (12-51) U/L, serum HBV DNA: 2.48×10^9 ($6.30 \times 10^6 - 1.20 \times 10^{10}$) copies/ml] and 19 in immune-clearance phase [group 2, ALT: 221 (71-1530) U/L, serum HBV DNA: 5.10×10^8 ($1.62 \times 10^6 - 1.77 \times 10^{10}$) copies/ml] were enrolled in the study. The relative mRNA expression levels of *Ebi3, Il12α* and *FOXP3* were determined by semi-quantitative PCR.
Results: The significant correlations were observed between the expression of *Ebi3* and *Il12α* (r=0.661, P<0.001), *Ebi3* and *FOXP3* (r=0.388, P<0.05), *Il12α* and *FOXP3* (r=0.431, P<0.01). The relative expression levels of *Ebi3* and *Il12α* in PBMCs were significantly higher in group 2 when compared with those in group 1 (1.46 ± 0.23 vs 0.80 ± 0.10 and 1.26 ± 0.19 vs 0.65 ± 0.09, P<0.05, respectively). Furthermore, the relative expression levels of *Ebi3* and *Il12α* in group 2 were significantly correlated with ALT levels (r=0.473, r=0.474, p< 0.05, respectively), but not with serum HBV DNA levels.
Conclusions: The expression levels of IL-35 in PBMCs were significantly higher in CHB patients in immune-clearance phase than that in immune-tolerant phase. Increased IL-35 expression levels were associated with liver injury.

PE157
Adefovir and Lamivudine versus Adefovir Alone in the Treatment of Lamivudine-Resistant Chronic Hepatitis B Infection- A Meta-Analysis
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Background: There are a number of oral antivirals approved for chronic hepatitis B. Lamivudine, the first oral nucleoside analog, is associated with increased rates of drug resistance with prolonged use-- from 20% at one year to 50% at three years. Therefore, an alternative or add-on treatment is necessary. Adefovir, an oral nucleotide analog, is used either in combination with lamuvudine or as monotherapy in lamivudine-resistant chronic hepatitis B. We did a meta-analysis to compare the efficacy of adefovir in combination with lamivudine versus adefovir alone in the treatment of lamivudine-resistant chronic hepatitis B infection.
Methods: A comprehensive literature search was performed using the following databases: Medline, Cochrane, and Embase. A total of 3 randomized controlled trials were retrieved and analyzed. Outcomes measured were virologic response, biochemical response and resistance rates.
Results: Meta-analysis on virologic response showed that combination treatment with adefovir and lamivudine is as effective as adefovir monotherapy (OR 1.04, 95% CI 0.50-2.15, P=0.92). Likewise, in terms of biochemical response, both regimens were equally effective (OR 1.06, 95% CI 0.47-2.40, P=0.90). One study showed statistically significant increase in adefovir resistance rate in the monotherapy arm compared to combination arm (P= 0.0182) after the first year of therapy.
Conclusion: In patients with lamivudine-resistant chronic hepatitis B infection and compensated liver disease, adding adefovir to lamivudine is as effective as switching to adefovir alone in terms of virologic and biochemical response.

PE158
The Efficacy of Switching to Telbivudine (LdT) In Chronic Hepatitis B (CHB) Patients Previously Treated with Lamivudine (LAM)
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Background: LdT produces greater viral suppression than LAM. We investigated whether patients receiving LAM can benefit from switching to LdT.
Methods: HBeAg positive and negative persistently viraemic patients (median HBV DNA 5.0 (LdT), 5.3 (LAM) log $_{10}$ copies/mL) and LAM treated for 3-12 months, were randomized to either switch to LdT or continue LAM. We report the benefit of LdT switch assessed by primary treatment failure (TF, <1 log HBV DNA decline) and viral breakthrough (VB, >1 log above nadir).
Results: 17% (21/122) of the LdT switch and 15% (18/124) continuing LAM patients had pre-existing M204 mutations at screening. TF was 5% (LdT) versus 21% (LAM, $p<0.05$). In patients with >24 weeks prior LAM treatment, TF was 10% (LdT) versus 41% (LAM). 83% LdT TF (5/6) was associated with resistance at screening versus 56% LAM TF. In LdT switch with <24 weeks prior LAM, no LdT TF occurred versus 12% LAM.
In HBeAg positive, TF occurred in 6% (LdT) versus 29% (LAM). Among HBeAg positive with >24 weeks prior LAM treatemtn, VB was 19% (LdT) versus 44% (LAM, $p<0.05$). Differences were not significant for HBeAg positive with >24 weeks LAM or for HBeAg negative regardless of duration of prior LAM treatment.
Conclusions: Early switch to LdT is associated with better virological outcomes in these patients. Persistent viraemia for >6 months on LAM treatment is associated with a high risk of TF and VB. For these patients, genotypic analysis is recommended prior to screening.

PE159

eAg-Ab Seroconversion as a Measurement of in Management of Antiviral Therapy with Chronic Hepatitis B Infection is Not Enough

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Objective: The aim of this study is to evaluate the proper endpoint in the treatment of chronic hepatitis B with antivirals by investigating the viral rebound ratio after one year's（nucleosides）or (three months) sustained treatment with lamivudine, adefovir, entecavir, or interferon when viral response and seroconversion response have been finished .
Methods: eAg positive chronic hepatitis B naïve patients with alanine aminotransferase (ALT) more than 2 ULN were assigned to receive 100 mg of lamivudine, 10mg of adeforvir, or 0.5mg of entecavir once daily, respectively. Patients in the interferon group were administrated with 5,000,000 IU of α－2a interferon on every other day, and the therapeutic duration lasted for another three months after eAg-Ab seroconversion appeared. HBV DNA and eAg-Ab in the serum were tested during the off-treatment period of 12 months.
Results: Thirty four patients in lamivudine group of 148 cases got eAg-Ab seroconversion after treatment with 20±5 months of average duration, and the viral rebound ratios in the off –treatment 6 an 12 months follow up period were 20.6%（7/34）and 40.1%（15/34）, respectively. In adeforvir group were 19%（4/21）and 33. 3 %（7/21）. In enticavir group were 20 %（3/15）and 46.7%（7/15）. In interferon group was 16.2%（6/37）in the off-treatment 6 months follow up period.
Conclusions: We conclude that eAg-Ab seroconversion in the treatment of eAg positive chronic hepatitis B patients is the goal but not an endpoint of therapy physicians should aim at. To gain everlasting effect, longer duration of treatment may be needed.

PE160

Hepatitis B Vaccination in HBsAg Negative (Low-risk) People: How Robust is the Evidence?

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Background: Universal hepatitis B(HB) vaccination of HBsAg negative people (especially infants) is widely recommended and practised.
Objective: To assess whether there is robust evidence of protective efficacy to back such practice.
Methods: This Cochrane review included randomised trials identified from six databases through detailed electronic searches. Trials comparing HB vaccine versus placebo/another vaccine, in HBsAg negative persons were included without any restrictions. The primary outcome was HB infection (developing HBsAg or anti-HBc). Robustness of evidence was assessed through comparison of available-case analysis versus intention-to-treat(ITT) analysis using four different models: (i)assuming unfavourable event for all missing data, (ii)assuming favourable outcome for all missing data, (iii)best-case-scenario and (iv)worst-case-scenario
Results: Twelve trials were eligible among 2964 citations; all were methodologically poor (high risk of bias). Data from four trials could be included in meta-analysis. Efficacy of vaccination varied with the type of data analysis. Available-case analysis suggested efficacy in reducing risk of developing HBsAg (RR=0.17;95%CI=0.09-0.31;n=1341) and anti-HBc (RR=0.42;95%CI=0.31-0.57;n=1235). ITT analysis results varied depending on the model chosen(Table), but liberal approaches suggested high efficacy, whereas conservative approaches did not.
Conclusion
The available evidence on efficacy of HB vaccination in HBsAg negative people is not robust; there are serious limitations in quality and quantity.

Analysis model	Relative Risk(95%CI)	
	HBsAg	Anti HBc
Available-case analysis	0.12(0.03-0.44)	0.36(0.17-0.76)
ITT assuming unfavourable outcome for missing data.	0.96(0.89-1.03)	0.81(0.61-1.07)
ITT assuming favourable outcome for missing data.	0.12(0.03-0.44)	0.45(0.25-0.50)
Best-case scenario	0.01(0.00-0.03)	0.08(0.01-1.03)
Worst-case scenario	9.45(2.14-41.7)	3.45(0.38-3.57)

PE161

Histologic Assessment of Long-term Entecavir (ETV) Treatment in Chronic Hepatitis B (CHB) Patients.

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Background: Open-label rollover study (ETV-060) assessed histologic improvement in CHB patients on at least 3 years ETV therapy.
Methods: 100% nucleoside-naïve patients and 98% lamivudine (LVD)-refractory patients from ETV-053 and ETV-052 studies, respectively, entered ETV-060 study and received ETV at 0.5/1mg for greater than 96 weeks. Improvement in Knodell necroinflammatory (NI) score and Knodell fibrosis score at Weeks 48 and 148 were studied.
Results: At Week 148, 95% of nucleoside-naïve patients and 56% of LVD-refractory patients achieved HBV DNA <400copies/mL. Furthermore, 95% of nucleoside-naïve patients and 93% of LVD-refractory patients had normalized ALT levels. Mean platelet counts in both naïve and LVD-refractory patients were improved at Weeks 48 and 148 compared with baseline.
Conclusions: Naïve and LVD–refractory CHB patients showed significant improvement in liver histology after 3 year ETV therapy, and improved DNA and serum ALT levels.

	Week 48	Week 148
Improvement in Knodell NI score (naïve patients)	31/37 (84)	37/37 (100)*
Improvement in Knodell fibrosis score (naïve patients)	6/36 (17)	17/36 (47)**
Improvement in Knodell NI score (LVD-refractory patients)	15/26 (58)	23/26 (89)*
Improvement in Knodell fibrosis score (LVD-refractory patients)	3/25 (12)	8/25 (32)***
*P<0.0001 compared to baseline;** P=0.0002 compared to baseline; *** P=0.043 compared to baseline; Denominators represent patients with biopsies evaluable for the end point		

PE162

Hepatic Pathology and Clinical Characteristics of Patients with Chronic Hepatitis B Virus in Immune Tolerant phase

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Objective: To investigate the hepatic pathology and clinical characteristics of patients with chronic hepatitis B virus (HBV) in immune tolerant phase.
Method: 98 chronic HBV carriers in immune tolerant phase were involved in this study. Statistical analysis included the ages and sex of patients, serum level of HBV DNA and hepatic pathology. Histological grade of inflammation and stage of fibrosis were also analysed in patients with different level of nomal ALT.
Results: 84.7 percent of patients were younger than 30 years old, 15.3 percent were older than 30 in this study. 48.0% patients' mothers were HBsAg positive. High levels of serum HBV DNA were founded in all patients, $>10^7$ copies/ml were 78.6%. Only 5 cases (5.1%) whose liver inflammation grade were G0, the rest patients were mild inflammation, in which G1 were 64 cases (65.3%), G2 were 29 (29.6%); there were 56 patients (57.1%) had no signifecant liver fibrosis, the rest 42 cases (42.9%) had different fibrosis, among those S1 were 23 cases (23.5%）, S2 were 14 （14.3%）, S3 were 5（5.1%）, none of patients had cirrhosis. The fibrosis stages of higher ALT level were markedly severer than lower ALT in patients with normal ALT（$P < 0.01$ ）.
Conclusions: Most of patients with chronic hepatitis B virus in immune tolerant phase present mild inflammation in liver, part of them have already appeared fibrosis, so some patients determinated by clinics are actually not in immune tolerant phase. Although ALT testing are in the normal range, but the possibility of liver fibrosis is increased in patients with relative higher ALT level, so liver pathology should be recommended to judge illness correctly.

PE163

Peginterferon alfa-2a in Chronic Hepatitis B Patients in Bangladesh: A Preliminary Study

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Background/aims: Hepatitis B virus infection (HBV) is a global health problem. In Bangladesh, 5-7% of people are HBsAg positive. This study was carried out to evaluate the efficacy and safety of peginterferon alfa-2a in chronic hepatitis B patients. Methods: A total of 60 patients with chronic hepatitis B, 32 (53.3%) were HBeAg positive (group A) while 28(46.7%) were HBeAg negative (group B) were included in this study after meeting the following criteria: age 18 to 60 years, HBsAg positive for more than 6 months, serum HBV-DNA was >5 log(10) copies/mL and ALT more than two times the upper normal limit. They were given peginterferon alfa-2a (180 microgram once weekly) for 24 weeks and followed for an additional 24 weeks. RESULTS: After 24 weeks of follow-up, the percentage of patients with normalization of alanine aminotransferase levels or HBVDNA levels below 20,000 copies per milliliter was significantly higher in HBeAg positive patients (59 percent and 43 percent, respectively) than among HBeAg negative patients (45 percent and 33 percent). Loss of hepatitis B surface antigen occurred in 3 patients in group A, as compared with 1 patients in the group B ($p<0.01$). Adverse events including pyrexia, fatigue, myalgia, headache and haematologic abnormalities were similar in both groups. CONCLUSIONS: Patients with HBeAg positive chronic hepatitis B had significantly higher rates of response, sustained for 24 weeks after the cessation of therapy, with peginterferon alfa-2a.

PE164

Prospective Study of the Effectiveness of Hepatitis B Vaccine in Healthcare Workers with Isolated Anti-hepatitis B Core Antibody

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Background: The effect of hepatitis B vaccination on individuals with isolated anti-HBc in endemic areas is not clear. We investigated the prevalence of individuals positive for anti-HBc only and their antibody response after hepatitis B vaccination in a single healthcare center.
Methods: The study included 1,812 healthcare workers. After screening for HBsAg and anti-HBs, the individuals negative for both HBsAg and anti-HBs were examined for anti-HBc and were vaccinated with a recombinant hepatitis B vaccine at 0, 1, and 6 months. The serum anti-HBs level was measured after the vaccination.
Results: Of the subjects, 334 (220 females) were negative for both HBsAg and anti-HBs. Forty (2.2%) subjects had isolated anti-HBc, including more males (60.0% vs. 30.6%) and older people (45.7±8.2 vs. 37.3±8.5 years), compared with individuals negative for all of the viral markers. The anti-HBs seroconversion rate and anamnestic response in the individuals with isolated anti-HBc after the first vaccine injection were 60% and 27.5%, respectively. In the 294 persons who were negative for all hepatitis B viral markers, the seroconversion rate after the first vaccination was 52.6%. The anti-HBs seroconversion rate did not differ between the isolated anti-HBc positive individuals and those negative for all hepatitis B markers (89.5% vs. 96.6%) after the full course of vaccination.
Conclusions: Serum HBsAg and anti-HBs tests are sufficient for screening before hepatitis B vaccination, especially in healthcare workers.

PE165

Quantity and Distribution Features of Liver CD83 + Mature Dendritic Cells in Patients with Chronic Hepatitis B Virus Infection in Their Immune Tolerant Phase

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Objective: To understand the quantity and distribution of $CD83^+$ mature dendritic cells in patients with hepatitis B virus in immune tolerant phase.
Methods: There were 30 immune tolerant phase patients with hepatitis B virus infection (fibrosis stages were S0), 10 immune clerance phase patients, 10 non-active status patients and 5 healthy controls involved in our research. The quantity and distribution of $CD83^+$ mature dendritic cells in liver were determined by immunohistochemical staining.
Result: The liver inflammation grades were between G1-G2 in patients who in inmmune tolerant phase and non-active status, moreover, patients in immune clerance phase were between G2-G4. There were a small amount of $CD83^+$ dendritic cells in healthy liver tissue, scattered in portal areas and hepatic lobules. The quantity and distribution of $CD83^+$ dendritic cells in patients who in inmmune tolerant phase and non-active status were similar to

the healthy, and the quantity were no difference among them（p＞0.05）.The number of $CD83^+$ cells in patients of immune clerance phase was significant increased compared with other groups, there were differences among them（p ＜0.05）, the $CD83^+$ cells mainly distributed in portal areas infiltrated with inflammatory cells and hepatic lobules with inflammatory necrosis.
Conclusion: $CD83^+$ mature dendritic cells are involved in liver immune response in patients of inmmune clerance phase, is likely to related to hepatitis B virus clearance. Lack sufficient mature dendritic cells may be one of the mechanisms of immune tolerance.

PE166
Antenatal Hepatitis B Screening in Women from the Mainland China versus Local Residents
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Background: Local hospitals provide obstetric services including antenatal care to women normally living in the Mainland China, whose prevalence of hepatitis B carrier is unknown.
Objectives: Compare prevalence of HBV carrier of pregnant women from the Mainland China with local counterparts and discuss the implications of results.
Materials and Methods: Antenatal serological results were retrieved from corporate laboratory information system databases. Pregnant women from the Mainland China were identified by a specific set of temporary-allocated identity number during January 2007 - October 2008.
Results: 7491 pregnant local residents and 1397 pregnant women from the Mainland China underwent antenatal serological tests for hepatitis B surface antigen. Positive hepatitis B surface antigen results were more frequent in pregnant women from the Mainland China (12.7%) than in local pregnant women (8.17%) ($p<0.001$).
Discussion: Because infected pregnant women can transmit the hepatitis B virus to the infant at delivery, specific management could entail maternal medication, injection of hepatitis B immune globulin to the infant at birth and immunization later on. However, early repatriation to the Mainland China, which is common, will make completion of immunization program difficult. These babies will be at a higher risk to be infected by HBV, particularly when breast-fed by HBV carriers. Their return to Hong Kong later will dilute the effects of local immunization program. The volume of work derived from the provision of obstetric services to women from the Mainland Chinese is larger with regard to medication, counseling and immunization for babies born to HBV carriers.

PE167
Prevention of Viral Hepatitis B Reactivation in Patients Undergoing Immunosuppressive or Anticancer Therapy
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Background/Aim: We compared the prevention of HBV reactivation in (HBsAg)-positive patients with HBsAg-negative patients who were positive for antibody to (anti-HBc) and/or (anti-HBs) undergoing immunosuppressive, anticancer or molecular target therapy.
Methods: From Sep 2004 to Nov 2008, 17 HBsAg-positive patients and 22 anti-HBc and/or anti-HBs-positive patients were enrolled in this study. We compared with 2 groups about background disease, age, blood examination, and nucleoside analogues.
Results: In HBsAg-positive patients mean age were 56.6±10.2 years old, median AST levels were 30 (18-706) IU/L, and median ALT levels were 36 (13-544) IU/L for 8 (47%) haematological disease and 9 (53%) collagenosis disease. In anti-HBc and/or anti-HBs-positive patients mean age were 71.3±9.6 years old, median AST levels were 20 (9-106) IU/L, median ALT levels were 16.5 (5-247) IU/L for 17 (77%) haematological disease and 5 (23%) collagenosis disease. Serum HBV-DNA levels >5.0 log copies/ml were 8 (47%), 2.6~5.0 were 7 (41%), <2.6 were 2 (12%) in HBsAg-positive patients, and serum HBV-DNA levels <2.6 were all cases in anti-HBc and/or anti-HBs-positive patients. 14 (82%) of HBsAg-positive patints received nucleoside analogues (7 LAM and 7 ETV), and 12 (55%) of anti-HBc and/or anti-HBs-positive patients received nucleoside analogues (8 LAM and 4 ETV). Mean duration of treatment for 14.2 months in HBsAg-positive patients, and for 4.1 months in anti-HBc and/or anti-HBs-positive patients, the resistance virus occurred to 3 (75%) of 4 HBsAg-positive patients treated with LAM for collagenosis disease more than two years.
Conclusion: When HB carriers of collagenaous disease undergoing immunosuppressive therapy required the nucleoside analogues more than two years, we recommended treatment to prevent HBV reactivation with ETV.

PE168
Low Rate of Adefovir Resistance-related Mutations in Polymerase Gene of Hepatitis B Virus in Lamivudine-resistant Chronic Hepatitis B Patients not Treated with Adefovir Dipivoxil
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Background: Adefovir dipivoxil is used for the initial treatment of chronic hepatitis B or rescue treatment of lamivudine-resistant chronic hepatitis B, and exhibits excellent antiviral activity. However, the presence of resistance to adefovir dipivoxil was more frequently in lamivudine-resistant chronic hepatitis B patients than in lamivudine-naïve patients during adefovir dipivoxil monotherapy. But the rate of adefovir resistance related mutations is little known in lamivudine-resistant patients before adefovir dipivoxil treatment. The aim of this study was to investigate the rate of adefovir resistance-related mutations in polymerase gene of hepatitis B virus in lamivudine-resistant patients not treated with adefovir dipivoxil.
Methods: The existence of adefovir resistance-related mutations was examined in 240 lamivudine-resistant chronic hepatitis B patients with breakthrough hepatitis and 100 antiviral-naïve chronic hepatitis B patients. Both polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) and directly sequencing of PCR product were used to detect resistant viruses.
Results: rtA181T mutants were detected in only two sera of lamivudine-resistant patients, while none in the antiviral-naïve chronic hepatitis B patients. There was no rtN236T detected in the two groups.
Conclusion: Our results suggest that the rtA181 mutant virus were present in a few lamivudine-resistant chronic hepatitis B patients before they have been treated with adefovir dipivoxil, but the rtN236T mutant was not detected in any of the two groups. The rate of adefovir resistance-related mutations in polymerase gene of hepatitis B virus was low in such lamivudine-resistant patients before adefovir dipivoxil treatment.

PE169
Comparison Proteomic Study on HBV Related Chronic Hepatitis, Liver Cirrhosis and Primary Hepatic Carcinoma
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Objective: In this study, we tried to detect and identify the special protein of HBV related chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. To find new opinion on the developing of chronic liver disease.
Methods: The sera of health adult, HBV related chronic hepatitis, liver cirrhosis and hepatocellular carcinoma were respectively detected by surface enhanced laser desorption/ionization time-of- flight mass spectrometry (SELDI-TOF-MS). The arrays of every group were analysised by clustering analysis and to establish disease predictive model. Then the sample was eluted with different pH Tris, trypsinization on-chip, mass determination and peptide database comparison.
Results: ① According CM10 chip we find 18 protein with obviously deviation ($P<0.05$) among HBV related chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. ②Clustering analysis for the data from SELDI-TOF-MS confirmed 42 differentially expressed proteins. Then we developed disease predictive mathematic models (Decision Tree Model, DT model) with average validity up to 73.9%. ③ The 5805 Da protein peak was identified to be Chondroitin sulfate synthase 2 (CHSS2), which is a potential molecule involved in the pathologic process and a potential serum marker for the HBV related hepatic diseases as well. **Conclusions:** Our results suggest that SELDI-TOF-MS is a usefull technique for differential expressed proteins screening and analysis in HBV related chronic liver

disease. CHSS2 may be useful during the developing of HBV related chronic liver disease.

PE170

Early Virologic and Biochemical Response to Clevudine in Cirrhotic Patients with Chronic HBV Infection

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Backgound: Clevudine is a new nucleoside analogue with potent antiviral activity in chronic hepatitis B patients. However, the efficacy and safety of clevudine in cirrhotic patients are not well recognized. This study was conducted to evaluate the early virologic and biochemical response rate as well as safety of clevudine in cirrhotic patients with chronic HBV infection.
Methods: 46 patients with chronic HBV infection who visited Korea University Ansan Hospital and Guro Hospital between May 2007 and May 2008 were included. 24 patients had chronic hepatitis B (group A) and 22 had liver cirrhosis (group B). Early virologic response was defined as HBV DNA less than 200 IU/mL at week 12. Early biochemical response was defined to be normalization of ALT (<45 IU/L) at week 12.
Result: Pretreatment HBV DNA levels were higher in group A compared with group B (8.06 log IU/mL vs 7.09 log IU/mL, p=0.06). Pretreatment ALT levels were not significantly different between the two groups (166 IU/L vs 139 IU/L, p=0.725). The rate of early virologic response was significantly higher in group B compared with groups A (72.7% vs 33%, p=0.01). The rate of early biochemical response were not significantly different in both groups (75% vs 72.7%, p=0.725).
Conclusion: Clevudine is considered to be safe and effective in cirrhotic patients with chronic HBV infection as well as chronic hepatitis B patients. Long term safety and efficacy need to be evaluated in the future.

PE171

Nucleos(t)ides as Prophylaxis for Reactivation of Hepatitis B in Immunosuppression

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Objective: The aim of this study was to evaluate the role of nucleos(t)ide analogues against HBV reactivation in immunosuppression.
Methods: Non-active HBsAg carriers suffering from cancer, autoimmune diseases and needing the treatment of immunosuppressants or cytotoxic chemotherapy were enrolled in the study. The outpatients or in-patients from April 2007 to July 2008 were enrolled. The nucleos(t)ide analogues were used in cancer patients 1-2 weeks before chemotherapy, and the duration lasted 6-12 months according to patients' compliance after completion of chemotherapy. Patients with other diseases used nucleos(t)ide analogues in 1-3 months before using glucocorticoids or other immunosuppressive agents, and continued to use for 6-12 months after accomplishing the course of immunosuppressant treatment. The characheristics and clinical manifestations about HBV reactivation were investigated.
Results: Of the thirty two patients in prospective group, twenty two patients suffered from cancer, eight patients suffered from idiopathic thrombocytopenic purpura, two patients suffered from chronic nephritis. The amount of HBV DNA was detected in the first, third, sixth and 12th month after the use of nucleos(t)ide analogues. After chemotherapy or immunosuppressant treatment, only 9.4% (3 / 32) of them suffered from HBV reactivation, which presented with HBV DNA positive and abnormal liver function.
Conclusion: Non-active HBsAg carriers would appear potential incidence of HBV reactivation during use of chemotherapy or immunosuppressant. Nucleos(t)ide analogues could be used in early phase as prophylaxis for reactivation of hepatitis B in immunosuppression and to improve clinical prognosis.

PE172

No Significant Drug-Drug Interaction Between Clevudine and Tenofovir Dipivoxal in Healthy Volunteers

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Background: HBV therapies are evolving toward combination antivirals. This study evaluated the combination of clevudine (CLV), a potent nucleoside analog, with tenofovir dipivoxil (TDF).
Methods: A phase I, single-arm, multi-dose study in 18 healthy adult volunteers to evaluate pharmacokinetic and safety interactions between CLV and TDF. Subjects received 21 days of CLV 30mg followed by 7 days of CLV 30mg +TDF 300mg. PK profiles were obtained on Days 1, 21 and 28. CLV AUC and Cmax were compared on Days 21 and 28. Day 28 tenofovir PK was compared to historical data. Safety assessments were conducted throughout.
Results: 18 subjects were enrolled (13M/5F);17 completed the study. The mean (range) age was 37y (22-49) and body mass index (kg/m2) was 27.6 (22.9-31.9). 22 AEs were reported by 6 subjects, with 10 AEs reported during CLV-only dosing and 12 AEs reported during CLV+TDF dosing. AEs included nausea (2) and pharyngolaryngeal pain (2). The majority of the AEs were mild. There were no clinically significant changes in ECGs or laboratory parameters. Comparisons of CLV AUC and Cmax on Day 21 and 28 revealed no significant impact of TDF upon the plasma CLV exposure (D28/D21 AUC ratio=0.98, D28/D21Cmax ratio=0.89). There is no significant effect of CLV on tenofovir when comparing AUC and Cmax of TDF to historical values.
Conclusion: Safety and pharmacokinetic results demonstrate that CLV and TDF may be safely co-administered, supporting the further study of this drug combination for the treatment of chronic HBV infection.

PE173

Urinary Dolichol as a Predictor of HBV Drug Resistance

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Background: Dolichyl (Dol), the main lipid intermediator of Dolichyl Phosphate Cycle (DPC) has been reported to be elevated in urine of patients with multidrug resistance in cancer. Drug resistance poses a major threat to nucleoside analogue-based therapies for chronic HBV infection.
Methods: With focus on a risk predictor for susceptibility to the development of HBV drug resistance the present study was carried out to estimate urinary levels of Dol in chronic HBV infection. The samples obtained every week before and during the course of treatment from 42 patients with HBV. The occurrence of exacerbations of chronic HBV were registered for 2 years. Dol in urine was assayed by HPLC method.
Results: The normal amounts of Dol in healthy persons urine (n=1500) are 6,0 $\pm$ 10,0 mkg/mmol creatine. During the period of observation 36 (86%) of patients treated with nucleoside analogue-based therapies were diagnosed with exacerbations due to resistance of hepatitis B virus to antiviral drugs. From this group of HBV patients 35 (98%) have had elevated urinal Dol excreation (45,8±5,2 g/ml vs. 8,2±1,9 g/ml, $p<0.0001$) in more than 3 months of observation.
Conclusion: There is a reason to suggest that elevated urinal Dol detected in patients with exacerbations during HBV treatment may evidence of possible defect of host mechanism of drug resistance development to nucleoside analogue-based therapies. The interest drawn to the employment of Dol as a predictor for exacerbation of chronic HBV is explained by the role of DPC in P-glycoprotein regulation in human hepatocytes.

PE174

Prevalence and molecular characterization of Hepatitis B virus in migrant workers from Myanmar, Cambodia and Lao to Thailand

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Background/Aim: Hepatitis B virus (HBV) is endemic in Southeast Asia. However, data on HBV prevalence among the populations of Myanmar, Cambodia and Lao are limited. In this study, HBV prevalence among

migrant workers in Thailand was established and virus isolated from serum samples was molecularly characterized. Methods: We tested 1975 sera of immigrants (752 from Cambodia, 429 from Laos and 794 from Myanmar) by HBsAg ELISA screening. HBsAg-positive sera were further tested for HBV DNA by PCR and subsequently subjected to sequencing of the Pre-S/S and Pre-C/C regions for genotyping

Results: The details of the results are shown below.

Conclusion: This study has shown the high prevalence of HBV infection (8-12%) among migrant workers from Myanmar, Cambodia and Lao. HBV genotype C was commonly found.

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	Cambodia (n = 752)	Laos (n = 429)	Myanmar (n = 794)	Total (n = 1975)
No. HBsAg positive (n; %)	78; 10.37	37; 8.62	98; 12.34	213; 10.78
No. PCR positive (n; %)	65; 83.3	28; 76.7	72; 73.5	165; 77.5
No. sequencing (n)	65	28	72	165
Gender (M : F)	48:17	22:6	47:25	117: 48
Age (yr ± SD)	28.82±7.96	25.54±6.32	28.32±7.14	28.57±7.52
Genotype				
A2	1	0	0	1
B				
- B2	5	0	0	5
- B3	1	8	0	9
- B4	3	3	0	6
C				
- C1	53	17	70	140
- C2	0	0	1	1
Suspected B2/C1 Recombinant	2	0	0	2
Suspected B2/C5 Recombinant	0	0	1	1

PE175

Entecavir (ETV) Therapy for Chronic Hepatitis B Patients with Suboptimal Response to Adefovir (ADV)

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Background: A significant proportion CHB patients treated with ADV have a suboptimal response, increasing the risk of disease progression and development of resistance. We report clinical results from patients who either failed or relapsed following ADV therapy and were subsequently switched to ETV.

Methods: Study ETV-079 was a randomized, open-label study comparing antiviral efficacy of ETV (0.5mg/day) vs ADV (10mg/day) in nucleoside-naïve HBeAg-positive patients. After up to 96 weeks of treatment in ETV-079, 24 patients treated with ADV (13 suboptimal responders) rolled over into study ETV-901 (1.0mg/day). HBV DNA viral suppression and safety was evaluated during 48 weeks of ETV treatment.

Results: At entry to ETV-901, the median HBV DNA was 5.72$\log_{10}$ copies/mL. Median exposure to ETV (1.0mg) in ETV-901 was 46 weeks and 18 patients currently remain on study therapy. At Week 24, the mean reduction in HBV DNA was 4.5$\log_{10}$ copies/mL and 8/16 (50%) reached HBV DNA levels <300 copies/mL. Nine patients have achieved Week 48 and all have achieved HBV DNA <10^4 copies/mL and 8/9(89%) had HBV DNA levels <300 copies/mL. No patients experienced virologic breakthrough on ETV. The safety profile of ETV in ADV-treated patients remained consistent with the previously reported experience.

Conclusions: The majority of patients who were suboptimal responders or virologic rebounders following ADV treatment in study ETV-079, experienced rapid reductions in HBV DNA levels when switched to ETV. HBV DNA levels continued to decline to undetectable levels with 48 weeks of ETV treatment.

PE176

Quantification of Hepatitis B Virus Total DNA and Covalently Closed Circular DNA in Chronic Hepatitis B, Cirrhosis of Hepatitis B and Hepatitis B Relevance Hepatocellular Carcinoma Patients

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Aim:To quantify hepatitis B virus (HBV) total DNA and covalently closed circular DNA (cccDNA) in liver biopsies and sera which from Chronic hepatitis B(CHB)、liver cirrhosis of hepatitis B(LC) and hepatitis B relevance hepatocellular carcinoma(HCC) patients, and analysis HBV replication under the circumstances of different diseases.

Methods:Total HBV DNA and cccDNA in serum and liver biopsy samples were measured in 21 CHB、23 LC and 25HCC patients by the real-time PCR assay.

Results: The levels of total HBV DNA in serum,intrahepatic total HBV DNA, intrahepatic cccDNA, as well as the proportion of intrahepatic cccDNA in total HBV DNA decreased progressively in CHB,LC and HCC ,moreover CHB had significantly higher levels of total HBV DNA in serum and liver biopsy samples than LC (log [total serum HBV DNA] P = 0.024;log [total intrahepatic HBV DNA] P = 0.034); CHB and LC had significantly higher levels of intrahepatic cccDNA and the proportion of intrahepatic cccDNA in total HBV DNA than HCC(P <0.01); cccDNA couldn't be detect in all patients'serum. In CHB ,the levels of serum's total HBV DNA,intrahepatic total HBV DNA and cccDNA in HBeAg-positive group had significantly higher than the HBeAg-negative group(P <0.01) ,but in LC only intrahepatic total HBV DNA had statistical difference between HBeAg-positive and negative group (P=0.026) , no statistical difference between HBeAg-positive and negative group in HCC.

Conclusions: The replication activity of hepatitis B virus in CHB,LC were higher than HCC, HBV reproduction reduced significantly in HCC. Duplication of HBV in LC was lower than CHB but had no statistical difference. The levels of HBV reproduce in HBeAg-positive group was higher than HBeAg-negative group of all three desease.

PE177

Treatment Outcomes of 48 Week Clevudine Therapy in Patients with Chronic Hepatitis B

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Background: Clevudine is a pyrimidine analogue with potent and sustained antiviral activity against HBV in the 24 week therapy. The present study assessed the efficacy and viral resistance of 48 week clevudine therapy in patients with chronic hepatitis B.

Method: A total of 42 patients (26 HBeAg positive and 16 HBeAg negative) who were received clevudine 30 mg once daily for 48 weeks were included in this analysis. Serum HBV DNA was quantified by real time PCR assay.

Result: At week 48, median reductions of serum HBV DNA from baseline were 4.98 $\log_{10}$ IU/mL (5.00 $\log_{10}$ IU/mL for HBeAg positive and 4.95 $\log_{10}$ IU/mL for HBeAg negative) and 76.2% of patients showed undetectable serum HBV DNA (<60 IU/mL) (65.4% for HBeAg positive and 93.8% for HBeAg negative). The normalization of ALT levels (<35 IU/L) was achieved in 81.0% (88.5% for HBeAg positive and 68.8% for HBeAg negative). 15.4% of HBeAg positive patients showed HBeAg loss or seroconversion. HBV DNA negativity at week 48 was associated with HBeAg negativity (P =0.037), HBV DNA <2,000 IU/mL at weeks 4 and 24 (P =0.019 and 0.001, respectively). Two HBeAg positive patients showed viral breakthrough with M204I mutation during 48 week.

Conclusion: Clevudine therapy in patients with chronic hepatitis B showed potent virologic responses at week 48, especially in those with HBeAg negativity and complete early virologic response (HBV DNA <2,000 IU/mL at weeks 4 and 24). But clevudine resistance can occur in HBeAg positive patients.

PE178

Normal Ranges of Serum Alanine - Aminotransferase Level and Its Modulating Factors in Thai People

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Background: Serum alanine aminotransferase (ALT) activity, the variable most commonly measured to assess hepatic disease, fails to identify many patients with hepatic injury. Current standards for "normal" ALT level were defined by using populations that included persons with subclinical liver disease. There is no study regarding normal level of ALT and its modulating factors in healthy Thai people.
Objective: To definitions of Normal ranges for serum ALT level in Thai people.
Design: Prospective observational study
Setting: Phramongkutklao hospital and Army Institute of Pathology Pramongkutklao Medical center(A.I.P.), Bangkok, Thailand
Participants: 200 persons who were first-time blood donors from August through December 2007 were negative for anti–hepatitis C virus(HCV), negative HBsAg(HBV), and had no contraindications to donation.
Measurements: Univariate and multivariate analyses examined associations between clinical and laboratory factors and ALT levels. Normal ranges for ALT were computed from the population at lowest risk for liver disease.
Results: Serum ALT activity was independently related to body mass index, age, alcoholic consumption and to laboratory indicators of abnormal lipid or carbohydrate metabolism. Normal ranges for serum ALT level in Thai people upper limits for men 26 U/L and for women 21.67 U/L.
Conclusion: In men serum ALT is strongly associated with body mass index, age, alcoholic consumption and to laboratory indicators of abnormal lipid or carbohydrate metabolism. The normal range of ALT should be defined for male and female separately.

PE179

Evaluation of Long-term Entecavir (ETV) Treatment in Chronic Hepatitis B (CHB) Patients Switched from 24 weeks Lamivudine (LVD) Therapy

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Background: The open-label rollover study ETV-060 was conducted after ETV phase II clinical study ETV-047 for nucleoside-naïve adult CHB patients in Japan. In this analysis, we report ETV long-term efficacy and safety in patients who were switched from 24-week LVD treatment to ETV therapy.
Methods: Ninety-seven percent (33/34) of LVD-treated patients from ETV-047 were rolled over into ETV-060 treated with 0.5mg of ETV. Thirty patients completed 96 weeks of ETV therapy and were evaluated for HBV DNA level, ALT normalization, HBeAg seroconversion, resistance and safety.
Results: Comparing to baseline before switching to ETV, after 96 week of ETV treatment, the proportion of patients achieving undetectable HBV DNA (<400 copies/ml) increased from 21% to 90%. Increases were also observed for ALT normalization (81% to 90%) and HBeAg seroconversion (10% to 19%). Three patients had detectable HBV DNA at Week 96 after ETV treatment and samples from two were tested for resistance. Neither demonstrated substitutions associated with ETV or LVD resistance. Five patients had Grade 3–4 laboratory abnormalities, including increased AST/ALT and increased lipase levels.
Conclusions: Switching patients from LVD therapy to ETV resulted in increased proportions of patients achieving HBV DNA suppression, ALT normalization and HBeAg seroconversion, with no evidence of ETV resistance. ETV was well tolerated during treatment.

PE180

Clinical Prediction of Failure in Anti-viral Prophylaxis for Patients with Hepatitis B Infection Undergoing Cytotoxic Chemotherapy for Malignant Tumors

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Backgrounds/aims: Hepatitis B virus (HBV) reactivation in patients undergoing chemotherapy hampers an adequate administration of cytotoxic agents and even causes an treatment failure. Prophylaxis failure occasionally results from viral breakthrough or withdrawal flare. The aims of this study were to identify predictors of anti-viral prophylaxis failure and to determine the optimal strategy for anti-viral prophylaxis.
Methods: Cancer patients with positive HBsAg who underwent cytotoxic chemotherapy in a tertiary medical center from January 2005 to June 2008 were included. Prophylactic lamivudine was started with initiation of chemotherapy, continued during the chemotherapy, and discontinued within 6 months after the completion of chemotherapy. All patients were followed up even after withdrawal of lamivudine.
Results: 115 patients were enrolled. Twenty-nine patients (23.7%) had hematologic malignancies and eighty-six (76.3%) had solid tumors. Median follow-up duration was 15.9 months and twenty-six patients (22.6%) experienced the prophylaxis failure: viral breakthrough (11 patients, 9.6%), withdrawal flare (15 patients, 13.0%). YMDD mutation developed in four patients. Withdrawal flare occurred at a median 2.5 months after discontinuation of lamivudine. Using log-rank test and Cox multi-variate analysis, our results showed that the type of underlying malignancies (HR 2.46, 95% CI, 1.11–5.43; P=0.026) and baseline HBV DNA titer (HR 3.91, 95% CI, 1.63–9.39; P=0.002) were significant independent risk factors for antiviral prophylaxis failure.
Conclusion: Cancer patients with high viral load of HBV and hematologic malignancies may need more prolonged and potent anti-viral prophylaxis to avoid interruption or delay of chemotherapy.

PE181

Viral Dynamics for Predicting Hepatitis Flares during or after Antiviral Treatment in Patients with Chronic Hepatitis B

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Back Ground: The usefulness of hepatitis B virus (HBV) DNA and HBV core-related antigen (HBcrAg) was evaluated for timing hepatitis flare after viral breakthrough or withdrawal of antiviral treatment in chronic hepatitis B.
Method: A total of 32 events of HBV reactivation due to withdrawal of lamivudine (LAM) or emergence of mutants resistant to LAM or adefovir dipivoxil (ADV) virus were analyzed in 25 patients with chronic hepatitis B (20 men, median age 56 years [range: 30–66]). They were followed monthly for serum ALT, HBV DNA and HBcrAg before, during and after the treatment.
Result: High ALT flare (ALT > 100 IU/ml) after viral breakthrough or withdrawal was related with baseline HBeAg positivity (p=0.016), HBcrAg level at HBV DNA elevation (p=0.038) and duration from HBcrAg elevation to salvage therapy (p=0.044). In multivariate analysis, HBcrAg > 4.0 log

U/ml (OR 22.9, 95%C.I. 1.7-304.1, p=0.018) and Salvage therapy after 8 weeks from HBcrAg elevation (OR 10.6, 95%C.I. 1.6-71.4, p=0.015) were selected as related factor with high ALT flare. After appearance of resistant-virus or withdrawal of LAM or ADV therapy, HBV DNA re-elevated without increase of HBcrAg, then HBcrAg elevated with HBV DNA. Re-elevations of ALT occurred in 27 of the 32 (84%) events. In 23 of the 27 (85%) events, ALT re-elevated within 8 weeks from the start of HBcrAg increase.
Conclusion: HBcrAg was useful for timing the re-elevation of ALT after HBV DNA re-elevation induced by drug-resistant virus or withdrawal of LAM or ADV therapy.

PE182
109 Weeks of Sequential Lamivudine + Placebo to Adefovir Therapy Suppresses HBV Replication in a Lamivudine Mutation Patient with Personalized Modeling
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Background and Objectives: The aim of the study was to observe the efficacy of a patient's therapy for switching lamivudine + placebo to adefovir dipivoxil (ADV), and modeling the viral dynamics.
Methods: The studied object was a Chinese CHB patient with lamivudine mutation. Used the LVD + placebo for 12 weeks' therapy. Then switched ADV for another 95 weeks. After that stopping the treatment and following up for 24 weeks. Based on our modified basic virus infection model, we introduce a personalized model consisting of four variables: *x, y, v, e* , representing uninfected cells, infected cells, free virus, and CTL cells, respectively.
Results: Selected the model parameters, the simulation data of HBV DNAs of our model are good in agreement with the clinical ones. Observe that after 24 weeks' treatment cessation, the benefit (HBV DNA < 250 copies/mL) for suppressing HBV replication can still be kept. Numerical simulation show that if the patient's immune functions can be kept after therapy stops, it needs 9 years to replace all infected cells by normal ones.
Conclusion: For LVD mutation patients, LVD+ placebo to AVD therapy scheme may help patients to suppressing HBV replication. Further researches are promising.
Acknowledgments: This work is jointly supported by the NNSF of China (No. 60674095), and the Yang Scientific Research Foundation of Beijing Healthy Bureau and Beijing Chinese Medicine Administrative Bureau.

PE183
Chronic HBV Infection in Children: Pre-Core Defective Variants Continue to Emerge after HBeAg/anti-HBe Seroconversion
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Background: G-A-1896 pre-Core mutants (P-C-mt) cause HBeAg-negative chronic hepatitis (CHB) in genotype D infected Mediterranean adults. We studied their emergence during chronic HBV infection in children.
Methods: Eighty consecutive HBsAg carriers (50/30 males/females, age 11y, range 0.2-17y) with vertical (66%) or intra-familial (16%) transmissions were followed-up for 12.5y (range 1-25 y). HBV genotype and HBeAg status were determined at the admission, HBeAg/anti-HBe every 2 years thereafter. During the follow-up, HBV-DNA was measured in 185 sera (1-7 sera/patient) (Cobas-Amplicor, Roche); P-C populations were characterized by direct sequencing (DS), by oligo-hybridization (OHA) and allele-specific-PCR (AS-PCR) with 30%, 10% and 0.1% sensitivities, respectively.
Results: Seven children were genotype A and 73 D; 70 (87.5%) were HBeAg-positive. Fifty-five (78.6%) underwent HBeAg/anti-HBe seroconversion (median age 13y, range 1.3-27y). Baseline HBV-DNA (cp/ml) was lower in seroconverters (7.9±1.9 vs 9,4±0,6, ANOVA p=0.012). DS/OHA P-C-mt were 4.2% at the admission and 45.8% after follow-up; AS-PCR P-C-mt 33.3% and 50% respectively. After seroconversion 47 (85.5%) became inactive carriers, 6 (14.5%) lost HBsAg (5 genotype D/P-C-wt); 8 P-C-mt had CHB. HBV-DNA (cp/ml) was lower in 31 P-C-wt than in 14 P-C-mt inactive carriers (3.42±1.05 vs 4.58±0.91; ANOVA p=0.007).
Conclusions: In genotype-D infected children P-C-mt is selected progressively after HBeAg/anti-HBe seroconversion to become predominant in HBeAg-negative CHB. Early and efficacious immune control of HBV replication avoids P-C-mt selection and leads to HBsAg loss.

PE184
Adefovir Dipivoxil anti-HBV Infection Treatment with Personalized Modeling
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Background and Objectives: A total of 40 chronic hepatitis B patients were received adefovir dipivoxil for over 96 weeks. Based on our modified basic virus infection model and a patient's clinic data, a mathematical model is set up in aim to explain the clinic data and predict the long time curative effect.
Methods: The model is described by four variables: *x, y, v, e* represent uninfected cells, infected cells, free virus, and CTL cells, respectively. The equation includes 11 parameters: λ, a, β, d, k, u, m, n, k_1, k_2 and k_3. Here k_1, k_2, and k_3 are the rate of CTL production and dead, killing virus, respectively.
Results: The patients with HBV DNA levels less than 1000 copies/ml were reported in 17.5% (7/40). A patient whose HBV DNA levels were higher than 40000 copies/ml can keep treatment benefits even stopping the therapy for over ten weeks. The simulation data of our model are in agreement with the patient's HBV DNA data. Our simulation also shows that it needs to spend about 18 years for clearing all infected cells.
Conclusion: The simulation result implies that some Chinese patients may need long term's therapy to clear all infected cells. Patients' CTLs assays are needed to confirm the effectiveness of the personalized modeling, and help doctors to decide whether stop the drug treatment even patients' HBV DNAs are higher than undetectable levels.

PE185
Programmed Death 1 Expression on T Cells Correlates with Early Response of Antiviral Treatment in Chronic Hepatitis B Patients
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Background/Aim: Recent reports have shown that programmed death 1(PD-1) expression is associated with T cell exhaustion and persistent viral infection. We studied longitudinally 28 chronic hepatitis B(CHB) patients undergoing treatment with nucleos(t)ide analogues or pegylated interferon-α(PEG-IFN-α) in 12-16 weeks to determine the relationship between PD-1 expression levels on T cells and early reduction of viral load induced by treatment.
Methods: Our investigations were focused on three points: baseline (time point 1, T1), treatment weeks 4-6(time point 2, T2) and treatment weeks 12-16(time point 3, T3). PD-1 expression on total CD4 and CD8 T cells in CHB patients during antiviral therapy was detected by flow cytometry. Serum Hepatitis B virus (HBV)-DNA load was measured by real time polymerase chain reaction.
Results: Between T1 and T2, PD-1 expression on total CD8 ($P<0.01$) and CD4 T cells ($P<0.01$) dropped concurrently with treatment-induced HBV-DNA decline($P<0.01$). Between T2 and T3, however, only the HBV-DNA levels reduced significantly ($P<0.01$).
Conclusion: Early suppression of HBV replication induced by antiviral treatment results in a significant decrease in PD-1 expression on total CD8 and CD4 T cells in CHB patients.

PE186
Proteomic Analysis of HBsAg Expressing Cell Lines Revealed Putative Pathways in Association with Apoptosis
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Background/Aims: Hepatitis B virus (HBV) is still regarded as one of the major causes of chronic hepatitis, cirrhosis and hepatocellular carcinoma worldwide. The interactions between hepatitis B surface antigen (HBsAg) and host cells still remain largely unknown and need to be explored in detail.
Methods: Differential protein expression profiles of HepG2-S-G2(Stably expressing HBsAg cell line) and HepG2-Neo-F4 (control cell line) were compared using two dimensional gel based differential proteomic approach. Cell proliferation assay and survival assay were used for further studies on the candidate protein.
Results: Compared with the control down regulation of 44 proteins and up regulation of 38 proteins were found in HepG2-S-G2 cell. All these regulated proteins were identified by MS/MS and could be fell into several categories including metabolism-associated, immune-response-related, protein modification, signal transduction and others. Among them, a group of proteins in putative pathways associated with apoptosis were found out and discussed, including glucose-regulated protein 78kD (GRP78/Bip), heterogeneous nuclear ribonucleoprotein (hnRNP), Far upstream element-binding protein (FUSEbp), Rho GDP Dissociation Inhibitor (GDI), cystatin B and some scaffold proteins. GRP78, an important chaperone protein involved in multiple functions in host cells, was consistently decreased in HepG2-S-G2 and in Huh7 cell transiently transfected with HBsAg expression plasmid. Decreased CRP78 inducing by HBsAg or blockage of RNAi consistently led to the less resistance to staurosporine-induced cell death.
Conclusions: These results revealed a possible pathogenesis induced by HBsAg via GRP78.

PE187

Adefovir Dipivoxil for Treatment of Lamivudine-resistant Hepatitis B e antigen- positive Chronic Hepatitis B

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Background/Aim: To evaluate the efficacy of adefovir dipivoxil alone and in combination with lamivudine in treating patients with lamivudine-refractory HBeAg-positive chronic hepatitis B.
Methods: Eighty-five HBeAg-positive patients who had received lamivudine treatment for various periods and had a lamivudine-resistant liver function abnormality, documented YMDD mutations and persistent viremia were randomized to adefovir dipivoxil 10 mg, lamivudine 100 mg, or addition of adefovir dipivoxil to ongoing lamivudine daily. The primary efficacy measure was virological response. The secondary efficacy measure was serological response (HBeAg loss rate and HBeAg seroconversion rate) and ALT normalization rate.
Results: After 24 weeks of therapy, mean reduction of HBV-DNA level, the percentage of patients with HBV-DNA lower than 5 log10 copies/ml and the percentage of patients with HBV-DNA level decrease of more than 2 log10 copies/ml in patients of adefovir dipivoxil/lamivudine and adefovir dipivoxil monotherapy groups were significantly higher than those in patients of lamivudine group (2.58, 2.21 log copies/ml vs. 1.02 log copies/ml, 92.3%, 88.5% vs. 33.6%, 76.9%, 75.8% vs. 28.8%; $P < 0.001$, respectively). At the end of 52 weeks, mean reduction from baseline in serum HBV-DNA level at was 0.08, −4.25, and −4.12 log10 copies/mL in the lamivudine, adefovir dipivoxil/lamivudine, and adefovir dipivoxil groups, respectively. ALT normalization rates were significant hihger in adefovir dipivoxil/lamivudine and adefovir dipivoxil recipients than those in lamivudine recipients (62%, 55% vs. 8%, $P < 0.001$, respectively). A similar pattern was observed in HBeAg loss among three groups.
Conclusions: Adefovir dipivoxil is an effective treatment option for patients with lamivudine-refractory HBeAg-positive chronic hepatitis B.

PE188

Prevalence and Risk Factors of Virologic Flare in Inactive Chronic Hepatitis B

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Aim: To find the prevalence of HBV virologic flare as defined by HBV DNA viral load of ≥ 2,000 IU/mL in inactive chronic hepatitis B (HBV DNA less than 2,000 IU/mL), HBeAg-negative patients who have not received any treatment and to identify if there are any predictors that can predict virologic flare.
Methods: We retrospectively analyzed medical records of the patients who have attended Hepatitis Clinic, Siriraj Hospital from January 1, 2002 to February 28, 2008. The patients were eligible if they were naïve to any treatment and HBV DNA less than 2000 IU/mL at entry. Co-infection with HIV and/or hepatitis C virus were excluded. HBV DNA measurement determine by Roche Amplicor® (detection limit of 60 IU/mL). HBV virologic flare was defined as HBV DNA more than 2000 IU/mL during follow up period.
Result: There were 84 patients with mean follow up time was 598 days with annual prevalence of HBV virologic flare of 12.8, 4.8, and 4.2% for the first, second and third year of follow up, respectively. Initial HBV DNA level was the only predictor that can predict reactivation. No patients with HBV DNA at entry below detection limit developed flare and the patients with HBV DNA above 740 IU/mL had 22 times higher chance to develop flare during follow up.
Conclusion: HBV DNA flare is not uncommon in inactive chronic hepatitis B patients. Most of the virologic flares occur in the first year. The most important predictor or virologic flare is higher HBV DNA at beginning.

PE189

Analysis of 23 Cases of Patient with Multiple Drug-resistant HBV to Lamivudine and Adefovir

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Background: Multi-drug resistant HBV developed with multiple antiviral agents. There existed difficulty in dealing with Multi-drug resistant HBV.
Methods: Retrospective analysis of 23 consecutive patients who exhibited chronic hepatitis B associated with multiple drug-resistant mutations to lamivudine and adefovir during antiviral treatment. Multiple drug-resistant mutations were detected in those patients by DNA direct sequencing.
Result: Before multiple drug-resistant HBV emerged, 20 patients accept sequential antiviral therapy, 3 patients accept NA monotherapies. There were 16 cases of rtA181T/V＋rtM204V/I mutation, 2 cases of M204V/I +N236T mutation, 4 cases of A181T/V+M204V/I +N236T mutation, 1 case of L180M+A181T/V mutation. 14 cases received rescue therapy of Interfron-α and HBV DNA level of 8 cases decreased; Other 9 cases received combination treatment and HBV DNA level of 4 cases decreased.
Conclusion: The main reason of multiple drug-resistant mutations was sequential antiviral therapy. Another reason may be pre-exist drug-resistant mutation before nucleoside or nucleotide analogue treatment. De novo combination of antiviral agents should be recommended. Combination therapy directed against mutants resistant to each treatment may not be adequate in suppressing multi-drug resistant HBV. Interfron may be one choice for HBV of multiple drug-resistant mutations.

PE190

The Relationship Between Clinical Features and Pathological Changes in HBeAg Negative Chronic Hepatitis B

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Background: To furnish basis for an accurate evaluation of HBeAg negative chronic hepatitis B (e^-CHB), the present study studies the clinical features and hepatic pathology, and analyzes the relation between the data and the grade and stage of hepatic pathology in e^-CHB.
Methods: A study is performed in 120 Chinese e^-CHB patients (106 men and 14 women; mean age SD, 34.3 9.4 years). The relationship between the clinical features and the grade and stage of hepatic pathology was analyzed by Spearman's rank correlation test or Kruskal-Wallis test by applying STATA 7.0 software.
Result: Negative correlation is shown between the grade and leucocyte count (r_s: -.029，P<0.01), erythrocyte count (r_s: -0.21，P<0.05), haemoglobin (r_s: -0.20，P<0.05), while positive correlation is shown between the grade and prothrombin time (r_s: 0.29，P<0.01), activated partial thromboplatin time (r_s: 0.26，P<0.01), α-fetoprotein（r_s: 0.49，P<0.01）. Negative correlation is shown between the stage and prealbumin (r_s: -0.39，P<0.01), thrombocyte count (r_s: -0.37，P<0.01), erythrocyte count (r_s: -0.27，P<0.01), haemoglobin (r_s: -0.23，P<0.05), leucocyte count (r_s: -0.23，P<0.05), while positive correlation is shown between the stage and prothrombin time (r_s: 0.32，P<0.01), activated partial thromboplatin time (r_s: 0.24，P<0.01), α-fetoprotein (r_s: 0.46，P<0.01), lactate dehydrogenase (r_s: 0.19，P<0.05).
Conclusion: Erythrocyte count, haemoglobin, leucocyte count, thrombocyte count, prothrombin time, activated partial thromboplatin time, prealbumin, α-fetoprotein and lactate dehydrogenase is significantly associated with the stage or grade of hepatic pathology in e^-CHB.

PE191

A Short-term Clinical Trial of Telbivudine Treatment in Patients with HBeAg-positive Chronic Hepatitis B

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Aim: To evaluate the efficacy and safety of Telbivudine (LDT) in hepatitis B e antigen (HBeAg)-positive chronichepatitis B (CHB) patients in early stage.
Methods: 80 patients with HBeAg-positive compensated CHB with HBV DNA >6 log10 copies/ml, serum ALT 2 x ULN were divided two groups:one treated with Telbivudine，and the other treated with Entecavir.
Results: Baseline characteristics were well balanced between treatment groups. At 12wk of the treatment，the HBV DNA undetectable rates of HBeAg-poitive patients in the Telbivudine group and the Entecavir were respectively 50%、52.5%(p > 0.05), the rates of HBeAg negative were 10%、0%respectively, the rates of HBeAg seroconversion were 20%、5% respectively; At 24wk of the treatment，the HBV DNA undetectable rates of HBeAg-poitive patients in the Telbivudine group and the Entecavir were respectively 80%、70%(p > 0.05), the total rates of HBeAg negative were 20%、15% respectively, the total rates of HBeAg seroconversion were 27.5%、17.5%respectively(p > 0.05).No adverse reactions were found in both groups
Conclusion: There was no significant difference in HBV DNA undetectable rates between two nucleotide analogs in short-term (24 weeks).The Telbivudine group has better effect in HBeAg seroconversion rate than the Entecavir group in early stage,but no statistical significance.

PE192

The Development of Biosensor Based Microarray for Hepatitis B virus Pre-C/BCP Region Mutation and Its Reliability Study

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Background: To develop a equipment free, and can be widely used in clinical practice biosensor-based microarray for hepatitis B virus Pre-C/BCP mutation assay.
Methods: A thin film optical biosensor were applied for amplification the microarray signal in situ. And HBV sites 1762, 1764,1768,1770 and 1896 were selected as the targets and the microarray were be fabricated. The 5 mutated plasmids contained 1762, 1764,1768,1770 and 1896 sites and 30 HBV sera were be tested in our study and all the plasmids and sera PCR products were be assayed by really time PCR and sequencing.
Results:

1. The biosensor based microarray signal can be easily record by digital camera or even by the naked eyes And the detection signal for positive discriminated from negative were sharply contrasted as whole yes or no and it looks be significantly superior to classical microarray technique;
2. The sensitivity of the detection limitation of sera HBV load is 2X10E3 copies/ml with 95% reproducibility. The concordance index of 50 times negative and mutated plasmids were 98%(Kappa=0.932).
3. 30 sera samples of HBV>10E4 load and 20 sera of HBV negative tested by PCR fragment sequencing were showing very good agreement between sequencing with our biosensor based microarray and the concordance index kappa was 0.7619.

Conclusion: Our biosensor-based microarray for Pre-C/BCP mutation assay were a both sensitive and accurate method. And its advantages of equipment free, sharply contracted signal of positive vs negative and easily be perform in testing were make it be a promised assay for clinical application.

PE193

Study of Characteristics of Cord Blood CD4+CD25+ Regulatory T Cells from Fetuses whose Mothers had Chronic Hepatitis B Virus Infection

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Objective: To investigate the frequencies of $CD4^+CD25^+$ regulatory T cells in the cord blood of fetuses whose mothers are patients with chronic hepatitis B, we assayed the differences among HBsAg-positive and healthy subjects by flow cytometry. The results might offer some experimental evidence to explain the high rates of HBV persistent infection in vertical transmission of HBV from HBV-infected mothers.
Methods: 12 newborns born from HBsAg positive mothers were recruited , 10 healthy subjects being used as a control group. The cord blood and peripheral blood of mothers were collected respectively .Frequencies of $CD4^+CD25^+$ regulatory T cells in the cord blood of fetuses whose mothers are patients with chronic hepatitis B were analyzed by flow cytometric analysis.
Result: The number of $CD4^+CD25^+$ regulatory T cells/PBMCs in the cord blood of newborns born from HBsAg positive mothers （4.49%±1.18%）significantly exceeded that in normal controls（2.26 %±0.97 %,P＜0.001）;And newborns born from HBsAg positive mothers presented a much higher fraction of cord blood $CD4^+CD25^+/CD4^+$（9.62%±2.34%）than those in normal controls（7.93%±1.43%,P＝P=0.0025，P＜0.05）.
Conclusions: The results indicate that the proportion of $CD4^+CD25^+$ regulatory T cells in HBsAg positive mother cord blood was higher than those of healthy cord blood.

PE194

The Clinical Features of Chronic Severe Hepatitis B with Negative Hepatitis B e-antigen (HBeAg) and Nositive Hepatitis B e-antigen (HBeAg)

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Objective: To study the clinical features of chronic severe hepatitis B with negative hepatitis B e-antigen (HBeAg) and positive hepatitis B e-antigen (HBeAg)
Methods: A total of 353 in-patients with chronic severe hepatitis B were recruited into the study and divided into two groups according to the HBeAg status. The serological chemistry data, hepatitis B virus (HBV) DNA quantification data were detected, and morbility of cirrhosis, its complications and prognosis were also studied.
Results: Of the 353 in-patients, 236(66.8%) patients were HBeAg-negative. 117(33.2%) patients were HBeAg- positive. The ratio of HBeAg-positive patients was significantly higher than that of HBeAg-positive patients (p<0.05).The average age of HBeAg-negative patients was older than that of HBeAg-positive patients (P=0.048). The serum HBV DNA level of HBeAg-negative patients was significantly lower than that of HBeAg-positive patients (5.49±2.02) vs(6.64±1.41) log copies/ml

(p<0.01).The ratio of patients who had a serum HBV DNA level less than 5log copies/ml in HBeAg-negative patients was significantly higher than that in HBeAg-positive patients (41.8% vs 11.9% ,p=0.000). There was no significant difference in serological chemistry data, morbility of cirrhosis and its complications on infections, ascites, hepatoencephalopathy, gastrointestinal hemorrhage, as well as prognosis of the patients between those two groups.
Conclusions: The study suggested that serological chemistry data, morbility of complications and prognosis of the disease of HBeAg-negative patients mimics that of HBeAg-positive patients. The HBeAg-negative patients had a higher level of age, while a lower level of serum HBV DNA. To reduce the incidence of liver failure, more frequent monitoring and earlier antiviral therapy prone to be reasonable for chronic hepatitis B patients with negative hepatitis B e-antigen.

PE195

Related Factors of Lamivudine-Resistant In HBeAg Positive Patients with Chronic Hepatitis B

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Background: The emergence of LAM-resistant virus greatly limits the efficacy of therapy and induces the liver injury. The aims of this study were to assess the related factors of LAM-resistant mutation in HBeAg positive CHB patients.
Methods: Thirty-five patients carrying LAM-resistant with HBeAg positive were enrolled in this study. All of them underwent percutaneous liver biopsy, histological findings and had detectable viral load. Age, viral load, levels of ALT, types of mutation and HBV genotype was monitored.
Result: The median year of mutation found was 23months. 85.71% were genotype C and 14.29% were genotype B. The mutation of L80I, L80V, G173L, L180M, M204V and M204I were detected. The emergence rates were 34.3%(12/35), 25.7%(9/35), 17.1%(6/35), 60%(21/35), 57.1%(20/35), 54.3%(19/35) respectively. The rate of patients with two or three mutation were much more than one or four mutation. 62.9% patients were found to have significant histological findings, even 5 had established cirrhosis. Two had no histological finding. One had rtL80I and rtM204I. The other had rtL80V, rtL180M and rtM204V. The number of resistant mutation has no significant finding with histological finding, basic ALT level and basic viral load.
Conclusions: The emergence rate of L180M, M204V and M204I were higher than that of L80I, L80V, G173L in HBeAg positive CHB patients with LAM-resistance. Most of them have two or three LAM-resistant mutation regardless of histological finding severity, level of basic ALT and viral load. We must select the efficacious method to treat the patients with LAM-resistant.

PE196

The Therapeutic Efficacy of Foscarnet Sodium in the Treatment of Patients with Severe Chronic Hepatitis B

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Objective: To investigate the therapeutic efficacy of foscarnet sodium in the treatment of patients with severe chronic hepatitis B.
Methods: Forty four patients were randomly divided into foscarnet sodium treatment and placebo groups.Each group consisted of 22 patients, 22 patients in foscarnet sodium group were treated with foscarnet sodium twice daily 3.0g given by intravenous infusions ,in addition to general therapy for 28 days.The other 22 cases were treated without any form of antiviral therapy as control.All patients were followed up for 6 months.The HBV markers, quantification of HBV-DNA, serological chemistry data were measured at baseline , during therapy period and the end of follow-up period .
Results: Clinical symptoms were improved in Two groups patients, meanwhile alanine aminotransferase (ALT) and total serum bilirubin (TBiL) decreased. Compare ALT and TBiL at the end of trentment, there were no significant differences between the two groups (p>0.05). In foscarnet sodium treatment group, the level of serum HBV-DNA descreased from (6.993±0.898) log copies/ml to(4.033±1.286) log copies/ml (p<0.05), the rate of HBV-DNA descrease of more than two log was 81.1%（18/22）. In the control group, the level of serum HBV-DNA descreased from(7.068±0.938) log copies/ml to (5.188±1.926)log copies/ml, the rate of HBV-DNA descrease of more than two log was 45.4%（10/22）.A comparison of serum HBV-DNA showed significant differences between the two groups(p<0.05)
Conclusion: foscarnet sodium administered can inhibit HBV replication in treating severe chronic hepatitis B.It can rapid lower the level of serum HBV-DNA obviously.But the relapse rate was 47.0% in foscarnet sodium treated at the end of follow up period

PE197

Five Years Trial of Entecavir for Chronic Hepatitis B Patients Failed with Lamivudine Therapy in the Chongqing Area

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Objective: Evaluation of efficacy and safety of five years trail of entecavir for chronic hepatitis Bpatients failed with lamivudine therapy in the Chongqing area.
Methods: Thirty-two eligible patients were enrolled who had documented LVD failure.In the double-blind phase,patients were randomized(4:1)to ETV1.0mg/d (n=28)and placebo (n=4) for 12 weeks.In the open-lable phase ,patients received ETV 1.0mg/d for 240 weeks.HBV-DNA level,liver function tests,HBV serology and safety assessments were conducted.
Results: The mean reduction in HBV DNA levels at week 12 was 4．05 logl0 copies / ml in ETV group compared to 0.08logl0 copies / ml in placebo group(P< 0．05). The mean of HBV DNA levels after 240 weeks of ETV treatment decreased to 2.58logl0 copies / m1． The proportion of HBV DNA<3log10copy/ml raised from 0 at baseline to 6.25% at week 8,to 15.6% at week 24,to 50% at week 96,and raised to 57.14% at week 240.There were two patients with HBsAg seroconversion and four patients with HBeAg seroconversion at the end of study. The mean of ALT became normal at week 12 and remained normal throughout week 240.There was one patient who had a severe adverse event during the trail.
Conclusion: The findings from this study demonstrated the antiviral activity and safety of ETV in adults with CHB who have failed LVD．

PE198

Efficacy of HBV Vaccination in Bayan-ulgii Province of Mongolia

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Background: Established that the HBV infection is wide spread in Mongolia, So, HBV vaccination introduced as mandatory immunisation since 1991. In Bayan-ulgii province, there is living mostly Kazakh ethnic group. But, on the efficacy of HBV vaccination no conducted any study in the among Kazakh ethnic group.
Objective: To study the efficacy of HBV vaccination among the Kazakh ethnic group of Mongolia and compare with another ethnic group of Mongolia.
Method of study and materials: This was a cross-sectional study. We have randomly selected from Bayan-Ulgii province 154 subjects (1-19 ages) in 2008. In all serum samples the anti-HBs was determined (General Biological, Taiwan).
Results: The serology results of anti-HBs illustrated in table in by age groups.

Age group	1	3	5	7	9	11	13	15	17	19
N	8	14	16	17	16	18	18	18	10	19
Anti-HBs/n	7	4	1	3	2	4	3	5	1	3
anti-HBs/ %	87.5	28.6	6.25	17.6	12.5	22.2	16.7	27.8	10.0	15.8

Discussion and Conclusion: By our previous study (2003) the seroprevalence of anti-HBs was age related and lowering tendency by age. Also, the rate of anti-HBs in Urban living children is high and in rural nomadic children is low. In Kazakh ethnic group, the efficacy of HBV vaccination is low and similar to the rural nomadic population of main ethnic group from Mongolia.

PE199

Early Innate Immune Responses Following HBV Vaccine: A Novel Insight through Pattern Recognition Receptor Studies

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Background: Innate immunity components provide faster-acting immune responses a necessary first line of defense because of relatively slow nature of adaptive immunity.Hepatitis B vaccination is effective in protecting HBV infection in 90-95% adults.How HBV vaccine activates innate immunity remains largely unknown.
Aim: To study competence of HBV vaccine in modulating innate and adaptive immune cells in comparison to non-specific Tetanus toxoid (TT) vaccine by evaluating the expression of TLR molecules.
Methods: Isolated peripheral blood mononuclear cells(PBMCs)from nine healthy subjects(Mean Age: 26.3±3.1 M::F 3:3),of which 6 subjects at day0,3,7and15 weeks after hepatitis B vaccine and 3subjects after 0.5LT TT vaccine were stained for T cells,CD209andTLR2,3,4,9.mRNA expression ofMyd88,TRAF6,NF-KB,IL-2,IL-6,IL-5,TNF-α and IFN-γ by syber green RT-PCR.
Results: Expression of all TLR's on dendritic cells was unregulated on day 3,significantly TLR2(p=0.003)increased and was down regulated by day 15,no changes on T cells. Whereas, in TT vaccinated volunteers, TLR2(p=.03),TLR4(p=.03)significantly increased on day 3 on DC's whereas showing delayed response on T cells as increased on day 7.The mRNA expression of IL-5 and IL-2 showed no response to HBV vaccine but highly regulated in TT after day 7(p=0.00,0.001).MyD88andTRAF 6(p=0.042)upregulated in HBV vaccine group followed by of IFN-α(0.012)no change of IFN found in TT
Conclusions: i) HBV vaccine stimulates innate response by day 3 which potentiates further cascade,peripheral dendritic cells plays significant role in generating immune flare follows MYD88 pathway and releases IFN-α .ii) Whereas T cells Marjory involved in TT showed delayed immune response.iii) Identification of key factors at different time points may prove to be a novel model to study the initial events after vaccination.

PE200

The Dynamic Change of Th1/Th2 Type Cytokines in Peripheral Blood and Its Clinical Significance in the Hepatitis B e Antigen Positive Patients Treated with Telbivudine

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Objective: To Compare TH1/TH2 cytokines' dynamic change and its clinical significance in hepatitis B e antigen-positive patients treated with Telbivudine.
Methods: Twelve hepatitis B e antigen-positive patients treated with telbivudine.The blood sample was collected at baseline, week 4, week 8, week 12, week 24 and week 48 and stored at -70C; serum IL-2, IL-4, IL-6, IL-10, TNF-α and IFN-γ were tested at each time point by Cytometric Bead Array (CBA), Compare TH1/TH2 cytokines' dynamic change at different time point in each group and Compare TH1/TH2 cytokines' dynamic change cross four different groups: complete response, partial response, non-response and break through .
Results:The level of Th1 type cytokines in complete response group are Obviously higher than the group of partial response、non- response and breakthrough,but the level of Th2 type cytokines are lower than the group of partial response, non- response and breakthrough.
Conclusions: Th1/Th2 cytokines is essential for the regulation of the immune function of the body. After treated with Telbivudine, the level of Th1-type cytokines in the complete response group increased significantly, while the level of Th2 cytokines declined trend.

PE201

Clinical and Biochemical profile of Incidentially Detected Asymptomatic HbsAg Positive Subjects (IDAHS)

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Background: Chronic infection with hepatitis B virus causes spectrum of manifestations ranging from asymptomatic carrier state (often inactive with low replication) to the development of cirrhosis-related complications.The characterization of asymptomatic state has not been done in this part of the country, which forms important objective of present study.
Methods: 61 incidentally detected asymptomatic hepatitis B surface antigen positive (IDAHS) subjects having HBsAg positivity for >6 month presenting to our liver clinic were enrolled after appropriate consent. Detailed clinical, laboratory and sonographic evaluation was done. They were divided into two groups according to presence or absence of e antigen.
Group A - HBeAg + (n=48)
Group B - HBeAg - (n=13)
Results: Most of our patients (49%) were young adults (21-30 years) with male to female ratio of 3.6:1. Approximately half of our patients were detected during routine medical checkup, followed by family screening of contacts. Most of our patients were asymptomatic, and Fatigue was most common symptom found in 16%. All demographic and biochemical parameters other than AST & ALT were comparable in both groups. Among HBeAg negative 48 (79%) subjects, HBV DNA level $>10^5$ copies/ml was found in 31%. Subjects with positive HBeAg as compared to non-replicative infection (antiHBe positive and HBV DNA negative) had more frequent elevation of transaminase levels (62% versus 31%, $p<0.05$). AntiHBe antibody was positive in all HBeAg negative subjects. Mean age of seroconverted (antiHBe positive) individuals was a decade older than HBeAg positive.
Conclusion: From our study we can suggest that ongoing liver disease is present in approximately one-thirds of incidentally detected asymptomatic hepatitis surface antigen positive subjects previously referred to as carrier state. HBsAg testing should be mandatory in all routine medical checkup and family and sexual contacts of index case should be screened.

PE202

Prevalence of HBcAb among the HBsAg negative first-time blood donors in Khorramabad and Borujerd blood centers, Lorestan, Iran

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Background and Objectives: This research was carried out to determine the prevalence of HBcAb among the HBsAg negative first-time blood donors who had referred to Khorramabad and Borujerd centers for blood donation.
Materials and Methods: This study was established on a descriptive cross-sectional basis in which HBsAg test (ELISA) was primarily performed on all of the donors having referred to Khorramabad and Borujerd blood centers; then, out of all those referred 1000 subjects, who were first-time and HBsAg negative, were selected for furthur investigation. The information concerning age, gender, job, blood transfusion, and HBV vaccine injection was included in the questionnaire of the study. HBcAb (total & IgM) and HBsAb tests were performed on the selected donors. Data were collected and finally the prevalence rate of HBcAb was determined.
Results: The results of the study showed that out of 1000 HBsAg-negative first-time blood donors, only 47 were HBcAb+, from which 27 were HBcAb (total)+, and 3 were HBcAb (IgM)+. 18 were both HBsAb+ and HBcAb+, and 53 were seropositive only for HBsAb.
Conclusions: It was demonstrated that the first-time blood donors who are seronegative for HBsAg marker will be easily identified through HBcAb test if they are in the so-called core window period of the virus. Meanwhile, this group of donors have been implicated as high-risk for transfusiontransmitted HBV infection. So, detecting this marker will remarkably reduce the chance of latent cases of HBV infection and help promote blood safety.

PE203

Tumor Necrosis Factor-α-308 Gene Promoter Polymorphism in Chronic Hepatitis B Virus Infection: Meta-analysis of 4338 Cases and 3013 Controls

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Background: Tumor necrosis factor-α (TNF-α) plays a pivotal role in the viral clearance and host immune response to HBV, and the capacity for TNF-α production in individuals is influenced by a major genetic component. The studies of TNF-α-308 gene promoter polymorphism in chronic HBV infection have reported apparently conflicting results.
Objective: To derive a more precise estimation of the relationship between the polymorphism of TNF-α-308 gene promoter and chronic HBV infection.
Method: Meta-analysis was done of 22 case-control studies in relation to TNF-α-308 gene promoter, involving a total of 4338 chronic HBV infection cases and 3013 controls. The pooled odds ratios (ORs) for the risk associated with the genotypes of GA, AA, and GA+AA (A-allele carriers) compared with the GG genotype were calculated.
Results: Overall meta-analysis indicated that -308A heterozygotes (GA) had 22% decreased risk of developing CHB with a borderline significance (OR = 0.78; 95% CI: 0.60–1.02; $P = 0.065$). For the -308A allele homozygotes (AA) and carriers (GA+AA), the pooled ORs both indicated a significantly decreased risk of CHB (OR = 0.39; 95% CI: 0.21–0.73; $P = 0.003$; and OR = 0.74; 95% CI: 0.57–0.96; $P = 0.026$, respectively) (Table 1). In the subgroup analyses by ethnicity, significantly decreased risks were associated with -308 variant genotypes (GA and AA) in Mongoloid populations in all genetic models. However, no significant associations were found in Caucasoid.
Conclusion: The meta-analysis suggests that the TNF-α-308A allele is a low-penetrant protective factor for chronic HBV infection, especially in Mongoloid.

PE204

Immunologic Mechanism Study of Matrine Injection on HBV

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Aim: To observe the effect of Matrine Injection on HBV-DNA in HBV transgenic mice and further stuy the immunologic mechanism.
Method: 20 HBV transgenic mice were randomly divided into physiologic saline group and Matrine Injection group. Another10 normal mice at the same species and age with HBV transgenic mice were regarded as the normal group. The mice in Matrine Injection group were administrated at dosage of 82.2 $mgkg^{-1}d^{-1}$by intraperitoneal for 30 days. The mice in physiologic saline control group and normal group were administrated normal saline with the same volume at same time. The contents of HBV DNA in serum and liver were quantitated by PCR. And the spleens were separated for cultivating dendritic cells. The surface molecules of dendritic cells were tested by flow cytometry. IFN-γmRNA and TNF-αmRNA in liver were tested by RT-PCR.
Result: There was no significant difference of the serum HBV-DNA level between physiologic saline and Matrine Injection groups. The content of serum HBV-DNA after treatment showed a significant decrease in two groups. The content of serum HBV-DNA in Matrine Injection dropped significantly as compared with that in the physiologic saline group. But there was no significant difference in the content of HBV-DNA in liver between physiologic saline and Matrine Injection groups. The expression level of MHC-II on dendritic and hepatic IFN-r mRNA and TNF-a mRNA showed a significant decrease in HBV transgenic mice than normal mice. In comparison with physiologic saline group，the expression level of them in Matrine Injection group showed a significant increase.
Conclusion: Matrine Injection was effective on depressing HBV-DNA in HBV transgenic mice. Its antiviral action may be achieved through regulating MHC-II on DCs surface and promoting the production of antiviral factor such as IFN-γand TNF-α.

PE205

HBV-DNA and Non-specificity Immunity Reply Function and Level Low Relations

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Purpose: To stimulate non-specific immune response capacity as the main content of the study to explore the HBV-DNA and non-specific immune responses in the relationship between the low response capability, Methods: 190 cases of asymptomatic carriers, double-blind, randomized into Mycobacterium FU 36, lamivudine and traditional Chinese medicine for the treatment group, Mycobacterium FU36 with traditional Chinese and lamivudine with traditional Chinese medicine were in the control group, a total of 12 weeks of treatment, follow-up six months after the termination of treatment.
Results: different treatment of HBV -DNA effect of the existence of significant differences; P> 0.01, the performance of different types of asymptomatic carriers negative rate of HBV-DNA there is a significant difference; P> 0.01, as well as the performance of the different types of asymptomatic carriers continued application A treatment plan presented HBV-DNA rebound rate there is a significant difference; P> 0.01,
Conclusion: HBV-DNA and non-specific immune responses in response to the lower capacity, anti-HBV therapy is not associated with non-specific immune response capacity or improve Is the anti-HBV drugs alone can not solve the asymptomatic carriers in anti-HBV therapy where the cause of the problem, solve the asymptomatic carriers in the anti-HBV treatment although the need for anti-HBV drugs with non-specific immune activation synchronous drugs on the basis of the Joint application , but the simultaneous combination of two drugs rather than as a result of HBeAg and HBV-DNA can HBeAg-positive asymptomatic carriers receive HBV-DNA negative effect of the results.

PE206

Initial Viral Response is the Most Important Predictor of the Emergence of Resistant Mutants after Adefovir Treatment in Lamivudine-resistant Chronic Hepatitis B

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Background: Adefovir dipivoxil (adefovir) effectively inhibits both wild-type and lamivudine (LAM)-resistant hepatitis B virus (HBV) replication and resistance to this drug is infrequent compared with LAM. In this study, we tried to identify factors affecting the emergence of resistant mutants after adefovir monotherapy in LAM-resistant chronic hepatitis B (CHB) patients.
Methods: The subjects were 87 CHB patients with LAM-resistance who had received adefovir for more than 12 months (range 12-39 months). The initial viral response (IVR) was defined as HBV DNA <4.0 log copies/mL. The adefovir resistant mutant was assayed at baseline and every 6 months during adefovir administration.
Results: IVR was observed in 38% of patients. The cumulative emergence rates of adefovir resistance were 2.6% at 6 months, 10.4% at 1 year, 14.6% at 2 years and 21% at 3 years. In univariate analysis, factors contributing to the emergence of adefovir resistant virus were baseline HBV DNA > 6 log copies/mL (P=0.003) and IVR (P<0.0001). The presence of precore mutation and type of YMDD mutants were not related. In multivariate analysis, only IVR was an independent factors affecting the emergence of adefovir resistant virus (P<0.0001).
Conclusion: IVR is a useful predictor for emergence of adefovir resistant mutants after adefovir monotherapy in LAM-resistant CHB patients. For IVR-negative patients, the change of therapeutic options such as add-on LAM or switch to other drugs should be considered because of the high incidence of the emergence of adefovir resistant mutants.

PE207

The Early Viral Suppression Effects of Entecavir (ETV) versus Lamivudine (LVD) in Chinese Nucleoside Naïve HBeAg positive Chronic Hepatitis B (CHB) Patients.

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Background: Elevated HBV DNA is strongly associated with the risk of disease progression. This study investigated the early viral suppression effects of ETV and LVD in nucleoside-naïve Chinese patients with active HBeAg (+) CHB.
Methods: This open-label study was conducted in 5 major hospitals in China. At study entry all patients had HBV DNA levels $\geq 10^7$copies/mL, elevated ALT (1.3–10xULN) and compensated liver function. Patients received either 0.5mg ETV or 100mg LVD daily. HBV DNA measurements were taken at baseline and at Weeks 2, 4, 12 and 24 during treatment, using Roche Cobas Amplicor assay (LLOD 300 copies/mL).
Results: A total of 97 patients were enrolled; 42/50 ETV patients and 40/47 LVD patients completed 24 weeks of treatment. At baseline, mean HBV DNA levels were 8.45 0.81 in ETV group and 7.67 1.76 $\log_{10}$ copies/mL in LVD group (P<0.05). The mean change in HBV DNA from baseline ($\log_{10}$ copies/mL) was -2.96±0.68 versus -2.03±1.28 (P<0.05), -4.11±0.71 versus -3.57±1.67 (P=NS), -5.39±1.07 versus -4.19±1.63 (P<0.05) and -6.82±1.31 versus -4.18±2.18 (P<0.05) at Weeks 2, 4, 12 and 24 in ETV and LVD groups, respectively. At Week 24, ETV-treated patients demonstrated undetectable HBV DNA rate of 80.7% compared with 54.5% in the LVD group (P<0.05).
Conclusions: This data supports previous reports that ETV is superior to LVD in early viral suppression in nucleoside-naïve Chinese CHB patients and a significantly higher proportion of patients on ETV achieved undetectable viral load at Week 24 compared with LVD.

Poster Exhibition – HCC
Poster Session, Hall 5B

PE208

New-drug-development for Hepatobiliary-diseases in Developing Nations : NGO's Role in Improving Access to Hepatitis Treatment & Vaccines

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Issues: Anti-cancer drugs for hepatocellular-carcinoma out of reach of>92% populations of Asia. Price reduction, appropriate drug-supply-chain, monitoring of chemotherapeutic-agents necessary. We need to address access to affordable treatment. Resource-poor-nations have no platform for raising these issues of hepatitis-sufferers.
Description: In-developing-countries unaffordable-chemo-cost leads to poor therapeutic-compliance. Since 2005 schemes offer discounted Anti-hepatitis-drugs, diagnostics/technical assistance scutinised. Common methodology to facilitate development of sound/sustainable Low-cost vaccine supply chain needed
Results: In last 4 years, 66 patients diagnosed for hepatobiliary-carcinoma in rural/tribal India. 14 NGOs, 28 governments, 24 private-entities. Major Lacunae is absence of co-ordination between Chemo-centres & primary-healthcare-workers. Drug distribution/cost/nurses-training are neglected issues [Our NGO-Operational-Performa handouts available to 19th APASL-Congress-Participants]
Lessons learned: must identify/design newer-treatments available to masses. Specific-NGO-FORUM needed to implement/expand cost-cutting-measures. We Plan to expand our-NGO-Chemo-advocacy-program to larger-population.
Recommendations: New-drug-development for hepatobiliary-carcinoma in infantile stage & expensive in developing-nations. Vaccines hope for future. But Promoting dialogue between public-hospitals/NGO/Pharmaceuticals must improve access to chemo-therapy. NGO's/Funding-agencies representative at APASL2009-conference need to address-this-issue. We NGO-representatives from developing-nations need exposure to research treatments used by European/American experts. Do we all failed in addressing socio-economic issues of cancer-sufferers? We need to address these socio-economic issues of affected population in resource-poor-nations.

PE209

A Garlic Derivative S-allylcysteine Suppresses Liver Tumor Growth and Metastasis by Sensitizing Chemotherapy

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Background: A garlic derivative S-allylcysteine (SAC) has anti-cancer effect in human prostate and colon cancers. We aimed to investigate the effect of SAC and combination of chemo-drug on tumorigenesis and metastasis of liver cancer.
Methods: The orthotopic liver tumor model using a metastatic liver cancer cell line MHCC97L labeled with luciferase gene was applied. SAC was given at day 7 after tumor implantation at 1mg/g/day, or 1mg/g/day combined with low dose Cisplatin for 5 weeks. Tumor growth and metastasis were monitored by Xenogen *in vivo* imaging system. Hepatic stellate cell (HSC) activation and tumor-associated macrophage (TAM) in the tumor tissue were detected by α-SMA and ED1/ED2 staining. Tumor micro-vessel density (MVD) and apoptosis were also analyzed. *In vitro* functional tests including proliferation assay, cell cycle analysis and apoptosis analysis were performed.
Results: Tumor growth was inhibited by SAC combined with Cisplatin treatment at different time points accompanied by lower incidence of lung metastasis compared with other groups. The observation of Xenogen IVIS was confirmed by histopathological examination. The HSC activation by α-SMA staining in the liver tumors was suppressed by SAC and Cisplatin treatment accompanied with less TAM infiltration. Consistent with *in vivo* study, *in vitro* functional study also demonstrated that SAC not only induced cell cycle arrest, apoptosis, and inhibited tumor cell proliferation, but also sensitized the anti-cancer effect of Cisplatin.
Conclusion: SAC treatment inhibited liver tumor growth and metastasis by inhibiting tumor cell proliferation, inducing apoptosis and sensitization of chemotherapy.

PE210

VEGF-targeted Therapy against Insulin-resistance-based Rat Hepatocarcinogenesis with Clinically Available Agent: Branched-chain Amino Acid (BCAA) Granules

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Background: Anti-angiogenic therapy would be a promising approach against hepatocellular carcinoma (HCC). Although a sorafenib has survival benefits in patients at advances stages of HCC, there seem to be several serious concerns to employ this agent for chemoprevention against HCC. Branched-chain amino acid (BCAA) reportedly inhibits the incidence of HCC in patients with insulin resistance (IR). However, the possible mechanism is still obscure. The aim of the current study was to examine the effect of BCAA on hepatocarcinogenesis under the condition of IR, especially in conjunction with angiogenesis.
Methods: The effect of BCAA on the development of liver enzyme-altered pre-neoplastic lesions and angiogenesis in the obese diabetic Otsuka Long-Evans Tokushima Fatty rats was examined. We also performed an in-vitro study to elucidate the possible mechanisms involved.
Result: Treatment with BCAA markedly inhibited the glutathione-S-transferase placental form (GST-P)-positive pre-neoplastic lesions along with suppression of neovascularization in the liver. The hepatic expression of the vascular endothelial growth factor (VEGF), a potent angiogenic factor, was also attenuated. BCAA treatment significantly suppressed the glucose- and insulin-induced in-vitro angiogenesis in the presence of VEGF. These results indicate that BCAA exerted a chemopreventive effect under the condition of IR via suppression of VEGF-mediated angiogenesis.
Conclusion: Since BCAA is widely used in the clinical practice for patients with chronic liver diseases, this agent may represent a new strategy for chemoprevention against IR-based HCC in the future.

PE211

Krüppel-like Factor 8 Regulates Proliferation, Invasiveness and Epithelial to Mesenchymal Transition in Hepatocellular Carcinoma Cell Line HCCLM3

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Background: Krüppel-like factor 8 (KLF8) is a member of transcription factors. Whether and how KLF8 signaling pathways contribute to Hepatocellular carcinoma (HCC) development and progression is unknown. This study investigated role of KLF8 in Hepatocellular carcinoma cell line HCCLM3 proliferation, invasiveness and Epithelial to Mesenchymal Transition (EMT).
Methods: The expression of KLF8 in different liver cell lines was detected by Quantitative real-time PCR and Immunocytochemistry. We used small interfering RNA (siRNA) to down-regulate KLF8 expression in HCCLM3. The change of proliferation and invasive ability of KLF8 down-regulated HCCLM3 was investigated by MTT Reduction Assay and Trans-well Invasive Assay respectively. The change of proliferation, invasiveness and EMT related gene in KLF8 down-regulated HCCLM3 was evaluated by Quantitative real-time PCR.
Result: KLF8 protein expressed predominantly in the nuclei of cancer cells and its expression is positively correlated with metastatic potential of these cell lines. HCCLM3 has the highest KLF8 level. Decreased KLF8 expression can notably inhibit the proliferation (p<0.001, n=6), mobility and invasiveness of HCCLM3 (p<0.001, n=8). We found that the mRNA level of N-cadherin, Fibronectin and Vimentin is much higher than that of E-cadherin in HCCLM3. The expression of Cyclin D1, Focal Adhesion Kinase (FAK) and fibroblast markers including N-cadherin and Fibronectin was obviously suppressed in KLF8 down-regulated HCCLM3.
Conclusion: KLF8 plays an important role in the process of HCCLM3 proliferation, invasiveness and EMT.

PE212

Insulin Resistance Plays a Pivotal Role in the Liver Fibrosis Development and Hepatocarcinogenesis in Rats

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Background: Insulin resistance (IR) has shown to play an important role in the progression of chronic liver diseases, including liver fibrosis development and hepatocellular carcinoma. The aim of this study was to elucidate the possible mechanisms of IR on the liver fibrosis development and hepatocarcinogenesis using obese diabetic Otsuka Long-Evans Tokushima Fatty (OLETF) rats.
Methods: To induce liver fibrosis, 1.0ml/kg of pig serum was injected twice a week for 4 weeks in the OLETF and LETO rats. In the hepatocarcinogenesis model, glutathione-S-transferase placental form (GST-P)-positive pre-neoplastic lesions were induced by a single injection of 200mg/kg of diethyl nitrosamine (DEN). We also performed in-vitro studies to examine the mechanistic insights.
Results: The liver fibrosis development and GST-P-positive pre-neoplastic lesions were both markedly accelerated in OLETF. In the fibrosis experiment, -smooth muscle actin-positive activated hepatic stellate cells (HSC) also increased in OLETF along with augmentation of the hepatic collagen content and transforming growth factor-b1. In the DEN model, the neovascularization was up-regulated in OLETF almost in parallel with the pre-neoplastic lesions development and a potent angiogenic factor, the vascular endothelial growth factor. Our in-vitro study showed that both glucose and insulin stimulated the proliferation of the activated HSC and augmented the neovascularization.
Conclusion: These results indicated that the IR status directly accelerated the liver fibrosis development and hepatocarcinogenesis at least partly through the stimulation of activated HSC proliferation and hepatic neovascularization, respectively, in the rat.

PE213

Well-differentiated Hepatocellular Carcinoma Vascularizing Like Focal Nodular Hyperplasia (FNH) on Contrast-enhanced Ultrasonography

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Case: A 68 years old man diagnosed with chronic hepatitis C regularly visited our hospital. In April of 2005, ultrasonography revealed a tumor 20mm in diameter in S2 of the liver and another tumor 15mm in diameter in S6/7 of the liver. The patient was hospitalized for further examination. Computer tomography (CT) revealed that the tumor localized in S6/7 presented a pattern of hypervascular hepatocellular carcinoma (HCC). For the tumor localized in S2, the following were revealed. 1) Contrast-enhanced ultrasound findings: A tumor vessel passed from outside the tumor to the center of the tumor in the early vascular phase, then radiated in a wheel-like shape at the center of the tumor; parenchymal phase perfused imaging in the area produced a similar imaging obtained from the area surrounding the liver. 2) CT: No tumor was detected. 3) SPIO-MRI (T2 weighted imaging): Iso-low intensity images were obtained. Although these imaging findings indicated FNH, the patient was HCV positive. In order to disprove the possibility of HCC, a biopsy was performed on the tumor at S2 in the liver. The resulting diagnosis was well-differentiated HCC.
Discussion: Until now, a characteristic finding of FNH has been spoke-like vascularization, which is considered diagnostically quite important. However, some recent cases of HCC have been reported to present FNH-like vascularization. From now on, when evaluating a tumor that presents spoke-like vascularization underlining chronic hepatitis, the possibility of HCC should be considered and a close examination may be needed.

PE214

Fibrosure, APRI and FORNS Score versus Liver Biopsy in Chronic HCV Infection in Egypt

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Chronic infection with HCV is problem .Clinical management of chronic HCV depend on extent liver fibrosis .Liver biopsy gold stander an invasive procedure responsible for severe complications and sample variability interpretation. Serum biomarkers for inflammation/fibrosis investigated to wave liver biopsy.
Diagnostic accuracy panel of Non-invasive serum biomarkers for hepatic fibrosis (Fibrosure , APRI score, Forn's score) versus liver biopsy.
20 HCV patients subjected for: APRI, Forn's , Fibrosure scores PCR quantitative HCV-RNALiver functions .Lipid Profile CBC . Ultrasound guided liver biopsy.
FORNS score; AUROC (0.917) with 95% CI(0.791-1.042) for(f_0f_1) vs. ($f_2f_3f_4$) while(0.688)with 95% CI(0.464- 0.91)for($f_0f_1f_2$) vs.(f_3f_4). Cutoff(>6.9)sensitivity for significant fibrosis($f_2f_3f_4$)and extensive fibrosis (f_3f_4)were (100%) and with low specificity ,with accuracy(40%) and (20%)respectively.-APRI score; AUROC(0.792)with 95% CI(0.568 – 1.015)comparing(f_0f_1) vs.($f_2f_3f_4$)while was(0.875)with 95% CI(0.703 – 1.047)for($f_0f_1f_2$)vs.(f_3f_4).Cutoff(<0.5) had low sensitivity and specificity(100%)with accuracy(60%)for significant fibrosis and(80%)for extensive fibrosis.-Fibrosure(fibro-acti test); showed best AUROC(1.00)in different fibrotic stages with 95 % CI (1.00–1.00).Cutoff(>0.59) sensitivity(50%)for significant fibrosis and(100%)for extensive fibrosis while specificity(100%)in all fibrotic stages. The PPV (100%)for significant and extensive fibrosis .NPV and accuracy(75%, 80%)respectively for significant fibroses,while it was (100%) for extensive fibrosis respectively.Significant correlation between liver biopsy and Fibro-test(P0.002)and Acti-test(P0.000).Significant correlation between liver biopsy hepatitis activity score and APRI (P 0.047)and FORNS score (P0.000).
Conclusion: FORNS score wasn't considered since does not discriminate between significant and extensive fibrosis. Low sensitivity of APRI prohibtes detection of minmal fibrosis and allow undetermined results. Fibrosure classified all cases of chronic HCV sufficient to wave liver biopsy

PE215

Glypican-3 Amino Terminal Marker for Early Detection of HCC.

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Introduction: HCC is the 6th common cancer. Global increase of hepatitis B and C infection, the incidence of HCC steadily increasing. Egypt seroprevalence of HCV in Nile delta 20 -35%. AFP had limited sensitivity 60% and specificity 90% for small HCC. GPC-3 oncofetal protein over expressed in HCC.

Evaluating validity of Glypican-3 as early detector of HCC.:10 healthy controls and 40 HCV positive patients:10 patients chronic hepatitis C virus infection.10 patients compensated cirrhosis [child-Pugh class A and B].10 patients decompensated cirrhosis [child-Pugh class C]. 10 patients HCC.

liver functions: ALT, AST, Bilirubin(T), Albumin, γGT.Tumor markers: AFP and GPC-3.Viral markers: HCV antibodies, HBs Ag and HBc Ab. The median value of GPC-3 in HCC, DC, CC significantly higher than chronic hepatitis and control groups. No significant correlation between AFP and GPC-3. AUROC of AFP 0.85 & AUROC of GPC-3 0.84. The diagnostic Sensitivity of AFP (20 ng/ml) 70% with PPV 53.8%. The specificity85% with NPV 91.9%. While the diagnostic Sensitivity of GPC-3 (2 ng/ml) 100% with PPV 27%. The specificity 42.2% with NPV 100%. Combined serial approach of AFP and GPC-3 improved specificity to 87.5%.

Conclusion:GPC-3 although a serological test for early detection of HCC, showed limited specificity, where detected in different stages of chronic liver disease,it is oncofetal protein produced by regenerating liver cells. The diagnostic signature approach for simultaneous determination of AFP and GPC-3 improve prediction accuracy of HCC patients in those showing seronegativity to AFP.

PE216

Characteristics and Outcomes of Patients with Hepatocellular Carcinoma and Dual Hepatitis B and C

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Background: Patients with hepatocellular carcinoma (HCC) due to dual hepatitis B and C virus (HBV, HCV) infection may constitute a distinct disease group that is different from patients with single virus infection. This study compared the clinical characteristics and outcome among patients with HBV, HCV and dual virus infection.

Methods: A prospective database of 1,215 HCC patients with chronic hepatitis B, C or dual virus infection was investigated.

Results: Patients with HCV infection (n=388) were significantly older (mean age, 69 years) than patients with dual virus (n=75, 65 years) and HBV infection (n=752; 60 years) ($p< 0.0001$). The male-to-female ratio for HBV, dual virus and HCV group was 5.2, 3.4 and 1.3, respectively ($p< 0.0001$). Patients in the HBV group more often had higher total tumor volume (mean, 409 cm^3) than the dual virus group (244 cm^3) and HCV (168 cm^3) group ($p< 0.0001$). No significant differences of the severity of liver cirrhosis, performance status, cancer staging and tumor cell differentiation were noted among the three groups. Patients in the HCV group had a significantly poor survival in comparison to the HBV group only in the subset of patients with small tumor volume (< 50 cm^3) in the Cox proportional hazards model (relative risk: 1.44, p=0.041).

Conclusions: Dual HBV and HCV virus infection does not accelerate the speed of HCC formation in patients with chronic hepatitis B, and appears to have a modified course of carcinogenesis pathway diverted away from the biological behavior of HBV and HCV infection.

PE217

Aetiology of HCC in Bangladesh

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Background: Patients presenting with HCC is not infrequent in our clinical practice. The aetiology vary ranging from HBV, HCV, NASH and alcohol. The aim of this study was to see the aetiology of HCC in Bangladeshi patients.

Methods: In this retrospective study, records of 976 patients who attended our OPD between July 2004 to August 2008 were reviewed. Patients having hepatic SOL and/or heterogeneous echotexture of liver on USG and/or CT scan were included. Diagnosis of HCC was confirmed at USG guided fine needle aspiration cytology with or without elevated serum AFP (>500 ng/ml).

Results: Of the 976 patients, 75% (732/976) had HBV infection. HCV infection was diagnosed in 17% (165/976). NASH was responsible for 5% (49/976) cases, alcohol in 1% (10/976), while in the rest 2% (20/976) cases no specific aetiology could be established.

Conclusion: The study shows that HBV is the commonest cause for HCC in Bangladesh followed by HCV.

PE218

The Influence of Hepatitis B Viral Load and Antiviral Therapy on Recurrence after Initial Curative Treatment in Patients With Hepatocellular Carcinoma

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Background: The aim of this study was to determine whether the hepatitis B virus (HBV) DNA viral load and antiviral therapy is associated with hepatocellular carcinoma (HCC) recurrence.

Methods: This retrospective study involved 93 patients who underwent hepatic resection or radiofrequency ablation for initial HCC curative treatment. The patients were divided into four groups. Fifteen patients with low serum HBV DNA levels (≤ 4 $\log_{10}$ copies/ml) at the time of initial HCC treatment received antiviral therapy (lamivudine, adefovir, dipivoxil, entecavir) before HCC appeared (pre antiviral therapy group; pre-TG). Thirty-four had low serum HBV DNA levels without antiviral therapy (low virus group; LVG). Fourteen had high serum HBV DNA levels and received antiviral therapy after HCC appeared (post antiviral therapy group; post-TG). Thirty patients had high serum HBV DNA levels without antiviral therapy (high virus group; HVG).

Results: The cumulative HCC recurrence rates at 3 years in the HVG, LVG, pre-TG, and post-TG groups were 68.9%, 42.2%, 44.3%, and 57.1%, respectively. There were significant differences in the HCC recurrence rates between the HVG and LVG groups ($P = 0.016$), and between the HVG and pre-TG groups ($P = 0.013$). The recurrence rate was lower, though not significantly, in the post-TG group than in the HVG group ($P = 0.18$).

Conclusions: Not only HBV DNA viral load but also antiviral therapy is associated with HCC recurrence. Antiviral therapy before HCC appears is important for patients with high serum HBV DNA levels to prevent HCC recurrence.

PE219

Risk Factors for Death in 224 Cases of Hepatocellular Carcinoma after Transcatheter Arterial Embolization

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Background/aims: Few reports have described methods for predicting prognosis in unresectable hepatocellular carcinoma (HCC) patients, especially those treated by repeated transcatheter arterial chemoembolization (TAE). To determine risk factors for death and determine prognosis in patients treated with repeated-TAE, we evaluated clinical data.

Methodology: We retrospectively analyzed clinical parameters of 224 unresectable HCC patients treated with repeated-TAE from January 1997 to December 2007. TAE was repeated when recurrence was diagnosed by tumor marker elevation and/or dynamic computed tomography findings. Factors affecting survival were evaluated using multivariate analysis after univariate analysis. Next, we combined the score for each significant factor into a single prognostic score, after which the results were compared with JIS and CLIP score methods.

Results: Multivariate analysis revealed that bilobular HCC, alpha-fetoprotein (≥400 ng/ml), tumor invasion of the portal vein, tumor size (≥10 cm), and

albumin (<2.8 g/dl) were related to poor prognosis, Using those 5 factors, we developed a new prognostic scoring system. The 50% survival period was 29.2 months for all subjects, while it was 54.6, 29.2, 15.0, 5.6, and 1.0 months for those with scores of 0, 1, 2, 3, and 4 or over, respectively (P<0.0001), using our new system. CLIP score was not useful to predict prognosis, while JIS score was better. However, subjects with JIS scores of 1 and 2 were difficult to differentiate.
Conclusion: Our scoring system was easy to perform and the results showed that repeated-TAE was effective for unresectable HCC with a score of 2 or less.

PE220
Local Ablative Therapies and Intrahepatic Pressure
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Background: Some of the unexpected recurrence observed after radiofrequency ablation (RFA) might be caused by increased intratumoral pressure. The present study examined the relationship between local ablative therapies and intrahepatic pressure.
Methods:
A. Basic study: Under general anesthesia, laparotomy was performed on 19 pigs. A LeVeen needle and a percutaneous ethanol injection (PEI) needle were inserted into the liver and intrahepatic pressure was monitored using an invasive blood pressure monitor.
Ablation was performed as follows:
1. RFA. 1) Single-step method: After fully deploying the electrode, the power was initially applied at 30 W, then increased in increments of 10 W/min until power roll-off. 2) Multi-step method: The array was deployed in 8 steps. At each step, the power was fixed at 30 W until power roll-off.
2. PEI. Injection of ethanol (2 ml).
B. Clinical study: We examined the multi-step RFA and PEI for HCC. Under local anesthesia, intratumoral pressure was monitored.
1. RFA. 39 patients with a mean tumor size of 15.3±4.9 mm were studied. 2. PEI. In 10 patients with a mean tumor size of 21.4±8.8 mm, 5 to 10 ml of ethanol was injected per session.
Results :
A. Basic study: The intrahepatic pressures were: single-step method, 154.5±30.9 mmHg; multi-step method, 24.1±18.2 mmHg; and PEI, 12.0±8.5 mmHg.
B. Clinical study: Intratumoral pressure was 39.5±27.9 mmHg for RFA and 12.2±9.0 mmHg for PEI.
Conclusion: These results suggest that consideration of intrahepatic pressure is crucial in local ablative therapies.

PE221
The Effect of a Late Evening Snack in Patients Undergoing Hepatic Arterial Infusion Chemotherapy for Advanced Hepatocellular Carcinoma
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Background: A late evening snack (LES) is recommended for liver cirrhosis. However, no clinical study has evaluated the nutrition status and the effect of LES in cirrhotic patients with hepatocellular carcinoma (HCC). We investigated the effect of LES undergoing hepatic arterial infusion chemotherapy (HAIC) in patients with HCC.
Method: Nineteen patients with HCC were enrolled. Ten patients were LES group, and nine were control group. In the LES group, the patients received LES supplementation with a branched-chain amino acid (BCAA)-enriched nutrient mixture. In the control group, the patients received ordinary food. There were no significant differences in relation to age, gender, etiology, Child-Pugh scores, tumor stage, clinical responses to HAIC between two groups. Blood biochemical data, nutrition status using an indirect calorimeter were evaluated at before and at the end of chemotherapy.
Results: The non-protein respiratory quotient (npRQ) and molar ratio of branched-chain amino acid to tyrosine (BTR) were significantly improved in the LES group but not in the control group. There were no significant differences in the area under the concentration curve for glucose between before and the end of chemotherapy in two groups.
Conclusions: LES in patients undergoing hepatic arterial infusion chemotherapy for advanced HCC improved the energy malnutrition.

PE222
Prognostic Implication of Tumor Vascularity and its Relation to Cytokeratin 19 Expression in Patients with Hepatocellular Carcinoma
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Background & Aims: Hepatocellular carcinomas (HCCs) often show hypo- or mixed vascularity, and the prognosis of these relatively hypovascular HCCs is not fully elucidated. Cytokeratin (CK) expression profiles may also be useful prognostic indicators, and specifically CK19 may reflect metastastic potency in HCCs. This study was to assess the prognostic implication of tumor vascularity and its relation to CK19 expression in HCC patients.
Methods: A total of 150 patients who underwent surgical resection for HCC were enrolled. Tumor vascularity was evaluated according to arterial enhancement pattern on CT scans and CK19 expression was evaluated using tissue microarray methods. Clinicopathologic data were analyzed using Kaplan-Meier and Cox proportional hazard model.
Results: During follow-up period, 91 (60.7%) patients experienced tumor recurrence. Forty-five patients (30%) had hypovascluar tumor at the time of diagnosis, and they showed significantly higher positivity for CK19 expression (p=0.001) and shorter disease-free survival (p=0.023) than patients with hypervascular HCCs. In addition, recurred tumors in these patients showed more frequently hypovascular pattern than in patients with hypervascular HCCs (p=0.001). Hypovascularity at initial diagnosis and microvascualr invasion were independent poor prognostic factors predicting survival. Following treatment of recurred HCCs, hypovascular tumors showed poor response to transarterial chemoembolization (TACE), which resulted in shorter overall survival than hypervascular tumors (P=0.057).
Conclusions: These results demonstrate that tumor hypovascularity in HCCs is associated with positive CK19 expression, early tumor recurrence, poor TACE response and poor survival. Therefore, tumor vascularity may also be a prognostic indicator in HCC patients.

PE223
Gene Different Expression Between Culture-activated and Hepatocellular Carcinoma Cells Induction-activated Rat Hepatic Stellate Cells
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Background: Hepatic stellate cells (HSCs) transdifferentiate to become extracellular matrix-producing myofibroblasts during liver injury. Myofibroblasts can also promote invasion and metastasis of hepatocellular carcinoma(HCC). In this study, we determine gene expression changes in two different models of HSCs activation and investigate whether induction-activated HSCs(iHSCs) gene expression changes are different from culture-activated HSCs(aHSCs).
Methods: HSCs were isolated by density centrifugation and exposed to conditioned medium from rat HCC cell lines C5F. Twenty-seven thousands and one hundred gene expression between quiescent HSCs(qHSCs), aHSCs and iHSCs was analyzed by microarray and confirmed by real-time RT-PCR and Western blot.
Results: Sixteen hundreds and seventy-one probe sets were differentially expressed in aHSCs, including genes that encode proinflammatory factors, adhesion molecules, cell surface receptors, signaling transduction and immune factors. Seven hundreds and eleven probe sets were differentially expressed in iHSCs. Induction-activated HSCs showed specific gene expression patterns, including Raf1, Rac2, Adam17, Wnt6, MMP-9 and TNF, suggesting that HCC cells can specifically induce HSCs activation. Induction-activated HSCs might play a important role in invasion and metastasis of HCC.
Conclusions: Induction-activated HSCs gene expression patterns are different from aHSCs. Culture-activated HSCs does not properly regulate

gene expression in HSCs, suggesting that iHSCs may be considered the model for the study of HSCs biology in HCC.

PE224

Association of the Polymorphsims of EphB 1 with the Occurrence of Hepatocelluar Carcinoma in Korean Population

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Background: Hepatocellular carcinoma (HCC) is a hypervascular tumor, and angiogenesis is important for tumor growth. Ephrin receptors are related with vascular system development and the polymorphism of EphB1 in the carcinogenesis of digestive tract has been reported. Our aim was to examine the polymorphsims of EphB 1 with the occurrence of Hepatocelluar carcinoma in Korean population.
Methods: Genomic DNA was extracted from 182 patients with hepatocellular carcinoma (HCC), 266 healthy subjects. EphB 1 polymorphism was determined by polymerase-chain reaction-based assays, and the association with HCC was investigated.
Results: With regard to EphB 1 polymorphism, A/A genotype at rs11926992, T/T genotype at rs7644369, A/A genotype at rs6776570, T/T genotype at rs3821502 and G/G genotype at rs6766459 were significantly associated with HCC but these were not associated with clinical characteristics of HCC.
Conclusions: Five out of seven polymorphisms on Ephb1 gene were statistically associated with HCC, in the Korean population. Therefore, more studies of Ephb1 gene polymorphisms including various risk factors should be performed to use as genetic markers of HCC occurrence.

PE225

Hepatic Resection for Hepatocellular Carcinoma in the Elderly

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Background: We aimed to compare the results of hepatectomy for HCC in patients older than 70 years old with those for younger patients.
Methods: Clinicopathological data and outcomes for 155 elderly patients and 333 younger patients with HCC who underwent hepatectomy between 1992 and 2007 were retrospectively compared.
Results: Although postoperative delirium was more common in the elderly group, there were no significant differences between the 2 groups with regard to operative morbidity, hospital death, disease-free survival, and overall survival. The overall recurrence rate was significantly higher in the elderly patients with alcohol abuse than in younger patients with alcohol abuse. Multivariate analysis revealed that preoperative alcohol abuse was a prognostic factor for elderly patients.
Conclusions: Elderly patients with preoperative alcohol abuse should be followed closely, even after R0 surgery, because alcohol abuse is strongly correlated with postoperative recurrence and worse survival.

PE226

Impact of Fresh Frozen Plasma on Hepatectomy for Hepatocellular Carcinoma

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Background: Little is known about the effect of transfusing fresh frozen plasma on the outcome after hepatectomy for hepatocellular carcinoma.
Methods: Among 410 patients who underwent curative resection between 1992 and 2005, 180 patients had perioperative transfusion with whole blood or packed red blood cells and fresh frozen plasma (group A), while 46 patients were only transfused with packed red cells (group B), 43 patients were only transfused with fresh frozen plasma (group C), and 141 patients had no transfusion (group D).
Results: Group C had significantly fewer postoperative complications and a shorter hospital stay than group A. Preoperative coagulation was significantly worse in group C. Survival was significantly better in groups C and D than in group A.
Conclusions: Perioperative transfusion of fresh frozen plasma improves clotting factors without an adverse influence on the survival of patients with liver dysfunction undergoing resection of hepatocellular carcinoma.

PE227

HA/GSA-Rmax Ratio as a Predictor of Postoperative Liver Failure

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Background: This study investigated risk factors for postoperative liver failure after resection of hepatocellular carcinoma to detect markers that could identify candidates for hepatectomy.
Methods: Perioperative risk factors for liver failure after hepatectomy were analyzed in 191 patients with hepatocellular carcinoma.
Results: Liver failure occurred postoperatively in 16 patients, 3 of whom died. The hyaluronate/GSA-Rmax ratio was a risk factor for postoperative liver failure by univariate analysis and was the only risk factor according to multivariate analysis. All 3 patients who died had a hyaluronic acid/GSA-Rmax ratio 500 mg min/dl.
Conclusions: To reduce postoperative liver failure, preoperative planning should employ various measures of the hepatic functional reserve, including tests of both parenchymal and nonparenchymal liver function. The hyaluronate/GSA-Rmax ratio can predict liver failure after hepatectomy, and a ratio greater than 500 mg min/dl is a relative contraindication to liver resection.

PE228

A Clinical Case of Hepatocellular Carcinoma which Developped 13 Years after Sustained Virological Response to Interferon Therapy against Chronic Hepatitis C

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The patient was a 73-year old Japanese man with chronic hepatitis C(CH-C) who achieved a sustained virological response(SVR) to interferon(IFN) therapy. As a result the liver functions were normalized and the histological findings of the liver also improved. However, 13 years after SVR, mild liver dysfunction was noticed along with a marked increase of tumor markers. Several modalities revealed huge liver tumors about 13 cm in greatest diameter in the left lobe invading the bile ducts and another tumor about 3 cm diameter in segment V. We performed liver biopsy and confirmed that this tumor was well-differentiated hepatocellular carcinoma (HCC). Only mild fibrosis development could be observed in the adjacent non-cancerous lesions. We successfully treated these tumors with transcatheter arterial chemoembolization and stereotactic radiosurgery.
Recent studies revealed that the risk of developing HCC still exists even after SVR. Since most of HCC that develop in patients with SVR are usually detected within 5 years, several investigators speculate that HCC is already present but too small to be detected at the time of completion of IFN therapy. This speculation is not the case in our patient, since SVR was achieved 13 years ago and no HCV-RNA could be detected when HCC appeared. Therefore, another possible mechanism should be considered. An annual follow-up with strict surveillance program for HCC should be performed for more than 10 years after the completion of IFN therapy.

PE229

Comparison of Oxidative Stress Expressed in the Liver Tissue between the Patients with Hepatocellular Carcinoma Positive and Negative for Hepatitis Viral Marker

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Background/Aims: In order to investigate the role and importance of oxidative stress as to carcinogenecity of hepatocellular carcinoma (HCC) we analyze the expression of 8-Hydroxydeoxyguanosine (8-OHdG) in the liver tissue of the HCC patients with and without hepatitis viral marker.
Methods: Patients undergoing hepatic resection for the first HCC from 1995 to 2004 were enrolled into the study. Only the cases that took no alcohol or small amount of alcohol were enrolled. 24 cases were negative for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCVAb) (NBNC group). 24 were positive for HBsAg and negative for HCVAb (B

group). 21 were positive for HCVAb and negative for HBsAg and antibody to hepatitis B core antigen (C group). Staining with hematoxylin and eosin (H&E) and Berlin-Blue, and immunohistochemical staining for 8-OHdG were performed using the non cancerous liver regions. The degree of 8-OHdG immunostaining was expressed as the labeling index, which means the percentage of positive hepatocytes per 1000 hepatocytes.
Results: The labeling index of 8-OHdG for NBNC group is 19.3(±55.3), significantly lower (p=0.014) than that for B group 49.7(±89.5), and also lower (p=0.016) than that for viral group (B group and C group)(35.4±71.8). The labeling index of 8-OHdG had no correlation with Grading, Staging, fatty and iron deposit among all cases.
Conclusions: There is possibility that oxidative stress might not associate with the carcinogenesis of HCC in some cases without hepatitis viral infection.

PE230

Suppressive Effect on the Cumulative Recurrence of Hepatocellular Carcinoma with Combination Treatment of Clinically Available Vitamin K2 and Angiotensin-converting Enzyme Inhibitor

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Background: No effective chemopreventive agent has been approved against hepatocellular carcinoma (HCC) yet. Since neovascularization plays a pivotal role in HCC, an angiostatic agent is considered as one of the promising approaches. Recently, it has reported that vitamin K2 (VK) and angiotensin-converting enzyme inhibitor (ACE-I) exert anti-angiogenic activity. The aim of the current study was to elucidate the combination effect of the clinically used VK and ACE-I on cumulative recurrence after curative treatment, especially in consideration of neovascularization.
Methods: VK (menatetrenone; 45 mg/day) and/or ACE-I (perindopril; 4 mg/day) were administered for 36 to 48 months after the curative therapy for HCC. The cumulative recurrence and several indices were analyzed.
Results: A 48-month follow-up revealed that the combination treatment with VK and ACE-I markedly inhibited the cumulative recurrence of HCC in association with suppression of the serum level of vascular endothelial growth factor (VEGF); a central angiogenic factor. The serum level of lectin-reactive a-fetoprotein was also suppressed almost in parallel with VEGF. These beneficial effects were not observed with single treatment of VK or ACE-I for 36 months.
Conclusions: The combination treatment of VK and ACE-I may suppress the cumulative recurrence of HCC after the curative therapy, at least partly through suppression of the VEGF-mediated neovascularization.

PE231

A long-term Follow-up and Management Study of Patients with Hepatocellular Carcinoma after Curative Hepatectomy over 30 Years at Single Institution

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Aim: The aim of this study was to clarify the cilnicopathologic features and management of hepatocellular carcinoma (HCC) patients surviving more than 5 years after hepatectomy.
Materials & Methods: Retrospective study was carried out on 823 HCC patients who underwent curative hepatectomy between 1973 and 2002. Clinicopathologic factors in 5-year survivors and patients who died within 5 years were compared. The prognostic factors affecting survival were examined among the 5-year survivors.
Results: There were 290 patients who survived for more than 5 years after initial hepatectomy, and 83 of those patients survived for more than 5 years after HCC recurrence. The overall 3-, 5-, 10- and 20-year survival rates were 57.4%, 40.9%, 17.2%, and 8.5% respectively. In multivariate analysis, absence of underlying cirrhosis, solitary tumor, alfa-fetoprotein less than 1000 ng/mL, and absence of microscopic vascular invasion were favorable independent factors associated with 5-year survival. Negative hepatitis C virus antibody status was favorable independent factor associated with longer disease-free interval and survival after tumor recurrence. Multimodal treatments such as repeat hepatectomy or percutaneous ablation led to improved survival after recurrence, compared with the survival after transarterial chemoembolization ($p<.05$).
Conclusions: The results suggest that patients without underlying cirrhosis who have a solitary HCC that does not demonstrate vascular invasion or high AFP levels might survive for longer than 5 years after the initial hepatectomy. Close follow-up and multimodal treatment could contribute to prolongation of survival in such patients, even if cancer recurrence occurs.

PE232

Carbon Ion Radiotherapy for Hepatocellular Carcinoma Adjacent to the Gastrointestinal Tract Using a Spacer: A Case Report

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The history of the use of carbon ion radiotherapy (CIRT) for treating hepatocellular carcinoma (HCC) goes back to 1995, when clinical trials were initiated at the National Institute of Radiological Sciences. We have already reported that CIRT used for the treatment of HCC is safe and effective, and that it causes only minor liver damage. In a phase II clinical trial, the local control and cumulative overall survival rates were 94 % and 35 % at 5 years, respectively. However, the patients with tumor adjacent to the gastrointestinal tract are thought to be ineligible for CIRT because of the high risk of radiation injury of the digestive organs. In order to extend the indication of CIRT, we have challenged the CIRT for such patients under the use of spacers.
A case was a 67-year-old female with 8cm tumor in Segment 4. In radiological findings, the tumor revealed typical enhancement pattern for HCC, and was near the EC junction. She had been judged ineligible for hepatectomy because of the high retention rate of indocyanine green. She could undergo the 42.8 GyE/2-fraction CIRT after the placement of GORE-TEX Soft Tissue Patch under the laparoscopic procedure. Up to the present date, no adverse effect due to the spacer has been occurred, and an apparent anti-tumor effect has been observed. This method seems to have a promising efficacy for extension of the indication of CIRT to the patients with tumors adjacent to the gastrointestinal tract.

PE233

Effect of PTEN Gene Polymorphisms on the Development of Hepatitis B Virus Associated Hepatocellular Carcinoma

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Background/Aim : Phosphatase and tensin homologue(PTEN) is known as a tumor suppressor for many tumor types and the expression of the PTEN is reduced or absent in almost half the Hepatocelluar carcinomas(HCCs). In the present study, we investigated association between single nucleotide polymorphisms(SNPs) in the PTEN gene and the development of HCC in hepatitis B virus infected patients.
Methods : Between March 2002 and December 2006, the 139 HCC patients and 99 chronic HBV carriers without HCC, enrolled in this study. We analyzed SNPs at six polymorphic sites in the PTEN gene at positions –7748 G>T, -4017 A>G, +21246 C>T, +2-97 C>T, +80492 A>G and +96024 C>T in study subjects.
Result: The PTEN -4017 A allele (OR;0.590, CI;0.409-0849, P=0.004), the +2-97 C allele (OR;0.492,CI;0.320-0.755, P=0.001), the +80492 A allele(OR; 0.593, CI; 0.415-0.847, P=0.001) and the +96024 C allele were significantly associated with the development of HCC. Additionally, the haplotype 1(GGCTGT) showed preventive effects on HCC occurrence.
Conclusions : This study indicates that PTEN gene polymorphisms are associated with the HBV related HCC development

PE234

Bortezomib Inhibit the Proliferation of Hepatocellular Carcinoma Cell Line with the Activation of HHM Expression

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Background: Previously we reported that high ubiquitination was marker of human hepatocellular carcinoma. On the basis of these finding, we firstly analyzed the effect of Bortezomib(proteasome inhibitor) on human HCC cell line. We also reported that HHM/DIP1/GCIP1 was early marker for human hepatocarcinogenesis. HHM was suggested to be a new tumor suppression gene, but the mechanism was not well confirmed. We analyzed change of HHM signal by Bortemib.
Method and Result: We used HCC cell line (HuH7, HLF, HepG2). The inhibitory effect of Bortezomib was evaluated using MTT assay. 20nM Bortezomib significantly inhibited proliferation of HCC cell line. The inhibitory effect by 20nM Bortezomib was similar with 10μM Cisplatin. On the other hand, Bortezomib has no inhibit effect in isolated hepatocyte from Rat. In this condition, we analyzed the expression of Cyclin D1, Phospho-Rb and HHM in HCC cell line by Western Blot analysis. Expression of Cyclin D1, Phospho-Rb decreased, but HHM was increased with time. Next we analyzed cell cycle by FACS. Bortezomib induced HCC cell line into cell cycle arrest in G2/M. The transcriptional activity of HHM was also activated by Bortezomib administration using pTimer-promoter-HHM plasmid.
Conclusion: Bortezomib has specific anti-proliferative effect on hepatocellular carcinoma. The induction of HHM by Bortezomib might be related with cell cycle arrest. Bortezomib will be a useful drug for HCC.

PE235

Neovascularization is required for carcinogenesis of non-alcoholic steatohepatitis: experimental and clinical study

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Background/aim: Non-alcoholic steatohepatitis (NASH) may progress to liver cirrhosis, and finally hepatocellular carcinoma. Recent study suggested that development of hepatic angiogenesis correlates the risk for hepatocarcinogenesis in liver cirrhosis patient.
We therefore examined the role of angiogenesis in the hepatocarcinogenesis of NASH in both experimental and human study.
Methods: As an experimental NASH model, Zucker (Z) rats, which naturally develop leptin receptor mutations, and their lean littermate (L) rats were fed a choline-deficient, amino acid-defined (CDAA) diet. In human study, 11 patients with NASH-related cirrhosis or pre-cirrhosis, regarded as high risk group of hepatocarcinogenesis, and 13 with simple fatty liver (FL) were enrolled and underwent clinico-pathological examinations. Immunohistochemical analysis of 4-hydroxy-2-noneal (4-HNE) and CD34 were employed for detection of reacrive oxidative stress (ROS) and angiogenesis in the liver tissues, respectively.
Results: In experimental NASH model, both groups showed marked steatohepatitis by feeding CDAA diet. In sharp contrast, the development of glutathione-S-transferase placental form (GST-P)-positive pre-neoplastic lesions and HCC could be observed only in the L-rats. The hepatic neovascularization was also significantly increased only in the L-rats. In human study, Both NASH and FL exerted a marked elevation of ROS. In sharp contrast, significant development of hepatic neovascularization was observed only in NASH, whereas almost no neovascularization could be observed in FL.
Conclusion: In conclusion, these results suggested that neovascularization might play a important role in hepatocarcinogenesis in NASH.

PE236

A transgenic mouse that targets the expression of human genetic imprinted gene PEG10 in hepatocyte

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Background: Paternally expressed gene 10 (PEG10), which was an imprinted gene with an active paternal allele but silent maternal allele, was highly expressed in a great majority of hepatocellular carcinoma(HCC). The aim of this study was to generate transgene mice expressing PEG10 in the liver under the control of mouse albumin (ALB) promoter and study the integration, transcription, expression of PEG10 gene in the transgenic mice
Methods: The linearized 1716bp transgene fragments, which contained ALB promoter and structural gene of PEG10, were microinjected into fertilized eggs of mice. Then manipulated embryos were transferred into the oviducts of pseudo-pregnant female mice. All the newborn mice were screened and identified by PCR detecting genomic DNA in tail tissue. As the transgene was driven by the ALB promoter, we examined its expression in the liver of transgenic mice by RT-PCR and western blotting.
Results: The transgene fragment was microinjected into the male pronucleus of 3741 fertilized oocytes. The injected eggs were implanted into oviducts of 94 pseudo-pregnant foster mothers, of which 22 mice became pregnant and give birth to 108 offspring. 65 of them died from unknown reason. Among the 43 offspring, 3 were identified to carry PEG10 cDNA as demonstrated by PCR, and PEG10 transgene could be expressed successfully in the liver of the established transgenic mice. The ratio of transgene integration were 6.97% (3/43) by PCR.
Conclusions: The PEG10 transgenic mouse model should be valuable for studying the in viro function of this imprinted gene in HCC.

PE237

Characterization of Brivanib Pharmacokinetics in Asian and non-Asian Subjects with Advanced or Metastatic Solid Tumors

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Background/Aims: Brivanib alaninate is the L-alanine ester prodrug of BMS-540215, an oral selective dual inhibitor of vascular endothelial growth and fibroblast growth pathway receptors. It is being developed in treating hepatocellular carcinoma (HCC), a disease highly prevalent in Asia-pacific region. This analysis investigated whether BMS-540215 exposure was different between Asian and non-Asian subjects.
Methods: A population pharmacokinetic (PPK) model was developed with data collected in 125 subjects (78 non-Asian, 47 Asian) with advanced and metastatic solid tumors (including HCC) from 2 clinical studies. Potential effects of the following covariates on model parameters were examined: age, gender, race, and baseline body weight. Model-based simulation was performed to examine BMS-540125 exposure in Asian and non-Asian patients following brivanib doses of 800 mg QD (Phase III dose).
Results: The PPK of BMS-540215 was characterized by a 2-compartment model with first-order absorption and elimination. Clearance was found to slightly increase with body weight ($p<0.01$). However, effects of age, gender and race on clearance were not statistically significant. The median of apparent clearance in Asian was 9.5% lower than that of non-Asians, which was adequately explained by 16% lower body weight in Asians. There was substantial overlap in steady-state BMS-540215 AUC of Asian and non-Asian patients, simulated based on their observed body weight distributions in these patient groups.
Conclusions: BMS-540215 PK can be adequately described by a linear 2-compartment model; exposures in Asian and non-Asian subjects are similar following brivanib doses of 800 mg QD.

PE238

Multiple-site resection or combined resection and radiofrequency ablation in patients with multiple hepatocellular carcinoma

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Background/aims: Hepatic resection is the standard treatment for hepatocellular carcinoma. In some patients with multiple HCC, one-block resection can not be feasible due to either the tumor location or the reserved liver function. In this study, we attempted to analyze the outcome of multiple-site resection or combined resection and RFA in patients with multiple HCC. The prognostic factors for postoperative survival were also investigated.

Methods: Among 507 patients who received resection from January 1996 to August 2006, 58 patients had a radiologically detected multiple HCC. Patients with multiple HCC were divided into: group A, patients treated with one-block resection (n=40) and group B, patients with multiple-site resection or combined resection and RFA (n=18).
Results: In group B, 6 received multiple-site resection and 12 underwent combined resection and RFA. The clinicopathological variables and postoperative complication rate were not significantly different between the two groups. The 5-year disease-free survival rates for group A and B were 24.1% and 18.3%, respectively (p=0.386). The overall survival rates were also not significantly different (36.9% vs. 39.4%, p=0.528). The multivariate analysis revealed that radiological tumor number ≥3, Edmondsons-Steiner grade (III-IV) and indocyanine green retention rate at 15 minutes> 10% were adverse prognostic factors for overall survival.
Conclusions: Active treatments including multiple-site resection and combined resection and RFA showed similar treatment outcomes compared with one-block resection in patients with multiple HCC. The prognosis after treatment was associated with tumor number, tumor grade and ICG R15.

PE239

Gold(III) Porphyrin 1a Inhibited Intrahepatic Nasopharyngeal Carcinoma Metastasis and Exhibited Anti-Angiogenic Activity via Downregulation of Stanniocalcin

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Background: Nasopharyngeal carcinoma (NPC) is endemic to southern China. Mortalities are mostly associated with secondary metastases. Novel treatments for NPC metastases are thus urgently needed. We aim to test the efficacy of a physiologically stable gold compound, gold (III) *meso*-tetraarylporphyrin 1a (gold-1a), in treating intrahepatic NPC metastasis in athymic mice.
Methods: Twenty million of C666-1 human NPC cells were injected into the livers of athymic mice to induce primary tumors. Gold-1a was administrated by intraperitoneal injection. Survival times, tumor volumes and degrees of metastasis of the animals were evaluated. Intratumoral microvessel density was determined by immunohistochemical staining for CD34. Tube formation by MS1 mouse endothelial cells were conducted with an *in vitro* angiogenesis assay kit. Gene expression level was determined by semi-quantitative reverse transcription-polymerase chain reaction. Cell proliferation was performed by methylthiazolyldiphenyl-tetrazolium bromide assay.
Result: Gold-1a prolonged the survival and inhibited intrahepatic and lung metastasis of the tumor-bearing animals. The compound induced tumor tissue necrosis and reduced tumor microvessel formation. In *in vitro* studies, gold-1a inhibited tube formation and proliferation of MS1 cells, and downregulated the expression of stanniocalcin 1 (Stc1), which plays roles in angiogenesis. Furthermore, our preliminary data showed that overexpression of Stc1 in MS1 cells rescued cells from gold-1a-induced death.
Conclusion: Gold-1a is a novel anticancer agent that prolongs survival of the NPC metastases-bearing mice. It inhibits intrahepatic and lung metastasis *in vivo* and inhibits angiogenesis *in vitro*, in part via downregulation of Stc1.

PE240

Inhibition of hepatoma cell growth by Tbx3 antagonist peptides

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Tbx3 is a transcriptional repressor that is important for embryonic development. Overexpression of Tbx3 was found in a large variety of cancers, including breast cancer, ovary cancer, cervical cancer, lung cancer, bladder cancer and liver cancer. Tbx3 promote carcinogenesis by bypass cellular senescence via suppression of $p14^{ARF}$. Our resent studies revealed that two key motifs composed of 7 + 3 residues are essential for its transcriptional repression. Based on this finding, we designed a set of peptides to block its transcriptional repression activity and tested their antiviral effects. We found that TAT-tagged peptides (TAPs) effectively transduced hepatoma HepG2 and BEL7404 cells at almost 100% efficiency and inhibited cell growth in a dose dependent manner. Further studies revealed that the TAP treated cells underwent up-regulate apoptosis via suppression of $p14^{ARF}$ both at mRNA and protein levels, demonstrating the potential of novel TAPs for anti-HCC treatment in the future.

PE241

Safety and long-term outcomes of radiofrequency ablation therapy in elderly and cirrhotic patients with hepatocellular carcinoma

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Background and Purpose: A tendency of the aging in patients with hepatocellular carcinoma！(HCC) is predominantly seen in Japan. In fact, the mean age of patients with HCC in our institute in 1990 was 60.1 years old, while that in 1999 was 67.8 years old. It is not still remained whether the percutaneous radiofrequency ablation (RFA) therapy in elder patients with HCC is safety and equal in therapeutic usefulness compared to the non-elder patients with HCC.
Subjects and Methods: Two hundred six cirrhotic patients with HCC (376 tumor nodules) received RFA therapy curative intent since August, 2006 were enrolled. We divided all patients into two groups: over 65 years (elder group: n=135) and under 65 years (non-elder group: n=71), and compared the patient's characteristics, tumor factors and survival rate and causes of death in two groups.
Results: The characteristics of patients, tumor factors, cumulative survival rate and recurrence rate were not revealed in two groups. Although in elder group two patients complicated aspiration pneumonia and respiratory depression due to sedation under RFA respectively, total occurrence rate of complications did not differ between two groups.
Conclusion: RFA therapy is safety and effective even in elder patients with HCC, although their care is necessary to prevent any complications which are often occurred during the RFA therapy.

PE242

Supplementation of branched-chain amino acid enriched nutrient improves the nutritional status and quality of life in patients with hepatocellular carcinoma after radiofrequency ablation therapy

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Background and Purpose: The aim of this study is to evaluate whether administration of the branched-chain amino acid！(BCAA) enriched nutrient (namely, aminoleban EN, Ostuka Pharmaceutical Company, Japan) might improve protein-energy malnutrition (PEM) status and quality of life (QOL) in cirrhotic patients with HCC receiving RFA therapy.
Subjects and Methods: Thirty-five cirrhotic patients with HCC who had received RFA therapy from October 2005 to October 2006 in our institute were randomized into two groups: diet with supplementation of aminoleban EN (EN group: 20 patients, 420 kcal/day) and diet only (control group; 15 patients). The total intakes of calories (30-35 kcal/kg) and protein (1.0-1.5 g/kg) were equal between tow groups. The primary end point was event-free survival rate (development of liver cancer, rupture of esophageal varices, or progression of hepatic failure) and second end points were serum albumin levels and the health-related QOL by ShortForm-8 questionnaire (SF-8).
Results: Total intakes of calories and protein were similar during the one year after RFA. No significant differences in event-free survival rate were seen between two groups. However, decreased serum albumin levels and one (general health perception) of domains in SF-8 were significantly improved in EN group compared to the control group.
Conclusion: Supplementation of BCAA-enriched nutrient may improve the impaired liver function and QOL after RFA therapy. Large scale prospective study should conduct to confirm these results near the future.

PE243

The Combination Treatment of Cox-1 and Cox-2 Inhibitors Does Not Produce an Additive Effect on Proliferation and Apoptosis of Hepatocellular Carcinoma Cell

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Backgrounds and aims To investigate the effects of selective Cox-1 and Cox-2 inhibitor on proliferation and apoptosis of HCC cell.

Methods Hep3B and SNU 387 cells were treated with NS-398 and SC-560. MTT assay, caspase 3/7 activity assay and TUNEL assay were performed. Cox protein and mRNA expression were measured by Western blot and real time RT-PCR.

Results In Hep3B cell line, Cox-1, Cox-2 (50, 100, 200 uM) and combination (25+25, 50+50, 100+100 uM) treatment after 24hr showed a significant dose dependent inhibitory effect on cell growth ($p<0.05$). Cox-1, Cox-2 (100 uM) and combination (50+50, 100+100 uM) treatment after 24hr significantly increased caspase 3/7 activity ($p<0.05$) and induced apoptosis ($p <0.05$). However, the combination treatment could not showed a additive effect to Cox-1 or Cox-2 inhibitor ($p>0.05$). In SNU 387 cell line, Cox-1 inhibitor and combination treatment showed a inhibitory effect on cell growth ($p <0.05$) similar to Hep3B cell line but any of treatment could not induce apoptosis significantly ($p >0.05$). In Cox protein and mRNA expression, SNU 387 cell line showed significant Cox-1 predominency ($p=0.037$) but Hep3B cell line showed Cox-2 predominency ($p=0.032$).

Conclusions In HCC cells, no additive effect of the combination treatment of Cox-1 and Cox-2 inhibitors could be anticipated. The apoptosis inducing effect of Cox inhibitor could be different between HCC cell lines. More studies for the mechanism of different response to Cox inhibitor between cell lines is needed.

PE244

A Phase I/II study of combination chemotherapy with mitoxantrone and uracil/tegafur and for advanced hepatocellular carcinoma

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Background: The aim of this study was to determine the maximum tolerated dose and recommended dose of combination chemotherapy with mitoxantrone and uracil/tegafur (UFT) (phase I part), and to clarify its efficacy (tumor response, overall survival, and progression free survival) and safety in patients with advanced hepatocellular carcinoma (HCC) at the recommended dose (phase II part).

Methods: Patients eligible for study had histologically confirmed, chemo-naïve advanced HCC, who were unsuitable for resection, local ablation therapy or transcatheter arterial chemoembolization. The therapy consisted of mitoxantrone dosages (6, 8 and 10 mg/m^2/day) intravenously on day1 and oral administration of UFT 300 mg/m^2 on day 1 through day 21. The treatment was repeated every four weeks if there was no evidence of tumor progression or unacceptable toxicity.

Results: A total of 25 patients were entered into the study. All had a good ECOG performance status score of 0-1. In phase I part, dose limiting toxicities occurred in all three patients (two patients: grade 4 neutropenia, one patient: grade 3 creatinine elevation) given mitoxantrone at dosage of 10 mg/m^2/day, and the recommended mitoxantrone dosage was 8 mg/m^2/day. Among 19 patients administered at the recommended dosage, one patient (5.3%) achieved a partial response, 8 patients (42.1%) had stable disease and 10 patients (52.6%) had progressive disease. One-year survival proportion, median survival and median progression free survival were 26.3%, 8.4 months and 2.5 months, respectively. The most common toxicities were grade 3–4 leucopenia (15.4%) and neutropenia(10.3%).

Conclusion: Mitoxantrone 8 mg/m^2 with UFT 300 mg/m^2/day is recommended dose. This regimen is generally well tolerated, but appears to have little activity for advanced HCC. These findings do not support its use in practice, and further trials with this regimen in patients with advanced HCC are not recommended.

PE245

Transarterial chemoembolization is an effective palliative treatment for patients with unresectable recurrent hepatocellular carcinoma

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Background: Transarterial chemoembolization (TACE) is a commonly employed palliative treatment for unresectable hepatocellular carcinoma (HCC). This study aims to evaluate its efficacy in patients with recurrent disease and to find out the prognostic factors of survival.

Methods: We performed a retrospective review on patients with HCC treated with TACE from Feb 2005 to April 2008 in a tertiary referral hospital. Survival time was calculated by Kaplan-Meier method from the time of TACE. Patients with *de novo* HCC and recurrent HCC were compared. The prognostic factors of survival were assessed by log rank test in univariate analysis and Cox regression in multivariate analysis.

Results: There were 139 patients (115 Male & 24 Female) in this study, among which 46 patients (33%) had recurrent HCC and 93 patients (67%) had *de novo* HCC. The median age was 61 years (range: 39-86). The median duration of follow-up was 9.8 months (range: 0.1 to 35.3). There was no significant difference (P=0.249) in the median survival between patients with *de novo* (19.4 months) and recurrent disease (19.9 months). Ruptured HCC (P=0.015), portal vein thrombosis (P=0.031), albumin <35g/L (P=0.001) and Cancer of the Liver Italian Program (CLIP) score >2 (P=0.013) were independent prognostic factors of poorer survival.

Conclusion: Patients with recurrent and *de novo* HCC had comparable survival after TACE. Recurrent patients who are not candidates for further curative treatment can still be benefited from TACE provided that their liver functions are preserved and the disease statuses are not too advanced.

PE246

Clinical applications of computerized tomography 3-D reconstruction imaging for diagnosis and surgery in children

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The study assessed the benefits of 3-D reconstruction of spiral CT scans for the diagnosis of and surgical guidance to large liver tumors or tumors at the hepatic hilum. We retrospectively analyzed 33 cases of children with such tumors treated in past 5 years.The patients were examined by 3-D reconstruction using 64 slice spiral CT. In 28 cases, the volume of tissue removed exceeded 1/3 the entire volume of the liver. In 5 cases, the excised tissue represented less than 1/3 of the total liver volume, but the location of the tumor was adjacent to major hepatic vessels. Pathological diagnoses included hepatoblastoma (n = 20), hepatocellular carcinoma (n = 4), mesenchymal hamartoma (n = 4), teratoma (n = 1) and adenoma (n = 4). All children had curative resections with tumor-free microscopic margins. 3-D CT imaging can provide high quality images and accurate location of the tumors. It could help the surgeon identify the tumor borders accurately and devise a safe surgical strategy. With its help the surgeon could identify vital hepatic blood vessels before operation, and can avoid massive hemorrhaging during operation.

PE247

TGFβ1 gene variant changes its expression and is associated with the HBV-related hepatocellular carcinoma

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Background: To investigate the association between C-509T polymorphism of transforming growth factor (TGF)-β1 gene and HBV-related hepatocellular carcinoma (HCC).

Methods: Patients with HBV infection (196 cases were HBV carriers, 379 cases were HCC) and 299 healthy volunteers were enrolled. The polymorphism of TGF-β1 gene C-509T was identified by polymerase chain reaction-restriction fragment length polymorphism method. The concentrations of plasma TGF-β1 were measured by enzyme linked

immunosorbent assay (ELISA). TGF-β1 mRNA expression was quantified by real-time PCR. A recombinant construct containing -509C>T variant as promoter and CAT as reported gene was transfected into HepG2 cells. The reporter gene CAT was detected with ELISA.
Results: The CT genotype at position -509 of TGF-β1 gene prevailed in all three groups, the frequency of genotype CC and allele C at -509 in HCC were significantly higher than those of the HBV carriers and controls. The plasma TGF-β1 concentration among the three genotypes did not show any significant difference in three groups. However, both the TGF-β1concentration and liver mRNA levels were statistically higher in patients with CC genotype than in those with TT genotype in the HCC group. Reporter gene CAT was elevated when HepG2 were transfected with -509C-CAT recombinant construct compared to that with -509T-CAT one ($p<0.05$)
Conclusion: The presence of C allele at position -509 may play an important role in the development of HBV-related HCC through influencing TGF-β1 expression both at mRNA level and protein level.

PE248
N-glycome profiling improves diagnostic efficacy in HBV-related hepatocellular carcinoma
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Background: To assess diagnostic value of N-glycan markers in identifying hepatocelluar carcinoma (HCC) from liver fibrosis after HBV infection.
Methods: A total of 273 cases of HBV related liver fibrosis (n=128) and HCC (n=145) patients as well as matched healthy controls (n=120) were recruited. Routine liver function and tumor markers were detected by automatic biochemistry or immunological analyzer. N-glycome of serum protein was profiled by DNA sequencer-assisted fluorophore-assisted carbohydrate electrophoresis with a capillary electrophoresis-based ABI3130 sequencer.
Results: The abuncance of a single agalacto biantennary glycan (NG1A2F, peak 4) was increased in liver fibrosis and decreased in HCC, while that of a branching triantennary glycan (NA3Fb, peak 9) was decreased in fibrosis and increased in HCC. The efficacy of the log ratio of above two N-glycan abundance [log (p9/4)] was similar to AFP in differentiation HCC from fibrotic patients. With logistic regression analysis, the accuracy and sensitivity of the diagnostic model combining AFP with N-glycan analysis(Cscore B) were increased 7-10% compared to AFP. Log(p9/4) was even more powerful in monitoring the progresison of HCC with the specificity improved 16% and accuracy improved 8% compared to that of AFP. Besides, log(peak 9/4) was correlated well with other tumor markers and TNM stages.
Conclusions: The log ration of the abundance of a branching triantennary glycan (NA3Fb, peak 9) to a single agalacto biantennary glycan (NG1A2F, peak 4) and the model combining AFP with N-glycome markers are promising in HCC diagnosis and progression monitoring.

PE249
Electrode Tract Thermocoagulation during Radiofrequency Ablation: A Comparison of Different Techniques in Porcine Livers
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The low incidence of tumor seeding and post-procedure bleeding after radiofrequency ablation (RFA) of hepatic tumors has been attributed to the use of thermocoagulation of the tract, which results in necrosis, upon electrode withdrawal. However, different investigators use different techniques with no experimental evidence of the effectiveness of a particular technique.
Objective: We aimed to compare the necrotic zone produced using different electrode withdrawal techniques.
Methods: Eighteen tract ablation zones were created in ex vivo porcine livers by withdrawing an internally-cooled RFA electrode (Cool-tip radiofrequency system, Valleylab) 1-2 mm/second using energy-dependent (20 vs.40 vs.60 vs.80 watts) and temperature-dependent (80 vs. 90^0C) techniques. Horizontal necrotic diameter was compared using ANOVA with Bonferroni post-hoc tests.
Results: Withdrawing RFA electrode with constant energy of 80watts resulted in greatest necrotic diameter (1.3±0.1cm;range=1.1-1.4cm), which was significantly larger than 20watts (0±0cm;range=0-0cm;$p<0.0001$), 40watts (0.6±0.2cm;range=0.4 to 0.8cm;$p=0.002$) and the temperature-dependent techniques [(80degrees=0.6±0.2cm;range=0.4 to 0.7cm;$p=0.001$); (90 degrees=0.7±0.1cm;range=0.6 to 0.8cm;$p=0.008$)], but not significantly different from that at 60watts (1.0±0.1cm;range=0.9 to 1.1cm;$p=0.373$). Average temperatures achieved in energy-dependent technique were highest with 80watts (80watts=64.3±2.3degrees vs. 60watts=56.7±4.9degrees vs. 40watts=41.7±4.6degrees vs. 20watts=29±1.0degrees;$p<0.001$) while there was no difference in watts delivered in temperature-dependent technique (80degrees=35.3+2.9watts vs. 90degrees=30.7+11.2watts;$p=0.522$).
Conclusion: Electrode tract thermocoagulation with at least 60watts results in greater necrotic diameter than temperature-dependent techniques in ex vivo livers. However, temperature-dependent techniques may be more reliable in vivo because blood flow may alter the temperature and necrosis achieved with energy-dependent techniques.

PE250
Overlapping Radiofrequency Ablation Synergistically Increases Coagulation Diameter Compared to Single Ablation
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Mathematical modeling suggests an impractical number of radiofrequency ablation (RFA) zones needed in order to ablate a medium-large hepatic tumor. However, overlapping RFA zones may increase the necrotic diameter disproportionately to that deduced from single ablation alone.
Objectives: To compare the necrotic diameter in single (Group1), dual overlapping (Group2) and dual non-overlapping (Group3) ablation.
Methods: Single (n=5) and dual (overlapping n=18; non-overlapping n=6) ablation zones were created in ex vivo porcine livers using Cool-tip RFA electrodes. Necrotic diameter was measured at the midpoint (MaxD) of the single and the two distinct RFA zones of the dual ablation groups and compared with the necrotic diameter at the tip of the second ablation (MaxD-O), corresponding to the point of overlap in Group2. The RFA electrode was withdrawn 2.5 and 4.1 cm before re-ablating for Group2 and Group3, respectively.
Results: Despite no difference in end-RFA temperature between 3 groups (Group1=75.6±7.4Cvs.Group2=73.9±7.3Cvs.Group3=74.8±4.8C; $p=0.873$), MaxD was significantly greater ($p=0.011$) in Group2 (4.1±0.7cm) as compared to Group1 (3.3±0.6cm) and Group3 (3.3±0.4cm), with no difference between Group1 and Group3($p=1.00$). Further proof of synergism between two overlapping ablations is that the MaxD-O in Group2(4.3±0.6cm) was larger than MaxD of Group1 ($p=0.042$) and Group3 ($p=0.028$), and was similar to MaxD of Group2 ($p=1.00$).
Conclusions: Overlapping two RFA zones results in incremental increase in necrotic diameter compared to single and dual non-overlapping ablation. This may explain the discrepancy in the number of ablation zones needed between clinical and mathematical modeling studies.

PE251
Vitamin K2 suppresses the expression of fibroblast growth factor receptor 3 in Hepatocellular carcinoma cells
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Background: Vitamin (Vit) K2 has been reported to inhibit the growth of human hepatocellar carcinoma (HCC) cells in vitro and suppress hepatocarcinogenesis in vivo. However, its inhibitory mechanism has not yet been clarified. In this study, we analyzed the effects of Vit. K2 on the expression of fibroblast growth factor receptor (FGFR) in a HCC cell line.
Methods: HCC cell line Hep G2 was cultured in 10%FBS-DMEM, and treated with 10, 30 and 100 M of Vit. K2. The cell numbers were measured by MTT assay. The total RNA was extracted by Isogen, and the mRNA expressions were analyzed by semi-quantitative RT-PCR, DNA chip and real-time PCR. The protein expressions of FGFRs were detected by

western blot. The inhibition of FGFR3 promoter was analyzed by luciferase assay.
Results: The mRNA and protein expressions of FGFR1, 2 and 4 were not suppressed by Vit. K2. However, FGFR3 expression was significantly suppressed by Vit. K2. The mRNA expressions of FGFR3 were suppressed 61.5% by real-time PCR and decreased 2.54 times by DNA chip after Vit. K2 treatment for 96 hrs at 30 M. Protein content of FGFR3 was also suppressed by Vit. K2. The luciferase activity of FGFR3 promoter was also suppressed by Vit. K2.
Conclusions: These findings suggested that Vit K2 suppressed the proliferation of hepatocellular carcinoma through down-regulation the expression of FGFR3.

PE252
Glutathione-S-transferase and Microsomal Epoxide Hydrolase Polymorphisms and Viral Related Hepatocellular Carcinoma Risk in India
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Background: Hepatocellular carcinoma (HCC) is the fourth most common cancer worldwide, main etiological factors being chronic infections with hepatitis B and C viruses. The present study was undertaken to evaluate the association of *glutathione-S-transferase* (*GST*) *T1* and *M1* null genotypes and *microsomal epoxide hydrolas e*(m*EPHX*) polymorphisms with hepatitis virus related HCC risk in Indian population.
Subjects and Methods: Three groups of subjects were considered viz. control (n=169), chronic viral hepatitis (n=174) and HCC (n=63). PCR-RFLP was used for this polymorphic study. Genotype distributions between categories were compared using the χ^2 test; odds ratios (ORs) and 95% CI were calculated to express the relative risk.
Results: Presence of *GSTM1* null genotype significantly ($p<0.05$) decreased the risk for HCC development among chronic viral hepatitis subjects. However, *GSTT1* null genotype was associated with an increased risk for HCC by 2.23 and 1.42 times among control and hepatitis subjects respectively. In case of m*EPHX*, Tyr113His and His113His genotypes significantly ($p< 0.05$) reduced the risk of HCC development in both viral hepatitis and control subjects. In case of m*EPHX* exon 4 genotypes, Arg139Arg imposed an approximate 2 fold risk for HCC development in the two groups. Combination of heterozygous mutant genotypes at m*EPHX* exons 3 & 4 also imposed around 2 fold risk (non-significant) for HCC.
Conclusions: Polymorphic forms of *GST* and *mEPHX* share an association with viral related HCC risk in Indian population and should be further evaluated as the candidate genes to determine individual susceptibility for viral related HCC.

PE253
Relevance of diabetes mellitus and antidiabetic therapy in patients with Cirrhosis and Hepatocellular Carcinoma
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Background : the association between type 2 diabetes mellitus (DM2) and hepatocarcinoma (HCC) has been identified in the last ten years.
Methods: to clarify the temporal relationship between DM2 and HCC and the possible effects of antidiabetic therapy on HCC risk, we recruited 465 patients with HCC compared with 490 control subjects without liver diseases and 618 cirrhotic patients.
Results: prevalence of DM2 was 31.2% in HCC, 23.3% in cirrhotic and 12.7% in control group. In univariate and multivariate analysis, the odds ratio (OR) for HCC in diabetic patients were respectively 3.12 (CI 2.2-4.4; P <0.001) and 2.2 (CI 1.2-4.4; P= 0.01). OR in univariate analysis were higher in male than in female patients. In 84.9% of the patients DM2 pre-exists the diagnosis of HCC from a mean time of 141.5 months. Moreover, the insulin treatment was more frequent in diabetic HCC patients than controls and we report an OR for HCC of 2.99 (CI 1.34-6.65; P= 0.007) in patients treated with insulin or sulfonylureas, and an OR of 0.33 (CI 0.1-0.7; P= 0.006) in patients treated with metformin.
Conclusion: our study confirms that male patients with type 2 diabetes mellitus have a significantly increased risk of HCC independently of other cofactor such as HBV, HCV and alcoholic abuse. DM2 is a pre-existing disease in most HCC patients and suggests that insulin and sulphonylurea treatments in DM2 are associated with an increased risk of HCC development, while metformin may have a protective effect.

PE254
Gene loss expressed profiling of hepatocellular carcinoma
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Background & Aims: Over the last few years, techniques that allow systematic analysis of chromosome aberrations at a genome-wide level were applied to HCC. The purpose of this study is to apply gene loss expression profiling in the attempt to discover new related genomic regions not revealed by LOH or CGH, and search the new tumor suppression genes for HCC.
Methods: Primary HCC and corresponding non-tumor liver tissues were obtained from surgery. Serologically, 13 cases were with hepatitis B virus infection and 12 cases were with hepatitis C virus infection. Four non-viral infected tissues from four patients receiving surgical resection for hepatic adenoma or focal nodular hyperplasia.Affymetrix GeneChip, U133A, was used to compare the loss and gained gene expression in liver needle biopsy samples (n=54).
Results: After adjusting by chromosome arm length, 16p, 17p, 19p, 19q and 22q showed higher gene loss-expression ratio (>= 10 loss / cM) in the comparison between normal samples and tumor samples; 1q, 2p and 4q showed higher gene loss-expression ratio in the comparison between tumor and non-tumor tissues. More than 50 genes showed different loss expression level in this study. For example, CD10 was loss expression in all non-tumor samples comparing to four normal samples. Ficolin 3 and ficolin 2 were loss expression in HCC samples with HBV infection and with HCV infection, respectively.
Conclusion: Our results revealed the potential tumor suppression genes and the genomic region they harbored. Further study is needed to validate the observation.

PE255
The Relationship between Expression of Caspase 8 and Survivin and Clinicopathologic Features in Hepatocellular Carcinoma
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Background/Aims: Hepatocellular carcinoma is common malignancy in human, accounting for 1 million deaths in the world annually. Caspase 8, as an initiator caspase, is involved in the induction of apoptosis. Survivin, a novel inhibitor of apoptosis is related to the ability to inhibit caspases and involved in critical steps of onset and progression of HCC with unfavorable prognosis.
Methods: To explore the possibility that the epigenetic alteration of caspase 8 and survivin genes is implicated in the development and progression of HCC, promoter methylation of two genes was analyzed in 73 cases of primary HCC by methylation specific PCR. The relationship between immunohistochemical expression of gene products and proliferative/apoptotic indices, and clinicopathologic parameters was also investigated.
Results: The methylation of caspase 8 (34.2%, 25/73) and survivin (32.9%, 24/73) demonstrated a negative correlation with immunohistochemical expression of capsase 8 (47.9%, 35/73) and survivin (43.8%, 32/73) (p=0.042 and p=0.001 respectively). Methylation of caspase 8 and immunohistochemical expression of its gene product was significantly correlated with apoptosis (p=0.026 and p=0.032). Survivin nuclear immunoreativity revealed significantly correlated with proliferative activity of tumor cells (p=0.001). By survivial analysis, the negative caspase 8 expression and positive survivin expression showed worse prognosis in HCC, that was statistically insignificant (p>0.05).

Conclusion: In conclusion, caspase 8 and survivin may contribute an important regulatory mechanism for tumor cell proliferation and apoptosis, and may be prognostic predictors in HCC.

PE256

A Subanalysis of Asian and Non-Asian Patients with Hepatocellular Carcinoma (HCC) Treated in a Phase II Safety and Efficacy Study of Brivanib as First-line Therapy

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Background: Worldwide 70% of HCC occurs in the Asian population and until recently, no systemic treatment has demonstrated benefit in these patients. A recent trial in Asian patients showed an overall survival of 6.2 months on sorafenib vs 4.1 months on placebo, both approximately 4 months shorter than in non-Asians in SHARP.

Methods: Brivanib is an oral dual inhibitor of vascular endothelial growth factor receptors (VEGFR) and fibroblast growth factor receptors (FGFR). This is a subanalysis by race/geography of a Phase 2, open-label study of patients with unresectable, locally advanced, or metastatic HCC receiving brivanib 800 mg qd as first-line therapy. Endpoints included overall survival (OS), time to progression (TTP), and adverse events (AEs).

Results: Data from fifty-five patients (64% Asian) receiving first-line brivanib are presented.

Conclusions: This subanalysis demonstrates encouraging activity and tolerability of brivanib as first-line therapy in Asian patients with HCC.

	Asian (n=35)	Non-Asian (n=20)
ECOG PS 0/1	54.3%/40.0%	30.0%/65.0%
Child-Pugh A/B	100.0%/0	75.0%/25.0%
Hepatitis B/C	68.6%/11.4%	25%/40%
Baseline AFP >ULN	74.3%	70.0%
Prior Local Therapy (overall)	51.4%	45%
Median OS	10.0 mos.	5.7 mos.
Median TTP	2.7mos.	2.8 mos.

Overall, incidences of AEs were similar between both groups.

PE257

Combination Therapy of Transcatheter Arterial Cisplatin Embolization and Radiation for Advanced Hepatocellular Carcinoma with Portal Venous Invasion

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Background: Hepatocellular carcinoma (HCC) with portal venous invasion (PVI) has a very poor prognosis. The combination of continuous intraarterial 5-fluorouracil (FU) infusion and systemic interferon-alpha (IFNalpha) injection was recently reported to be effective against HCC with PVI, though the therapy is not always applicable for the patients with arterial abnormality. Therefore we tried combination therapy of transcatheter arterial cisplatin embolization and radiation, and will report the effectiveness and toxicity of the therapy.

Methods: The combined therapy was conducted in 7 HCC patients with PVI. Transcatheter arterial embolization with 1mg/kg cisplatin powder (IA call) was performed against intralobar lesions, followed by external radiation targeted for PVI (60Gy in 2 Gy fractions). The following variables were evaluated with the survival rate: gender, age, viral etiology, Child's class, performance status, and location of PVI.

Results: One (16%) patient showed complete response and another two (33%) partial response. Two (33%) showed no change, and one (16%) showed progress of disease. The survival rates at six months among overall patients were 85.7%. Adverse events were limited to nausea and appetite loss. One of the patients with partial response underwent curative resection, and is still alive without any recurrence for 530 days.

Conclusions: The combination therapy of cisplatin embolization and radiation is safe, effective and also feasible to the patients with arterial abnormality. This therapy is suggested to be a useful alternative therapy for the patients with extensive PVI.

PE258

Efficacy of Transarterial Chemo-Lipiodolization Using Cisplatin Powder Delivered Via an Injection Port for Advanced Hepatocellular Carcinoma

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Back ground: The treatment efficacy for inoperable advanced hepatocellular carcinoma (HCC) is poor. Recently, the injection port has been used for hepatic arterial infusion chemotherapy (HAI) in Japan. HAI is usually used for the treatment of multifocal bilobar tumors of the liver or HCCs combined with portal vein tumor thrombosis (PVTT), not amenable to TACE. This study examined the efficacy and toxicity of repeated hepatic HAI using lipiodol suspension mixed with cisplatin powder.

Methods: From April 2005 to September 2008, 20 patients with inoperable advanced HCC were enrolled in this study. All received cisplatin powder (50mg) and Lipiodol (2ml) suspension, with an intervening 4 weeks interval. The drugs were delivered from an injection port. 13 patients had HCC with PVTT, and 7 had HCC without PVTT. 11 patients with liver function of Child grade A, 7 of grade B, and 2 of grade C were enrolled.

Result: The mean number of HAI given during the follow-up period was 4.1 times. We found complete response in 1 case, partial responses in 6, no change in 6, and progressive disease in 7. The overall response rate was 35.0%. The 1-year survival rate was 36.7% and the 2-year survival rate was 12.1%. Although 3 patients had cisplatin-induced anaphylaxis, no severe adverse events (hepatic failure and renal failure) were observed.

Conclusion: Chemo-lipiodolization using cisplatin powder delivered via an injection port provides some clinical benefits without severe adverse events in patients with far advanced HCC.

PE259

Relationship between Vascular Endothelial Growth Factor and its receptor gene expression in hepatocellular carcinoma and its surrounding liver parenchyma

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Background: Recently, the antitumor efficacy of angiogenesis inhibitors is expected in the treatment to hepatocellular carcinoma. The gene expression relevant to the vascularization, which is a target of these inhibitors, has a difference according to each case and it is thought that it influences the therapeutic effect of them. However, there are still few reports of mRNA expression of Vascular Endothelial Growth Factor (VEGF) receptors in HCC.

Methods: The relative mRNA level of VEGF and its receptors (KDR and flt-1) was analyzed using quantitative RT-PCR in 51 patients with HCC. Matched samples of HCC (T) and non-tumor liver tissue (NT) were obtained by fine needle (21gauge) biopsy. Results: Gene expression level of VEGF and flt-1 was significantly higher in HCC than NT (VEGF; $p<0.001$, flt-1; $p<0.001$). According to the clinicopathological findings, gene expression level of VEGF and KDR in HCC was significantly high in hypervascular HCC compared to hypovascular HCC (VEGF; $p=0.002$, KDR; $p=0.042$). Additionally, flt-1 tended to be expressed higher in hypervascular HCC than hypovascular HCC ($p=0.09$). Moreover, gene expression level of VEGF, KDR and flt-1 tended to be higher in advanced-stage HCC than early-stage HCC. Conclusion: Not only VEGF but KDR and flt-1 were highly expressed in hypervascular and advanced HCC.

PE260

Efficacy and Safety of Sorafenib in Patients with Advanced Hepatocellular Carcinoma (HCC): Collective Results from the Phase III Sorafenib HCC Assessment Randomized Protocol (SHARP) and Asia-Pacific (AP) Trials

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Background: Because the etiology of HCC varies considerably by geographic region, we compared results of the SHARP and AP trials to evaluate the effectiveness of sorafenib in patients worldwide with advanced HCC. SHARP enrolled patients from Europe, North/South America, and Australia; AP, patients from the AP region.

Methods: Eligibility criteria were similar. Patients had ECOG PS 0-2, and no prior systemic therapy for HCC. Patients were randomized to sorafenib 400 mg BID or placebo, at a 1:1 (SHARP) or 2:1 (AP) ratio. Endpoints included overall survival (OS), time to progression (TTP), and safety.

Results: AP patients had more advanced disease (eg, more extrahepatic spread, poorer ECOG PS) than SHARP patients at baseline. OS and TTP hazard ratios were similar between SHARP/AP studies, despite more advanced disease in AP patients.

Conclusions: Sorafenib was effective and safe for the treatment of advanced HCC, despite a more evolved HCC stage in Asia.

Endpoint	SHARP Study		AP Study	
	Sorafenib/Placebo, median (months) (N=299)/(N=303)	Hazard Ratio (95% CI)	Sorafenib/Placebo, median (months) (N=150)/(N=76)	Hazard Ratio (95% CI)
Overall survival	10.7/7.9	0.69 (0.55-0.87)	6.5/4.2	0.68 (0.50-0.93)
Time to progression	5.5/2.8	0.58 (0.45-0.74)	2.8/1.4	0.57 (0.42-0.79)
Drug-Related AE (%)	**All Grades Sorafenib/Placebo (N=297)/(N=302)**	**Grade 3/4 Sorafenib/ Placebo (N=297)/ (N=302)**	**All Grades Sorafenib/Placebo (N=149)/(N=75)**	**Grade 3/4 Sorafenib/ Placebo (N=149)/ (N=75)**
HFSR	21/3	8/<1	45/3	11/0
Diarrhea	39/11	8/2	26/5	6/0
Fatigue	22/16	3/3	20/8	3/1
Hypertension	5/2	2/1	19/1	2/0

PE261

Fgl2 prothrombinase contributes to tumor hypercoagulability via IL-2 and IFN-γ

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Aims: Fibrinogen-like protein 2/fibroleukin (fgl2) has been reported to play a vital role in the pathogenesis in MHV-3 (mouse hepatitis virus) induced fulminant and severe hepatitis, spontaneous abortion, allo- and xeno- graft rejection by mediating "immune coagulation". Fgl2 functions as an immune coagulant with the ability to cleave prothrombin to thrombin directly. Therefore, this study was designed to examine the role of fgl2 in tumor development.

Methods: Tumor tissues from 133 patients with six types of distinct cancers and the animal tumor tissues from human hepatocellular carcinoma (HCC) model on nude mice (established from high metastasis HCC cell line MHCC97LM6) were obtained.

Results: Hfgl2 was detected in tumor tissues from 127 out of 133 patients as well as tumor tissues collected from human HCC nude mice. Hfgl2 was highly expressed both in cancer cells and interstitial inflammatory cells including macrophages, NK cells, and $CD8^+$ T lymphocytes and vascular endothelial cells. Hfgl2 mRNA was localized in cells that expressed hfgl2 protein. Fibrin (nogen) co-localization with hfgl2 expression was determined by dual immunohistochemical staining. *In vitro*, IL-2 and IFN-γ increased hfgl2 mRNA by 10-100 folds and protein expression in both THP-1 and HUVEC cell lines. One-stage clotting assays demonstrated THP-1 and HUVEC cells expressing hfgl2 had increased procoagulant activity following cytokines stimulation. Conclusion: The hfg12 contributes to the hypercoagulability in cancer and may induce tumor angiogenesis and metastasis via cytokine induction.

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PE262

Phase II study of IFN + Systemic 5-FU in patients with advanced hepatocellular carcinoma.

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Purpose: This phase II study of the combination therapy, interferon and systemic 5-FU, assessed efficacy in advanced hepatocellular carcinoma (HCC) patients.

Methods: Patients with inoperable HCC received peg-interferon (90 microgram on Day 1 of each week of treatment) and 5-FU (500mg d.i.v. on Day 1-5 of the first and second week of each 4-week cycle). The therapy was either terminated at the end of the first cycle in cases with progressive disease, or continued for at least 2 cycles, when responses to treatment were evaluated by Eastern Cooperative Oncology Group criteria.

Results: Of 146 patients treated (male, 79%; median age, 64 years), 64% had Child-Pugh A, and 31% had B. 90% had either metastasis or vascular invasion. 71% had metastasis and 49% had vascular invasion. On the basis of independent assessment, three (2.1%) patients achieved a complete response, thirteen (8.9%) had a partial response, and 42 (28.8%) had stable disease. There was no grade 3/4 drug related toxicities. Median overall survival was 6.9 months.

Conclusion: Combination therapy of IFN +5-FU has modest efficacy in HCC.

PE263

Pilot study with AURON MISHEIL THERAPY (AMT) in patients with advanced hepatocellular carcinoma

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Background: AMT is a mixture of approved pharmaceuticals in low therapeutic doses (human insulin and chlorpheniramine) and herbal components (aqueous camomile extract). Preclinical and phase I data in healthy volunteers showed a favourable safety profile for AMT. This pilot study should examine efficacy and safety of AMT in the patients with advanced hepatocellular carcinoma (HCC).

Methods: Thirteen patients with advanced HCC (TNM stage III-IV), who did not respond to existing therapy, were treated with i.m. AMT at 0.066 ml/kg up to a maximum volume of 5 ml twice daily for 1-10 months. Primary study objectives: Clinical Benefit Response (CBR). Secondary objectives: safety of AMT, tumor response according to WHO-RECIST criteria, quality of life (QOL) and iimmunomodulatory effects. The effects were evaluated by cytokine production of PBMCs before and after the treatment.

Results: There were no significant safety issues. Four and 3 patients showed positive and stable responses for CBR, respectively. Tumor response was 1 PR, 6 SD and 6 PD. Even in the patients with PD, 2 and 1 patients showed positive and stable responses for CBR. QOL data showed clear improvement.

Immune monitoring demonstrated effects of AMT on the functional immune parameters in about half of patients. In the patients with PR, histological examination showed tumor necrosis and many lymphocytes including plasmacytes infiltrating in the tumor.
Conclusion: These results suggest that a promising rate of patients with advanced HCC respond clinically to the AMT treatment without significant safety issue and AMT has some immuno modulatory capacities.

PE264

Electron Microscopic Study of Liver Dysplastic Nodule

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Background/Aims: Dysplastic nodules are important due to premalignant potential. The aim of this study was to evaluate the electron microscopic findings of liver dysplastic nodule in patients with liver cirrhosis.
Methods: A total of 5 patients (mean age: 64±9 years old, male 4) with dysplastic nodules which suspected as malignant nodule (mean size 1.38±0.22 cm) was enrolled from 48 cases of liver cirrhosis undergone ultrasonography-guided biopsy from December 2006 to January 2008. The etiologies of liver cirrhosis were as follows; alcohol (1 patient), hepatitis B virus (2), and hepatitis C virus (2).
Results: Hepatocytes showed rosette formation of regenerative hepatocyte or degeneration. The nucleus was round or oval shaped and the nucleus membrane was irregular. The nucleolus was prominent and clear, the mitochondria were crowded to one side in the cytoplasm with megamitochondria. Glycogen granules and lipofuscin pigments were abundant. Sinusoid formation was poorly developed and collagen fiber bundles were increased. The hepatocytes of rosette formation and bile ductules cell made of canal of Hering, which was dilated and microvilli was decreased. The number of canal of Hering was 7, which was composed of 1.7±0.8 with hepatocyte and 2.1±0.7 with bile ductule cell, respectively. There was no oval cell in the canal of Hering, which was relatively well developed. Schwann cells were clustered together in nerve plexus. Therefore, these electron microscopic findings showed that dysplastic nodule was similar to early hepatocellular carcinoma.
Conclusions: This study showed that dysplastic nodule in liver cirrhosis is nearly identified to early hepatocellular carcinoma.

PE265

DCP is an important risk factor for recurrence after radiofrequency ablation of single hepatocellular carcinoma -< 3cm in diameter

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Background and aims: The aim is to analyze the risk factors for local recurrence + intrahepatic metastasis after radiofrequency ablation (RFA) and hepatic resection (Hr) for single hepatocellular carcinoma (HCC) ≤ 3cm in diameter.
Methods: Between 1999 and 2007, 219 patients with single nodule ≤ 3cm in diameter and Child-Pugh grade A were treated by Hr and RFA, and recurrence rate and survival rate using Kaplan-Meier method, and important risk factors for recurrence using Cox's proportional-hazards regression model were analyzed. Factors used for multivariate analyses were age, gender, viral marker, tumor diameter, AFP, AFP-L3, DCP, and platelet count.
Results: Mean age was 66 years old, M/F ratio was 136/83, Hr/RFA was 59/160, and mean observation period was 1194 days. Five-year survival rates, and 2-year local recurrence-free + intrahepatic metastasis-free rates were not significant between Hr group and RFA group (82/72%, 92/89%). In RFA group, the only independent risk factor for local recurrence-free + intrahepatic metastasis-free survival was DCP (P=0.0034). Tumor diameter was not significant for recurrence. In Hr group, there was no risk factor for recurrence. In pathological analyses of Hr group, DCP had a tendency to associate with microvascular invasion (P=0.065).
Conclusions: RFA was effective for HCC ≤ 3cm in diameter and DCP ≤ 40 mAU/ml. Hepatic resection should be selected for single HCC with DCP > 40 mAU/ml even though HCC <3cm in diameter.

PE266

Tumor morphology and prognosis after radiofrequency thermal ablation for small hepatocellular carcinoma

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Background: Radiofrequency ablation (RFA) is now a common treatment for small hepatocellular carcinoma (HCC). However, critical complications after RFA such as rapid intrahepatic dissemination have been reported. In this study, we investigated the method how to estimate the malignant potential of small HCC by dynamic CT before RFA.
Methods and results: Firstly, 61 HCCs less than 3cm in diameter were analyzed. Those tissues were classified into 4 groups as followed, small nodular type with indistinct margin (type E),! simple nodular type (type 1), simple nodular type with extranodular growth (type 2), confluent multinodular type (type 3). In the type 2 and 3 groups, portal invasion over vp1 were observed more frequently than those in the type 1 and E groups. At the next step, these 61 HCCs were classified into above-mentioned 4 types by two radiologists according to the shape of early stain or defect of delay phase of dynamic CT before operation. The accorded rate was 87% between those classifications. Next, 45 patients, which had solitary HCC less than 3cm in diameter and treated with RFA, were classified into those 4 types by dynamic CT before RFA. The recurrence rate and prognosis of those patients were examined. In the type 2 and 3 groups, the recurrence rate was higher and significant worse prognosis was showed than those in type 1 and E group .
Conclusion: It was suggested that HCC with type 2 and 3 might process higher malignant potential and RFA should be carefully performed on those types of HCC.

PE267

Induction of Interleukin-8 Maintains the Angiogenic Response in HIF-1α blocked Hepatocellular Carcinoma Cell Lines

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Background/Aims: Hypoxia-inducible factor-1α (HIF-1α) is the central transcriptional factor in the cellular response related to various aspects of cancer biology, including proliferation, survival, angiogenesis, and extracellular matrix metabolism to hypoxia. IL-8 became known to replace HIF-1α functions in the other cancer cell lines. The aim of this study was to evaluate whether IL-8 may induce angiogenic factors without HIF-1α by inflammation signal of hypoxic condition.
Methods: HIF-1α knockdown cell lines of HCC (Huh7 and HepG2) were constructed by RNA interference tools, and cultured under normoxia (21%O_2, 24 hours) and hypoxia (1%O_2, 24 hours) conditions. Following transfection, the amounts of HIF-1α, IL-8, angiogenic factors and matrix metalloproteinase (MMP) were examined using RT-PCR and western blotting, respectively.
Results: The expression of HIF-1α, angiogenic factors, MMP, IL-8 was markedly enhanced in wild types that were cultured under hypoxia, and the hypoxic induction of angiogenic factors and MMP was partially blocked in HIF-1α knockdown HCC cell lines. NF-κB inhibitor suppressed angiogenic effects by blocking IL-8 activity.
Conclusion: These data suggest that IL-8 induced tumor angiogenic factors in HIF-1α knockdown HCC cell lines.

PE268

The Relationship between the Quantity of Hepatocellular HBV cccDNA, tDNA and the Primary Liver Cancer

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Background：There were some reports that liver caner related to the levele of sera HBVDNA Our research focused on the relationship between the quantity of hepatocellular HBV cccDNA , tDNA and liver cancer.
Methods：The samples included the liver tissue of 24 CHB patients (CHB group) and the para-liver cancer tissue of 26 primary liver cancer patients (PHC group) The quantity of hepatocellular HBVcccDNA, tDNA were assayed by FQ-PCR in both groups.
Result: The quantity of hepatocellular HBV cccDNA in CHB group was 11.56±16.14 copys/cell higher than PHC group(3.96±9.27 copys/cell), P=0.011; The quantity of hepatocellular HBV tDNA in CHB group was 57.38±91.64 copys/cell higher than that of PHC group(35.07±93.03 copys/cell),P=0.13.;
Conclusion: The quantity of hepatocellular HBVcccDNA, tDNA can not be used as predictors of liver cancer for hepatitis B patients.

PE269

Cyclin D1 induction by Benzo(a)Pyrene Diol-Epoxide, via PI-3K/Akt/MAPKs-dependent Pathway, Facilitates G1/S Cell Cycle Transition and Tumorigenesis

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Background： Benzo[a]pyrene diol-epoxide (B[a]PDE) is the hepatic metabolite of Benzo(a)pyrene [B(a)P], which has been recognized as a ubiquitous liver carcinogen. Given that accumulating evidence has documented the potent carcinogenic effect of B[a]PDE, its molecular mechanism remains obscure.
Methods: DNA report assay and RT-PCR were utilized to examine the cyclin D1 level in hepatocytes exposed to B[a]PDE. Western blot was employed to determine the activation of the signal molecules. Flow cytometry sorting was used to analyze the cell cycle redistribution. Xenograft nude mice was established to evaluate the tumorigenecity of B[a]PDE.
Result：We observed hepatocytes treated with B[a]PDE present a significant increase of cyclin D1. Moreover, remarked activation of Akt, p70S6k, mitogen-activated protein kinases (MAPKs) including JNK, ERKs and p38 were detected in B[a]PDE-treated cells, while NF-κb, NFAT and Egr-1 not. We also demonstrated that JNK and Erks were involved in B[a]PDE-induced cyclin D1 expression, but p38 not. Furthermore, we found that overexpression of dominant negative mutant of p85 (Δp85) or Akt (DN-Akt) dramatically reduced B[a]PDE-induced JNKs and Erks activation and subsequently cyclin D1 expression, demonstrating cyclin D1 induction by B[a]PDE is via PI-3K/Akt/MAPKs-dependent pathway. Furthermore, knockdown of cyclin D1 by small interference RNA significantly blocked the G1/S cell cycle transition and tumorigenesis of B[a]PDE-treated cell.
Conclusion：These results will deepen our knowledge of the molecular mechanism involved in B[a]PDE-induced human liver cancer.

PE270

Influence of Pregnancy on the Development of Liver Cancer in Rats

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Hepatic cancer predominantly occurs in Males. This is almost a commonsense to most of us. But the detailed mechanisms underlying such phenomenon are still not well-known. The average age of liver cancer patients are about 30-40 years old. So most female patients have udergone pregnancy at least one time. Pregnancy is a very important event before or during the development of liver cancer in females. In this special period, not only sex hormones secrete in a strange manner, but also immune system functions in a special module which is very different from normal. So it is urgent to investigate the impact of process of pregancy on the development of hepatic cancer. In this study, 100 female SD rats are randomly divided into two groups: pregance group and controll group. Rats in both groups are injected IV Diethylnitrosomine(a chemical carcinogen). In pregnance group, rats are raised together with male rats in 3:1 ratio(3 female, 1 male) to make every rats undergo pregnancy. While in controll group, rats are coupled with spermaduct-ligated male rats. The size and amount of hepatic cancers in pregancy group are smaller and less than those in controll group. The survial rate is also significantly higer than that in controll group. We conclude that the process of pregnancy exerts an inhibitory role in the development of chemical induced hepatic cancer in rats.
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PE271

The use of alpha-fetoprotein measurement in detection of recurrent hepatocellular carcinoma after living donor liver transplantation

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Background: The recurrent hepatocellular carcinoma (rHCC) after liver transplantation (LT) can occur in 10 to 20 % of transplant recipients despite with a careful patient selection. For the surveillance of rHCC, frequent measurement of alpha-fetoprotein (AFP) and annual CT scan is commonly used. However, the usefulness of AFP is not clear. We report the update of our experience using our surveillance protocol.
Methods: Between 1996 and March 2008, 330 adult living donor LT were performed at the University of Tokyo. Among them, 100 recipients with HCC in their explanted liver were subjected to analysis. We used monthly measurement of AFP and des-gamma carboxy prothrombin (DCP) with annual dynamic CT scan.
Results: 83 met Milan criteria pre-operatively and 12 did not. 5 were incidental HCC. rHCC was experienced in 9 patients at 10 (2-24) months after LT. Recurrence sites were graft (1), lung (2), bone (3), and multiple organs (3). rHCC was first suspected from elevation of tumor markers in 8; AFP in 4, DCP in 2, and both AFP and DCP in 2. rHCC was confirmed with CT scan (7) or MRI (2) in 4 (0-6) months after the first sign of rHCC. When the cutoff level of AFP>20ng/ml was used, the sensitivity and specificity for rHCC were 66% and 100%. Six cases were treated surgically of which two achieving prolonged survival.
Conclusions: Although the confirmation of the rHCC sites required multiple imaging studies, AFP measurement was useful as for the first sign of rHCC.

PE272

Heated Lipiodol as a Embolization Agent for Transhepatic Arterial Embolization in VX2 Rabbit Liver Cancer Model

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Purpose: To evaluate the therapeutic effect of heated (60 C) lipiodol via hepatic artery administration in VX2 rabbit liver cancer model.
Materials and Methods: Thirty male New Zealand white rabbits were randomly divided into 3 groups with 10 rabbits for each group. VX2 carcinoma cells were surgically implanted into the left liver lobe. The tumors were allowed to grow for 2 weeks, and studies were performed until the diameter of tumors detected by ultrasonograph reaching 2 to 3 cm. Under the anaesthesia, transcatheter hepatic arterial embolization was performed and Doxorubicin-lipiodol (37ºC) (1 mL), lipiodol (60ºC) (1 mL) and control (physiological saline (37ºC) (1 mL)) were injected into hepatic artery of the 3 different groups. One week later, the volume of tumor was measured by ultrasonograph again. The serum of all rabbits was collected before injection and at 4 and 7 days after injection and the level of aspartate aminotransferase (AST) was checked. The survival period of 3 groups of rabbits after treatment was also recorded. During the last course of their disease, the rabbits were given some analgetics to relieve suffering.
Results: The tumors' growth rate in lipiodol (60ºC) group (0.92±0.21) was significantly decreased compared to control group (3.48±1.17) ($P<0.05$) and Doxorubicin-lipiodol (37ºC) group (1.69±0.26) ($P<0.05$). Consequently, the survival period of lipiodol (60ºC) group (41.0±3.0 days) was significantly higher than Doxorubicin-lipiodol (37ºC) group (38.0±2.5 days) ($P<0.05$). On the other hand, there is no statistical significance of serum level of AST

between lipiodol (60ºC) group (148.2±11.3 $U \cdot L^{-1}$) and Doxorubicin-lipiodol (37ºC) group (139.7±12.3 $U \cdot L^{-1}$) at 7 days after injection(P>0.05).
Conclusions: With the similar effect on the serum level of AST as Doxorubicin-lipiodol (37ºC), the treatment with lipiodol (60ºC) can greatly prolong the survival period of rabbits with VX2 cancer by inhibiting the tumors' growth.

PE273

Androgen signaling is involved in hepatitis C-related hepatocarcinogenesis

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Background/Aims: Hepatocellular carcinoma (HCC) is one of the male-dominant cancers, and hepatitis C virus (HCV) is one of the causes of HCC. It was reported that androgen receptor (AR) is expressed in HCC and its surrounding tissues. Androgen signaling and AR may be involved in hepatocarcinogenesis. In this study, we investigated whether HCV interacts with androgen signaling in human hepatocytes.
Methods: HCV protein expression vectors were co-transfected with AR-expression vectors and AR-responsive element-driven reporter vector into immortalized human hepatocytes (IHHs) and human hepatoma cell lines. Kinase inhibitors were used to examine the activation of the Akt, MAPK, and JAK/STAT3 pathways. Real-time PCR and Western blotting were performed. Cell culture grown HCV (HCVcc) were also used, and angiogenesis was evaluated by tubule formation assays in human coronary microvascular endothelial cells in the presence of 5 -androgen-1 -ol-3-one.
Results: HCV enhances AR-responsive gene expression in the presence of androgen. HCV core protein has the strongest effects and induced AR activation associated with JAK/STAT signaling. HCVcc enhances VEGF mRNA expression and angiogenesis.
Conclusions: HCV core protein is an enhancer in androgen signaling and can be expected to play an important role in HCV-related hepatocarcinogenesis.

PE274

Arsenic trioxide combined with Chinese traditional Jianpiliqi formula in the treatment of advanced hepatocellular carcinoma: an analysis of 32 cases

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Background: To evaluate the therapeutic outcomes and the toxicity of the combination of arsenic trioxide and the Chinese traditional Jianpiliqi (JPLQ) formula in the treatment of advanced hepatocellular carcinoma (HCC).
Methods: Patients with advanced HCC, not suitable for resection but with normal major organ functions, were enrolled to receive a therapeutic regimen consisting of intravenous arsenic trioxide (6 mg / m^2) administration from days 1-14, and an oral administration of JPLQ formula twice daily from days 1-28. Each cycle was composed of 28 days and treatment could expand up to 4 cycles before evidences of intolerable toxicity or disease progression.
Result: One patient had partial response, one had minor response, 15 showed stable disease and 15 (46.9%) had disease progression. Total disease control rate was 53.1%, median survival time was 5.8 months (2-23.9 ms), and time to progression was 4.2 months (1-16.9 months). The incidences of grade 1-3 abdominal distention and nausea/vomiting were 65.6% and 37.5%, respectively. Increases in GGT occurred in 4 patients (2 grade 2, 1 grade 3, and 1 grade 4) and increases in serum creatinine in 2 patients (1 grade 3 and 1 grade 4), respectively.
Conclusion: Compared with the single arsenic trioxide treatment reported in past literature, treatment by arsenic trioxide combined with JPLQ showed modestly higher anti-tumor activity and tolerable toxicity in patients with advanced HCC; its manageable toxicity and increased tumor response rate may offer a better treatment regimen, and deserve further investigation.

PE275

The inhibition of gene silencing of osteopontin in the invasion and metastasis of human hepatocellular carcinoma cell lines

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Aim: To investigate the effect of osteopontin (OPN) expressions down-regulated by RNA interference (RNAi) on the invasion and metastasis of human hepatocelluar carcinoma (HCC).
Methods: HCC cell line (HCC-LM3) was transfected with the chemically synthesized small interfering RNA (siRNA) in study arm and with non-specific siRNA in control arm. Real-time PCR and Western blotting were used to quantify the mRNA and OPN protein levels. The malignant phenotypes including cellular growth rates, colony formation and Matrigel invasion activities of the HCC cell line were analyzed.
Results: In study arm OPN mRNA expressions decreased 75% and OPN protein decreased 80% compared to those of blank arm. The number of formed colonies and migrating numbers of the cells in vitro decreased significantly (64.6% and 59.6% respectively) in study arm compared to these of blank controls ($p<0.05$). The parameters in the control arm did not differ from those of the blank arm ($p>0.05$).
Conclusion: The specific siRNA was able to reduce OPN expressions at both the mRNA and protein levels and significantly diminished the invasiveness of HCC cells.

PE276

The inhibition of MIF siRNA in the expressions of VEGF in hepatocellular carcinoma cells

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Aim：To investigate the inhibitory effect of MIF siRNA on the expressions of MIF and VEGF in hepatocellular carcinoma (HCC) cells.
Methods: The expressions of MIF and VEGF in HCC and adjacent tissues were detected from 4 patients. Specific siRNA targeting MIF gene was synthesized, and transfected into the HCC cell lines (PLC and HepG2) in study group and non-specific siRNA was used in controls. The mRNA and protein expressions of MIF and VEGF were examined by PCR and western blot.
Results: MIF and VEGF mRNAs were overexpressed in the HCC tissues compared with adjacent tissues (RQ=8.91±1.85 and 3.00±0.86, $P<0.01$). The mRNA and protein expressions of MIF and VEGF of HCC cell lines significantly decreased in study group compared with controls ($P<0.01$). VEGF mRNA levels decreased 75.6%±2.6%; 79.8%±1.2% in PLC, and 73.6%±4.6%; 80.7%±2.2% in HepG2 cells when disposed with siRNA 50nM and 100nM. VEGF protein levels also significantly reduced in study group（$P<0.01$）.
Conclusions MIF and VEGF mRNAs were overexpressed in the HCC tissues in vivo, and MIF siRNA was able to knock down the expressions of MIF and VEGF in HCC cell lines in vitro.

PE277

Identification of differentially expressed genes in hepatocellular carcinoma by laser capture microdissection and microarray

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Aim: To identify tumor-associated genes by constructing transcription profiles of pure hepatocellular carcinoma (HCC) tissues and normal liver tissues with the combination of laser capture microdissection and microarray.
Methods: HCC cells and normal liver cells from resection samples of 4 patients were laser capture microdissected. Micro-RNA was isolated from them for linear amplification，then cRNA was tested with whole genome microarray. Differentially expressed genes were screened.
Results: The quality control of this technique was satisfactory with RNA Integrity Number>7, A260/A280 ratio for cRNA measurement=2.0~2.1 and good pictures for microarray. Compared with normal liver tissues, HCC had 1361 differentially expressed genes, with 607 being up-regulated and 754 being down-regulated genes respectively. Among the top ten ranked up- and down-regulated genes (total 20), 5 genes were known as HCC differentially expressed genes, 11, known as other tumors expressed genes previously.

Four unknown tumor related genes (DEPDC1B, ASPM, FCN2 and BBOX1) were detected in this study.
Conclusion: The combination with laser capture microdissection and microarray was effective in screening the differentially expressed genes of HCC.

PE278

The Computed Tomography (CT) imaging Characteristics of Hepatocellular Carcinoma In Young Patients on Initial Presentation and Their Relationship with Clinical factors and Prognosis

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Background/Objective: Young patients present with large HCC on initial presentation are not uncommon. Our aim is to study the computed tomography(CT) imaging of HCC and the clinical features of this special group of patients.
Methods: 521 HCC patients had CT imaging of liver peformed in a three year period, 385 patients had CT imaging peformed at the time of initial HCC diagnosis in our centre and were selected. They were divided into three age groups: Young patients with age </= 40 year-old(Group 1), Age 41 to 60(Group 2), Age >60(Group 3) to study imaging and clinical factors. Univariate and multivariate analysis by Cox regression model done to look for prognostic predictive factors.
Results:

Table 1. Basic characteristics of HCC patient classified according to age

Characteristics	Group 1 ≤40y.o. (n=13)	Group 2 41-60 y.o. (N=193)	Group 3 >60 y.o. (N=180)	p-value
Male(%)	13(100%)	176(96.2%)	167(88.4%)	0.01*
Family of HCC, +ve:-ve	0:0	23:122	21:105	0.46*
Symptomatic at diagnosis, +ve: -ve	11:2	113:70	86:103	<0.01*
HBs Antigen positive, +ve: -ve	12:1	166:16	134:54	<0.01*
HBe Antigen positive, +ve: -ve	4:3	18:120	13:79	0.01*
HCV antibody, +ve: -ve	1:9	11:131	22:117	0.11*
Alcoholic, drinker:non-drinker	1:11	39:127	32:141	0.30*
Haemoglobin,g/dL	14(10-16)	13(7.3-18)	12(4.1-16)	<0.01*
AFP, ng/ml	46000 (131-7.4X10^6)	118(2-3.6X10^5)	96(1-3.6X10^6)	<0.01*
Platelet count, 10^9/L	244(65-308)	179(12-763)	156(11-990)	0.06*
Child stage, no. (%)				
A	7(63.6%)	131(72.8%)	120(65.2%)	0.01*
B	4(36.4%)	41(22.8%)	38(20.7%)	
C	0(0%)	8(4.4%)	26(14.1%)	
CT imaging findings -				
Bilobe involvement, yes: no	10:3	87:96	83:106	0.07*
Size of lesion, cm	10(3.5-20)	5.5(0.6-20)	6(1.0-20)	0.0*
Infiltrative type, Yes: No	6:7	39:144	29:160	0.02*
T staging				
1	1(7.7%)	17(9.3%)	18(9.5%)	0.51*
2	3(23.1%)	52(28.6%)	68(36%)	
3	2(15.4%)	35(19.2%)	40(21.1%)	
4	7(53.8%)	78(42.9%)	63(33.3%)	
M staging				
0	9(69.2%)	125(68.3%)	114(60.3%)	0.26*
1	4(30.8%)	58(31.7%)	75(39.7%)	
N staging				

Table 3. Positive findings in Multivariate analysis of prognostic factors

	Odd ratio	95 % CI
Symptomatic disease at diagnosis	1.65	1.23-2.34
Child' s stage		
B	2.02	1.49-3.73
C	3.28	2.31-5.26
Tumour stage		
2	1.50	0.76-2.96
3	3.54	1.77-7.06
4	4.04	2.05-7.97
Metastasis stage		
M1	2.60	1.72-3.94
Infiltrative tumour	1.49	1.07-2.07

PE279

A public survey of the knowledge, attitudes and beliefs of adult Singaporeans on liver cancer screening

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Background: Most Singaporean patients with hepatocellular carcinoma(HCC) present late with advanced disease. This may be due to inadequate knowledge about HCC or benefits of screening.
Aims: To evaluate the knowledge, attitudes and beliefs of the Singaporean public on HCC and screening for liver cancer.
Methods: Self-administered questionnaires to obtain information on knowledge of HCC and attitudes/beliefs towards cancer screening were distributed to attendees of the 2006 National Foundation of Digestive Disease Day public lecture.
Results: 235 questionnaires were distributed with a response rate of 83%. Mean age was 56(±10) years. 55.6% were female and 96.4% Chinese. Only 3.6% of responders were hepatitis B carriers. Most identified alcohol, hepatitis B and liver cirrhosis as risk factors for HCC(86.2%,71.9%,75.5% respectively) but not hepatitis C(49%). 49.5% believed hepatitis A to be a risk factor. 84.7% knew HCC detected early is potentially curable. 62.8% knew HCC may be asymptomatic. Only 33.7% knew where to find information on HCC. Responders <55years would mainly use the Internet whereas those >55years would consult their GP/Polyclinic doctor($p<0.001$). Majority(59.2%) thought HCC was best diagnosed by blood tests and 29.6% believed HCC is contagious through sharing of food. Majority(72.4%) felt that annual screening for HCC is worthwhile. Main reasons against screening were cost and perceived low HCC risk.
Conclusions: From this survey of predominantly elderly, Chinese, non-hepatitis B carriers, most had adequate knowledge of HCC and had a positive attitude towards screening for HCC. Primary care physicians play an important role in educating the older public (age>55years) about HCC.

PE280

Selection and analysis of aptamers binding Lens culinaris agglutinin-reactive alpha-fetoprotein

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Background/Aims: Lens culinaris agglutinin-reactive alpha-fetoprotein (AFP-L3) is a specific protein produced by hepatocellular carcinoma(HCC), which is more valuable than AFP in the diagnosis of HCC. Aptamers are oligonucleotide ligands binding to target molecules sensitively and specifically, which are screened from a great capacity of synthetically oligonucleotide library by systematic evolution of ligands by exponential enrichment (SELEX). Our aims were to select the aptamers against AFP-L3 from a self-designed ssDNA library for potential application in diagnosis of HCC.
Methods: A random ssDNA library and its corresponding primers were designed and synthesized. Aptamers against AFP-L3 were selected by SELEX. Individual aptamers were separated by polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP) analysis and characterized.
Results: A ssDNA library of 78 nucleotides with 40 random nucleotides in middle were designed and used for the selection. The binding rate of library against AFP-L3 was increased from 5.1% to 48.2% after 13 round selection. Seven aptamers (S1 to S7) were isolated, and their sequences in random region and secondary structures were different from each other. All aptamers could bind AFP-L3 in a different extent, and the dissociation constants of S4 and S7 are 650nmol/L and 132nmol/L. Conclusions: Aptamers for AFP-L3 are successfully screened out and could bind AFP-L3 specifically.

PE281

Expression change of NK cells receptor NKG2D from human peripheral blood in patients with primary carcinoma of liver

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Aim: To investigate the expression change of NK cells receptor NKG2D from human peripheral blood in patients with primary carcinoma of liver，and study the relationship between NKG2D expression and cytotoxicity of NK cells.
Methods: Flow cytometry was used to determine the number of NK cells and the expression of NK cells receptor NKG2D from human peripheral blood in patients with 20 case primary carcinoma of liver，23 case hepatitis B cirrhosis，20 case hepatitis B and 20 healthy cases，and enzyme mark instrument was used to detect cytotoxicity of NK cells in all cases.
Results: killing rate of NK cell for K562 cell,NKG2D expression level of NK cells, and the number of NK cells in the patients with primary carcinoma of liver decreased significantly（$P<0.05$），compared with those in the healthy subjects and hepatitis B group ,And decreased a little compared with those in the hepatitis B cirrhosis ($P>0.05$).The activity of NK cells showed a obvious

positive- correlation with the number of NK cell and expression level of NK cell receptor NKG2D.
Conclusion: The cytotoxicity of NK and the NKG2D expression of NK cells decreased significantly from human peripheral blood in patients with primary carcinoma of liver .The activity of NK cells is closely related to the NKG2D expression level of NK cells. enhancing the NKG2D expression level of NK cell may provide a new idea for Adoptive immunotherapy of primary carcinoma of liver.

PE282

Diagnosis of Glypican-3 protein for primary hepatic cancer is superior to alpha-fetoprotein

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Aim: To investigate diagnostic value of glypican-3(GPC3) and alpha-fetoprotein （AFP ）in serum and tissues for primary hepatic cancer(PHC).
Methods: Sixty-six PHC and 32 cirrhotic patients were enrolled. In PHC patients,male /female was 48:18, age was 55.4 ± 9.91.of them, 16 patients were defined as stage Ⅰa-Ⅱa. In cirrhotic patients, male /female was24:8, age was 53.3 ± 5.81. SerumGPC3 was detected using ELISA. Serum AFP was detected using electrochemiluminescence. The hepatic expressions of GPC3 and AFP were measured using immunohistochemistry in 21 PHC and 6 cirrhotic patients.
Results: The cutoff value of AFP diagnosis for PHC was 400 μ g / L or more, AFP positive in PHC patients was 28.8% (19/66); The cutoff value of GPC3 diagnosis for PHC was 300ng / L or more, GPC3 positive was in 47.0 % (31/66), P = 0.031. In Ⅰa-Ⅱa stage PHC patients,the positive of GPC3 and AFP was 62.5% (10/16), 0(0/16), respectively,P = 0.000. In serum AFP negative or positive patients, the positive of GPC3 was 46.7% (14/30) , 47.2% (17/36), respectively,P = 0.964. The relationship between GPC3 with age, sex, Child-pugh grade, HBV infection, tumor size and metastasis were not observed.The positive expression of GPC3 and AFP in hepatocellular carcinoma tissue was 85.7% (18/21), 4.8% (1 / 21), respectively, P = 0.000. Neither GPC3 ,nor AFP in the paracarcinomatous and cirrhotic tissue, was expressed.
Conclusions: Diagnosis of Glypican-3 protein for primary hepatic cancer is superior to AFP.GPC3 can be regared as a early marker to diagnosis PHC.

PE283

Inhibitory effects of curcumin on the proliferation and the metastasis of hepatocellular carcinoma HCCLM3-RFP cell line in vitro and in vivo

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Objective: To investigate the effects and the possible mechanism of curcumin on the proliferation and the invasion of human hepatocellular carcinoma in vitro and in vivo.
Methods: HCCLM3-RFP cell lines were maintained in DMEM medium supplemented with 10% fetal bovine serum. The fluorescent areas of HCCLM3-RFP were photographed daily and repeated in 4 consecutive days after curcumin treatment for obtaining cell growth curves. The cell morphologic changes were also observed. Cell invasion experiment was performed with Boyden chamber array. The RFP-expressing human HCC xenograft model in nude mice was established to study the anti-tumor effects of curcumin. The CTC was detected by FACS. The expression of cyclinD1 and MMP-2 was detected by SYBR Green Real-time PCR.
Results: After incubation with 20 M, 10 M and 5 M curcumin respectively for 24, 48 and 72 hours, the growth of HCCLM3-RFP was significantly inhibited and some morphologic changes were observed. The mean tumor size in nude mice treated with curcumin since day 21were significantly less than those of the control group($p < 0.01$). The mean metastasis area of lung and the number of CTC in curcumin group on day 35 were remarkably less than in the control group($p < 0.01$). The mRNA levels of cyclin D1（$p < 0.01$） and MMP-2（$p < 0.05$） in curcumin group on day 35 were significantly lower than in the control group.
Conclusion: Curcumin can inhibit the proliferation and invasion of HCCLM3 cell line not only in vitro but also in vivo mainly by down-regulating the expression of cyclin D1 and MMP-2 in mRNA levels.

PE284

Phosphorylated ERK is a potential predictor of sensitivity to therapy with sorafenib in hepatocellular carcinoma – evidence from in vitro study

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Background: Sorafenib is the first agent that has demonstrated an improved overall survival benefit in advanced hepatocellular carcinoma (HCC) and thus sets the new standard for the first-line treatment of advanced HCC. However, it remains unresolved to predict the drug sensitivity in treating HCC with sorafenib. Pretreatment pERK level has been shown to be associated with favorable response to such therapy in a phase 2 preclinical study, indicating that pERK may be a potential biomarker for treatment of HCC with sorafenib.
Methods: The effects of sorafenib and 5-Fluorouracil on cell proliferation were evaluated by cell viability assay in four types of HCC cell line (SMMC-7721, MHCC97-L, MHCC97-H and HCCLM6), with different metastatic potential and basal pERK expression. Levels of pERK expression were determined by immunocytochemical analysis and quantification, along with Western Blot analysis. Correlation analysis was carried out between the IC_{50} values of drugs and Mean Optical Density values of pERK.
Results: The basal pERK levels increased stepwise in cell lines in accordance with their metastatic potential. Sorafenib inhibited ERK phosphorylation at a concentration between 5 and 20 μM dose-dependently, while no changes were observed after 5-FU treatment. Correlation analysis between the IC_{50} values and MOD values of pERK revealed that the effects of sorafenib were significantly correlated with basal pERK levels (Spearman r=-0.8671, P=0.0003). On the other hand, the resistance to 5-FU were significantly associated with basal pERK expression in these HCC cell lines (Spearman r=0.7846, P=0.0009).
Conclusions: In this vitro study, pERK was confirmed to be a useful biomarker predictive of sensitivity in treating HCC with sorafenib. The RAF/MEK/ERK pathway may be involved in invasion, metastasis and drug resistance to traditional chemotherapy in HCC.

PE285

Mechanisms of hepatic IGF-II dynamic expression and apoptotic-related bcl-2 during malignant transformation of hepatocytes

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Background: To investigate the dynamic expression of IGF-II and IGFBP-3 and its alteration of bcl-2 in HCC.
Methods: HCC models were induced with 2-FAA on male SD rats. Morphological changes of livers were observed and the dynamic changes of liver or serum IGF-II, IGFBP-3, and bcl-2 were quantitatively analyzed by ELISA. The expression and distribution of liver IGF-II were observed by immunohistochemistry.
Result: Hepatocytes from granule-like degeneration to a typical hyperplasia to HCC and the progressing increasing of the levels of hepatic IGF-II after rats induced by 2-FAA. The levels of IGF-II in hepatoma and sera were significantly higher than any of other groups. The positive relationship of IGF-II was found between liver and sera ($P<0.01$). The IGFBP-3 levels in hepatoma were significantly lower than that in other groups ($P<0.01$)，and the progressing increasing of the levels of hepatic bcl-2 expression during the course. The levels of bcl-2 in hepatoma tissues were significantly higher than those in normal and degeneration ones. The immunohistochemistry evidences indicated the positive expression and hepatocyte distribution of bcl-2 in rat hepatoma.
Conclusion: Hepatic IGF-II, IGFBP-3 and bcl-2 may participate in hepatocyte canceration and accelerate the occurrence and development of HCC. The expression of IGF-II and IGFBP-3 could be useful molecular markers for early diagnosis and prognosis of HCC.

PE286

Role of HBV, HCV and aflatoxin in hepatocellular carcinoma in Bangladesh and comparison of PIVKA-II and AFP as diagnostic marker

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Background: This study was done to assess the etiological role of hepatitis B virus (HBV), hepatitis C virus (HCV) and aflatoxin B1(AFB1) in development of hepatocellular carcinoma (HCC) in Bangladesh. It was also investigated whether alpha-feto protein (AFP) and protein induced by vitamin K absence or antagonist II (PIVKA-II) has any diagnostic advantage over each other

Methods: Fifty five histologically proven HCC patients were tested for serological markers of hepatitis B and hepatitis C, and AFB1-DNA adduct. During the diagnosis, they were also investigated for liver function tests, AFP PIVKA-II.

Results: Out of fifty five HCC patients, 41(74.5%) were found positive for serological markers of HBV, 21(38%) for HCV and 15(27%) for both. Eight cases (14.5%) were negative for the markers of HBV and HCV. However, none had AFB1-DNA adduct above normal range. Both PIVKA-II and AFP is strong marker for HCC with satisfactory level of sensitivity and specificity; but PIVKA-II is more sensitive (92.7%) and AFP is more specific (96%).

Conclusions: HBV and HCV is the major etiological agent responsible for the development of HCC in Bangladesh.

PE287

Expression features of NF-κB and intervention of its single transduction pathway on influences of malignant transformation of hepatocytes

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Background: To investigate the influences on the malignant transformation of hepatocytes through the intervention of NF-κB activation pathway.

Method: HCC models were induced with 2-FAA on SD rats, thalidomide was administered intragastrically and rats were sacrificed fortnightly interval to the twelfth week. Morphological changes were observed by HE staining. NF-κB expressions were detected by IHC. The relationship between NF-κB expression and pathological characteristics in HCC and non-HCC were analyzed.

Results: Rat hepatocytes showed vacuole-like denaturations at the early stages, then dysplastic nodules appeared at middle stage, and finally progressed to tubercles of cancerous nest, all of which were highly differentiated HCC. Thalidomine can repress the morphologic change of liver cells. There were only punctiform denaturations at the early and middle stage; Nodosity hyperplasy and minority atypical hyperplasia were found at the finally stage. The IHC results demonstrated that NF-κB level was significantly higher than those in normal ones, and the NF-κB level of livers in HCC was higher than those in thalidomide group. An increasing tendency of NF-κB was found from normal to HCC. NF-κB in HCC were significantly higher than those in NC. The NF-κB levels with thalidomide intervence raised first and decreased later. NF-κB expressions in HCC were higher than that in their non-cancerous tissues. No positive relationship presented between NF-κB expression and histological differentiation grade or the number of tumor, and size of tumor.

Conclusion: Decrease NF-κB expression can inhibit HCC development and NF-κB is expected to be a new molecular target of HCC therapy.

PE288

Clinical Values of quantitative analysis of vascular endothelial growth factor in liver tissues and sera of patients with hepatocellular carcinoma

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Backgroud: To quantitative the expression levels of vascular endothelial growth factor (VEGF) in tissues and sera of hepatocellular carcinoma (HCC) for exploring the clinical values of VEGF in development and metastasis of HCC.

Method: The cellular distributions of VEGF expression in HCC tissues were investigated by immunohistochemistry. The levels of total RNA and VEGF were quantitatively detected in HCC, their paracancerous, and distal cancerous tissues, respectively. Simultaneitily, serum VEGF were analyzed in patients with chronic liver diseases for clinical values.

Results: The positive expression showed palm-yellow or palm- brown granules and distributed in hepatocyte plasma of HCCs. The incidence of VEGF was 63.9% in HCC tissues, 78.3% in non-encapsulated HCCs, and 90.9% in HCCs with extrahepatic metastasis, respectively. No significant difference was found between hepatic VEGF and HCC diameter or differentiation degree. The specific concentration (pg/mg liver) of VEGF expression was significantly higher ($P<0.01$) in HCC than their paracancerous or distal cancerous tissues, respectively. The circulating VEGF was abnormally elevated in HCC. If the cut off values was more than 280 pg/mL, the incidence of serum VEGF was 88.4% in HCC, 14.3% in chronic hepatitis, and 10% in liver cirrhosis, respectively. The combined VEGF and AFP can increase positive rate up to 94.2% for HCC.

Conclusion: The VEGF overexpression is a useful marker for vascular invasion and metastasis of liver tumors.

PE289

Treatment Of Hepatocellular Carcinoma By Radiofrequency Thermal Ablation Versus Transcatherter Hepatic Arterial Chemoembolization With Or Without Subcutanous Viscum (Fraxini 2) Injecton.

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[1] Hepatology, [2] Radiodiagnosis

Background: Hepatocellular carcinoma (HCC) represents a major health problem world wide. It accounts for 90% of all primary liver cancers and is the fifth most common malignancy (1).

Objectives: Evaluation of radiofrequency thermal ablation versus transarterial hepatic chemoembolization with the effect of Viscum (Fraxini 2) on tumour recurrence.

Methods: 60 patients with HCC were enrolled in the study. Group 1 include 30 patients and were treated with radiofrequency thermal ablation (15 patients of them received viscum 2 by subcutaneous route for 2 years). Group 11 included 30 patients with HCC and were treated by TACE (15 patients of them received viscum 2 subcutaneously for 2 years).

Results: Group 1 patients showed total ablation in 70% with persistant inactivity during 2 years follow up. Group 11 did not show significant difference from Group 1 as regards relapse rate nor the performance status.

Complications as nausea, vomiting, fever, jaundice, and elevation of transaminases were significantly more encountered with TACE. Viscum 2 did not significantly arrest tumour recurrence.

Conclusion: Non surgical patients with HCC can achieve curative treatment with radiofrequency with minmal side effects. TACE is a palliative treatment option for large HCC.

PE290

Breaking The Needle Diameter Limit For Radiofrequency Thermal Ablation For Hepatocellular Carcinoma.A New Technique

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A new technique had been attempted to increase the field of radiofrequency ablation of expandable electrode needles in the treatment of hepatic neoplasms much larger than the routinely covered size of 5-7 cm according to the needle size overcoming the technical difficulties usually met with in the overlapping balls technique due to the hyperechoic focus that develops at the needle tip making reinsertion difficult and inaccurate.

In this technique, two or three needles were inserted from the start into the mass with accurate estimation of the exact field of ablation of each needle trying to cover the whole extent of the mass before application of radiofrequency waves. 40 patients were included in the study, all presented with hepatic neoplastic mass lesion that range in size between 7 and 10 cm in its maximum diameter. All had a pretreatment helical (triphasic) CT study for accurate delineation of the whole extent and vascularity of the mass. Two

needles were sufficient to cover the whole extent of the mass in 23 patients (57%) while in the remaining 17 patients (43%) three needles were necessary. The procedure was done under general anathesia and ultra sound guidance, patients tolerated procedure well with smooth recovery. No major complications. Follow up spiral (triphasic) CT was done 2 weeks after ablation revealed percentage of tumour necrosis of 90% or more in 30 patients (75%), 70-90% in 6 patients (15%) while in the remaining four patients (10%) the percentage was 50-70% necrosis.
In conclusion this technique should be considered in the treatment of hepatic masses larger than the usual field of the needle.

PE291

Glypican-3 amino terminal marker for early detection of HCC

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Introduction: HCC is the 6th common cancer. Global increase of hepatitis B and C infection, the incidence of HCC has been steadily increasing. Egypt seroprevalence of HCV in Nile delta was 20 -35%. AFP had limited sensitivity 60% and specificity 90% for small HCC. GPC-3 oncofetal protein over expressed in HCC.
Aim: Evaluating the validity of Glypican-3 as an early detector of HCC.
Material: 10 healthy controls and 40 HCV positive patients:
10 patients with chronic hepatitis C virus infection.10 patients with compensated cirrhosis [child-Pugh class A and B].10 patients with decompensated cirrhosis [child-Pugh class C]. 10 patients with HCC.
Methods:Liver functions: ALT, AST, Bilirubin(T), Albumin, γGT.Tumor markers: AFP and GPC-3.Viral markers: HCV antibodies, HBs Ag and HBc Ab.
Results: The median value of GPC-3 in HCC, DC, CC was significantly higher than chronic hepatitis and control groups. No significant correlation found between AFP and GPC-3. AUROC of AFP was 0.85 & AUROC of GPC-3 was 0.84. The diagnostic Sensitivity of AFP (20 ng/ml) was 70% with PPV 53.8%. The specificity was 85% with NPV 91.9%. While the diagnostic Sensitivity of GPC-3 (2 ng/ml) was 100% with PPV 27%. The specificity was 42.2% with NPV 100%. Combined serial approach of AFP and GPC-3 improved the specificity to 87.5%.
Conclusion:GPC-3 although it is a serological test for early detection of HCC, it showed limited specificity, where It is detected in different stages of chronic liver disease, as it is an oncofetal protein produced by regenerating liver cells. The diagnostic signature approach for simultaneous determination of AFP and GPC-3 may improve the prediction accuracy of HCC patients in those showing seronegativity to AFP.

PE292

Outcome of inoperable hepatocellular carcinoma patients receiving transarterial chemoembolization: Retrospective analysis in an Asian regional hospital

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Background: Hepatocellular carcinoma (HCC) is a common cancer worldwide causing substantial mortality. Although surgical resection is a form of curative treatment in HCC, only a minority of patients is suitable for this treatment and the postoperative recurrence remains high. Transarterial chemoembolization (TACE) is a treatment option for inoperable HCC and it was proven by randomized control trials that TACE can prolong survival in selected patients. The aim of this study is to evaluate the survival and the prognostic factors in patients with advanced HCC treated by TACE.
Methods: Seventy four patients with inoperable HCC diagnosed from January 1998 to December 2003 were analyzed retrospectively in this study. Only patients with unresectable HCC or who refused operation were included. Patients with advanced cirrhosis, extrahepatic metastasis or previously treated HCC were excluded. Multiple host, tumor and treatment variables were analyzed in order to evaluate the predictive factors of favorable response to treatment and better survival.
Results: The median survival of the study patients was 213.5 days. The cumulative survival rates at 1 year, 2 year and 3 year were 28.4%, 12.2% and 6.8% respectively. By multivariate analysis, superselective cannulation performed in TACE (hazard ratio: 0.47, 95% CI: 0.23-0.95, p=0.034), embolization with gelfoam (hazard ratio: 0.30, 95% CI: 0.11-0.80, p=0.017), treatment interval more than 45days (hazard ratio: 0.33, 95% CI: 0.15-0.72, p=0.006), Child-Pugh grade B (hazard ratio: 5.62, 95% CI: 2.11-14.97, p=0.001), and pre-treatment serum αFP level (hazard ratio: 2.93, 95% CI: 1.50-5.73, p=0.002) were independent predictors of survival.
Conclusions: Survival of patients with inoperable HCC is still grave despite treatment. This study provided information in predicting the survival of patients with inoperable hepatocellular carcinoma treated by transarterial chemoembolization.

PE293

Predictors Related To Survival Of Cancer Of The Liver Italian Program (Clip) 0-1 And Clip 2-6 Hepatocellular Carcinoma (Hcc) In Japan.

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Background: Differences of predictors relating survival between early and intermediate / advanced hepatocellular carcinoma (HCC) remains unclear. The aim of this study was to elucidate the differences of predictors relating survival between CLIP 0-1 and CLIP 2-6 HCC patients in Japan.
Methods: Between 1985 and 2005, 362 CLIP-0-1 and 182 CLIP 2-6 HCC patients were recruited in the present study. Among 14 factors tested, factors related to survival were analyzed.
Result: Age <65, total bilirubin (TB) <2.0mg/dl, albumin (Alb) ≥3.5g/dl, prothrombin time (PT) ≥70%, platelet counts (Plt) ≥10.0 $10^4/mm^3$, single nodule, and type of treatment (surgery or local ablation therapy) were linked to increased survival at univariate analysis of CLIP 0-1 HCC patients. Of CLIP 2-6 HCC patients, TB <2.0mg/dl, Alb ≥3.5g/dl, des-gamma-carboxy prothrombin (DCP) <100mAU/ml, absence of vascular invasion, and type of treatment were correlated with survival. The following factors were related to survival by multivariate analysis: CLIP 0-1 HCC patients; age, Alb, single nodule, and absence of vascular invasion, CLIP 2-6 HCC patients; age, TB, Alb, alpha-fetoprotein (AFP) <100ng/ml, DCP, absence of vascular invasion, and type of treatment.
Conclusion: Age, albumin, vascular invasion were significant predictors of survival both CLIP 0-1 and CLIP 2-6 HCC patients. CLIP 0-1 HCC patients: single nodule; CLIP 2-6 HCC patients: lower levels of tumor markers and patients receiving promising treatment had a better chance of prolonged survival.

PE294

The role of gross classification as the predictor of microvascular invasion in hepatocellular carcinoma.

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Background; The presence of microvascular invasion (MVI) as the risk factor in hepatocellular carcinoma (HCC) is controversial. The aim of this study was to determine the outcomes and predictive factors after hepatic resection for HCC with MVI.
Methods; One hundred and ten patients who underwent curative resection for HCC were included in this retrospective study. The risk factors of these patients for recurrence-free and disease-specific survival were investigated, and the clinicopathological factors predicting the presence of MVI were also evaluated.
Result; Multivariate analysis showed that cirrhosis and MVI were identified as independent risk factors for recurrence-free survival. The 2-year recurrence-free survival rates for patients with and without MVI were 44.6% and 76.7%, respectively. Multivariate analysis showed that the number of tumors, presence of MVI, and IM were identified as independent predictors of disease-specific survival. The 5-year disease-specific survival rates for patients with and without MVI were 59.3% and 92.0%, respectively. By univariate analysis, MVI was significantly associated with greater tumor size, gross classification, histological grade, and intrahepatic micrometastasis (IM). Gross classification proved to be the only independent predictive factor

for MVI by multiple logistic regression analysis. The gross classification could be evaluated by preoperative imaging diagnosis.
Conclusion; MVI is strongly associated with recurrence and survival in HCC patients after curative resection. Furthermore, gross classification of HCC can be helpful in predicting the presence of MVI.

PE295

A phase I study of PXD101 (belinostat) in patients with unresectable hepatocellular carcinoma (HCC): a multicenter study by the Cancer Therapeutics Research Group (CTRG).

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Background: HCC is a common cause of cancer morbidity and mortality. PXD101 is a novel, low molecular weight, histone deacetylase inhibitor. This phase I study aims to determine dose limiting toxicity (DLT) and maximum tolerated dose (MTD).
Methods: Patient eligibilities include unresectable disease, ECOG 2, adequate organ functions. PXD101 was given intravenously on day 1-5 every 3 weeks; dose levels were: 600 (level 1), 900 (level 2), 1200 (level 3) and 1400 mg/m^2/day (level 4). DLTs are defined as grade 4 hematological toxicity or grade 3/4 non-haematological toxicity during cycle 1 (according to NCI CTC v3), or treatment delay >2 weeks. The MTD is defined as the dose below which > 2 of 3 or > 2 of 6 patients experiencing DLT.
Results: 18 patients were entered; level 1 (3), level 2 (3), level 3 (6) and level 4 (6). Grade 3/4/5 toxicities in cycle 1 included: raised ALT 1/0/0, diarrhea 1/0/0, abdominal distension 1/0/0, anaemia 1/0/0. A total of 56 cycles were administered; overall grade 3/4/5 toxicities: raised ALT 1/0/0, bilirubinaemia 1/0/0; cardiac ischaemia 1/0/0; diarrhoea 1/0/0, abdominal distension 2/0/0, anaemia 2/0/0; variceal haemorrhage 1/0/0; hypercalcaemia 1/0/0; hyperkalaemia 0/1/0; hyponatraemia 1/1/0; infection 2/0/0; liver dysfunction 0/2/0; muscle weakness 1/0/0; abdominal pain 1/0/0; prolonged QTc 1/0/0; syncope 1/0/0; seizure 1/0/0. There were 3 SD and 15 PD.
Conclusion: At the maximum dose of 1400 mg/m^2/day, MTD has not been reached. PXD101 is very well tolerated.
Sponsor: The Division of Cancer Treatment and Diagnosis, National Cancer Institute, USA.

PE296

Researches On Tumor Thrombus Of The Portal Vein In Hepatocellular Carcinoma

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Tumor thrombus (PVTT) is prone to be produced in the portal vein near the main tumor nodule for hepatocellular carcinoma (HCC) patients and its molecular mechanism is still unclear. In this study, we first established a HCC cell line named CSQT-01 from resected tumor thrombus in portal vein in a patient with histopathologically proved to be a moderately differentiated hepatocellular carcinoma . This cell line was composed of polygonal shaped cells and its peaks of the chromosome number was 69 and 77. Study on stem cell biology in this cell line suggests that CD133 cells represent about one fourth of the tumor cell population and CD133(+) cells possess a greater colony-forming efficiency, higher proliferative output, and greater ability to form tumor in vivo. With this cell line model and resected tumor thrombi specimen, we also studied the different expression of proteins in primary tumor and tumor thrombus and found 20 proteins expressed differentially between primary tumor and the PVTT. from these proteins, AnnexinV, Prx I , CycB were selected for further analysis to find potential biomarkers of PVTT in hepatocarcinogenesis.
For clinical study, we recommended a new tumor thrombus type system (type I～IV) according to anatomic features of portal vein and tumor thrombus of HCC developing modes, then evaluate this type system to predict prognosis of HCC patients. The retrospective data of 406 HCC patients with PVTT underwent resection shows that the 1y, 2y, 3y overall survival rates were 44.7％, 26.3％ and 19.7％ for type I, 29.9％, 20.6％ and 12.4％ for type II, 25.0％, 12.5％ and 3.6％ for type III, 27.3％, 0％ and 0％ for type IV, respectively, suggests tumor thrombus type system may be helpful to determine treatments and prognosis of HCC patients with PVTT.

PE297

Polyprenol could decrease the risk of hepatocarcinogenesis in HBV

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Background: Over-expression of P-glycoprotein (Pgp) is associated with liver cancer development from HBV . Glycoprotein synthesis in malignant tissues is limited by Dolichyl Phosphate (DolP). The aim of the present study was to investigate the effect of polyprenol (PP) which provides a DolP substitute in regulation of N-glycosylation on Pgp over-expression in the development of liver cancer in HBV infection.
Methods Human hepatocytes, infected with HBV and human hepatocarcinoma HEP 3B cell line were used. Pgp was assessed by an immunohistochemical technique. DolP fractions were analysed by HPLC methods.
Results It is confirmed that plasmatic membrans of hepatocytes cells contain 7,9 – 9,4% of Pgp (the total protein amount) as a resistance marker. HBV infected cells differ from normal hepatocytes in Pgp content by 4-5 times and HEP 3B cells differ by 10-12 times The study showed 5-fold DolP decrease in HBV infected cells and 10-fold DolP decrease in HEP3B cells. The investigations demonstrate that the situation can be changed by treatment with DolP and PP. The DolP concentration in HBV infected hepatocytes was returned to the normal level. It is established that DolP in the concentration 10^{-6} M aid 6-8-fold reducing Pgp in membranes of HBV infected cells.
Conclusions: These results indicate that noncontrollable accumulation of Pgp in HBV infected cells can be overcomed using stimulation with DolP substitution. Polyprenol is a promising new agent which usage can open up possibilities in liver cancer prevention in HBV infection.

PE298

The transcriptional factor Snail simultaneously triggers cell cycle arrest and migration of human hepatoma HepG2

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Background: Metastasis is one of the most complicated and major pathological processes responsible for poor prognosis of hepatocellular carcinoma. Snail was recently highlighted as a critical transcriptional factor for tumor metastasis.
Method & Result: Real time RT/PCR and Western blot analysis demonstrated that Snail mRNA and protein, respectively, were induced by 12-Otetradecanoylphorbol-13-acetate (TPA) in hepatoma cell HepG2. Blockade of gene expression of Snail by antisense oligodeoxynucleotide and/or siRNA technique can prevent not only the TPA-triggered EMT/cell migration and growth inhibition of HepG2 but also TPA-induced down-regulation of E-cadherin and up-regulation of p15INK4b. Moreover, the TPA-triggered promoter activation of p15INK4b was also prevented. On the other hand, two of the HepG2 clone overexpressing Snail, namely S7 and S15, had a scattered fibroblastic morphology and acquired higher motility than parental HepG2. Also, the proportion of G0/G1 phase of S7 and S15 was higher than that of parental HepG2, consistent with the longer doubling time of both cells. Semiquantitative RT/PCR analysis demonstrated a greatly elevated gene expression of Snail accompanied with decreased E-cadherin and increased p15INK4b in both Snail-overexpressing cells. On the transcriptional level, p15INK4b promoter activity was 2.6-fold higher in S7 as compared with parental HepG2. Furthermore, electrophoretic mobility of DNA fragments encompassing proximal p15INK4b promoter can be retarded by incubation of nuclear extract of S7.
Conclusion: Our results demonstrated that Snail play diverse trans-regulatory roles in HepG2. Notably, we suggested that Snail may upregulate p15INK4b gene expression by directly activating its promoter.

PE299

Intermediate Filament Protein Synemin is Implicated in Sinusoidal Remodeling in Hepatocellular Carcinoma.

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Background/Aims: Synemin is an intermediate filaments (IF) protein which affects the motility of several cell types by modulating the dynamic properties of alpha-actinin and F-actin. We have previously shown that synemin is expressed in resident hepatic stellate cells (HSC) and myofibroblasts (MF) in hepatic inflammation and fibrosis. In the present study we evaluated systematically the expression of synemin in a large cohort of western European hepatocellular carcinoma (HCC).
Methods: Single and double immunolabelin for alpha-smooth muscle actin (SMA), vimentin, CD31, CD34, CD68, CEA, CD10, cellular retinol-binding protein1 (CRBP-1) and synemin were performed on 75 paraffin-embedded HCCs and 10 controls.
Results: Synemin-positive HSCs/ MFs were a hallmark of non-neoplastic fibrotic liver tissue at the border to the neoplastic lesion but were absent from normal controls. Tumour cell plates of the trabecular and pseudoglandular types of HCC were covered by scattered synemin-positive cells outlining sinusoidal structures. A subpopulation of these cells showed features of pericytes while others resembled endothelium. This pattern correlated with the degree of differentiation and was not observed in poorly differentiated HCCs which generally contained rare intratumoral MFs.
Conclusion: The presence of synemin-positive HSCs/MFs in the vicinity of HCCs suggests a possible contribution of mesenchymal cells to the promotion of liver carcinogenesis. Since synemin expression is linked to motility, a migration of this cell type into the tumour and a differentiation in vascular mural cells may be implicated in sinusoidal remodeling and the expansion of the neoplastic population.

PE300

Comparison of clinical, laboratory characteristics and initial treatment response among patients with viral marker negative and viral marker positive Hepatocellular Carcinoma

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Aim: To estimate the prevalence of viral marker negative HCC and to compare the clinical, biochemical, histological, radiological characteristics and initial treatment response among patients with viral marker negative and viral marker positive HCC.
Methods: Medical records of patients diagnosed to have HCC visiting Aga Khan University Hospital, Karachi during January 1998 to December 2007 were reviewed. Patients were divided in to NBNC-HCC(those who have negative HBsAg and Anti-HCV antibody)and viral HCC(those who have positive HbsAg and Anti-HCV antibody)group.
Results: Out of 433 patients 68(15.7%) had NBNC-HCC. Over all mean age was 57.48± 10.9 years and 69.5% were males. The proportion of HCC detected under surveillance was significantly smaller in NBNC-HCC group(p0.02). There was no difference in distribution of age, gender, BMI, child score, bilirubin, serum albumin, prothrombin time and Alfa Feto protein in both groups. However, patients with viral-HCC were found to be more thrombocytopenic(52.67±86.7vs.226.15±153.9,p<0.001) and had hepatopulmonary syndrome. On liver biopsy greater proportion of moderate to poorly differentiated HCC was observed in NBNC group(19.2%vs.7.9%,p<0.001).
HCC measuring 5cm in diameter(60.3%vs.41.9%, p 0.01), non-solitary HCC(p0.038) and portal thromboses(p0.01) were strongly demonstrated in NBNC-HCC group. Involvement of right hepatic lobe and extra hepatic tumor spread was greater in NBNC-HCC group but that difference was not statistically significant. Out of 178 patients who underwent for liver transplantation(0.5%),TACE(36.7%),Resection(1%),ethanol ablation(2%) and chemotherapy(2%), poorer responses were observed in NBNC-HCC group (p 0.04).
Conclusion: HCC secondary to NBNC-cirrhosis is not uncommon. Patients with NBNC-HCC tended not to be under surveillance that leads to diagnoses at more advanced stage and poor prognosis.

PE301

Factors associated with survival in Asian Americans with hepatocellular carcinoma: a seven year experience at UCLA

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Background: Hepatocellular carcinoma is a common malignancy in Asia and is related to the high prevalence of chronic viral hepatitis. We examined the clinical features, treatments and survival rates in Asian Americans with HCC.
Methods: Retrospective cohort study of 278 HCC patients who presented to the UCLA Liver Cancer Center in Los Angeles, California, USA from September 2000 to December 2007.
Results: Two hundred and seventeen of 278 (78%) HCC patients were male, 58% and 30% had HBV and HCV infection respectively, and 73% had cirrhosis. HCC patients detected by surveillance had smaller tumor sizes, more within the Milan and UCSF criteria, lower HCC Tokyo system scores and had improved 1,3,5 year overall patient and disease free survival rates compared to HCC patients who presented with symptoms ($p<0.01$ to $p<0.0001$). By multivariate analysis, independent predictors of patient survival were tumor volumes greater than 5cm (HR1.48, p=0.04), AFP per unit $\log_{10}$ increase (HR 1.12, p=0.02), HCC Tokyo score per unit increase (HR 1.3, $p<0.0001$), liver transplantation (HR 0.14, $p<0.0001$), hepatic resection (HR 0.18, $p<0.0001$), RFA (HR 0.17, $p<0.0001$), TACE (HR 0.44, p=0.0006), and Hepatitis B infection (HR 0.71, p=0.03). Factors associated with disease free survival were age per year increase (HR 1.01, p=0.03), MELD per unit increase (HR 0.97, p=0.0049), liver transplantation (HR 0.23, $p<0.0001$), and hepatic resection (HR 0.39, $p<0.0001$).
Conclusion: HBV and HCV infection accounts for the majority of HCC in Asian Americans. HCC detected by surveillance resulted in treatments which improved overall patient and disease free survival.

PE302

Vimentin Biomarker for Detection of Small Size (2 cm) Tumor of hepatocellular carcinoma

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Treatment of small (≤2cm) HCC tumours can be achieved by surgical resection and complete eradication always correlates with good patient's outcome, with low local recurrence and high survival rates. Indeed, surveillance program for the early detection of small HCC tumour is imperative to facilitate curative treatment, and hence better survival. Discovery of new blood-based biomarkers is obligatory and vimentin is a distinct novel small HCC tumour marker herein identified using proteomics. **Experimental design:** A total of 76 liver tissues were evaluated by 2-DE analysis. Differentially expressed proteins were unequivocally identified by MALDI-TOF/TOF and validation of the best candidate from protein to gene levels. Indirect ELISA assay was developed to detect soluble vimentin from 152 serum samples. **Results:** Vimentin was significantly over-expressed in small HCC tumours compared to non-malignant controls and maintained expression in >2cm tumours using 2-DE analysis. Blind verification displayed over-expression of vimentin in both transcripts and proteins levels. Soluble vimentin was significantly detected at high level in small HCC as well as in overt HCC tumours. Receiver operating characteristic analysis showed vimentin exhibited 40.91% sensitivity and 87.50% specificity in detecting small HCC at a cutoff of 245ng/ml. Combined diagnostic performance of soluble vimentin and serum AFP increases the detection sensitivity and specificity to 50.53% and 98.15%, respectively. **Conclusion**: In this context, over-expression of vimentin is associated with the favourable ≤ 2cm sub-class of HCC thus may potentially be used as an effective serum-based diagnostic marker for cancer surveillance in high-risk cirrhotic patients.

PE303

Yes Associated Protein (YAP) Is An Independent Prognostic Marker for Overall and Disease-Free Survivals In Hepatocellular Carcinoma

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Purpose: Our recent comparative oncogenomic analysis in mouse model has identified YAP (Yes associated protein) as a novel oncogene in HCC. However, its clinical significance is unknown. In this study, we aimed to investigate the clinical values of YAP as an independent prognostic marker

in HCC. Experimental Design: A total of 177 HCC cases with retrospective clinicopathologic and follow-up data were recruited in this study. Both tumor and adjacent non-tumor tissues were examined for immunoreactivity of YAP expression by immunohistochemistry. Clinicopathologic features and YAP expression were investigated with Pearson χ^2 test. HCC-specific disease free survival and overall survival with YAP expression were analyzed by Kaplan-Meier curves and Log-rank test. Cox regression was used to test the independence and magnitude of the effects. Results: YAP was found over-expressed in HCC (62.1%) with nuclear expression pattern. Positive YAP immunoreactivity was significantly correlated with worse tumor differentiation grade (P=0.021) and high serum alpha-fetoprotein (AFP) level >400 ng/ml (P<0.001). Kaplan-Meier plot and Cox Regression showed that YAP was an independent predictor for HCC-specific disease free survival (hazard ratio, 1.653; 95% CI, 1.084-2.522; P=0.02) and overall survival (hazard ratio, 2.226; 95% CI, 1.312-3.778; P=0.003). Conclusions: YAP expression in HCC is correlated with tumor differentiation and serum AFP level. It served as an independent prognostic marker for HCC.

PE304

Understanding of Cellular and Molecular Physiology of Hepatocellular Carcinoma through Integrative Analysis of Tissue Proteome and Transcriptome Data

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Background: Integrative analysis of global protein and mRNA expression patterns could help researchers to understand cancer cell physiology without the need of any prior hypothesis.
Methods: We used a 2D-PAGE approach to profile and compared the global protein expression profiles of hepatitis B virus-related HCC tissues, adjacent non-tumor liver tissues, normal liver tissues and HCC cell lines. Subsequently, we established the bioinformatic tools for integrative analysis of gene expression and protein expression data. We compared the dysregulated protein list and the dysregulated gene lists obtained by meta-analysis of microarray gene expression data from 6 research centers in different countries.
Results: We identified 66 proteins dysregulated in HCC. Hierarchical clustering analysis revealed that there was a progressive change of protein expression patterns from normal liver, adjacent non-tumor liver tissues, HCC tissue, then to HCC cell lines. According to the biological functions, the differential proteins could be classified into various groups, including heat shock protein, chaperone, kinase substrate, cell signaling, apoptosis regulation, transcription regulation, free-radical scavenger and metabolic enzyme. Ontology analysis of the genes with consistent dysregulations at both mRNA and protein levels identified specific pathways down-regulated during the progression of HCC. The inhibition of those pathways provides new insights in the hepatcarcinogensis and treatment strategies.
Conclusion: Integrative analysis of tissue proteome and transcriptome data is useful in identifying dysregulated pathways in HCC, and provides insights in treatment strategies. (This project was supported by RGC Central Allocation and Li Ka Shing Foundation.)

PE305

Combined Mutations in Pre-S/Surface and Core Promoter/Precore Regions of Hepatitis B Virus Increase the Risk of Hepatocellular Carcinoma: A Case Control Study

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Background: To investigate the role of sequence variations in pre-S/surface and basal core promoter (BCP)/precore regions of the hepatitis B virus (HBV) in hepatocellular carcinoma (HCC).
Methods: The direct sequencing in pre-S/surface and BCP/precore regions of HBV was determined from 80 HCC patients and 160 controls with HBV infection.
Results: In pre-S/surface regions, HCC patients had higher frequencies of pre-S deletions, amino acid substitutions at codon 4, 7, and 81 in pre-S1 genes, at the start codon in pre-S2 genes, and at codon 68 in surface genes. But they had a lower frequency of amino acid substitution at codon 2 in pre-S2 genes than those without HCC. In BCP/precore regions, HCC patients had higher frequencies of C or G1753, A1762/T1764, T1846, and A1899 than those without HCC. Multivariate analysis showed that pre-S deletions, I68T in surface gene, T1762/A1764, and A1899 were independent factors for HCC. The HBV with a complex mutation pattern (pre-S deletion, T1762/A1764, and A1899) rather than a single mutation was associated with HCC. Patients with combined mutations of T1762/A1764 and pre-S deletion, T1762/A1764 and A1899, pre-S deletions and A1899, and T1762/A1764, pre-S deletions and A1899 had a 7.81, 7.7, 7.0, and 16.88 fold increased risk of HCC, respectively, compared to patients with wild-type at both or three genomic regions.
Conclusions: Pre-S deletions, I68T in surface gene, T1762/A1764, and A1899 were independent factors for HCC. Combination of these viral mutations appeared increasing HCC risks.

PE306

High peritumoral expression of placental growth factor in hepatocellular carcinoma is a poor factor for survival after curative resection

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Background/Aims: Angiogenesis plays a significant role in the metastasis and recurrence of hepatocellular carcinoma (HCC). Placental growth factor (PlGF), which is one member of the vascular endothelial growth factor family, may have prognostic values in patients after curative resection of HCC.
Methods: Expression of PlGF was assessed by immunohistochemistry in tissue microarray containing paired peritumoral liver tissue and tumor from 105 patients underwent hepatectomy for histologically proved HCC. Prognostic values of PlGF and clinicopathological factors were evaluated.
Result: PlGF staining was mainly on the cytoplasm of tumor cells or hepatocytes. The mean integrated optical densities of peritumoral and intratumoral density of PlGF were 0.018±0.018 and 0.006±0.007 respectively. Peritumoral PlGF density was significantly higher than that in tumor (p<0.001), and this result was also validated in another cohort of 37 patients by quantitative real-time reverse transcription-PCR (p=0.007). Intratumoral density of PlGF was not correlated with common clinicopathological factors (eg, TNM stage, tumor size, microvascular invasion, intra-hepatic metastasis) or overall survival (OS) (p=0.425) and time to recurrence (TTR) (p=0.419). However, peritumoral density of PlGF, which was correlated with tumor size (p=0.003) and intrahepatic metastasis (p=0.004), was a prognostic factor for both OS (p=0.015) and TTR (p=0.018). In multivariate analysis, peritumoral expression of PlGF was also an independent prognostic factor for OS (p=0.015, RR: 2.500，95% CI: 1.191-5.253) and TTR (p=0.045, RR: 2.013，95% CI: 1.014-3.996).
Conclusion: Peritumoral expression of PlGF in HCC patients is an independent risk factor for survival and recurrence, and may be a target of anti-angiogenic therapy in preventing post-operative recurrence.

PE307

RFA in Combination with hepatic artery-portal vein chemotherapy and ethanol injection for treatment of advanced HCC

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Purpose: To further research RFA in combination with hepatic artery-portal vein chemotherapy and ethanol injection for treatment of advanced hepatocelluar carcinoma (HCC).
Methods: 25 cases were treated with transhepatic artery chemoembolization (TACE) + radiofrequency ablation (RFA) + introportal vein chemotherapy (PVC) + percutaneous ethanol injection (PEI) (four combined group) and this method was compared with 23 cases that were performed TACE + PEI (two combined group) . The serum level of AFP was measured respectively after 2 and 6 months, CT scan and color Doppler ultrasound were measured after treatment for six months.

Results: The serum level of AFP declined in two groups after 2 months. For treatment after six months, AFP in four combined groups was rose lower than two combined group (X^2=5.06, p<0.05). CT and Doppler ultrasound examination, four combined groups was superior than two combined groups to the control in tumor shrinkage (X^2=8.29, p<0.01) and blood supply (X^2=6.81, p<0.01), relapse and mortality are also less.
Conclusions: RFA in combination with hepatic artery-portal vein chemotherapy and ethanol injection is a safe, effective combined method and has less complication in treatment of advanced HCC.

Poster Exhibition – HCV
Poster Session, Hall 5B

PE308

Relationship between hepatitis c virus genotyping and haematological changes in patients with chronic hepatitis c infection.

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On the average, hepatitis C virus infects 1.2% of the population worldwide. In Egypt, the prevalence rates reach 20% in some areas. Ability of the virus to persist in about 75-85% of infected individuals is related to the virus higher mutation rate. Six major HCV genotypes have been identified. Genotype 4 seems to be confined to the Middle East and Central Africa. Extra hepatic syndromes have been reported in up to 1/3 of HCV patients. We aim in this study to determine the relationship between viral genotypes and specific extra hepatic haematological disease in patients with chronic hepatitis C. The study group included 60 selected patients with chronic hepatitis C having various haematological problems. We studied hepatitis C virus genotypes using RT-PCR. We found among 60 patients , 57 genotype 4 (95%) and 3 patients genotype 1a (5%).28 patients (46.66%) were diagnosed as chronic hepatitis C with associated thrombocytopenia, 16 patients (26.66%) were diagnosed Mixed Essential Cryoglobulinemia(MEC), 13 patients (21.66%) were diagnosed Non- Hodgkin's lymphoma, and 3 patients (5%) were Aplastic anemia.
Positive serum cryoglobulins level was found in 20 patients (33.3%).No significant correlation was found between the level of viraemia and specific haematologic disease, biochemical liver markers or liver enzymes (P>0. 05).
We did not find correlation between HCV genotype and specific extrahepatic haemological disorder in HCV infected patients. Several environmental, genetic and immunological factors may contribute in disease progression.

PE309

Knowledge , Attitude and Practices of Barbers and their regular clients regarding the Hepatitis B & C disease in Hyderabad, Pakistan.

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Background: Hepatitis B & C are rapidly emerging a major public health problem. The objective of this study was to assess knowledge, attitude, practices among barbers and their regular shaving clients.
Material & Method: A questionnaire based, sero-surveillance Cross-sectional descriptive study conducted during May to September 2007 funded by the World Health Organization.
Results: In the targeted area 111 shops of barbers were successfully interviewed and total 715 questionnaires were filled by both groups. The mean age were found in both groups of Barbers (n=186) and Clients (n=529), 28.47 years. The both groups showed that there are no any drugs which can protect us from diseases. Both of the groups were not vaccinated for hepatitis B diseases. Regarding the care providers the barbers replied that they prefer registered medical practitioners and the clients generally prefer the Hakeems. Those who knew Hepatitis as liver disease, were 73 (39.2%), out of 186 barbers only 68 (36.6%) were knowing about Hepatitis-B&C, When we enquired about routes of HBV& HCV transmission only (37%) replied correct routes of transmission in both groups. About HBV vaccination (49.7%) were aware, only (14.8%) were vaccinated against HBV. 60% barbers claimed for disinfection of instruments before shaving (88.9%) claimed for use of new blades. In the sero-surveillance the HBV found was very low and HCV became epidemic (5.7% - 14.4 %) respectively.
Conclusion: The both groups need awareness for transmission. The use of new blade for the clients reduces the burden of HBV and HCV.

PE310

Hepatocellular Carcinoma Risk in Patients with Chronic Hepatitis C: a Cohort Study Focusing on HCV RNA Level and Other Clinical Risk Factors

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[1] *Tainan Municipal Hospital, Taiwan*

Background: Hepatocellular carcinoma (HCC) occurs frequently in patients with chronic hepatitis C (CHC) infection. The aim of the study was to verify possible clinical and laboratory factors affecting development of HCC in CHC patients.
Methods: A total of 373 patients with CHC were collected. 185 patients did not fulfill the including criteria. The remaining 164 patients (90 males; 74 females; mean age: 58.2±14 years old) were prospectively recruited and followed up.
Results: During the follow-up period between January 2000 and May 2008, HCC was identified in 19 (11.6%) patients. The incidence rate of HCC was 14.5 per 1,000 person-years. Fifteen patients (9.1%) developed cirrhotic liver. By Cox model, only male sex (p=0.006; hazard ratio:22.22; 95% CI: 0.005-0.414), genotype 1b (p=0.014; hazard ratio: 15.13; 95% CI: 1.715-133.508), and older age (≧65 y/o) (p=0.02; hazard ratio: 1.124; 95% CI: 1.018-1.241) are significant risk factors for HCC . Overall, there was 8.8-fold increased risk in non-cirrhotic patients with HCV RNA≧1 million to develop HCC. The incidence rate of HCC was 8.8% for IFN-treated patients and 14.3% for IFN-untreated patients (p=0.352).
Conclusion: The study highlights the roles of male sex, older age, and genotype 1b in the progression from CHC infection to HCC. Patients with higher HCV viral load potentially tend to develop HCC; however, HCC occurrence could be prevented using antiviral treatment. These two points need to be clarified further by a larger study population with longer follow-up period.

PE311

Transfer of Hepatitis C virus (HCV)-reactive T cell specificity for the treatment of HCV-associated hepatocellular carcinoma

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[1] *Medical University of South Carolina,* [2] *University of Colorado*

An approach have recently been described that retroviral vectors encoding T cell receptor (TCR) genes are used to redirect the specificity of normal peripheral blood lymphocyte (PBL)-derived T cells to recognize the tumor antigens. The therapy in which T cells have been genetically modified with TCR genes to recognize HCV would represent a novel approach for the treatment of HCV infections and HCV-related malignancies. We have previously shown that HCV+ liver transplant patients that have received HLA disparate liver allografts have HCV reactive T cells of host origin in their peripheral blood that are restricted by the donor HLA molecules. Initial studies indicate that the TCRs expressed by HCV reactive T cell clones from these patients have relatively high affinity for their ligands. We have cloned and expressed two TCRs which mediate recognition of the 1406-1415 and 1073-1081 epitopes from the HCV NS3 protein. The results indicate that these TCR transduced T cells can recognize the wild type epitopes, as well naturally occurring mutant variants of these epitopes. Most importantly, the TCR transduced T cells could also recognize HCV+ hepatocellular carcinoma cells. These data suggest this high affinity HCV-specific TCR might have potential new immunotherapeutic implications.

PE312

Factors predicting treatment efficacy in chronic hepatitis C patients without a rapid virologic response

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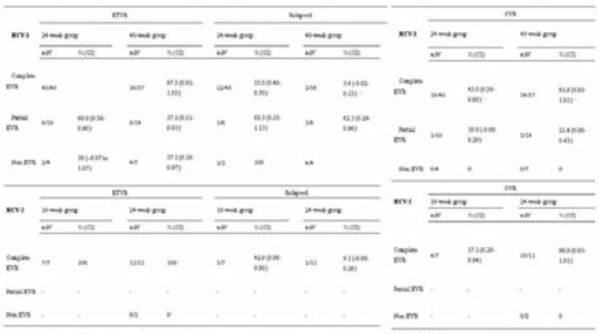
Kaohsiung Medical University, Kaohsiung, Taiwan., [4] Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung

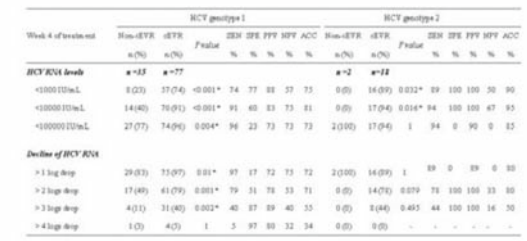
Background: Factors associated with SVR in patients without an RVR remains unclear.
Methods: 200 HCV-1 (100 for 24 and 48 weeks, separately) and 150 HCV-2 (100 for 24 weeks, 50 for 16 weeks) patients were randomized to peginterferon-alpha-2a and ribavirin for analysis.
Results: Multivariate analysis showed that treatment duration and a complete EVR were the strongest independent factors associated with an SVR. A higher SVR rate and a lower relapse rate were observed in the standard regimen group than in the abbreviated group in patients who had a cEVR (table 1). The best levels of viral loads in predicting cEVR at week 4 were < 10^4 IU/mL (table 2).
Conclusion: It was crucial to achieve a cEVR with adequate treatment duration in patients who failed to achieve an RVR.

Table 1. The rates of end-of-treatment virological response, relapse, and sustained virological response, according to early virological response status and regimen in patients without rapid virological response stratified by genotype



CI, 95% confidence interval; ETVR, end-of-treatment virological response; SVR, sustained virological response; Complete EVR, seronegative of HCV RNA at week 12; Partial EVR, HCV RNA positive but have a > 2-$\log_{10}$ drop in HCV RNA at week 12. Statistical significance: a,b,c,d,f,g, $P < 0.001$; e,h, $P=0.013$; i, $P=0.038$

Table 2. Accuracy of viral kinetics at week 4 in predicting complete early virological response in patients without rapid virological response



Notes: EVR, complete early virologic responder; HCV, hepatitis C virus; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; ACC, accuracy; *, statistical significance.

PE313

Negative Predictive Factors For Early (Evr) And Sustained (Svr) Virological Response In Patients With Chronic Hepatitis C Treated With Peginterferon And Ribavirin

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Our aim was to evaluate the impact of some biochemical, histological and viral factors on both EVR and SVR in patients with genotype 1 chronic hepatitis C (CHC) treated with peginterferon plus ribavirin.
Patients and methods: We evaluated retrospectively 188 naïve patients with CHC treated with peginterferon plus ribavirin at standard weight-based doses for 48 weeks. Biopsies were assessed for inflammatory activity and fibrosis. Steatosis was categorized by the proportion of hepatocytes per low-power field with fatty changes: >5%, >5–33%, 34–66%, >66%. Biopsies were also assessed for stainable iron using the Brissot scoring system. All patients were evaluated for metabolic syndrome (MS) using the NCEP-ATP III criteria.
Results: EVR was achieved in 115/188 pts (61.17%) while SVR occurred in 82/115 (71.3%). After adjusting for sex and age, independent factors that negatively interfered with both EVR and SVR were: fibrosis score, steatosis, iron score, HOMA-IR index and viral load. After excluding the patients with MS criteria (n=32), EVR was observed in 102/156 (65.4%) and SVR in 82/102 (80.4%). Factors that independently influenced both EVR and SVR were: fibrosis score, steatosis, iron score and viral load.
Conclusion: Fibrosis, steatosis and iron scores, as well as viral load are independent parameters that can affect both EVR and SVR in genotype 1 CHC patients, regardless the presence of MS. If MS is present, high HOMA-IR index can also additionally impair viral response.

PE314

Development of Newer Hepatitis-Vaccines & Ethical Issues : NGO efforts to protect human rights of Hepatitis patients

P. Sankpal[1], V. Sankpal[1]
[1] *Health Alert Organisation of India*

Issue/Argument: Asia has rising cases of hepatitisB/C. Alcohol/Food-habits cause high prevalence in rural/tribal areas. Lack of monitoring/follow-up complicates management. vaccines emerge as hope. Clinical-trials of vaccines debated-issue. Design of hepatitis-vaccine-trials in developing-countries complex ethical-issue. We focus on controversies identified in international/regional/local CME/pharma programs as vulnerability of volunteers to exploitation by foreign/local research-groups/funding-agencies. Critical task is protect interests of vaccine-subjects in face of substantial-risks. Determine if hepatitis-Vaccine-volunteers will have access to treatment during trial. Access to Vaccine-trial-outcome. Interaction with seniors 19th APASL-Congress from developed-countries will give voice to such burning-issues.
Methodology: Researchers/pharmaceuticals/Govt-policy planners need to develop forum to solve these problems. NGO's can play pivotal role. Obligation on part of researchers to create mechanisms to offset anticipated risks of participation in controversial, Risky vaccine-development.
Conclusion: counselling/right to withdraw from trial be made basic guideline. Apart from monetary aspects unsuspected adverse reactions/deaths be properly evaluated/monitored. Researchers need to evolve policy-guidelines to overcome barriers as variation in interpretation of essential ethical ideas, legal-system-differences, educational/economic-status. Need to develop common consensus between research-community/pharma sector to reduce suffering of hepatitis-affected patients community.
Recommendations: Researchers/NGOs should come together at 19th APASL-congress platform to form workgroup to settle these issues. We shall raise our this burning issue & present Hepatitis-Prevention-Advocacy plan of our NGO graphically to APASL-2009 participants.

PE315

Improving QOL Hepatitis Patients in Resource poor developing nations: Supportive care Efforts by an Non-Govt-Organisation [NGO] in rural/tribal india

P. Sankpal[1], V. Sankpal[1]
[1] *Health Alert Organisation of India*

Issues: Fatigue/sexual-dysfunction/depression commonly seen in Hepatitis-sufferers. Most patients of hepatitis treated symptomatically. Active treatment very expensive. Palliative-care inaccessible in rural/tribal areas. Hence our NGO-nurses took initiatives to improve QOL with alternative-medicines since October 2005.
Objective: Around 112 patients die each-year from Hepatitis. Statistically over 90% express sexual-dysfunction, 68% experience fatigue/weakness; 70% suffer social neglect/humiliation ; 54% sleeplessness, nausea/vomiting; 64% depression. Our NGO-nurses followed-up Hepatitis-sufferers unable to afford Rx Or who needed of palliative care.
Methods: 81 patients [58 hepatitis-B & 23 hepatitis-C] included. After 14 weeks-Rx-with alternative-medicines. Counseling/palliative support with nutrition, we noted QOL improved to statistically. Assessment performed on weekly-basis. Traditional-faith-healers involved for giving traditional Indian-medicinal-plant extracts [non-commercial].

Results: 53% patients expressed that alternative-medicines-Rx most important factor to cope with hepatitis. higher scores of QOL (ANOVA $p < 0.001$) correlated with alternative-medicines-Rx. Our NGO-initiative suggests that over 70% patients will need well trained specialist for home-based-care unit.
Conclusions: Life-span/QOL of Hepatitis-sufferers depends on appropriate-palliative-care. NGO-personals should be trained in Palliative-care-services. Our data is being used for palliative care advocacy. Field of Spiritual/psycho-social/community support is fertile ground for further investigations. Such use of complimentary Indian medicinal plant extracts needs further evaluation in a large group in multicentre trial.

PE316

Treatment with Adacolumn in patients with hepatitis C related who have undergone kidney transplantation: Preliminary study

G. Novelli[1]
[1] *La Sapienza University*

Introduction: Patients who have undergone kidney transplant and suffer from hepatic C related (HCV) cannot be treated with standard therapy (PEG-IFN combined with ribavirine) due to acute rejection risk. Furthermore, immuno-suppressive therapy facilitates progression and infection and chronic hepatopathesis. Monocytes and macrophages are known to produce extra-hepatic breeding sites and spread disease. Our aim was to lower macrophages, granulocytes,monocytes, pro-inflammatory cells and viremia levels using an extra-corporeal device:Adacolumn®(OTZUKA).
Methods: The Adalcolumn filter is filled with 2mm. cellulose acetate beads immersed in sterile saline solution. These carriers absorb granulocytes and monocytes/macrophanges through FCR receptors. Six patients were treated in our department. All patients were affected by virale genotype 1b. Patients underwent five 1hour treatments for five consecutive days according to protocol.
Results: During treatment cycles and successive follow ups we observed a stabilization of kidney parameters and a non significant decrease in transaminase levels. At 3rd month follow up we observed a significant decrease in plasma HCV-RNA in 3 patients ($p<0.01$) associated with attenuation of inflammatory phase ($p<0.2$) and variations in immuno-modulation. only one patient presented altered CD4+ and CD8+ where positive was observed at 3rd month. In another patient, even though immuno-modulation improved, there was no reduction in viremia.
Conclusions: Considering the results this method should be used on a greater number of patients evaluating successive treatment times in case of viremia increase.

PE317

Treatment with Adacolumn in patients with hepatitis C related who have undergone kidney transplantation: Preliminary study.

G. Novelli[1], M. Rossi[1], L. Poli[1], V. Morabito[1], F. Ruberto[1], G. Ferretti[1]
[1] *La Sapienza University*

Background: Patients who have undergone kidney transplant and suffer from hepatic C related (HCV) cannot be treated with standard therapy (PEG-IFN combined with ribavirine) due to acute rejection risk. Furthermore, immuno-suppressive therapy facilitates progression and infection and chronic hepatopathesis. Monocytes and macrophages are known to produce extra-hepatic breeding sites and spread disease. Our aim was to lower macrophages, granulocytes,monocytes, pro-inflammatory cells and viremia levels using an extra-corporeal device:Adacolumn®(OTZUKA).
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Conclusions: The treatment was found to be safe without hemodynamic or infective complications. Considering the results this method should be used on a greater number of patients evaluating successive treatment times in case of viremia increase.

PE318

Serum Levels of IL-1 Beta and IL-6 In HCV Infected Patients As Markers for Liver Disease Progression

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Aim: We aimed to characterize serum cytokine levels of interleukin-1 Beta (IL-1β) and interleukin -6 (IL-6) in HCV infected patients & in patients with hepatocellular carcinoma (HCC) in comparison to control group and their possible use as markers of disease progression.
Patients and Methods: Sixty Patients were divided into three groups: Group I: twenty HCV infected patients without cirrhotic changes. Group II: twenty HCV infected patients with liver cirrhosis (LC). Group III: twenty HCV infected patients with HCC and 20 healthy subjects as control group. All patients and control group were subjected to biochemical and serological tests, anti HCV, HCV (RT-PCR) and cytokines measurements of serum IL-1 β & serum IL-6 levels.
Results: Showed a high statistically significant elevated serum IL-6 and IL-1 β levels in patients with chronic HCV infection in comparison to control group. Highly statistically elevated levels of IL-6 and IL-1 β in liver cirrhosis and higher levels were found in HCC group in comparison to control group. The levels of Il-6 and IL-1 β increased significantly in HCV infected patients as the disease progress.
Conclusion*:* Serum IL-1 β, and IL-6 levels are elevated in patients with hepatitis C-related liver diseases, especially in LC and HCC patients. Their levels reflect hepatic dysfunction better than liver inflammation parameters; accordingly, we may use serum IL-1 β and IL-6 as markers for Liver disease progression in HCV-infected patients instead of invasive techniques.

PE319

Low-dose pegylated interferon therapy for patients with compensated HCV-related liver cirrhosis

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Background and Aim: Pegylated interferon (PEG-IFN) therapy is not indicated for many cases with HCV-related cirrhosis due to various adverse effects. However, patients with HCV cirrhosis are at high risk for development of hepatocellular carcinoma (HCC). Thus we have introduced low-dose PEG-IFN treatment for patients for compensated HCV cirrhosis.
Patients and Methods: Selection criteria for low dose PEG-IFN is 1) compensated HCV-related cirrhosis, and 2) either the elderly (>65) or presence of thrombocytopenia ($<8.0 \times 10^6$/ l). We have treated patients who met these criteria with low-dose PEG-IFN, consisting of either PEG- 2a 90 g/1-2w or PEG- 2b 0.5 g/kg/w+ribavirin 200mg/d. [Results] Twenty patients with compensated HCV cirrhosis (all patients genotype 1b) have been treated with low-dose PEG-IFN (PEG- 2a:9, PEG- 2b+rib:11). The age, platelet counts ($\times 10^6$/ l), and ALT (IU/l) of 20 patients at baseline were 64.1±8.3, 7.8±4.6, and 90.4±68.6 respectively. All patients were well tolerated. Low-dose PEG-IFN has been continued 59.6±43.8 weeks on average. Although viral response was not detected, biological response (BR), defined as maintenance of ALT within normal range, was obtained in 12 patients (12/20=60%). Of note, neither development of HCC nor decompensated cirrhosis was observed in these 12 BR cases. By contrast, HCC and decompensation developed in 5 and 1 patients respectively among 8 patients who failed to achieve BR.
Conclusion: Low-dose PEG-IFN treatment was safe and well tolerable, and could potentially prevent HCC or decompensation in patients with liver cirrhosis when BR was obtained.

PE320

High Response Rate of Combination Therapy Of Pegylated Interferon And Ribavirin In Treating Chronic Hepatitis C With Genotype 6A In Hong Kong Chinese

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Aims: To study the efficacy of peginterferon and ribavirin in treating chronic hepatitis C (CHC) with genotype 6a in Hong Kong Chinese.

Methods: To assess sustained virological response (SVR) (serum HCVRNA< 500IU/mL) at 6-months follow-up.

Results: Nine patients with genotype 6a CHC (included from Jan2003 to Dec2007) received peginterferon and ribavirin. Mean age: 50 (range 28-64). Mean ALT before treatment: 96 IU/L (range 29-173 IU/L). Seven patients had liver biopsy performed, only one showed stage 3-4 fibrosis and others showed active hepatitis without advanced fibrosis. Mean serum HCV-RNA: $9.17x10^5$IU/mL(range $9.0x10^3$–$3.3x10^6$IU/mL). Six patients had received peginterferon alfa-2b (1.5mcg/kg/week), other 3 received peginterferon alfa-2a (135mcg/week). Ribavirin dosage ranged from 600mg-1000mg/day depending on body weight and baseline haemoglobin. Treatment durations were 48-52 weeks in 7 patients, 24-26 weeks in 2 patients as one showed rapid virologic response at week 4 and the other was intolerant to side effect of peginterferon. Eight patients had early virologic response at week 12 and one had >2log drop of HCVRNA. Eight patients had end-of-treatment response. Eight patients (88.9%) achieved SVR at end of follow-up. Two patients who received only 24-26 weeks of combination therapy also achieved SVR. The one who failed to achieve SVR was at older age of 60 and had advanced fibrosis.

Conclusions: The efficacy of pegylated interferon and ribavirin in treating Chinese patients with chronic hepatitis C genotype 6a can achieve high sustained virologic response rate of 88.9%.

PE321

Prevalence of Hepatitis C virus genotypes in hepatocellular carcinoma: A Comparative analysis from New Delhi and Madurai

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Introduction: HCV is a recognized cause of HCC. Information on HCV genotypes in HCC are scanty in India.

Methods: A total of 154 HCC cases from Delhi, 96 HCC cases from Madurai and 246 cases of chronic hepatitis without HCC were controls in the study. RT-PCR for HCV RNA and genotyping were carried out in all the cases

Results: In group-I, HCV RNA was positive in 26.58% HCC cases in which genotype 3 was found in 57.1% Genotype 1 was observed in 26.2% HCC cases. Whereas 16.6% cases remained nontypable. In group-II, HCV RNA was positive in 23.95% HCC cases, with genotype 3 in 30.4% cases, Genotype 1 in 52.2% cases and Genotype 4 in 4.34% cases. However, 13.04% cases remained nontypable. Out of the 246 control cases, 187 were CH and 59 were cirrhosis. In CH group, HCV RNA was positive in 22.45% cases in which, genotype 3 was detected in 71.4% cases whereas Genotype 1 was observed in 21.4% cases . However 7.1% cases remained nontypable. In Cirrhosis group, HCV RNA was positive in 37.2%cases. Genotype 3 was found in 59.1% cases. While genotype 1 was present in 31.8% cases and 9.1% cases remained nontypable.

Conclusion: Genotype 3 in Delhi and Genotype 1 in Madurai were predominant. in HCC cases. Our study demonstrates that no particular HCV genotypes were associated with HCC and genotype did not appear to influence the development of HCV-associated HCC.

PE322

24 Weeks Treatment with Pegylated Interferon Alfa plus Ribavirin may be Enough in Patients with Chronic Hepatits C Infected with Genotype 1 Who Have Low Pretreatment Viremia and Rapid Virologic Resoponse

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Background/Aims: The standard treatment for chronic hepatitis C infected with HCV genotype-1 is a combination of pegylated interferon alfa and ribavirin for a 48weeks. It is unclear if 24weeks treatment is possible for patients showing a rapid virologic response (RVR) without compromising the sustained virologic response (SVR) in Korea.

Method: Between June 2005 and July 2008, among patients chronically infected with the HCV genotype-1 (HCV-1) who were treated with pegylated interferon alfa subcutaneously once weekly plus ribavirin (weight-based), 20 consecutive paients who had low pretreatment viral load ($\leqq 1.5x10^6$copies/mL) and RVR were treated for 24weeks and then followed up for 24weeks. The HCV RNA was quantitatively assessed pretreatment, at 12weeks of treatment and was qualitatively assessed at 4weeks of treatment, the end of treatment (24weeks), 24weeks after end of treatment. RVR was defined as undetectable HCV RNA at the 4weeks.

Results: Baseline characteristics of patients was as followed; age (30-65years:mean 45years), BMI (21-27kg/m²:mean 23.5kg/m²), HCV RNA titer ($0.3\text{-}1.4\times10^6$copies/mL:mean 0.5×10^6copies/mL), ALT (5-751IU/L:median 77IU/L). Among the 20 patients, all patients (100%) had sustained virologic response (SVR).

Conclusions: HCV-1 infected patients with a low baseline HCV RNA concentration ($\leqq 1.5\times10^6$copies/mL) who had HCV RNA negative at week 4 of treatment may be treatment for 24weeks without compromising sustained virlolgic response. However, an additional trial will be needed to optimize the treatment duration.

PE323

Effectiveness of interferon therapy in Korean patients with acute hepatitis C

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Background/Aims: Acute hepatitis C (AHC) has a high chronicity rate of up to 50~84% if it is not treated. Although the good treatment response to pegylated interferon (peg-interferon) therapy has reported, there is not definite guideline to treat of AHC in Korea yet. The aim of our study was to investigate the clinical course and treatment outcome of AHC in single center of Korea.

Methods: We performed a retrospective analysis of 35 patients who were diagnosed with AHC during the period from May 1996 to December 2007. The diagnosis of AHC was based on seroconversion to anti-HCV antibody or the clinical and biochemical diagnostic criteria satisfactory to AHC and on the presence of HCV RNA in first serum sample. The spontaneous resolution was defined as loss of HCV RNA in serum for 6-month in untreated group, and in treatment group, the sustained virological response (SVR) was defined as a index of treatment success.

Results : Thirteen of thirty-five patients were treated, six of thirty-five were untreated and observed clinical course, and sixteen patients were not followed up after diagnosis. In treatment group, nine of thirteen (69%) acquired SVR, and two of six (33%) showed spontaneous resolution in untreated group. Ten of thirteen treatment patients used conventional interferon, and another three patients used peg-interferon.

Conclusion : Compared with untreated group, there was higher SVR rate in treatment group (33% vs. 69%). So early interferon treatment in acute hepatitis C should be considered.

PE324

Predictors of the development of thyroid dysfunction in patients with chronic hepatitis C during peginterferon and ribavirin combination therapy

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Background: This study was conducted to identify predictors of thyroid dysfunction and to determine whether virologic factors or treatment response affect thyroid dysfunction development during peginterferon (pegIFN) therapy in chronic hepatitis C patients.

Methods: Sixty chronic hepatitis C patients treated with pegIFNα-2a or α-2b

in combination with ribavirin from 1st July 2004 to 30th July 2008 were included in this study. Treatment responses were evaluated and thyroid functions were assessed every 4 weeks.
Results: Seventeen patients (28.3%) experienced thyroid dysfunction during treatment, and that occurred more frequently in women and in patients with a lower body mass index (BMI). The proportion of patients with a high viral load (a serum HCV RNA titer >750,000 IU/mL) was significantly higher in the thyroid dysfunction group rather than in the euthyroid group(88.2% vs. 48.8%, p=0.005). Among patients with HCV genotype 1, the rate of sustained virologic response was lower, and relapse occurred more frequently in the thyroid dysfunction group than in the euthyroid function group during pegIFN-based therapy(SVR, p=0.024; relapse, p=0.017). The female gender and the high viral load were independent predictors of thyroid dysfunction in multivariable analyses (female, OR 9.44, 95% CI 1.76-50.8, p=0.009; high HCV RNA titer, OR 8.40, 95% CI 1.23-57.64, p=0.030).
Conclusion: The risk of thyroid dysfunction during pegIFN therapy for chronic hepatitis C was found to be higher for women and for those with a low BMI and a high viral load.

PE325

Changes of hyaluronic acid levels predict the outcome of combination therapy of peginterferon alpha2b and ribavirin for patients with chronic hepatitis C

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Background: In peginterferon alpha2b (PEG-IFNα2b) and ribavirin (RBV) combination therapy for 48weeks for patients with chronic hepatitis C, it is still difficult to predict which patients will achieve sustained viral response (SVR) at the completion of this therapy.
Aim: To predict SVR and non-SVR (relapse) at the end of this combination therapy by determining changes of serum hyaluronic acid (HA) levels.
Methods: Eighteen patients were enrolled and their serum HA levels were measured before therapy, and after the 1st, 2nd, 3rd, and last trimesters during therapy.
Results: Eleven patients achieved SVR and 7 became relapsers. All patients showed higher HA levels in the 1st trimester than the pretreatment levels. In the SVR group, 3 of 11 (27.2%) patients in the 2nd, 5 of 10 (50.0%) in the 3rd, and 9 of 11 (81.8%) in the last trimester showed lower HA levels than the pretreatment levels. By contrast, in the relapser group, none in the 2nd, 1 of 6 (16.7%) in the 3rd, and 1 of 7 (14.3%) ($p<0.05$) in the last trimester showed lower HA levels than the pretreatment levels. This study revealed that as the 48-week therapy went on, HA levels were more likely to fall below the pretreatment levels by the last trimester in patients achieving SVR. However, HA levels of relapsers tended to continuously be above the pretreatment levels.
Conclusion: Determination of changes of serum HA levels during PEG-IFNα2b and RBV therapy predicts SVR and non-SVR at the completion of this therapy.

PE326

Non-Hodgkin Lymphoma and the HCV infection

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Background: to evaluate the prevalence of the HCV infection in patients with NHL.
Methods: We included 40 patients admitted in the Hematological Clinic in January – July 2000, diagnosed with non-Hodgkin B-cell lymphoma with clinical, biological, histological criteria and no history of transfusion.
Results: The most frequent lymphomas were with high malignancy (40%), intermediate (32.5%) and low degree (27.5%). Cryopathy was negative (87.5%). The presence of viral markers was performed soon as possible after the NHL diagnosis, at the same time (52.5%) or during the first year of evolution (32.5%). The prevalence of the HCV infection was 15%, comparable to the one in the control patients group (22.68%), admitted in a gastroenterological clinic. On the other hand, this prevalence is significantly increased compared to the one in the general Romanian population (4.9%). The patients with NHL and HCV infection belonged especially to the low and intermediate malignancy degrees; the survival was influenced by the malignancy degree and not by the presence of HCV infection. The prevalence of HBV infection in the tested patients was 2.5%, being lower than that of HCV infection (2.5% vs. 15%, p = 0.113) but comparable to the one in the general population (2.5% vs. 6.3%, p = 0.525).
Conclusions: The prevalence of HCV infection in the patients having NHL was 15%, comparable to the one in the control group, but significantly increased compared to the one in the general population, leaving open the issue of a causal relationship between HCV infection and NHL.

PE327

Iron hepatic overload and hepatitis C

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Aim: evaluation of the prevalence and the degree of iron loading and the relationships with the clinical, biological and morphological changes.
Method: 212 patients with chronic hepatitis C were included, to whom we tested the blood iron level. In order to evaluate the hepatic iron accumulation we performed the Perls staining, using a qualitative analysis and a semiquantitative scoring system (Deugnier).
Results: From a total of 212 patients, 16.5% presented increased blood iron level (p = 0.000). The evaluation of the liver iron loading was performed in 54 patients, some having normal blood iron level (n = 34) and others (n= 20) increased (p = 0.007). The stainable iron was observed in 27 patients.
The iron loading was usually low, the deposits were observed mostly at the sinusoid cells and the hepatocyte and less in the portal spaces, usually as a pale staining or of small, nonmerging granules. The total iron score Deugnier was low.
The increased blood iron correlated with the ALT and GGT levels, the necroinflamatory activity and fibrosis. No correlationships between stainable iron and increased blood iron.
The presence of liver iron accumulation only correlated with the fibrosis degree.
Conclusions: Of the 212 patients to whom we tested the blood iron, 16.5% had increased levels.
The Perls staining was positive in 50% of the patients.
The iron loading was mainly low, with a more frequent distribution in the sinusoid cells and in the hepatocytes and correlated only with the stage of fibrosis.

PE328

A PEG-Interferon /Ribavirin Combination Treatment for Genotype 1b with High Viral Load - The Characteristics of the Non Sustained Viral Response Patients whose HCV RNA Became Negative at 12 -16 Weeks

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Background/aim: Chronic hepatitis patients whose HCV RNA became negative at 4 weeks of PEG-Interferon/ribavirin treatment achieved excellent SVR(sustained viral response) rate of almost 90%. However, in patients whose RNA became negative after 20 weeks, the SVR rate is very low. Since many patients became RNA negative at 12-16 weeks, it is important to clarify the characteristics of the patients.
Material and Method: Among 234 patients, 41 became RNA negative at 12-16 weeks and the therapy completed (total 48-60 weeks). The characteristics were analyzed by using sex, age, weight, BMI, ALT, γGTP, hemoglobin, platelet counts, Ccr, hyaluronic acid, the mutation of HCV core region (aa70, 91) and interferon sensitivity determining region, adiponectine, HOME-IR, RNA dynamics, dose and the treatment period.
Result: The SVR rate was 75.6%(31/41). Because all 10 patients of non SVR were female, we compared these 10 patients and 15 female SVR. The platelets counts were low in non SVR (non SVR 15.0 ± 2.8 ($x10^4/mm^3$) vs SVR 20.2 ± 4.8 ($P<0.05$)). The mean dose of ribavirin was lower (447 ± 126 mg/day) in non SVR ($P<0.05$) than in SVR (625 ± 127).
Conclusion: As for the characteristics of the patients whose HCV RNA became negative at 12-16 weeks but became non SVR, female, low platelet count and low dose of ribavirin were important factors. In the patients who received reduced ribavirin doses, the idea to increase the ribavirin dose and to maintain it are necessary. (ex, use 400mg and 600mg alternately)

PE329

Efficacy and Relapse: Peginterferon alpha-2a plus Ribavirin Combination Therapy in Chinese Patients with Chronic Hepatitis C in Clinical Practice.

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Background: Chronic hepatitis C virus (HCV) infection poses a challenge for a growing number of infected patients who exhibit disease complications, including cirrhosis, hepatocellular carcinoma, and liver failure in China. The combination treatment of peginterferon alpha (PEG-IFN alpha) plus ribavirin (RBV) is recommended as a standard care for HCV infections, which can improves hepatic markers and eradicates the virus in about 50% of patients. However, a significant number of patients do not respond to therapy or relapse following treatment discontinuation. Several viral, hepatic, and patient-related factors influence response to therapy.

Methods: In our clinical practice, a total of 77 interferon-naïve patients (61% male; median age 47 years) with chronic hepatitis C include 11 cirrhotic patients (no genotyping) received PEG-IFN alpha-2a 180 mcg/week plus RBV 900-1200mg/day for 48 weeks and follow up 24 weeks.

Results: show that the patients have more RVR and EVR rate (54% and 90.9% respectively). While the SVR (undetectable HCV-RNA 24 weeks after treatment completion) rate is only 51.5%

In conclusion: comparing with the data of clinical trail, the RVR, EVR and EOTR were higher, while SVR was the same in Chinese patient with chronic hepatitis C patients received the combination therapy of PEG-IFN plus RBV. The reason of high relapse was still unknow. Although optimal duration of retreatment and benefits and safety of maintenance therapy have not been determined, an extended duration is likely needed, even for the patients who achieved EVR.

PE330

Association of Hepatitis C Virus Mutation with Treatment Response in a Combination Therapy of Peginterferon and Ribavirin

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Background/Aims: Recently amino acid (aa) substitutions in hepatitis C virus (HCV) core region (double wild (DW); arginine at aa 70, leucine at aa 91) were reported to be associated with sustained virological response (SVR) in a combination therapy of peginterferon and ribavirin. We evaluated the viral factors influencing treatment response.

Methods: Nucleotide sequences of core region were determined directly in 104 patients with genotype 1 and high viral load (≥100 KIU/ml) treated with peginterferon-alpha 2b and ribavirin for 48 weeks. Rapid virologcal response (RVR) was defined as more than 2 log decrease of HCV-RNA during the first four weeks of therapy and early virological response (EVR) as that during the first 12 weeks. SVR was defined as negative HCV-RNA 6 months after the end of treatment and non-virological response (NVR) as less than 2 log decrease of HCV-RNA during the treatment.

Results: DW at aa 70 and 91 was shown in 17/44 (35%) patients with RVR and in 5/44 (11%) with non-RVR (p=0.003), in 25/72 (35%) with EVR and in 1/28 (3.6%) with non-EVR (p=0.001), in 16/37 (43%) with SVR and in 6/44 (14%) with non-SVR (p=0.003), and in 1/24 (4%) with NVR and in 25/79 (32%) with non-NVR (p= 0.005). In multiple logistic regression analysis, DW was significantly associated with RVR, EVR, SVR and NVR.

Conclusions: DW at aa 70 and 91 in HCV core region was closely associated with virological response in a combination therapy of peginterferon and ribavirin.

PE331

Probability of Virologic Relapse among HCV Genotype 1 Patients Treated with Peginterferon Alfa-2a (40KD) (PEGASYS®) and Ribavirin (COPEGUS®) Varies with the Speed of On-treatment Virologic Response

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Background: Among patients with chronic HCV treated with pegylated interferon and ribavirin, the highest sustained virologic response (SVR) rates are achieved in patients with a rapid virological response (RVR). Here we investigate how the time taken to become HCV RNA undetectable influences the probability of relapse during untreated follow-up.

Methods: Data from 569 patients treated for 48 weeks with peginterferon alfa-2a (40KD) 180µg/week plus ribavirin 1000/1200mg/day were included in the intent-to-treat analysis. Response was classified as RVR, complete early virological response (cEVR) slow responder and non-EVR.

Results: There was a correlation between the time required to become HCV RNA undetectable and the relapse rate after stopping treatment. Patients with an RVR had the lowest relapse rate (4%); this increased among patients with slower responses.

Conclusion: There was an inverse correlation between the time taken to achieve a virologic response and the probability of relapse.

Response	EOT response, n (%)	Relapse, n (%)	SVR, n (%)
RVR (n=90)	79/90 (88)	3/79 (4)	79/90 (88)
cEVR (n=240)	205/240 (85)	50/205 (24)	162/240 (68)
slow responders (n=129)	77/129 (60)	43/77 (56)	34/129 (26)
Non-EVR (n=110)	13/110 (12)	8/13 (62)	5/110 (5)

RVR = HCV RNA <50IU/mL at week 4; cEVR = non-RVR but HCV RNA <50IU/mL at week 12; slow responder = non-RVR/cEVR but ≥2$\log_{10}$ drop in HCV RNA at week 12; non-EVR = <2$\log_{10}$ drop at week 12
Three patients with RVR and seven patients with cEVR had no end-of treatment (EOT) response (five due to missing EOT values, five due to detectable HCV RNA at EOT), but achieved an SVR

PE332

Categorical Response at Week 4 Allows a Refined Prediction of Week 12 Response and Sustained Virological Response in HCV Genotype 1 Patients Treated with Peginterferon Alfa-2a (40KD) (PEGASYS®) and Ribavirin (COPEGUS®)

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Background: Rapid virologic response (RVR; HCV RNA <50IU/mL) at week 4 of treatment with pegylated interferon plus ribavirin can be used to predict the probability of achieving an SVR. Patients with detectable HCV RNA at week 4 have a lower probability of achieving an SVR than those with an RVR; further subdivision of these patients may be useful in predicting outcomes.

Methods: We conducted a retrospective analysis including 569 genotype 1 patients treated for 48 weeks with peginterferon alfa-2a (40KD) 180 g/week and ribavirin 1000/1200 mg/day. Patients were categorized as RVR and non-RVR. Those without an RVR were further subdivided into detectable but unquantifiable, ≥3, ≥2, ≥1 or <1 $\log_{10}$ drop in HCV RNA. The proportion of patients with undetectable HCV-RNA at week 12 and achieving an SVR was calculated within each category.

Results: RVR and non-RVR patients had an 88% and 43% rate of SVR respectively. Among non-RVR patients, rates of SVR depended on the categorical response at week 4: detectable but unquantifiable HCV RNA, 77%; ≥3 $\log_{10}$ drop in HCV RNA, 61%; ≥2 $\log_{10}$ drop, 43%; ≥1 $\log_{10}$ drop, 27%; and <1 $\log_{10}$drop, 13%. Independent of week 4 response, undetectable HCV RNA at week 12 was also highly predictive of SVR.

Conclusions: Patients achieving an RVR have high rates of SVR. Among patients who do not achieve an RVR a more precise prediction of SVR can be achieved by considering the extent of viral load reduction at week 4 and week 12.

PE333

Retrospective Japanese Validation Study of FibroTest and ActiTest in patients with chronic hepatitis C.

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Background: Fibrotest (FT) and Actitest (AT) are biochemical markers of fibrosis and activity for use as a non-invasive alternative to liver biopsy in patients with chronic hepatitis C virus. The aim of this study was to perform a validation study the discordances between FT and AT(FT/AT) and liver biopsy in patients with chronic hepatitis C in Japan.
Methods: 117 serum samples of chronic hepatitis C patients sended at -80°C at the Biochemistry Department of Pitié Salpetrière Hospital were analysed between july and august 2007. FT/AT components were assessed on thawed sera for 110 patients. 96 from 110 patients had liver biopsy at the moment of serum analysis. Liver biopsy fibrosis and activity scores were assessed by a pathologist in Japan according to METAVIR scoring system. For each individual test– FT/AT the following statistical analysis were performed
Result: FT observed AUROC for the diagnosis of advanced fibrosis was 0.81 and after adjustment according to the prevalence of different stages of fibrosis the AUROC was 0.89. This difference could be explained by the non-homogenous distribution of different stages of fibrosis (low prevalence of extremes stages of fibrosis –F0 and F4- and high prevalence of adjacent intermediate stages –F1 and F2). The observed AUROC of FT for the diagnosis of precirrhosis and cirrhosis was 0.86 and the observed AUROC of AT for the diagnosis of moderate to severe activity was 0.74 .
Conclusion: These results are similar to those observed in all independent validations worldwide.

PE334

Evaluation of Measurement Efficiency for HCV-RNA Quantification across Different Genotypes by Two Real-time Polymerase Chain Reaction Based Techniques

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Background: Accurate monitoring of HCV-RNA level throughout anti-HCV therapy is key factor for predicting sustained virological response (SVR). Real-time detection polymerase chain reaction (RTD-PCR) based methods are sensitive, have wide dynamic range of quantification and carryover contamination caused by classical PCR. Aim: To compare RTD-PCR based assays; Cobas Ampliprep/Cobas TaqMan (CAP/CTM) and recently developed Abbott RealTime HCV for HCV RNA quantification and measurements differences by 2 assays in different genotypes.
Methods: In total, 253 serum samples were used including, 135, 39, 24, 15, and 40 with genotypes 1b, 2a, 2b, 3a and 4 respectively were tested quantatively for HCV-RNA by CAP/CTM and Abott RealTime.
Results: Good correlation between two assays as overall (r=0.96) with correlation coefficient (R) in genotypes 1b, 2a, 2b, 3a ranged between 0.99 to 0.98 and least in genotype 4 (r=0.78). Mean differences between CAP/CTM and Abott RealTime was significnat in genotypes 1b and 4. Significantly HCV-RNA genotype 4 underestimation by CAP/CTM (4.3±0.9 log IU/ml) than Abbott RealTime (4.8±0.9 log IU/ml; *P=0.01)*. In genotype 1b, significantly higher HCV-RNA measurement by CAP/CTM (5.7±1.7log IU/ml) than Abbott RealTime (5.0±1.4log IU/ml, P=0.001). Two HCV genotype 4 samples showed measurement differences (CAP/CTM minus Abbott RealTime) of -3.75 and -1.68 log IU/ml. Studying genotype 4 sequences within 5′ UTR , target for CAP/CTM RT-PCR amplification, revealed nucleotide polymorphisms at positions A107, A165, T203, A205, and A243.
Conclusion: Different measurement efficiency by commonly used CAP/CTM in different genotypes compared to Abbott RealTime.

PE335

Risk Factors for the Spread of Hepatitis C Virus (HCV) Infection in Bahawalpur (South Punjab, Pakistan)

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Objective: To find out the risk factors for the spread of HCV infection in Bahawalpur.
Background: HCV infection is a major public health problem worldwide. The risk factors varies substantially between countries and geographic regions
Design: A case control Study.
Place and Duration of Study: The study was conducted in Bahawal Victoria Hospital / Quaid-e-Azam Medical College, Bahawalpur from 1st June 2005 to 30th july 2006.
Patients and Methods: A total of 2200 patients with dyspepsia were screened by anti-HCV antibody test (ELISA). Two groups were made, one was anti-HCV+ve while the other was anti-HCV-ve. The following risk factors were studied: H/O injection, blood transfusion, operation, sexual contacts, shaving by the barbers, visit to dentist and family H/O of HCV infection.
Results: Among a total of 2200 patients, 59.1% were male and 40.9% were female. Anti-HCV test was positive in 15.9% patients. In anti-HCV positive group H/O injections was present in 310(88.6%, P<0.001) patients, H/O Blood Transfusion in 45(12.9%, P<0.001) patients, H/O operations in 90(25.7%, P<0.001) patients, Family H/O HCV infection in 61(17.4%), H/O sexual contacts in 60(17.1%, P< 0.001) patients and H/O dental procedures in 240(68.6%, P<0.001) patients. While H/O shaving by the barber 177(84.7%, P=0.974) was insignificant.
Conclusion: HCV infection is common in patients with dyspepsia (15.9%). Important risk factors were H/O injections, blood transfusion, surgical procedures, sexual contact, family H/O HCV infection and dental procedures while shaving by barber was insignificant.

PE336

PROVE 1: Subgroup Analysis of a Phase 2 Study of Telaprevir with Peginterferon Alfa-2a and Ribavirin in Treatment-Naïve Subjects with Hepatits C

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Background: PROVE1 is a placebo-controlled study of 250 subjects with genotype 1 chronic hepatitis C randomized to 48 weeks of peginterferon-alfa-2a 180 ug/week (P) plus ribavirin 1000-1200 mg/d (R) (PR48, n=75), or 3 regimens of 750 mg q8h telaprevir (TVR) with PR: TVR/PR for 12wks followed by PR for 0wks (T12/PR12, n=17), 12wks (T12/PR24, n=79) or 36wks (T12/PR48, n=79). The impact of African American race (AA) and bridging fibrosis on sustained virologic response (SVR) was examined.
Methods: Subjects with cirrhosis were excluded from study. Fibrosis was categorized as mild/minimal, portal, or bridging from biopsy within 2 years. ITT analysis was performed.
Results: Overall, SVR was achieved by 41% of subjects in the PR48 group, 35% in T12/PR12 group, 61% in T12/PR24 group, and 68% in T12/PR48 group. Subgroup analyses indicated SVR was improved with TVR/PR (TVR/PR arms pooled) vs PR48 alone in AA subjects (44% (8/18) vs 11% (1/9)), and in subjects with bridging fibrosis (69% (22/32) vs. 26% (5/19)). Adverse events leading to discontinuations were more frequent in the TVR/PR groups (21% vs. 10%). Rashes, gastrointestinal events and anemia were more common in the T/PR arms, and rashes were more frequently severe (7% vs 1%).
Conclusions: TVR-based treatment for 24 or 48 weeks was associated with an increase in SVR rates compared to PR48. Subgroups with impaired response to standard Peg-IFN/RBV therapy appeared to benefit from the addition of telaprevir. Adverse events leading to discontinuation were more frequent in TVR-based regimens.

PE337

The Expression of TBK1s in HCV-infected Patients

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Background and aims: Induction of Type I IFNs is a core issue in antiviral responses and must be tightly controlled. The protein kinase TBK1 is critically involved in virus-triggered type I IFN signaling. In previous studies, an alternatively spliced isoform of TBK1, termed TBK1s, was identified to be induced in both human and mouse cells. Bound to RIG-1, it is able to

disrupt the interaction between RIG-I and VISA. This study was designed to observe the expression of TBK1s in HCV-infected patients.
Methods: Total RNA was extracted from samples of peripheral blood mononuclear cells obtained from 11 HCV patients, 9 HCV patients treated with IFN- /ribavirin and 9 healthy controls, and subjected to real-time PCR using the primer-probe sets for human Tbk1s, Tbk1 and IFN- genes.
Results: The TBK1s expression was significantly elevated in HCV-infected patients, while treatment of HCV-infected patients with IFN- /ribavirin resulted in down-regulation of TBK1s to the normal level.
Conclusions: The study strongly supports the idea that expression of TBK1s is correlated with HCV infection, and indicates that TBK1s may play an important role in the regulation of HCV infection.This work was supported by NSFC(30571643, 30672380, 30700702)；National Key Basic Research Program of China（2005CB522901, 2007CB512900）

PE338

Evaluation of Health-related Quality of Life in Rural Chinese Women with Chronic Hepatitis C

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Background/aims: To evaluate the health-related quality of life (HRQOL) in rural female chronic hepatitis C (CHC) patients and to identify factors associated with impairment of HRQOL.
Methods: Participants included 41 women with chronic (10-15 years) hepatitis C and a control group of 51 healthy women from the Guan area of Hebei province, China. HRQOL was assessed by the Short Form Health Survey (SF-36) administered during an interview.
Results: The CHC patients had significantly lower SF-36 scores in all domains than those of the women not infected with hepatitis C virus.
Conclusions: Rural female CHC patients have a reduced HRQOL. CHC alone is associated with significant impairment of HRQOL.
Acknowledgement This work was supported by the National Hi-tech Projects of the Tenth Five-year Programs (2001BA705B06).

PE339

Influence of Syndrome of Iron Overload and Hereditary Hemochromatosis on the Stable Virology Response during HCV Infection Treatment by Peginterferon Alpha-2a (40 kd) /Ribavirin.

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Background: Infringement of iron metabolism is one of fibrosis progressing factors during diffuse liver diseases. The interrelation between the syndrome of iron overload (SIO) and SVR achievement is studied during chronic HCV infection treatment.
Methods: 68 patients with chronic HCV infection (genotyping: 1- 34; 1+3- 5; 3- 22; 2- 6; 4-2) are investigated. SIO criteria: iron increase- more than 37 mkMol/l, ferritin - more than 200 mkMol/l, percent of transferriny saturation with iron (%Tf) - more than 50%.
Results: SIO revealed in 10 patients (14.7%): 5 patients - 1 genotype (2 assotiative with a diabetes) and 5 patients- genotype 3 (3 - in combination with liver steatosis and obesity). Venipuncture series were done up to getting ferritin referential parameter values before therapy beginning. RVR: SIO - 5 patients, normal metabolism - 48; EVR: 6 and 54, SVR: 4 and 54 relatively. 5 nonresponding patients (SIO) had steatosis and diabetes, hereditary hemochromatosis (C282Y/H63D) is verified in 1 case. Increase of ferritini values and %Tf during therapy and positive HLA-A3 and HLA-B7 is registered in nonresponding patients.
Conclusions: SIO in HLA-A3, HLA-B7 and C282Y/H63D positive patients is independent predictor of nonresponse during peginterferon alpha-2a (40 kd)" ribavirin treatment.

PE340

Distribution Pattern of HCV Genotypes and Its Association with Viral Load and Biochemical Profile

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Background: Hepatitis C virus (HCV) has emerged as a leading cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma worldwide. Genotyping and assessment of viral load in HCV patients are vital for designing therapeutic strategies. We aimed to determine the pattern of HCV genotypes and its association with viral load and biochemical profile.
Methods: 71 HCV RNA positive patients were included in the present study attending the medical-OPD and wards of Dr RML Hospital, a tertiary care hospital in New Delhi during 2006-2008. HCV genotyping was carried out by restriction fragment length polymorphism (Buoro et al 1999) followed by the type specific primers from the core region (Ohno et al 1997). Viral load estimation was carried out by Taqman real time PCR system using previously described method (Martell et al 2000).
Result: 67.6% of cases were having genotype 3 (3a, 3b, 3f & 3i) followed by genotyping 1 (1a & 1b) in 26.8% and genotype 2 in 5.6%. There was no statistical significant difference seen in the biochemical profile between the three groups of genotypes. Genotype one was associated with a significantly higher viral load as compared to the genotypes three and two. Parentral mode of transmission was accounted for the 68% of all the infected cases.
Conclusion: HCV genotypes 3 and 1 accounted for 94% of our cases. The genotype 1 is associated with higher degree of disease severity as assessed by viral load. Also two unusual subtypes 3i and 3f were identified from this geographical region.

PE341

To Determine the Polymorphism of Tumor Necrosis Factor-alpha and Interlukin-10 Genes in Chronic Hepatitis C Patients

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Background: The development and resolution of an inflammatory process is regulated by a complex interplay among cytokines that have pro and anti-inflammatory effects. Regulatory mechanisms that control the production of cytokines include genetic polymorphism in particular promoter/leader region. Polymorphisms may directly or indirectly affect the binding of transcriptional factors, consequently increasing or decreasing the production of mRNA, thus regulating cytokine production. We aimed to determine the polymorphism of tumor necrosis factor-alpha (TNF-alpha) and interleukin-10 (IL-10) genes in chronic hepatitis C patients.
Methods: 40 HCV RNA positive patients were included in the present study conducted during 2006-2008. 25 healthy controls were also included. Genomic DNA was extracted by using Q1A amp DNA blood kit protocol according to manufacture's instruction and desired fragment was amplified by using the primer's of Vidigal et al 2002.
Result: Genotyping of -308-promoter variant of TNF-alpha was performed by PCR. Polymorphism in the TNF-alpha (G/G, G/A and A/A allele) was different between HCV patients and healthy controls. IL-10 variants (C/T, C/C) were more frequent among HCV patients as compared to healthy controls.
Conclusion: Genetic polymorphism analysis on IL-10 promoter have indicated that distribution pattern of IL-10 polymorphism was significantly different between controls and HCV patients. Furthermore, polymorphism in promoter region of TNF-alpha (-308) was found, though the difference was not significant. Since this is a preliminary study, we believe that our findings may stimulate further research on larger number of patients.

PE342

Performance of Fibro-test in Patients with Chronic Hepatitis C Genotype 4

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Introduction: The assessment of liver fibrosis provides useful information not only for diagnosis but also for therapeutic decision. Although liver biopsy is the gold standard for fibrosis assessment, it is invasive and may have some risks, this has led to the development of non-invasive biochemical markers of liver fibrosis. Fibro-test which have five parameters used for the quantitative assessment of liver fibrosis. Our aim is to validate the performance of fibro-test in an independent cohort of patients with chronic hepatitis C genotype 4.
Methods: Subjects were 50 patients with chronic hepatitis C genotype 4. All biopsies were scored using METAVIR system by two independent pathologists. Fibro-test was done with (Biopredictive, Houilles, France) for the assessment of liver fibrosis. Sensitivity, specificity, PPV and NPV were measured for distinguishing between different degrees of severity of fibrosis.
Results: patients (45 male and 4 female) age ranged 21-56 years, liver biopsy showed 4% (F0), 40% (F1), 20 % (F2), 28% (F3), 8% (F4). The efficacy of Fibrotest is 63.26%, sensitivity 83.3%, specificity 53%, positive predictive value 50% and negative predictive value 85%.
Conclusion: Fibrofast has a low performance in assessment in fibrosis in chronic hepatitis C genotype 4.

PE343

Performance of European Liver Fibrosis (ELF) Markers in Patients with Chronic Hepatitis C Genotype 4

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Introduction: Liver biopsy is the reference method for assessing liver fibrosis. However, it is invasive, costly and has some limitations. European Liver Fibrosis (ELF) markers have shown to be accurate in assessing liver fibrosis in a range of chronic liver disorders. Our aim is to test the performance of ELF markers in an independent cohort of patients with chronic hepatitis C genotype 4.
Methods: Subjects were 199 patients with chronic hepatitis C genotype 4. All biopsies were staged for fibrosis using METAVIR system by two independent pathologist. ELF markers were done by (Diagnostic & Operations, England) and fibrosis scores were derived using the published ELF algorithm. The area under the curve (AUC) for receiver operator characteristic curves was measured along with sensitivity and specificity, positive (PPV) and negative (NPV) predictive values for distinguishing between different stages.
Results: patients (179 male and 20 female), age was ranged 25-51 years, liver biopsy showed 2% (F0), 27% (F1), 34% (F2), 26% (F3) and 11% (F4). ELF markers had no correlation with fibrosis score where r = - 0.003, P = 0.963, AUCs: 0.469, Specificity 87.9 %, Sensitivity only 9.3 %, PPV: only 6.03 %, NPV: 61.5 % and efficacy 58.2%.
Conclusion: The performance of ELF marker is low and can not be used for assessment of fibrosis in chronic hepatitis C genotype 4.

PE344

PROVE2: A Phase 2b Study of Telaprevir Combined with Peginterferon-Alfa-2a with or without Ribavirin for Treatment-Naïve Patients with Chronic Hepatitis C

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Background: The PROVE2 trial is a randomized, placebo-controlled study that assessed the safety and efficacy of 750mg q8h telaprevir (TVR) combined with 180 g/week PEG-IFN alfa-2a (P) ± 1000-1200mg/day ribavirin (R) in chronic HCV genotype 1-infected treatment-naïve patients without cirrhosis.
Methods: Overall, 323 patients received TVR + PR for 12 weeks (T12/PR12; n=82), TVR + PR for 12 weeks then PR for 12 weeks (T12/PR24; n=81), TVR + P for 12 weeks (T12/P12; n=78), or to PR for 48 weeks (PR48; n=82). Primary endpoint: sustained virologic response (SVR, undetectable HCV-RNA 24 weeks post-treatment).
Results: Baseline characteristics were well balanced across groups. Numerically higher SVR rates were observed in patients receiving T12/PR24 (69%; p=0.004 for difference vs. PR48) than T12/PR12 (60%), T12/P12 (36%) or PR48 (46%). Relapse rates were lower in the T12/PR24 group (14%) than the T12/PR12 (30%), T12/P12 (48%) and PR48 (22%) groups. The relapse rate in patients receiving T12/PR24 with 4-week and 12-week undetectable HCV-RNA was 7% (3/45). The AEs occurring more frequently with the T/PR regimen were pruritus, rash, asthenia, nausea and anemia. In the T/PR arms, 12 patients discontinued due to rash, 2 discontinued due to pruritus, and 2 patients due to anemia.
Conclusion: These results showed that a telaprevir-based regimen led to significantly higher SVR rates than PR, and indicate that this regimen could shorten the overall treatment duration from 48 weeks to 24 weeks for most patients infected with HCV genotype 1.

PE345

Sustained Virological Response is Associated with Decrease in Liver Stiffness Values in HCV Cirrhotic Patients

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Background/Aim: This study evaluated the effect of the response (SVR) to therapy on fibrosis stage, as assessed by LS, in patients with advanced fibrosis (F3) or cirrhosis (F4).
Methods: HCV patients with F3 or F4 who received interferon-based treatment were studded. LS was assessed after treatment (median delay of 36 months, 2-206) in patients with or without SVR. Correlations between LS and clinical and treatment characteristics were analyzed.
Results: 114 patients were included: male gender (72%), mean age (54±9 years), diabetes (26%), mean BMI (26±6 kg/m2), genotype 1 (59%). 33% had SVR. LS was performed 0-3, 3-6, >6 years following treatment.
By linear regression, the median of the LS was independently associated with SVR (p=0.005) and diabetes (P=0.008). SVR patients had lower LS (8.4 kPa; range 3.3-45) than non SVR patients (15.7 kPa; range 5.3-75) (p<0.001). Among the SVR patients the median LS was lower when the delay between LS and the end of treatment was longer (10.9,8.8,6.3) (p=0.02). On the opposite, among the non-SVR patients the median LS was not significantly different (p=0.57).
The median of liver stiffness was higher in patients with diabetes (p=0.006). BMI and dyslipidemia did not influence the median of the LS.
Conclusion: In patients with advanced fibrosis or cirrhosis, LS was lower in patients with SVR and decreased with time while it was higher and did not decrease in non-SVR patients. LS could be important for assessment of fibrosis stage during the post-treatment follow-up.

PE346

Peripheral Blood and Intrahepatic Natural Killer Cells In Patients With Chronic Hepatitis C: Relation To Disease Activity and Hepatic Fibrosis.

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Background: Although factors involved in viral persistence are not yet clearly identified, the cellular immune responses play an important role. *Aim:* To study peripheral blood and intrahepatic Natural Killer (NK) cells in patients with chronic hepatitis C in relation to disease activity and severity of hepatic fibrosis.
Patients & Methods: Fifteen untreated patients with histologically-proven chronic hepatitis C, and 12 matched healthy subjects. The NK cells and Natural Killer T (NKT) cells were identified in fresh whole blood samples using two-color flow cytometric assay as $CD3^{-}CD56^{+}$ and $CD3^{+}CD56^{+}$ positive cells. Immunohistochemical staining of liver biopsies taken from all patients was done using monoclonal antibody against CD56 for detection of NK cells and rabbit polyclonal antibody against smooth muscle actin (SMA) for identification of activated hepatic stellate cells (HSCs).
Results: Patients with chronic hepatitis C showed significant decreases in the percentages of NK cells and NKT cells in peripheral blood. A negative correlation was found between serum HCV RNA levels and the percentages of peripheral blood NK cells and the intensity of intrahepatic NK cells. The percentages of circulating NK cells and NKT cells and the intensity of

intrahepatic NK cells were inversely correlated with the METAVIR fibrosis stage and the steatosis grade, and also with the intensity of intrahepatic activated HSCs.
Conclusion: Patients with chronic hepatitis C had significant deficiency in circulating NK and NKT cells as well as in intrahepatic NK cells. This may provide a possible mechanism for the suppression of innate immunity against HCV.

PE347
Genotipic Frequency of Hepatitis C Virus in Distinct Populations, Para, Brazilian Amazon
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Background: HCV infection is the major cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma. The virus is classified in six genotypes and more 50 subtypes, which are related distinct with antiviral therapies reply. In Brazilian Amazon, epidemiologist's studies in blood donors had pointed high frequency of genotype 1 (74%) followed by genotypes 3 (25%) and 2 (1%). However, epidemiological research in populations of risk to the infection still is scarce.
Aim: To determine HCV genotypic frequency in 116 blood donors, 55 patients with blood transfusions multiples, 57 patients in hemodialysis and 52 drugs users in the State of Pará, Brazilian Amazon.
Methods: Using Real Time PCR and nucleotide sequencing followed phylogenetic analysis had been gotten viral diagnosis and genotyping.
Results: In blood donors, HCV distribution was constituted by genotypes 1 (93.1%) and 3 (6.9%). In multitransfunded patients occurs maximum prevalence of genotype 1 (100%), probably reflect of genotype 1 specific transmission of blood donors population. On the other hand, in hemodialysis patients had been detected genotypes 1 (85.7%), 2 (3.6%) and 3 (10.7%), result of a bigger diversity of transmission routes (transfusional, interfamilial, nosocomial, etc). In drug users occurs the biggest frequency of genotype 3 (38.1%) with prevalence of genotype 1 (61.9%), suggesting that the sharing of abuse machinery is allowing strains diffusion of genotype 3.
Conclusions: The genotype 1 possesses the biggest frequency in different population. Moreover, through HCV genotypic frequency if it detached the contribution of transmission distinct routes indicated by previous epidemiologists researches.

PE348
Real-Time PCR Assay for Rapid Detection of Substitution of Amino Acids 70 and 91 in Genotype 1b HCV Core Coding Region
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Background/Aims: The effects of hepatitis C virus (HCV) sequence variations on the success of antiviral therapy or the development of hepatocellular carcinoma (HCC) are complex for many reasons. Recently, there have been several reports concerning the effects of genotype 1b HCV core amino acids substitutions 70 and/or 91 on the outcome of antiviral therapies and the clinical course (Akuta N, et al. Intervirology 2005; Donlin MJ, et al. J. Virol. 2007). We established real-time polymerase chain reaction (PCR) assays for the easy detection of these HCV mutations.
Methods: Plasmids p-core-W, including wild type HCV core coding region (70R and 91L), and p-core-M, including mutant type HCV core (70Q/H and 91M), were constructed by cloning and PCR-based mutagenesis for control vector of wild type core and that of mutant core, respectively. Using serially diluted forms of these vectors, SyBr Green-based real-time PCR detections with mutation-specific primers were performed.
Results: Analysis of known scalar concentrations of references indicated that the detection limits of these methods were at least 10 copies, 10 copies, 1000 copies, and 10 copies of 70-wild, 70-mutant, 91-wild, and 91-mutant, respectively. Each primer could clearly distinguish the difference between p-core-W and p-core-M at the same copy numbers. Concerning substitution 70, the ratios 100:1, 10:1, 1:1, 1:10, and 1:100 of p-core-W versus p-core-M could be distinguished. On the other hand, for substitution 91, the ratios 100:1, 10:1, 1:1, 1:10, 1:100, and 1:1000 could be distinguished, confirming the sensitivity and specificity of the assay.
Conclusions: This method could represent a useful alternative for the detection of genotype 1b HCV core amino acid substitutions 70 and 91 and be reliably applied for rapid screening.

PE349
Efficacy and tolerability of HCV treatment in Asian patients according to age and genotype at a tertiary centre in Western Australia
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Introduction: Race and ethnicity can influence efficacy and tolerability to treatment in HCV. The higher response rate in Asians is thought to be associated with better adherence and tolerability.
Objectives: (1) To evaluate the adherence according to age and genotype (2) To assess the effect of age on treatment efficacy (3) To determine factors associated with discontinuation.
Methods: Retrospective analysis of all Asian HCV patients treated with pegylated interferon alfa 2a & 2b plus ribavirin from 2001-2007. Patient demographics, genotype, treatment type and duration, SVR, adherence, discontinuation & reasons were analysed.
Results: 85 patient (53 male, 32 females), age 24 - 77years (Mean 48.6). Genotype 1= 55, Genotype 2& 3 = 30. SVR in genotype 1 = 60%, genotype 2& 3 =60%. Discontinuation rate in genotype 1 = 21.8%, genotype 2&3 = 10%. Difference between ages and discontinuation rate <30yrs 1:6; 31-45yrs 1:19; 46-55yrs 11:42; >56yrs 2:18. The most common side effects are anaemia (60%) and psychiatric problems (20%). Adherence (80/80/80) = 80%. Compliance (clinic attendance) = 97.7%.
Conclusions: Discontinuation rate is low in Asian HCV patients with high adherence and compliance.

PE350
Frequency of Hepatitis C Virus Infection and its Genotypes Among Patients Attending a Liver Clinic and Voluntary Blood Donors in a Rural Area of Pakistan
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Background: Hepatitis C virus (HCV) infection is a major health problem. There is huge regional variation in its prevalence and genotypic distribution. Voluntary blood donors are thought to have somewhat lesser prevalence than the rest of the community. Reliable statistics are not available for the entire country, particularly for the rural areas. It is important to know local situation and rationalize use of limited resources.
Methods: Retrospective study of the records of patients attending the Free Liver Clinic (FLC) of our hospital located in a rural area of Pakistan, and those screened for HCV infection prior to voluntary blood donation.
Results: Patients at FLC (324 out of 1638 [20%; males 65%] were found to have higher chances of being reactive for HCV antibodies as compared to voluntary blood donors (121/804 [14%]; p = 0.004; OR 1.39 – 95% CI = 1.11 – 1.75). Out of a total of 1022 HCV reactive patients, 904 (88%) were found to be positive on HCV RNA testing. Out of a total of 166 typeable genotypes, 125 (75%; 95% CI = 68.7 – 81.9, estimated odds = 3.05) were infected with a single genotype, and only 7 patients (4%) were infected with genotype 1, either alone (n=4) or in combination with 3a.
Conclusions: One out of every 5 people tested in our FLC is seropositive for HCV, and 14% of "healthy" voluntary blood donors have the same results. Genotype 1 is very rare in our region.

PE351
How Good is Conventional Interferon-based Treatment in Eradication of Hepatitis C Virus (HCV) with Genotype 3?
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Background: Hepatitis C viraus (HCV) infection is common in our region. Data is not available on success rates of conventional Interferon (INF) based products here. We attempted to find out the dominant genotype, and to determine the success rate of conventional INF-based treatment in eradicating HCV.
Methods: Retrospective case series study of HCV infected patients' records treated with 14 different brands of INF.
Results: 320/1858 (17%) of all patients tested were positive for HCV antibodies. HCV-RNA was tested by PCR for 1022 patients, of which 904 (88%) turned out to be positive. Genotype type 3 was the dominant genotype - found in 118/168 (70%) patients. 101 men and 57 women were treated with various brands of INF with the same manufacturer's brand of Ribavirin. The overall ETR achieved was 100/142 (70%) - 58/85 (68%) men and 42/57 (74%) women. 41/62 (66%) of genotype 3 achieved ETR. There was no significant difference in average ages for those who achieved good ETR and those who did not (39 years each). The ETR achieved by different brands ranged from 48% to 91%. SVR was achieved by 17/30 patients.
Conclusions: 17% of all people tested positive for HCV antibodies, of which about 88% had evidence of active HCV infection. ETR achieved by different brands averaged 70%. This was 74% in female sex, although age did not appear to be a factor in determining a favourable ETR.

PE352

Alanine Aminotransferase (ALT) and Sero-Prevalence of Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Infection in Patients With Diabetes Mellitus (Dm)

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Background: DM and HCV infection are common problems of our society. HCV infection is associated with DM. DM is also causing increase in levels of serum ALT.
Objective: To study the frequency of HCV and HBV infections in diabetic patients and to note the relation of these infections with ALT.
Study Design: A cross-sectional Observational-descriptive analytic study.
Place and Duration of Study: Diabetic clinic Bahawal Victoria Hospital / Quaid-e-Azam Medical College, Bahawalpur (30th December 2006 to 30th June 2007).
Patients & Methods: A total of 439 consecutive diabetic patients of either sex were evaluated for HCV and HBV infection by using Enzyme Linked Immunosorbant Assay (ELIZA-3) along with serum ALT levels. On the basis of this test, the patients were divided into two groups, sero +ve and sero –ve. Different variables were: Age, sex, BMI, area of residence (rural or urban), type and duration of DM, smoking, literacy and ALT.
Results: Males 50.3% and females 49.7%. Age ranged from 18 to 95. Majority were married (98.4%), from rural area (70.4%), had type-2 DM (99.8%), normal weight (39.2%), normal ALT(60.1%) and non-smokers (78.6%).
Seroprevalence for HCV, HBV and both were 25.1%, 1.8% and 1.6%. Two groups were made, sero +ve and sero -ve. Raised ALT (59.2%) was significant ($P<0.05$) factor while all others variables were insignificant ($P>0.05$).
Conclusion: HBV and HCV infections are more prevalent in DM with increased ALT levels. While HCV infection is more common than HBV in patients with DM.

PE353

Expression and Characterization of Codon-optimized HCV Envelop Proteins and HCV Receptors Proteins in Mammalian Cell

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Hepatitis C virus (HCV) envelope proteins (E1 and E2) mediate the entry of virus into host cells by binding to its cellular receptors and resulting in the fusion of the viral membrane with host cell membrane. The expression and secretion of biologically active envelope proteins *in vitro* have proven to be a difficult task due to the high degree of glycosylation and the existence of hydrophobic domains within these sequences. In order to obtain glycosylated, correctly-folded HCV envelop proteins in large quantities, we optimized the DNA sequences of HCV envelop proteins by substituting the encoded sequence with human preferable codons and expressed them in human embryonic kidney (HEK) 293 cells. Both proteins were detected intracellularly, with a small portion secreted into supernatant. In order to enhance secretion, truncated forms of envelop proteins including E2 TM, $E2_{384-661}$, $E2_{484-661}$ were also expressed. Both full-length and truncated forms of envelop proteins were glycosylated and expressed at high level. In addition, we also expressed the codon-optimized HCV receptors CD81 and Claudin-1 in 293 cells. By comparing the expression level of codon-optimized sequences and the sequences that were obtained from cDNA library by PCR, we found that codon-optimization enhance protein expression significantly in 293 cells. These results not only lay solid foundation for further research concerning the mechanism of HCV entry, including the optimal pH and right protein conformation for fusion, cell types that permit viral entry; but also potentiate a useful cell model for testing antiviral agents.

PE354

Association of Prolactin Expression with Hepatitis C Virus in Chronic Viral Carriers

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Background: Prolactin (PRL) is an immunoregulatory hormone secreted from lymphocytes, however, PRL induction in relation to Hepatitis C virus (HCV) infection has not been elucidated.
Methods: Serum PRL levels were measured in both 232 subjects of our HCV cohort study and 31 male patients of the hospital, who were chronically infected with HCV. Furthermore, serum PRL levels were compared in 27 male patients before and after interferon therapy. We measured expression of PRL mRNA level in PBMCs in 12 male patients, and also investigated PRL mRNA of PBMCs collected from 5 healthy men that stimulated by HCV produced by Huh7.5 cells in vitro.
Result: Serum PRL levels were significantly higher in the HCV-infected subjects than in the controls ($p< 0.01$). They were significantly higher in HCV-infected male subjects than in the controls ($p< 0.001$). Serum PRL levels were significantly higher in male patients than in the controls ($p<0.01$). Serum PRL levels decreased significantly after interferon therapy in patients with sustained virological response to therapy ($p<0.05$). The levels of PRL mRNA in PBMCs derived from HCV-infected patients were significantly higher in 12 male patients than in the controls ($p<0.001$).
Conclusion: The high levels of PRL expression are associated with HCV infection in carriers.

PE355

Comparision of Antiviral Activity between Interferon Omega and Alpha 2a Based on Infectious HCV Cell Culture System and HCV 1b Replicon

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Background and Objectives: Hepatitis C virus (HCV) is a major cause of chronic liver hepatitis, cirrhosis, and hepatocellular carcinoma.Current clinic standard therapy is interferon alpha (IFN-α) combination with ribavirin, but this treatment is associated with adverse effects and often fails to induce a sustained response. Until recently, development of a HCV cell culture system (HCVcc) provides a suitable tissue culture system to study the complete HCV life cycle. In this study, we tested the effect of IFN omega (IFN-ω)—a member of type I interferon on HCV compared with IFN-α based on HCV 1b replicon and HCVcc.
Methods: We compared IFN-ω and IFN-α 2a effects on HCV RNA replication and protein expression, as measured by ribozyme protection assay and western blot. We also compared the intracellular protein level of phosphorylated signal transducer and activator of transcription 1 (p- STAT1) treated with different interferon type and concentration with western blot analysis.
Results: HCV RNA and protein level were inversely related with IFN-ω concentration and compared with IFN-α2a, at the same concentration, the

HCV RNA and protein levels treated with IFN-ω were lower than that treated with IFN-α 2a（$p<0.05$）.Also based on the HCV RNA analysis, EC50 of IFN-ω was 10 folds lower than IFN-α 2a. IFNs increased intracellular p-STAT1 level at a dose dependent manner and compared the same concentration of IFN-ω and IFN-α 2a, p-STAT1 protein level was higher in IFN-ω treated group（$p<0.05$）.
Conclusions: These results demonstrate distinct antiviral effect of IFN-ω compared with IFN-α 2a and this difference maybe partly caused by the stronger stimulation of IFN receptor . Outstanding antiviral activity of IFN-ω may be useful for developing new HCV treatment strategies.

PE356

Preponderance of Hepatitis C Virus Genotype 1b with Occult Hepatitis B Virus Infection in an Area with Intermediate Prevalence of HBV Infection

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Background & Aim: Hepatitis B virus (HBV) infection with undetectable levels of hepatitis B surface antigen (HBsAg) is called an occult infection, which although has been described among subjects with chronic hepatitis C liver disease in the western world, it's prevalence and clinical significance are still ambiguous in the Indian subcontinent.
Materials and Methods: We investigated HBV-DNA PCR in serum samples of 260 HBsAg negative subjects with chronic HCV-related liver disease, and 70 apparently healthy volunteers negative for HBsAg and anti-HCV as control.
Results: Serum samples found positive by at least two independent PCR assays were considered HBV DNA positive. HBV-DNA was detected among 19 HCV-related chronic liver disease (CLD) patients (7.3%), which was higher ($p = 0.2$) as compared with the control volunteers (4.3%). It was more frequent (37.5%) in 24 anti- HBs negative/anti-HBc positive patients than in 180 anti-HBs/anti-HBc positive (5 %, $p < 0.05$). HCV RNA by qualitative PCR was significantly ($p <0.001$) higher in occult HBV compare to non-occult. HCV genotype 1b was predominantly associated with occult HBV (73%), especially among subjects with hepatocellular carcinoma (HCC) ($p<0.05$) as compared to non-occult HBV cases. Though not significant, frequency of occult HBV infection was higher than healthy controls and HCV 1b genotype was significantly associated in patients with HCC.
Conclusion: This study suggests that in all HBV-endemic areas, the possibility of occult HBV in patients with HCV should be considered and HBV-DNA should be performed.

PE357

HIV, Syphilis and HCV Infections among Men Who Have Sex with Men in Shenzhen, China

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Background: Besides HIV and syphilis, hepatitis C virus (HCV) is also rapidly spread among men who have sex with men (MSM). This study was designed to identify the prevalence of these 3 sexual transmitted diseases in MSMs in Shenzhen, China.
Methods: A cross sectional study was conducted by using time location sampling method from April to July, 2008. 831 MSM participants (including 454 Male sex workers) were recruited and finished guided self-administered questionnaires (or interviews if they have difficulty in reading or understanding) in 37 venue-date-time randomly selected from 48 active venues.
Results: Results were analyzed using SPSS. 736 blood samples were collected for HIV, syphilis and HCV test. Participated MSMs were between the age of 18 to 51 years (25.5±5.9) with a majority of 20-29 years (73.7%). Most of them finished junior high school education (74.9%). 84.2% had high level of knowledge on modes of transmission and prevention. Likewise, 56.0% MSMs have ever sold sex to men, 38.3% of them were self identified as gay, 35.1% as bisexual. 78.3% MSMs had multiple male sexual partners and 50.3% MSMs always used condom. 48.6% of them had sex with women in the past 6 month, and the condom use rate decline to 35.1% during both male and female sex. HIV positive rate is of 6.7% and syphilis for 18.3%, HCV is only found in 3 cases (0.4%).
Conclusions: A greater number of the participants have both male and female sex partners. This survey shows that HCV infection rate is still low among MSMs in Shenzhen, although the HIV and syphilis rate is high and continuing increased in the past few years.

PE358

The Change of Insulin Sensitivity in Hepatitis C Patients with Normal Insulin Sensitivity

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Background: Hepatitis C virus (HCV) infection is associated with a high prevalence of diabetes mellitus (DM). Insulin resistance (IR) is known to play a crucial role in the development of DM in Chronic hepatitis C (CHC) patients. We prospectively investigated the change of insulin sensitivity in CHC patients during 5-year period, and analyzed factors significantly associated with IR.
Methods: Subjects consisted of 62 non-cirrhotic CHC patients with normal alanine aminotransferase (ALT) and normal insulin sensitivity (CHC group), and healthy control group of 172 subjects matched by age, sex, body mass index and life styles. We compared initial baseline insulin sensitivity, metabolic parameters and incidence rate of IR at the end of follow up period in both groups. The change of insulin sensitivity and metabolic parameters and development of IR was analyzed, and factors associated with development of IR were evaluated.
Results: IR developed in 22.5% of 62 CHC patients and 5.2% of 172 normal individuals ($P<0.001$). HCV infection per se and genotype 1 were independent risk factors of IR. Initial fasting glucose 90-100 mg/dL, fasting insulin≥10 uIU/mL, HOMA-IR 2.3-2.7 were significantly associated with development of IR in CHC group.
Conclusions: HCV infection is independent risk factor of IR. Even if CHC patients with normal insulin sensitivity, careful monitoring for IR is necessary.

PE359

Prevalence of Viral Hepatitis C in Latvia

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Background and aim: Viral hepatitis C (VHC) because of its prevalence and clinical course has become one of the most actual infectious diseases in the world. To date chronic hepatitis C affects over 170 million individuals worldwide. Chronic VHC is a leading cause of cirrhosis and hepatocellular carcinoma.
The aim of this study was to investigate how many residents of Latvia, that are over 18 years of age have been exposed to VHC (anti-HCV prevalence) and how many are infected at the moment (HCV-RNA prevalence). Until now such research has not been performed in Latvia.
Methods: From the register of general practitioners there were randomly selected 26 GP's from different regions of Latvia, 60 persons over 18 years of age were selected out of each GP register and tested for anti-HCV with screening test (ELISA). In case of positive result antibodies were confirmed with Western-Blot reaction and person was tested for HCV-RNA (PCR).
Results: In total 1591 person was invited by general practitioners for the test and 1442 persons responded (response rate 90.6%). Confirming test (Western-Blot) was positive in 34 participants and out of which HCV RNA test was positive in 25 patients.
Conclusions: There are 2.4% of people exposed to hepatitis C virus in Latvia and 1.73% are infected with hepatitis C virus, respectively, 1734 infected persons per 100 thousand individuals.

PE360

Genetic variation in the IKK/NF-κB pathway and the live fibrosis progression in chronic hepatitis C

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Background/Aims: IκB kinase/NF-κB (IKK/NF-κB) signaling pathway is thought to play critical roles in liver inflammation and fibrogenesis. We carried out a haplotype-based association study to examine the contribution of common genetic variations in the genes encoding NFκB inhibitor kinase alpha and beta (IKBKA and IKBKB; the major components of IKK/NF-κB pathway) to the progression of live fibrosis in chronic hepatitis C.
Methods: Based upon the common single nucleotide polymorphisms (SNPs; minor allele frequency(MAF)≥0.05) and linkage disequilibrium (LD) information derived from the HapMap, we selected 5 and 3 tag SNPs from IKBKA, and IKBKB, respectively, for genotyping. By using melting curve analysis, SNPs were genotyped in 217 chronic hepatitis C patients, including 80 patients with hepatocellular carcinoma. Association between common genetic variations in IKBKA/IKBKA and platelet count (Plt) was tested by both genotype- and haplotype-based approaches.
Results: We succeeded in genotyping a total of 8 tag SNPs that efficiently capture common variation across the 32 kb-block of IKBKA and the 25 kb-block of IKBKB. For each of genes tested, 5 haplotypes were found in population studied. All SNPs were in Hardy-Weinberg equilibrium, but no significant association was observed between any single tag SNP or haplotype and decreased Plt in patients analyzed.
Conclusions: Our data suggest that it is unlikely that polymorphisms within the IKBKA and IKBKB genes are involved in the progression of live fibrosis in chronic hepatitis C. Further studies on genetic variations in other NF-κB-related genes in chronic hepatitis C are needed.

PE361

Efficacy of Interferon β Combined Cyclosporine a Treatment in the Retreatment of Chronic Hepatitis C - Promising Aspect of conquest of Posttransplant Hepatitis C

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Background: Hepatitis C virus infection is a major burden after liver transplantation. The effective treatment for patients who underwent liver transplantation has not been well established. Management of these patients is the most challenging task. Cyclophilins are essential host factors for HCV replication. We report here the efficacy of divided administration of IFNβ plus cyclosporine A in the treatment of chronic hepatitis C patients who failed Peg-IFN or IFN combined ribavirin.
Patients and method: We prospectively included 59 patients (median age, 63) with genotype 1b and, failures to combination IFN plus ribavirin or combination pegylated IFN plus ribavirin. The present treatments consisted of an induction therapy, an intensified therapy and a maintenance therapy. The induction therapy comprised intravenous 1 MU IFNβ every 4 hours for the first 3 days, 1.5 MU IFNβ every 6 hours for the next 4 days and 2 MU IFNβ every 8 hours for the following 3 weeks, totaling 168 MU of IFNβ. The intensified therapy was induction therapy shortened to 2 weeks. The maintenance therapy comprised of pegylated IFNα2b and ribavirin. CsA was given 4 times daily during the induction and the intensified therapies. Ribavirin was given twice daily during the maintenance therapy.
Results: The end treatment response and sustained virological response rate of the present study were 73 % (43/59) and 59% (35/59), respectively. The relapse rate was 19 %(8/43). Non-responders was 16 % (3/19). All adverse effects were completely reversible. The treatment protocol was well tolerable.
Conclusion: We concluded that our protocol should be effective in failures to the previous combination therapies. Host factor targeting treatment will become a promising treatment option.

PE362

Cyclophilin Targeting Treatment is a Promising New Anti-HCV Treatment

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Background: Hepatitis C virus (HCV) is the most common cause of chronic liver disease. However, the efficacy of currently available treatments is limited. We recently reported the effects of combined interferon- /cyclosporin A treatment. Cyclophilins are associated with HCV replication and bind cyclosporin A. Which cyclophilins are closely associated with HCV replication remains controversial.
In this study, several cyclophilins were found to be essential host factors for HCV replication and HCV replication was rescued by overexpression of cyclophilin A in the presence of cyclosporin A.
Methods: We evaluated the effect of cyclosporin A and its analogues on the replication of HCV in vitro using several types of HCV replicon. The gene expression of representative cyclophilins and Pin-1 was knocked down using small interfering RNA2 (siRNA) to identify cyclophilins associated with HCV replication. The specificity of the effect of siRNA was confirmed by western blot analysis. The effect of overexpression of cyclophilins on HCV replication in the presence of cycloporin A was also studied.
Results: Cyclosporin A and its analogues suppressed HCV replication in a dose dependent manner. Cyclophilin F, cyclophilin LC1 and cyclophilin LC2 as host factors which are closely associated with HCV replication, in addition to the previously reported cyclophilin A. Knockdown of chclophilin B showed little effect on HCV RNA replication. Cyclophiln-dependent HCV replication varied among the three HCV replicon cell-lines used. Overexpression of cyclophilin A rescued HCV replication in the presence of cyclosporin A.
Conclusions: These findings suggest several cyclophilins are essential host factors for HCV RNA replication. Thus potent cyclophilin inhibitors have the potential to be anti-HCV drugs.

PE363

HCV Genotype Distribution in Chronic Hepatitis C patients in Tertiary Care Hospital of Rawalpindi, Pakistan

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Background/Aims: Hepatitis C Virus (HCV) genotypes 1-6 have a worldwide distribution. Types 1a and 1b are predominant in Northern Europe and North America, and in Southern and Eastern Europe and Japan, respectively. Type 3 is endemic in south Asia and is variably distributed in different countries. Genotype 4 in Egypt, genotype 5 in Central and South America and genotype 6 is common in China, Japan and South East Asia. In Pakistan 3a is the commonest genotype, which is associated with the most favorable outcome regarding end treatment response and sustained virological response after 24 weeks of therapy. The aim of this study is to find out HCV Genotypes in newly diagnosed chronic hepatitis C patients.
Methods: This observational study was conducted in chronic hepatitis C patients. All patients had raised ALT levels for last 06 months, had positive polymerase chain reaction (PCR) for HCV RNA by real time method and liver biopsy was done in all patients under National program for prevention and control of hepatitis during year 2006 - 2007. Genotyping was done on Roche Genotyping Kit. Data was analyzed by SPSS 13.0
Results: Out of 164 patients, 85.9% (n=141) were genotype 3a. 6.1% (n=10) were genotype 3b. 3.0% (n=5) were genotype 1a. n= 01 had genotype 1b. 4.2% (n= 7) had mixed genotype (3a,3b/1a,1b,3a,3b).
Conclusion: Majority (85.9%) of chronic hepatitis C patients were genotype 3a which is associated with favorable outcome after 24 weeks of interferon and ribavirin therapy and only 3.0% had genotype 1a in this cohort.

PE364

Hepatitis B and Hepatitis C seroprevalence in children with human immunodeficiency virus-1 infection in China

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Background/aims: As human immunodeficiency virus (HIV) infected children who are receiving antiretroviral therapy (ART) are living longer in China, comorbidities of hepatitis B virus (HBV) and hepatitis C virus (HCV) coinfection should be carefully considered when making management decisions. However, the coinfection rate of either HBV or HCV is unknown in HIV-infected children in China. We evaluated the seroprevalence of HBV and HCV in the China national pediatric ART cohort of HIV-infected patients.

Methods: Patients were selected from HIV infected children medically eligible for ART who were enrolled into the China national pediatric ART cohort since 2004. Interviews, medical assessment, serology for HBsAg, anti-HCV antibody, transaminase levels, and HIV serostatus and CD4 counts at baseline of patients were obtained.
Results: 42 of 763 HIV-infected children were HBsAg seropositive (5.50%; 95%CI: 3.88%-7.12%), and 69 of 662 children were anti-HCV antibody seropositive (10.42%; 95%CI: 8.09%-12.75%). Only age was associated with HBV coinfection. Multivariate analysis revealed that children infected with HIV through contaminated blood or transfusion of blood products were 6.35 times more likely to be anti-HCV antibody positive than those infected with HIV through other routes. And children from central China provinces, Henan, Anhui, Shanxi, and Hubei were 2.5 times more likely to be HCV seropositive.
Conclusion: The high seroprevalence of HBV and HCV coinfection in HIV-infected children attending China national pediatric ART cohort calls for routine screening for hepatitis viral coinfection and modification of the management of HIV-infected children in China.

PE365

BMS-790052 is a First-in Class Potent Hepatitis C Virus (HCV) NS5A Inhibitor for Patients with Chronic HCV Infection: Results from a Proof-of-concept Study

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Background: BMS-790052 is a first-in class and highly selective hepatitis C virus (HCV) NS5A inhibitor with picomolar *in vitro* potency against genotypes 1a and 1b. In a SAD study with healthy subjects, BMS-790052 was safe, well-tolerated, and had a pharmacokinetic profile suggestive of once-daily dosing.
Methods: The objectives of this randomized, double blind, placebo-controlled, SAD study were to evaluate the safety, tolerability, antiviral effect and pharmacokinetics of BMS-790052 in patients with genotype 1 chronic hepatitis C (CHC). Treatment naïve or experienced patients were randomized to receive 1, 10, or 100 mg of BMS-790052 or placebo.
Results: All BMS-790052 single doses were well tolerated and had a safety profile similar to that of placebo. Following oral administration, BMS-790052 was readily absorbed with dose proportional exposures over the studied dose range. The mean terminal half-life of BMS-790052 was approximately 12 hours. Mean decline in HCV RNA 24 hours after a single 1, 10 and 100 mg dose of BMS-790052 was 1.8 $\log_{10}$ (range 0.18 to 3.0 $\log_{10}$), 3.2 $\log_{10}$ (range 2.9 to 4.0 $\log_{10}$) and 3.3 $\log_{10}$ (range 2.7 to 3.6 $\log_{10}$), respectively. The 100 mg dose resulted in a mean decline of 3.6 $\log_{10}$ (range 3.0 to 4.1 $\log_{10}$) 48 hours after dosing, which was maintained at 144 hours.
Conclusions: Single doses of up to 100 mg of BMS-790052 were safe and well tolerated in patients chronically infected with HCV genotype 1. BMS-790052 produced a robust decline in HCV RNA and has a pharmacokinetic profile that potentially supports once-daily dosing.

PE366

Viral Sequence Evolution of Full-length Open Reading Frame in Chronic Hepatitis C Patients Experiencing Treatment Failure during and after Antiviral Therapy

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Background: The global infection rate of HCV is approximately 3%, and nearly 3.2% in China. Only 42%-46% of patients with genotype 1b can achieve sustained virological response (SVR) after antivirus therapy, nearly half of them experienced treatment failure. The study aimed to determine HCV-1b sequence evolution in patients experienced treatment failure during and after therapy, and further analyze relations between the mutations and treatment outcome.
Methods: 19 patients with genotype 1b accepted antiviral treatment of IFN plus Ribavirin for 48 weeks, and long-term follow-up after therapy. 2 patients experienced treatment failure were further analyzed (one for relapser, another for nonresponder). Sera were reserved at baseline, 12W, 48W and 4-year after therapy. HCV-RNA was extracted. HCV full-length ORF was amplified by RT-nested-PCR and sequencing.
Result: 9 of the 19 patients achieved SVR (47.4%). From sequence alignments of relapser at baseline and 48W, we find that p7, NS5A and NS4A have higher mutation rate both in nucleotide and amino acid level (7.41% and 6.35%, 4.08% and 5.63%, 4.32% and 5.56%, respectively). But there is no significant difference in the alignments of 48W and 4-year after therapy, the mutation rate is lower. Mutation rates of the non-responder among baseline, 12W, 48W and 4-year after therapy are very low.
Conclusion: Antivirus effect is correlated with specific HCV sequences in chronic hepatitis C, mutations in HCV non-structure protein p7, NS5A and NS4A have important impacts on treatment outcome in IFN-based therapy.

PE367

The Result of Antiviral Therapy in Elder Patients with Chronic Hepatitis C

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Background: The results of antiviral therapy for hepatitis C (HCV) have improved recently with the use of peg-interferon (peg-IFN)/ribavirin therapy. However, age of patients are concerned because of side effects and safety. As we known, a few studies have targeted therapy in elder with chronic HCV.
Aim: We reviewed the results of interferon based antiviral therapy in the elderly with chronic HCV at our institution.
Methods: Patients were defined as elderly if they were 65 years and elder who received therapy for HCV. The prescribed treatment duration, end of treatment response were mention. The data recorded included laboratory tests, adverse events (AE), dose modification, and withdrawal rate of therapy.
Results: 304 of chronic HCV patients treated with peg-IFN/ribavirin between Nov 2004 and Feb 2008. 50 patients were older than 65 years old. The mean age of the elder patients was 70.3 ± 4.8 years old. 21 were male and 29 were female. Histological studies showed 18 with cirrhosis. Almost all patients had experienced AE/side effects. The most common abnormalities were anemia and neutropenia. Therapy was discontinued in 22% (11/50). The rate of dose modification was 46% (18/39) patients who received 24 weeks therapy. Transaminases were normalized in 66% (33/50) after 24 weeks treatment and sustained in 66% (29/44) one year later.
Conclusion: The elder patients are more at risk of developing AE while on treatment. Most patients should be discontinued or decreased dosage of medication. However, the elder patients with chronic HCV can be treated successfully.

PE368

Incidence of Interstitial Pneumonitis (IP) among HCV-infected Patients Treated with Pegylated Interferon

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Background: In the general population the incidence of interstitial lung disease is estimated to be 0.03% and has also been reported with the use of interferons. The higher reporting rate of IP in Japan has created interest and warrants further investigation.
Methods: Using both data from 12 randomized clinical trials (ex-Japan) and the Roche world-wide safety database (ADVENT), the frequency of IP was estimated in patients treated with peginterferon alfa-2a ± ribavirin. IP was defined as: interstitial lung disease, alveolitis, pulmonary fibrosis, pneumonitis and pulmonary toxicity.
Results: One case of IP was reported among the 6180 patients included in the clinical trials (0.02%). In the ADVENT database considering the estimated 926,000 patients with cumulative exposure to peginterferon alfa-2a (42,600 in Japan and 883,400 US/ROW) the 228 reported cases of IP represent a rate of 0.02% with a proportional reporting ratio (PRR) of 1.7 ($p<0.0001$). Of

these cases, 140 were reported in Japan (PRR 2.9; p<0.0001), 34 in the USA (PRR 0.7; p=0.06) and 54 ROW (PRR 1.2; p=0.11) representing reporting rates of 0.3% in Japan and 0.01% in the USA and ROW. Japanese patients with reported IP were older (66 versus 50-55 years) and were more likely to have been treated with peginterferon alfa-2a monotherapy (81% versus 21-39%). Furthermore, the yearly incidence rate has remained unchanged.
Conclusions: The apparently higher rate of IP reported in Japan may result from differences in patient demography, diagnostic criteria and treatment patterns. The overall incidence of IP remains low.

PE369

Serum Retinol-binding Protein 4 is Dysregulated in Chronic Hepatitis C Patients

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Background: Hepatitis C virus (HCV) infection carries a significant risk for development of insulin resistance (IR) and/or diabetes (DM). Recently, retinol-binding protein 4 (RBP4) has been reported as a protein contributing to IR. This study aimed to assess the different expression of serum RBP4 between chronic HCV infection (CHC) patients and non-CHC controls.
Methods: Serum RBP4 was measured in 105 treatment-naïve CHC patients and its correlation with the homeostasis model assessment of insulin resistance index (HOMA-IR), liver histology, virology and metabolic factors was investigated. Patients were stratified into different stages of glucose tolerance by oral glucose tolerance test. Another 100 sex- and age-matched non-CHC adults served as the controls.
Results: The mean RBP4 level of controls tended to be higher than that of CHC patients (32.46 ± 20.92 vs 25.48 ± 13.13 μg/mL, P=0.07). The mean RBP4 level of 34 IGT control-group subjects was 43.7 ± 24.0 μg/mL, which was significantly higher than that of 34 NGT (24.4 ± 13.0 μg/mL, P<0.001) and 32 DM controls (29.0 ± 19.5 μg/mL, P<0.01). In contrast, the mean RBP4 level (22.2 ± 10.3 μg/mL) of 32 DM/CHC patients was not significantly different from that of NGT/CHC (24.9 ± 10.5 μg/mL, n=28) and IGT /CHC (28.1 ± 15.8 μg/mL, n=45) patients. Amongst CHC patients, there was a significant decreasing linear trend of RBP4 dependent of both histological grading and staging progression, whilst a significant increment of HOMA-IR was found.
Conclusion: Serum RBP4 is dysregulated in CHC patients.

PE370

A Randomized Open Label Clinical Trial with Pregabalin in the Treatment Regime with Interferon Therapy For Chronic Hepatitis C

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Introduction: Sustained Viral Response (SVR) in Hepatitis C treatment with Interferon Alfa and Ribavirin is affected by adherence and compliance due to severe myalgia, fatigue-anxiety and disturbed sleep. Pregabalin, an orally effective GABAsergic drug is not metabolized via Cytochrome P450 and is used in fibromyalgia and fatigue-anxiety syndromes without hepatic toxicity.This study evaluates the addition of Pregablin to standard agents in achieving SVR by reducing side events.
Methods: Thirty patients with chronic hepatitis C {mean age – 46 years, male: female - 2:1,Genotype(G)1(n=29), G6 (n=1), Fibrotic score F2-3 (n=24) and F4 (n=6), mean BMI > 29 Kg/m^2, initial viral load > 800,000 IU/ml} were randomized to Pregablin100mg (n=15) or Duloxetine 20mg (n=15) both orally daily with Interferon Alfa 2a 180mcg sq once a week and Ribavirin 1200mg daily for 48 weeks. Myalgia anxiety scale, modified quality of life score - evaluated at entry and tri-monthly. All were tested for rapid viral response, early viral response and end treatment viral response and SVR.
Results: At the end of 48 weeks, in the Pregablin arm, 14(97.3%) completed the therapy without interruption, one stopped due to excessive somnolence. Duloxetine arm -10(66.6%) completed with interruptions, 4(22.2%) withdrew from the trial due to side events, one left the country. 9(62.2%) achieved SVR in pregablin arm and 5(33.3%) with Duloxetine.
Conclusions: Pregablin may be considered with IFN and RBV for better adherence and compliance in achieving SVR in treatment of Chronic Hepatitis C. Larger randomized studies are needed to confirm the findings.

PE371

Intravenous Silibinin as "Rescue Treatment" for on Treatment Nonresponders to Full Dose of Peginterferon/ribavirin Combination Therapy

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Background: Silibinin (SIL) given intravenously at a dose of 20 mg/kg/day for 14 days had marked antiviral properties in nonresponders to full dose of peginterferon/ribavirin (SOC) combination therapy with chronic hepatitis C (Ferenci et al, Gastroenterology 2008), confirming in vitro findings that SIL inhibited viral replication. In this study we extended this treatment approach to on treatment nonresponders (defined as having detectable HCV-RNA after at least 24 weeks of SOC).
Methods: So far, 5 pts. HCV-RNA pos. after 24 weeks of SOC (3 male, 2 female, genotype 1:4; genotype 3a:1, 3 with cirrhosis) participated in this protocol; 4 were treatment naïve pts, 1 relapser to two previous therapies (24 and 48 weeks). 20 mg/kg/d SIL was given for 14 days, SOC was continued. HCV-RNA was quantified by TaqMan (Roche Diagnostics, USA) at monthly intervals on standard treatment and weekly after starting SIL.
Results: All patients received at least 24 weeks of SOC, at week 24 3 had a log drop < 3, two patients had detectable but unquantifiable HCV-RNA (< 15 IU/mL). After 14 days of SIL all 5 had undetectable HCV-RNA, in one HCV-RNA increased to 100 IU/ml and recived after a second course of SIL. .All 5 patients are still on SOC and are HCV-RNA negative.
Conclusion: SIL iv. Is an effective "rescue treatment" for on treatment nonresponders to full dose of peginterferon/ribavirin combination therapy.

Poster Exhibition –Imaging Modalities
Poster Session, Hall 5B

PE372

Using Sonazoid-enhanced ultrasonography to evaluate hyperechogenic nodules and particularly to identify residual lesions after transcatheter arterial chemoembolization (TACE)

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Background: Levovist-enhanced ultrasonography using subtractions makes it possible to depict the perfusion of hyperechogenic nodules. Our institution performs Sonazoid-enhanced ultrasonography using a Toshiba APLIO80 that is set to a PS low images, as generally recommended. The resulting images, however, are difficult to evaluate the kind of staining image that is obtained from a hyperechogenic nodule. These staining images were then compared to Advanced Dynamic Flow (ADF) images of a hyperechogenic nodule recorded using Levovist-enhanced ultrasonography.
Methods: The subjects were five nodules who had undergone Sonazoid-enhanced ultrasonography. Two patients had experienced a recurrence of HCC after TACE, while three patients had a hyperechogenic nodule of HCC that had never been treated. One patient with HCC after TACE was imaged at a PS low. The second patient with HCC after TACE and the three patients with HCC showing a high echoic nodule, were imaged using ADF.
Results: In the patients with HCC after TACE, the remaining tumor was difficult to observe in both the vascular phase and the Kupffer phase taken at a PS low. In the other patients, however, images taken using ADF clearly showed the residual tumor. Also, with regard to the findings from the

perfused images obtained from the three patients with hyperechogenic nodules of HCC, the HCC was more easily detectable in the ADF images than in those taken at a PS low.
Conclusion: Hyperechogenic perfused nodules are easier to identify in images taken using ADF than in images taken using PS low.

PE373

Real-time Virtual Sonography and Sonazoid: Novel and Precision Navigation Tools for Percutaneous Radiofrequency Ablation of Hepatocellular Carcinoma

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Background: This study aimed to evaluate the usefulness of Sonazoid enhanced radiofrequency ablation under real-time virtual sonography (RVS) guidance in a series of patients with hepatocellular carcinoma (HCC).
Method: Twenty-five patients with a solitary HCC tumor measuring < = 2.5 cm in greatest dimension were enrolled in this study. Eight patients received an initial treatment, seven also received an additional treatment for local recurrent tumors, and the remaining ten had distant recurrent tumors. All patients were easy to scan by multiple detector CT (MDCT), but not by conventional ultrasound (US) examinations. Sonazoid enhanced US images can be observed on vascular imaging, micro-bubble tracing imaging (MTI), and post vascular (Kupffer) imaging.
Result: In all patients, MRP images of target HCC tumors were displayed at good positions corresponding with US by the RVS system. Ten of the 18 (56%) patients with primary or distant recurrent tumor showed well enhanced areas on vascular imaging, while all patients demonstrated well enhanced areas on MTI, and non-enhanced areas on post vascular imaging. Seven patients with local recurrent tumors after radiofrequency ablation showed well enhanced areas at post ablation sites on vascular imaging and on MTI, and demonstrated non-enhanced areas on post vascular imaging. MDCT scans after radiofrequency ablation showed non-enhanced areas at ablation sites, suggesting complete necrosis of the HCC tumor.
Conclusions: The combination of the RVS system with Sonazoid-enhanced US appears to have a high potential for use on patients that are difficult-to-scan by US examinations for percutaneous radiofrequency ablation.

PE374

Utility of Contrast Enhanced Ultrasonography with Sonazoid in Radiofrequency Ablation (RFA) of Hepatocellular Carcinoma (HCC)

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Background & Aims: Contrast enhanced ultrasonography (CEUS) with Sonazoid can be expected to be useful not only for detection of tumor but also for US guided ablation therapy because Kupffer imaging lasts for long time. The aim of this study is to investigate the usefulness of Sonazoid in RFA for HCC.
Material & Methods: A total of 716 HCC nodules in 316 patients admitted to receive RFA were studied. The detection ability of HCC was compared between CEUS and conventional US using dynamic CT as reference standard. The effectiveness in the treatment was assessed by comparing the mean numbers of treatment session of RFA in patient treated with CEUS assistance and that in historical controls matched for tumor and background conditions.
Results: The detection rate was 83.5% in conventional US and 93.2% in CEUS (P=0.04). Sixty-nine nodules in 52 patients were not detected by conventional US and detected after injection of Sonazoid. The mean increase in detected tumor number with contrast enhanced US were well correlated with serum albumin level (P=0.016). CEUS was not superior to conventional US in patients with low albumin level. The mean number of session was 1.33±0.45 as compared to 1.49±0.76 in the historical controls (P=0.0019).
Conclusions: CEUS with Sonazoid is useful for detection of tumor in patients with well-conserved hepatic reservoir. The decrease in the mean number of sessions compared to historical controls suggested that Sonazoid is an excellent supportive agent in RFA treatment of HCC.

PE375

Computational Simulation of Peri-operative Change in Portal Blood Flow Dynamics in Fibrotic and Non-fibrotic Human Livers

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Direct measurement of peri-operative change in portal blood flow and pressure is difficult in human. In the present study, computational simulation of pre- and post-operative portal blood flow and pressure was performed using computational flow dynamic (CFD) software in patients with primary liver cancers.
Methods: Patients with fibrotic or non-fibrotic livers were analyzed. According to preoperative MD-CT, mesh models of portal branches were constructed. CFD software (Fluent 6.2, Fluent Inc.) was employed for flow simulation. On the Fluent 6.2, changes in flow dynamics in the remnant portal branches were simulated by virtual cutting of an interested portal branch. The simulation was also performed 14 days after the operation using DICOM data obtained at that time.
Results: Relative increase in blood flow in each remnant portal branch was not uniform throughout the liver in each patient. The sudden increase in portal pressure just after the virtual cutting of interested portal branch was almost normalized by day 14 in non-fibrotic liver according to the flow simulation, while the increase in fibrotic liver did not return to the pre-operative values by day 14. These results suggest that responsive dilatation of remnant portal branches and subsequent regional regeneration could normalize the sudden increase in portal pressure after surgery in non-fibrotic livers, while the mechanism is impaired in fibrotic livers.
Discussion: Computational flow dynamic simulation is useful to analyze the differences in the peri-operative portal flow dynamics and liver regeneration between non-fibrotic and fibrotic livers.

PE376

Hepatocellular Carcinoma Wash-out on CT: Comparison of Quantitative Region of Interest Analysis with Qualitative Analysis

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Aim: To determine if ROI analysis can characterize washout in Hepatocellular Carcinoma (HCC) better than visual analysis.
Methods: Surgically proven HCCs from a single institution were studied. The patients' gender, age, date of scan, date of surgery were recorded. 94 patients with pre-operative triphasic (n=67) and quadriphasic CT scans (n=27) were included.
A representative section containing the lesion was selected for each case. The HU change between the precontrast and arterial ($HU_{absolute\ hypervascularity}$) and the HU change between the peak attenuation and late portovenous phases ($HU_{absolute\ washout}$) were recorded. Cases were deemed positive if the HU change was more than the standard deviation (11 HU). This was compared against visual analysis to determine if our method would increase sensitivity of CT for HCC.
Results: The mean patient age was 63.7 years (range 19 to 84 years); there were 77 males and 17 females. The mean duration between surgery and the scan was 39.5 days (range 1 to 348 days).
Peak enhancement was seen in the early portal venous phase in 76.6% cases. The mean $HU_{absolute\ washout}$ was 23.8 HU (range -5 – 54). ROI analysis detected 86/94 cases (91.5%). This was 12.8% more than visual assessment, which detected 74/94 cases. This was statistically significant (p=0.014).
Conclusion: Visual assessment of lesion density is subjective. Quantitative measurement of lesion attenuation changes between scan phases is a simple and objective method that is more sensitive than visual assessment in determining lesion washout.

PE377

Characteristics of the missed hepatocellular carcinomas in the abdominal ultrasonogram

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Background: Abdominal ultrasonogram(USG) is a common available diagnostic tool to screen and follow up for hepatocellular carcinoma(HCC). But it has been reported that the specificity of ultrasonogram is high but the sensitivity of it is insufficient. We investigated the characteristics of HCCs that was missed in the USG but was detected in the CT.
Methods: Total 122 patients who were diagnosed with HCC between December, 2003 and February, 2008, were enrolled and analysed retrospectively. All patients were performed with a USG prior to a spiral CT. The period between USG and spiral CT was limited within 1 month. We investigated age, gender, cause(HBV, HCV, alcohol), the size of HCC(the length of long diameter), stage(modified UICC), Child-Pugh Grade, cirrhosis, tumor number, portal vein thrombosis, diffuse type of HCC, regenerative nodules(RNs), and the tumor location at segement 8 as the possible related factors.
Results: The mean period between USG and spiral CT was 3.04±5.70 days. The diagnostic accuracy rate to HCC was 84.4%(103/122). There was no interobserver variation. In analysis of associated factors, there was no statistical significance in age, gender, cause(HBV, HCV, alcohol), stage(modified UICC), Child-Pugh Grade, cirrhosis, portal vein thrombosis, diffuse type of HCC, regenerative nodules(RNs) ($P > 0.05$). There was statistical correlation in the tumor size less than 2 cm, the solitary tumor and location at segement 8. ($P > 0.05$).
Conclusion: Tumor size less than 2 cm, solitary lesion and location at segment 8 are significant factors to miss HCCs in USG diagnosis.

PE378

Percutaneous Liver Biopsy: Comparison between Blind versus Sonographic Guided Approach in Terms of Safety and Diagnostic Utility

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Background: Histopathological examination is required in the evaluation of various liver diseases for both diagnosis and prognosis. Earlier blinded percutaneous liver biopsy was done commonly but now there are various studies suggesting that sonographic guided percutaneous liver biopsy could be more precise and safer. Our aim was to compare the safety and diagnostic utility of sonographic guided versus blind percutaneous liver biopsy.
Methods: It was a retrospective single center study done between June 2003 and May 2007. Trucut Liver biopsy needle was used in all patients. Demographic, clinical and histological characteristics between the two groups were evaluated. Insufficient biopsy was defined as a sample with less than 6 portal spaces. We reviewed the type of complications and if hospitalization was required, or any mortality related to the procedure.
Results: Out of 256 liver biopsies done in this period after excluding 16 patients we included 240 patients, 144 in Group A(60%, blind approach) and 96 in Group B (40%, sonographic guided approach). Mean age was 38±12.4 years and male: female ratio was 1.6:1. Biopsy was sufficient in 76% in Group A and 94% in Group B ($p < 0.05$). Minor complications occurred in 58% in Group A and 49% in Group B which was not significant. Major complications occurred in 2.8 % in Group A and 1.2% in Group B which was statistically significant. Mortality was 1.2% in Group A and 0.4% in Group B which was statistically significant.
Conclusion: Our study suggest that sonographic guided percutaneous liver biopsy is superior in the diagnosis of liver diseases in all aspects when compared to blind approach as it is more safe, has more diagnostic utility with significantly less complications and mortality.

Poster Exhibition – Liver Fibrosis
Poster Session, Hall 5B

PE379

Effect of Lipid Lowering Agents on Acute and Chronic Liver Damage in a Rat Model

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Background/Aims: HMG-CoA reductase inhibitors have been shown to reduce hepatic stellate cell proliferation and collagen production and decrease oxidative stress and hepatic vascular tone in cirrhotic patients. Therfore, the aim of the present study was to examine whether the lipid lowering agents atorvastatin (Ato) or rosuvastatin (Ros) would prevent experimentally-induced acute or chronic hepatic damage in rats.
Methods: Liver cirrhosis was induced by thioacetamide (TAA, 200 mg/kg, I.P.) twice a week, for 12 weeks. Acute damage was induced by two consecutive TAA injections (200 mg/kg in a 24 h interval). Rats were treated concurrently with TAA only or TAA and either Ato or Ros daily by nasogastric gavage. Another group was treated with TAA+pentoxifyline (PTX), an agent with known antifibrotic effect through a different mechanism and served as positive control.
Results: Presented in the table (Means ± SD, n=7 in each group, *$p<0.05$):

Chronic (mg/kg/day)	**ALT (IU/l)**	**MDA (nmole/ g liver)**	**Hydroxyproline (mg/g protein)**	**Fibrosis Score (0-4)**
Control	62±33	26.2±4.1	2.6±0.6	0
TAA	65±30	38.1±10.7	11.5±3.2	3.5±0.7
TAA+Ros 5		37.3±10.3	10.5±4.0	2.7±1.8
TAA+Ros 10	51±7		11.9±2.8	3.3±0.8
TAA+Ros 20	51±3		10.5±5.0	2.7±1.8
TAA+Ato 1	49±17	37.9±9.0	11.3±3.3	3.8±0.2
TAA+Ato 10	54±5	38.0±8.9	9.8±3.2	3.9±0.2
TAA+Ato 20	52±10	35.9±12.6	10.1±4.5	3.9±0.2
TAA+PTX 50	50±12		5.9±2.2*	2.3±0.4*
Acute (mg/kg/day)	**ALT (IU/l)**	**MDA (nmole/ g liver)**	**Blood ammonia (µg/dl)**	**Hepatic Necroinflammation (0-3)**
TAA	2150± 928	14.0±2.8	640±159	2.5±1.5
TAA+Ato1	2462± 2475	12.9±1.2	632±240	2.7±1.6
TAA+Ato10	1124± 507	12.0±2.4	302±302	2.0±1.3
TAA+Ato 20	1433± 718	12.8±2.0	548±236	2.3±1.5

Conclusions: The lipid lowering agents used in our study had no effect on the development of acute or chronic hepatic damage in rats or on oxidative stress induced by TAA.

PE380

A New Noninvasive Method for Assessment of Hepatic Fibrosis - Usefulness of the Strain Rate Imaging Method

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Purpose: The development of hepatic fibrosis in patients with chronic liver disease increases the risk of liver cancer. The present study was conducted to determine whether an easily performed myocardial examination technique can be applied to the assessment of hepatic fibrosis. Strain Rate Imaging is a new method based on Tissue Doppler Imaging (TDI). The usefulness of Strain Rate Imaging in assessing the degree of hepatic fibrosis was evaluated. This time, it mede comparative study with Fibroscan in 11 cases.
Methods: Strain Rate Imaging was performed using a diagnostic ultrasound system (Aplio™, Toshiba Medical Systems Corporation, Tochigi, Japan) in a total of 47 subjects:25 in the chronic hepatitis group, 12 in the cirrhosis group, and 10 in the normal control group. TDI-Q, the Tissue Doppler analysis software installed in the Aplio system, was used for analysis. Measurement was performed five times from the epigastrium, with the ROI size set to 10 mm and the derivative pitch to 3 mm.

Results: The mean strain value was 0.156 in the chronic hepatitis group, 0.055 in the cirrhosis group, and 0.26 in the normal control group.The correlation was not thought to be Fibroscan.
Conclusion: The results of the present study suggest that this noninvasive method permits quantitative assessment of the degree of hepatic fibrosis to be performed easily and in a short time. It is expected that the accuracy of the Strain Rate Imaging method in determining the degree of hepatic fibrosis will be improved when it is used in combination with histological examination.

PE381

Elevated serum levels of 15-deoxy-Δ12, 14-prostaglandin J2 in patients with hepatitis C induced liver fibrosis and with hepatocellular carcinoma propose therapeutic approaches with PPARgamma inducing drugs

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Background: Current knowledge attributes connective tissue growth factor (CTGF/CCN2) a crucial role in enhancing TGF-β actions during hepatic fibrogenesis. Recently, we demonstrated that caffeine leads to an upregulation of PPAR in hepatocytes, thus sensitizing these cells to the well known inhibitory effect of 15-deoxy-$\Delta^{12,14}$-prostaglandin J_2 (15-d-PGJ_2) on CTGF expression. However, upregulation of the receptor alone is not sufficient *per se*, its physiological ligand 15-d-PGJ_2 is required for exerting its inhibitory effect on CTGF synthesis.
Aim and Methods: This study compares serum concentrations of 15-d-PGJ_2 in Caucasian patients with fibrotic liver diseases (n=289), Caucasian controls (n=136) and Caucasian non-liver disease sick (n=307), as well as of Chinese patients with hepatocellular carcinoma (n= 43) and Chinese healthy controls (n=63) in order to characterize their suitability for therapeutic approaches with PPAR inducing (i.e. CTGF inhibitory) drugs such as caffeine.
Results: Presented data show that Caucasian patients with ongoing hepatic fibrogenesis (mean 6.2 ± 5.9 µg/L) display impressingly higher serum concentrations of 15-d-PGJ_2 than healthy probands (mean 2.3 ± 1.0) and Caucasian patients with non-liver disease (mean 2.7 ± 1.4 µg/L). Similar results are found in Chinese patients with fully developed HCC (mean 1.3 ± 0.7 µg/L) compared to Chinese healthy controls (mean 0.4 ± 0.2 µg/L).
Conclusion: In conclusion, our data thus propose an increased suitability of these patient groups for therapeutic approaches with drugs inducing PPAR expression, such as caffeine.

PE382

Non-Invasive Assessment of Fibrogenic Liver Diseases as Exemplified by Serum Based Fibrotest/Actitest: How Reliable are the Results?

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Introduction: Non-invasive, i.e. serum-based multiparametric panels of biomarkers have been proposed for the diagnostic assessment of liver fibrosis.
Aims/Methods: (i) Haptoglobin, ALT, GGT, alpha 2-macroglobulin, apolipoprotein A1 and bilirubin in sera of 4 patients with histological proven fibrosis (F1-F4, A1-A3) were determined in 6 different quality-controlled laboratories. Interlaboratory variations of the calculated Fibrotest Score for staging and Actitest Score for grading (both BioPredictive™), and their error ratios compared to biopsy results were calculated. (ii) The variability of obtained Fibrotest/Actitest Scores depending on 64 differential combinations of the allowed analyt-specific maximum/minimum permissible values as determined by the external quality control of the German Association of Laboratory Medicine was determined and the frequency distribution of the results calculated.
Results: (i): Both scores were largely reproducible among the different laboratories. However, compared to the histological findings, the error ratio was 77% for all results calculated by Fibrotest and Actitest. (ii): Calculated scores varied among F2 (9%), F3 (31%), F3-F4 (6%), and F4 (54%) (Fibrotest), as well as A1/A2 (48%), A2 (9%), A2-A3 (5%), and A3 (38%) (Actitest).
Conclusion: Despite reproducibility of Fibro- and Actitest results among the six laboratories, large scale investigation (n=64) displayed increasing variability of the results depending on interlaboratory differences that were still in a quality controlled, analytically acceptable range. Furthermore, calculated scores coincided with histological findings only in less than 25% of all cases. Thus, the diagnostic accuracy of these tests seems low, if histology is accepted as gold standard.

Chronic (mg/kg/day)	**ALT (IU/l)**	**MDA (nmole/g liver)**	**Hydroxyproline (mg/g protein)**	**Fibrosis Score (0-4)**
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TAA+Ato 10	54±5	38.0±8.9	9.8±3.2	3.9±0.2
TAA+Ato 20	52±10	35.9±12.6	10.1±4.5	3.9±0.2
TAA+PTX 50	50±12		5.9±2.2*	2.3±0.4*
Acute (mg/kg/day)	**ALT (IU/l)**	**MDA (nmole/g liver)**	**Blood ammonia (µg/dl)**	**Hepatic Necroinflammation (0-3)**
TAA	2150±928	14.0±2.8	640±159	2.5±1.5
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TAA+Ato10	1124±507	12.0±2.4	302±302	2.0±1.3
TAA+Ato 20	1433±718	12.8±2.0	548±236	2.3±1.5

PE383

Low P2/MS Value Is an Independent Risk Factor for Early Recurrence of Hepatocellular Carcinoma after Radiofrequency Ablation Therapy

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Background: The influence of liver fibrosis on the recurrence of hepatocellular carcinoma (HCC) after local ablation therapy has not been fully elucidated. In this study, we aimed to evaluate the effect of P2/MS [(platelet count [10^9/L])^2/(monocyte fraction [%]×segmented neutrophil fraction [%])], which reflects the degree of liver fibrosis (presented in the 18th APASL meeting), on HCC recurrence after radiofrequency ablation (RFA) therapy.
Methods: Chronic hepatitis B patients who underwent RFA for hypervascular stage I HCC at Seoul National University Hospital, Seoul, Korea between September 2004 and August 2007 were prospectively included. We identified the predictors of tumor recurrence using Cox-regression model.
Results: A total of 51 patients (mean age, 54.3±9.8 years; male, 78.4%) were included. Median follow-up duration was 14.2 months (range, 5.6–37.3) and 20 patients (39.2%) experienced local tumor recurrence during the observational period. Multivariable analyses showed that low P2/MS level (relative risk, 0.98; 95% confidence interval [CI], 0.96–0.99; *P*=0.035) and serum alpha-fetoprotein level >100 ng/mL (relative risk, 5.41; 95% CI, 1.59–18.18; *P*=0.007) were independent risk factors for tumor recurrence. Patients with P2/MS level <45.0 revealed 3.79-fold (95% CI, 1.05–13.76; *P*=0.042) increase in the risk of recurrence after adjustment for serum alpha-fetoprotein level, as compared to those with P2/MS level >45.0.

However, tumor size, Child-Pugh score, and hepatitis B virus DNA level failed to significantly affect the time-to-recurrence.
Conclusion: Our study suggests that lower P2/MS value, which means more severe liver fibrosis, is an independent predictor for HCC recurrence after RFA.

PE384
Severity of Liver Cirrhosis And Prevalence of Osteoporosis
H.S. Woong[1], G.P. Gohn[1], N.G. Woo[1], K.D. Soon[1], K.J. Il[1], K.S. Hyoung[1], K.E. Mi[1], K.S. Hyun[1], L.B. Seok[1], L.H. Young[1]
[1] *Chungnam National University College of Medicine*

Background/Aims: Despite of its high prevalence, osteoporosis is an underestimated complication of liver cirrhosis. The aims of this study is to prove the prevalence of osteoporosis and osteopenia in patients with liver cirrhosis and to identify the principal risk factors associated.
Methods: The prevalence of osteoporosis and osteopenia was studied in patients with alcoholic or viral liver cirrhosis who were admitted to the Institute of Gastroenterology and Hepatology, CNUH between March 2008 and September 2008. Osteoporosis and osteopenia was evaluated by measuring their bone density using dual energy X-ray absorptiometry (DEXA) at lumbar spine and femoral head. The variables taken into consideration were: sex, body mass index (BMI), presence of cholestasis, severity and duration of liver disease.
Results: Total 45 patients (male 32 and female 13, respectively) were estimated for association of liver disease and osteoporosis. Of these, 39 patients were estimated for bone density of lumbar spine and neck of femur by dual X-ray absorptiometry (DEXA). Morning blood samples were taken for hormonal and biochemical analysis from all patients. Among 39 patients, 25 patients (64%) were found to have osteopenia or osteoporosis. There was no statistically significant correlation between age, BMI, severity and duration of liver disease, PTH, Vitamin D, ALP and IGF-1.
Conclusion: There is high prevalence rate of osteopenia or osteoporosis in liver cirrhosis. Although the causes of osteopathy are heterogeneous, the early diagnosis and treatment of osteopathy in patients with liver cirrhosis is important.

PE385
Mathematical Models using Conventional Laboratory Indicators to Predict Hepatic Fibrosis Progression in Chronic Hepatitis B
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Background: To build and to evaluate mathematical models for predicting liver fibrosis progression by using conventional laboratory indicators in chronic hepatitis B.
Methods: Liver biopsy and routine laboratory tests were performed in 391 patients with chronic hepatitis B. Using Multiple logistic regression to analyze evidently relevant indicators, then the predicting models were built and analyzed by ROC curve.
Results: After Spearman analysis, factors such as age, platelet count(PLT), international rate(INR), total bilirubin(TBIL), albumin(ALB), aspartate aminotransferase (AST), gamma glutamyltranspeptidase (GGT), total bile acid(TBA) and cholinesterase(CHE) were found to be correlated with liver fibrosis（$P<0.01$）. Three models ($s\geq2$, $s\geq3$, $s=4$, respectively) were built by PLT, INR, ALB, GGT and CHE, which were independent predictors after multiple Logistic regression analysis.Finally, Fibrosis Score (FS) was calculated to predict different liver fibrosis stages. ROC curve analysis revealed that the AUC of FS was 0.784 in $model_1$ ($s\geq2$), 0.768 in $model_2$ ($s\geq3$) and 0.806 in $model_3$($s=4$)（fig1）.The cut-off FS in $model_1$ was at 7.09 with 67.4% sensitive, 79.3% specificity and the accuracy was 71.1%. The cut-off FS in $model_2$ was at 5.67 with 75.0% sensitive, 67.7% specificity and the accuracy was 72.9%. The cut-off FS in $model_3$ was at 3.65 with 71.4% sensitive, 78.5% specificity and the accuracy was 73.7%.
Conclusions: The predicting models, built by using conventional laboratory indicators, have fairly well value for diagnosing hepatic fibrosis or hepatocirrhosis in chronic hepatitis B.

PE386
Impact of Liver Cirrhosis Induced by Carbon Tetrachloride on Atherosclerosis in the Rabbits Chronically Fed With High-Fat Diet
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Background: To investigate the effect of liver cirrhosis on the development of atherosclerosis in the rabbits chronically fed with high fat diet.
Methods: Normal male New Zealand white rabbits were randomly divided into four groups: a control group, a high fat diet group, a carbon tetrachloride (CCl_4) group and a complex group. Pathologic changes in ascending aortas and livers were observed. The levels of serum alanine aminotransferase （ALT）, lipid, C-reactive protein (CRP) were also determined.
Results: Significant hepatic steatosis, inflammation and fibrosis could be observed in the three treatment groups; while atherosclerosis and typical arteriosclerotic plaques in ascending aortas could only be observed in the two high fat diet groups. Compared with the control group, serum ALT and lipid levels in CCl_4 group were increased significantly ($P<0.05$), but no difference of arterial intima-media thickness (IMT) and I/M ratio between these two groups. The levels of serum ALT, lipid, CRP and IMT in two high fat diet groups were significantly increased compared with the control group ($P<0.05$). The level of serum ALT in the complex group was significant higer than that in the high fat diet group, but the I/M ratio was just opposite (all $P<0.05$), and there was no difference of IMT between the two groups.
Conclusions Rabbits treated with CCl_4 can elevate serum lipid levels, but can not induce atherosclerosis. Though the activity of liver inflammation was aggravated in the complex model group, it has no effect on atherosclerosis possibly partly because of malnutrition.

PE387
Higher Values of Liver Stiffness in Males with Mild Chronic Hepatitis C
C. Stern[1], A.C. Cardoso[1], R. Moucari[1], A.D. Pumpo[1], N. Giuily[1], P. Bedossa[1], P. Marcellin[1]
[1] *Hopital Beaujon*

Background/aim: Liver stiffness (LS) measured by FibroScan (EchoSens) is a noninvasive method to assess liver fibrosis in patients with chronic liver diseases. We evaluated the impact of factors on LS results in mild chronic hepatitis C (CHC).
Methods: CHC patients with METAVIR Fibrosis stage 1 at liver biopsy and a reliable LS exam were eligible. All patients had no prior antiviral treatment. The LS values were compared to clinical and biochemical data.
Results: 93 patients were included with the following characteristics: mean age 50 11, male gender (46%), mean BMI 23 2.7, median LS 5.8 kPa (3.2-21.8), diabetes (7%), genotype 1 (61%), METAVIR activity A1 (86%), A2 (10%), steatosis at biopsy 30% (92%), mean glucose 4.9 1, abnormal ALT (78%), abnormal GGT (47%), HOMA (2 1.2). The LS values were associated wtih male gender (median 6.1 in males *vs* 5.2 in females) (p=0.04), BMI (p=0.03), ALT (p=0.006), GGT (p=0.02) and glucose levels (p=0.04). No association was found between LS and activity stage (p=0.34) or steatosis (p=0.14). In the linear regression, the only factor independently associated with higher LS was gender (p=0.038). In men, higher LS was related to levels of ALT (p=0.005), but not to necro-inflammation grade (p=0.4). In women, LS was not associated with ALT levels, but with BMI (p=0.045) and GGT levels (p=0.035).
Conclusion: In patients with mild CHC, liver stiffness values are higher in males. These results suggest that different cut-off for fibrosis stage 1 should be proposed according to gender.

PE388
Effects of Shuanghu Qinggan Granule on Prevention and Treatment
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Aims: To investigate the effects of Shuanghu Qinggan Granule(SQG) on prevention and treatment of hepatic fibrosis induced by carbon tetrachloride in rats.

Methods: 60 SD rats were divided into 6 groups, normal control groupAmodel groupB, SQG largeC1, middleC2small dose groupsC3 and silymarin positive contrast groupD. The rats of BC1C2C3D were injected with carbon tetrachloride for 8 weeks. The rats of C1C2C3 were then administered with SQG for 8 weeks. The rats of D were then administered with silymarin for 8 weeks.
Results The liver structure of rats of B was severely damagedlarge amount of liver cells became obviously degeneratedand hepatic veins were clearly congested. The hepatic cells fatty degeneration and infiltration of inflammatory cells in rats of C1C2C3D reduced significantly. There was no fiber hyperplasia in liver tissues of rats of C1C2C3D. Blood serum HAⅣCPⅢP levels in rats of B were significantly higher than those in AC1C2C3D.
Conclusion: SQG has remarkable therapeutic effects on rats with hepatic fibrosis induced by carbon tetrachloride, the higher the dosage of SQG was, the more effective the results would be.

PE389

Does Sophisticated Biomarker Have Added Value In Prediction Of Significant Fibrosis In Chronic Hepatitis B? A Critical Appraisal

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[1] Chuncheon Sacred Heart Hospital, [2] Ajou University School of Medicine, [3] Korea University College of Medicine, [4] Pochon CHA University College of Medicine, [5] Inje University College of Medicine, [6] Pusan National University College of Medicine, [7] Catholic University College of Medicine

Background/aims: It has not been explicitly addressed whether new biomarkers additionally contribute to the prediction of liver fibrosis over readily available laboratory data. Our primary objective was to clarify whether new sophisticated biomarkers independently contribute to predict significant fibrosis (METAVIR F2) in chronic hepatitis B patients.
Methods: A total of 209 consecutive patients with chronic hepatitis B who underwent liver biopsy were recruited from 6 tertiary care medical centers between October 2005 and July 2007. The Risk Score (RS) models named RS-1 in 142 HBeAg positive patients and RS-3 in 67 HBeAg negative patients were derived from only routine laboratory data. The RS-2 in HBeAg positive group and RS-4 in HBeAg negative group were developed by using all correlates obtained from both routine laboratory data and sophisticated biomarkers [haptoglobin, apolipoprotein A1, α2-macroglobulin (α2-MG), hyaluronic acid, type III procollagenic peptide (PIIINP), matrix metalloproteinase-2 (MMP-2), and tissue inhibitor of metalloproteinase-1 (TIMP-1)].
Results: Comparison of area under the ROC curve between RS-1 [0.88 (95% CI, 0.81-0.94)] and RS-2 [0.89 (0.83-0.95)] showed no superior diagnostic accuracy of RS-2 over RS-1 (p=0.41). RS-4 [0.96 (0.92-0.99)] showed superior diagnostic accuracy over RS-3 [0.86 (0.76-0.95)] for prediction of significant fibrosis (p=0.003).
Conclusions: None of sophisticated biomarkers had value in addition to readily available laboratory data for the prediction of significant fibrosis in HBeAg positive patients. Two markers out of 7 sophisticated biomarkers provide additional diagnostic information in HBeAg negative patients. Before new biomarkers are accepted, their superiority to routine laboratory data should be meticulously appraised.

PE390

Observation of Therapeutic Effect of TINMAX HB-3 in Patients with Hepatofibrosis Post Hepatitis B and Cirrhosis

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Objective: To evaluate the efficiency and safety of "TINMAX" HB-3 Herbal Compound (cpd) in treatment of hepatofibrosis and cirrhosis post chronic hepatitis B.
Methods: A double-blind randomized method was employed. 60 patients of hepatofibrosis or cirrhosis post hepatitis B were separated into study group ("TINMAX" HB-3 group) and control group (natural vitamin group) by randomized method. The course was 52 weeks. Patients visited once every 12 weeks and the last visit at 12 weeks after the cessation of treatment. Part of patients had liver biopsy before and after treatment. Before, during the course and at the end of therapy, clinical symptoms and physical signs were evaluated, hepatic function, and serum markers of hepatofibrosis (such as hyaluronate acid, laminin, serum type III procollagen and collagen IV) were tested, and ultrasound evaluation was performed.
Results: 60 patients enrolled in the evaluation. 58 patients completed the evaluation according to the protocol. 20 patients had liver biopsy twice, 10 from the study group and 10 from the other one. At the end of therapy, the total effective rate of hepatofibrosis in histopathology is 74.13% in the study group, much higher than that of 21.95% in the control group ($P<0.05$). The total effective rate of serum markers of hepatofibrosis at the end of therapy in the study group was 70.10%, much higher than that of 30.24% in the control group ($P<0.05$). The total effective rate of non-invasion markers of hepatofibrosis at the end of therapy in the study group was 76.08%, much higher than that of 19.41% in the control group ($P<0.05$). The drugs of adverse event had not happened in both groups.
Conclusion: "TINMAX" HB-3 herbal compound (cpd) is effective and safe in treatment of hepatofibrosis and cirrhosis post chronic hepatitis B.

PE391

Clinical Value of Serum Indices for Hepatic Fibrosis in Chronic Liver Diseases

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[1] GI Department, First municipal hospital of Guangzhou, Guangzhou

Aim: To investigate the clinical value of serum indices for hepatic fibrosis in chronic liver diseases.
Methods: Competitive radioimmunoassay was used to determine the serum level of collagen type Ⅳ(ⅣC), laminin (LN) and hyaluronic acid(HA) in 193 patients with different severity degree of chronic liver diseases, and in 30 healthy subjects.
Results: The serum levels of ⅣC, LN, and HA in the patients with liver diseases increased to different extent, compared with those in the healthy subjects. Of which the highest of ⅣC, LN, and HA were found in the patients with primary carcinoma of liver or hepatocirrhosis，and the serum level of HA is highlight. The combination detection of serum ⅣC, LN, and HA is more valuable than single index.
Conclusion: Joint detection of serum ⅣC , LN, and HA is of higher significance in clinical diagnosis and prognosis of hepatocirrhosis, and is also available for successive observation on the development of liver diseases.

PE392

Fuzheng Huayu Decoction Prevents Hepatic Stellate Cell Activation through TGF-beta 1 Signal Transduction Pathway in Vitro

Q.L. Wang[1], Y.Y. Tao[1], L. Shen[1], C.H. Liu[1,2]
[1] Liver Disease Institute, Shanghai University of Traditional Chinese Medicine，Shuguang Hospital, [2] E-institute of TCM Internal Medicine, Shanghai Municipal Education Commission

Aims: To investigate the mechanism of Fuzheng Huayu decoction (FZHY) on hepatic stellate cells (HSCs) activation relating to TGF- 1 signal transduction pathway.
Methods: HSCs were isolated from normal rats by *in situ* pronase/collagenase perfusion followed by density gradient centrifugation. At day 4 after isolation, cells were stimulated with 100pM TGF- 1 for 24h, then incubated with 10% FZHY pharmacological serum or 10 M T R-I inhibitor (SB-431542) for 24h. Protein expression of –SMA, Smad3 was assayed by immunofluorescent stain; Total protein expression of –SMA, T R-I, Smad2/3 and nuclear expression of Smad3 was analyzed by Western blotting.
Results: FZHY pharmacological serum significantly decreased expression of α-SMA, T R-I, and inhibited Smad3 nuclear expression and translocation in TGF- 1 stimulated HSCs.
Conclusions: Fuzheng Huayu decoction can prevent HSCs activation through TGF- 1 signaling transduction pathway in HSCs, which may be the important molecular pharmacological mechanism of Fuzheng Huayu decoction action against liver fibrosis.

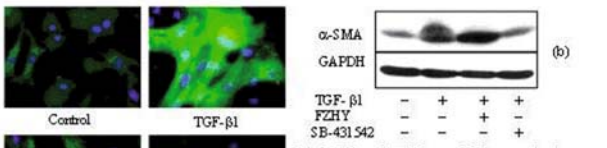

Fig.1. Effect of FZHY on α-SMA expression in HSCs. 4-day primary cultured rat HSCs were stimulated with 100pM TGF-β1 for 24h, then incubated with 10% FZHY pharmacological serum or 10μM SB-431542 for 24h. α-SMA expression was then determined by immunofluorescent stain (a) or Western blotting (b).

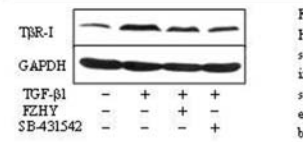

Fig.2. Effect of FZHY on TβR-I expression in HSCs. 4-day primary cultured rat HSCs were stimulated with 100pM TGF-β1 for 24h, then incubated with 10% FZHY pharmacological serum or 10μM SB-431542 for 24h. TβR-I expression was then determined by Western blotting.

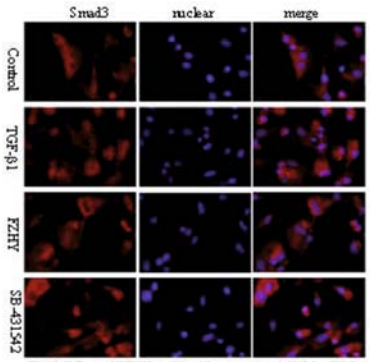

Fig.3. Effect of FZHY on Smad3 expression in HSCs. HSCs were stimulated with 100pM TGF-β1 for 24h followed by incubating with 10% FZHY pharmacological serum or SB-431542 for 24h. Smad3 expression was then determined by immunofluorescent stain.

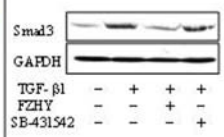

Fig.4. Effect of FZHY on Smad3 nuclear expression in HSCs. 4-day primary cultured rat HSCs were stimulated with 100pM TGF-β1 for 24h, then incubated with 10% FZHY pharmacological serum or 10μM SB-431542 for 24h. HSCs nuclear protein was isolated. Smad3 nuclear expression was determined by Western blotting.

PE393

Salvianolic Acid B Inhibits Hepatocytes Apoptosis in Vitro via TNFR1/Caspases Signaling Pathway

X.C. Yan[1], Y.Y. Tao[1], L. Shen[1], C.H. Liu[1,2]

[1] Liver Disease Institute, Shanghai University of Traditional Chinese Medicine，Shuguang Hospital，Shanghai, [2] E-institute of TCM Internal Medicine, Shanghai Municipal Education Commission, Shanghai

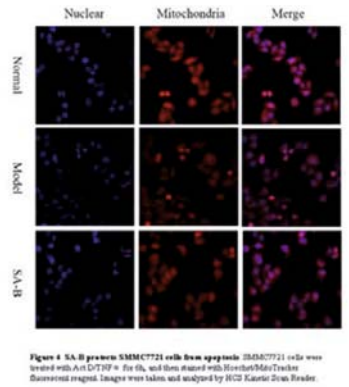

Figure 4 SA-B protects SMMC7721 cells from apoptosis. SMMC7721 cells were treated with Act D/TNF-α for 6h, and then stained with Hoechst/MitoTracker fluorescent reagent. Images were taken and analyzed by HCS Kaeter Scan Reader.

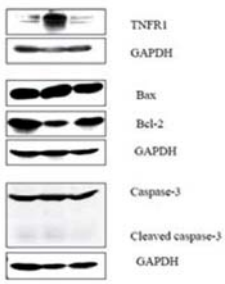

Figure 5 Antiapoptotic effect of SA-B is mediated through TNFR1/Caspases signaling pathway. Cultured SMMC 7721 cells were pretreated with SA-B (1 μ M), for 1 h before they were incubated for 6h with Act D/TNF-α. Protein expression was analyzed using Western blot.

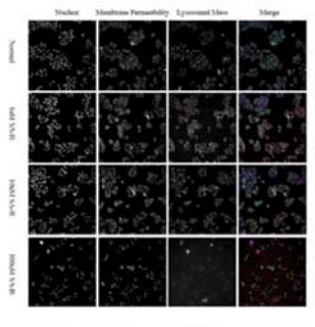

Figure 1 Effect of SA-B on proliferation of SMMC7721 cells. SMMC7721 cells were plated in 96-well plate with a density of 8000 cells/well. Cells were incubated with SA-B for 24 hours and then stained with Multiparameter Cytotoxicity Hst.

Figure 2 Agarose gel electrophoresis of DNA in SMMC7721 cells lane 1, Marker, lane 2, control, lane 3, model, lane 4, 1 μ mol/L SA-B, lane 5, 10 1 μ mol/L SA-B. DNA was purified by DNeasy Kit, 1.5% agarose gel electrophoresis for 45min.

Figure 3 Inhibition of apoptosis by SA-B in SMMC7721 cells. SMMC7721 cells were trypsinized and stained with Annexin V and PI, then analyzed by Calibur flow cytometer. FL1-H is Annexin V, and FL2-H is PI. Apoptotic cells (Annexin V positive and PI negative) and necrotic/ late apoptotic cells (both Annexin V and PI positive) are in the right lower or upper quadrant, respectively.

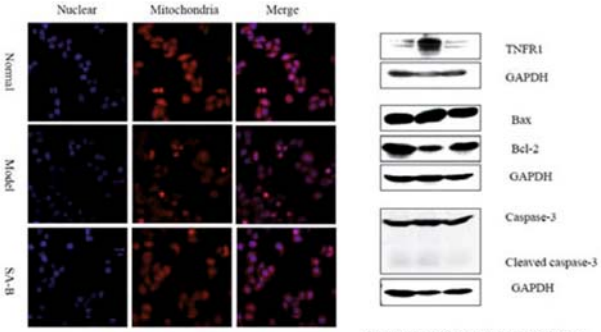

Figure 4 SA-B protects SMMC7721 cells from apoptosis. SMMC7721 cells were treated with Act D/TNF-α for 6h, and then stained with Hoechst/MitoTracker fluorescent reagent. Images were taken and analyzed by HCS Kaeter Scan Reader.

Figure 5 Antiapoptotic effect of SA-B is mediated through TNFR1/Caspases signaling pathway. Cultured SMMC 7721 cells were pretreated with SA-B (1 μ M), for 1 h before they were incubated for 6h with Act D/TNF-α. Protein expression were analyzed using Western blot.

PE394

The Effect of Salvianolic Acid B on TGF-beta 1 Signal Transduction Pathway in Rat Hepatic Stellate Cells

Y.Y. Tao[1], Q.L. Wang[1], C.H. Liu[1,2]

[1] Liver Disease Institute, Shanghai University of Traditional Chinese Medicine, [2] E-institute of TCM Internal Medicine, Shanghai Municipal Education Commission

Background and Aim: Our previous studies have showed that Salvianolic acid B (SA-B) is an effective compound against liver fibrosis, this study is designed to investigate the action mechanism of SA-B against liver fibrosis relating to TGF-β1 signaling.

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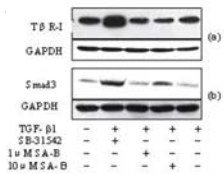

Fig.2. Effect of SA-B on TβR-I (a) and Smad3 nuclear (b) expression in HSCs. 4-day primary cultured rat HSCs were stimulated with 100pM TGF-β1 in medium containing 1 μ M S A-B, 10 μ M S A-B or 10 μ M S B-431542 for 24h. TβR-I and Smad3 nuclear expression was determined by Western blotting.

Table 1. Effect of S A-B on TβR binding ability

组别	Bmax (fmol/0.05mg蛋白)	Kd (pM)
Control	33.9±1.3	31.3±3.7
TGF-β1	31.1±3.5*	9.8±1.1**
SB-431542+TGF-β1	37.3±1.2#	13.3±1.7##
1 μ M SA-B+TGF-β1	38.1±1.5	13.9±1.3#
10 μ M SA-B+TGF-β1	31.1±1.8#	13.7±3.1#

Table 2. Effect of S A-B on TβR-I protein and mRNA expression

组别	TβR-I/GAPDH	TβR-I mRNA expression/Control
Control	0.35±0.07	1.0±0.1
TGF-β1	1.13±0.11**	3.3±0.3*
SB-431542+TGF-β1	0.38±0.08##	0.9±0.1##
1 μ M SA-B+TGF-β1	0.35±0.06##	1.1±0.1#
10 μ M SA-B+TGF-β1	0.35±0.04##	1.2±0.1#

vs Control, * $P<0.05$, ** $P<0.01$; vs TGF-β1, # $P<0.05$, ## $P<0.01$

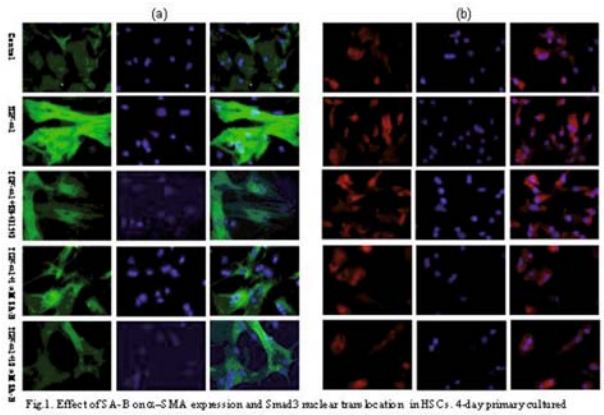

Fig.1. Effect of SA-B on α-SMA expression and Smad3 nuclear translocation in HSCs. 4-day primary cultured rat HSCs were stimulated with 100pM TGF-β1 in medium containing 1 u M SA-B, 10 u M SA-B or 10 u M SB-431542 for 24h, α-SMA (a) and Smad3 (b) nuclear translocation was then determined by immunofluorescent stain.

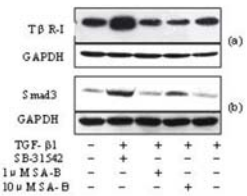

Fig.2. Effect of SA-B on TβR-I (a) and Smad3 nuclear (b) expression in HSCs. 4-day primary cultured rat HSCs were stimulated with 100pM TGF-β1 in medium containing 1 u M SA-B, 10 u M SA-B or 10 u M SB-431542 for 24h, TβR-I and Smad3 nuclear expression was determined by Western blotting.

Table 1. Effect of SA-B on TβR binding ability

组别	Bmax (fmol/10^6细胞)	Kd (pM)
Control	33.9±1.3	31.3±3.7
TGF-β1	31.1±3.8*	9.8±0.1**
SB-431542+TGF-β1	27.5±1.1#	15.3±1.7##
1u M SA-B+TGF-β1	28.1±1.3	13.9±1.1#
10u M SA-B+TGF-β1	31.1±1.9#	13.7±3.1#

Table 2. Effect of SA-B on TβR-I protein and mRNA expression

组别	TβR-I/GAPDH	TβR-I mRNA expression/Control
Control	0.35±0.07	1.0±0.1
TGF-β1	1.13±0.11**	3.3±0.5*
SB-431542+TGF-β1	0.35±0.03##	0.8±0.1##
1u M SA-B+TGF-β1	0.35±0.13##	1.4±0.3#
10u M SA-B+TGF-β1	0.35±0.04##	1.3±0.4#

vs Control, * $P<0.05$, ** $P<0.01$; *vs* TGF-β1, # $P<0.05$, ## $P<0.01$

Conclusion: SA-B can reduce protein expression of HIF-1α, ICAM-1, VCAM-1 and vWF, indicating the anti-fibrosis effect mechanism of SA-B is related to anti- hypoxia and anti-angiogenesis.

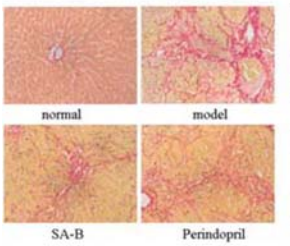

Fig.1.The effect of SA-B on collagen deposition in liver tissue. Sirius Red Staining.

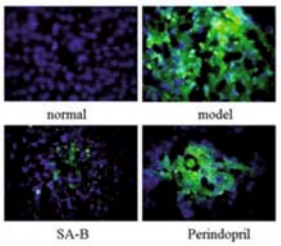

Fig.2.The effect of SA-B on gelatinase activity in liver tissue. *in situ* Flourescent Zymography.

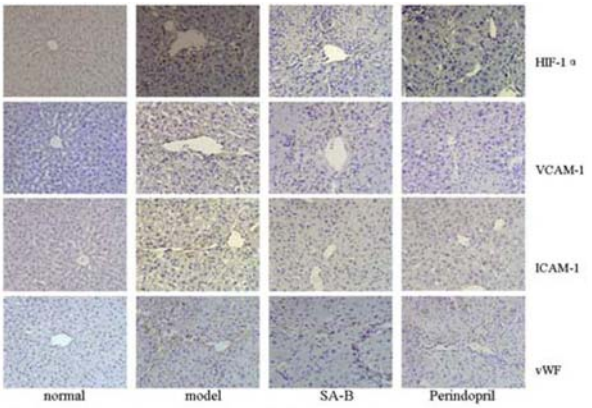

Fig. 3. The effect of SA-B on HIF-1α and angiogenesis in liver fibroitissues. Immunohistochemistry.

PE395

The Effect of Salvianolic Acid B on Hypoxia and Angiogenesis in Fibrotic Liver

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Aim: To investigate the action mechanism of salvianolic acid B (SA-B) against liver fibrosis relating to hypoxia and angiogenesis regulation.
Methods: The rats were divided into normal, model, SA-B and Perindopril control group. Rats in SA-B and Perindopril group were administrated with SA-B and Perindopril respectively. Liver fibrosis was induced by ip dimethylnitrosamine (DMN) for 4w. Fibrosis degree was observed by Sirius red staining. Col-I protein expression was analyzed by Western blot; Col-I , VCAM-1, ICAM-1, HIF-1α and vWF expression in liver tissue was checked by immunohistochemistry; gelatinase activities in liver tissue were detected by gelatin zymography and *in situ* flourescent zymography.
Result: Compared to normal group, Col-I, HIF-1α, ICAM-1, VCAM-1 and vWF protein expression and gelatinase activity in liver tissue were increased obviously in model group, while SA-B and perindopril treatment significantly decreased these protein expressions and gelatinase activity.

PE396

Involvement of Endoplasmic Reticulum Stress in the Development and Regression of Fatty Liver Fibrosis Induced by Methionine-Choline Deficient Diet in Rat

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Background: Fatty liver disease has become a health problem related to metabolic syndrome worldwide although its molecular pathogenesis has remained further studied and it is unclear whether advanced fibrosis induced by steatohepatitis will regress when diet is controlled. Aim of this study is 1) to study the involvement of endoplasmic reticulum stress (ER stress) in the occurrence of seatohepatitis and 2) to obtain the evidence of resolution of fibrosis by changing the diet.
Methods: Non-alcoholic steatohepatitis with advanced fibrosis was produced in rats by giving methionine-choline-deficient diet (MCDD) for 10 weeks. Methionine-choline-control diet (MCCD) instead of MCDD was given for the last 2 weeks in an experimental group. Fibrosis and inflammation was determined by several tissue stainings. Gene expression related to fibrosis and inflammation was determined by immunoblotting and real-time PCR. Expression of caspase-12, caspase-7, and glucose-regulated protein 78 was evaluated to clarify the presence of ER stress
Results: 1) Changing the diet from MCDD to MCCD triggered the reduction in fat in hepatocytes, the decrease of inflammatory gene expression and oxidative stress, and the regression of fibrosis accompanied by the disappearance of activated stellate cells and macrophages. 2) Immunohistochemistry, immunoblotting, and RT-PCR analysis all indicated the occurrence of ER stress in steatohepatitis while it recovered immediately after changing the diet from MCCD to MCDD.

Conclusions: This simple experiment clearly shows that the changing diet from steatohepatitis-causing MCDD to MCCD triggers the resolution of inflammatory and fibrotic reaction in the liver, suggesting that food intake is a very important factor for controlling the state of fat and pathology of the liver. ER stress is involved in the process.

PE397

GABA Inhibits the Activation of Hepatic Stellate Cells

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Gamma-aminobutyric acid (GABA) is a major inhibitory neurotransmitter in the nervous system. Increasing evidences have shown that GABA plays an important role in regulating liver function. In this study, we found that GABA had no effects on cell proliferation and DNA synthesis. However, GABA could block hepatic stellate cells (HSCs) activation through inhibiting myofibroblast activation and collagen deposition. This experiment may provide an alternative therapeutic approach to the prevention and treatment of liver fibrosis.

PE398

Proteomic Analysis of the Effect of Fuzheng Huayu Decoction on Fibrotic Liver in Rats

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Aim: To investigate the effects of Fuzheng Huayu Decoction (FZHY) on the proteome of fibrotic liver induced by DMN (dimethylnitrosamine) in rats and discover potential molecular mechanism of anti-fibrosis at molecular level.
Methods: Liver fibrosis was induced by DMN in male Sprague-Dawley rats; The rats were divided into normal (N), model (M) and FZHY group. Rats in FZHY group were administrated with FZHY. Total liver protein was separated by two-dimensional gel electrophoresis (2-DE). Protein identification was done by peptide mass fingerprinting (PMF) with matrix assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF-MS). The expression levels of vimentin in the liver tissues were validated by Western blot and RT-PCR analyses.
Result: There were 1120±154, 1122±113, 932±160 protein spots on the maps of N,, M and FZHY group respectively. A total of 61 spots exhibiting significant ($p < 0.05$) changes in intensity, and 22 spots, corresponding to 16 different proteins or polypeptide chains were finally identified. Of these proteins, the typical one, vimentin, was further examined by Western blotting and quantitative real-time RT–PCR, resulting in coincident data with the proteomic evidence.
Conclusion:
1. There are various proteins joined together in the fibrogenesis of rat liver induced by DMN, including molecular chaperones, antioxidant proteins, enzymes involved in material metabolism, structural molecules, and calcium-binding proteins.
2. The mechanism of FZHY decoction on anti-liver fibrosis may be associated with modulation of Proteins associated with metabolism, stress response, attachment, migration, and cell signaling.

PE399

The Molecular Mechanism of Gynostemma pentaphyllum-reduced Type1 Procollagen Expression in Rat Hepatic Stellate Cells

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[1] *National Chiayi University,* [2] *Chang Gung Memorial Hospital,* [3] *Chiayi Christian Hospital*

Background: Liver fibrosis results from chronic damage to the liver in conjunction with the accumulation of extracellular matrix proteins, which is a characteristic of most types of chronic liver disease. Under injury conditions, hepatic stellate cells (HSCs) are activated to transdifferentiate into myofibroblasts, which are capable of secretion of many connective tissue elements, especially collagens I, III, and IV. *Gynostemma pentaphyllum* is a popular folk medicine that has been used for treatment of hepatitis in Asia. Gypenosides are the major saponins derived from *G. pentaphyllum*. In previous study, gypenosides have hepatoprotective and anti-fibrotic activities in rat chronic liver injury induced by CCl_4, and anti-proliferative effect in rat isolated HSCs.
Methods: In cultured HSCs model, we detected type1 procollagen protein and mRNA by Western blot and RT-PCR.
Result: we found that *G. pentaphyllum* inhibited type1 procollagen protein expression in 66% at 48 hours. Furthermore, *G. pentaphyllum* also inhibited type1 procollagen α1 and α2 mRNA expression in 39% and 11% respectively. In addition to transcriptional inhibition, we found that *G. pentaphyllum* also enhanced the degradation rate of type1 procollagen protein. Base on the effect of enhancing protein degradation, we used some protease inhibitors like CA-074 Me, z-FA-fmk, AEBSF, TPCK and TLCK to identify the potential target of *G. pentaphyllum*. On the other hand, in the ubiquitin-proteasome system analysis, we quantified the change of some target proteins of proteasome in the presence or absence of *G. pentaphyllum*.
Conclusion: *G. pentaphyllum* reduced type1 procollagen protein by inhibiting transcription and enhancing protein degradation.

PE400

Restoration of Lipid Metabolic Profiles and Hepatic Injuries with Ginger Supplementation in STZ-induced Diabetic Rats

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Aim: Excessive oxidative stress in diabetic patients has been implicated in the pathology and complication of liver. The present study was designed to examine whether ginger has a direct hepatoprotective effect in diabetic cases.
Methods: Wistar strain albino rats were selected for this study. The rats were divided into 4 groups: (i) control, (ii) ginger treated (200mg/kg b.w. orally, 30 days) (iii) diabetic (50 mg/kg b.w., i.p.) and (iv) diabetic + ginger treatment. The lipid metabolic profiles such as total cholesterol, triglycerides, phospholipids and lipid peroxidation as stress markers and histopathological studies were carried out to assess the damage in hepatic tissue.
Results: Ginger treated diabetic rats demonstrated significant reduction in glucose levels as compared to the nontreated diabetic animals. Diabetic rats have shown increased total cholesterol, triglycerides, phospholipids and lipid peroxidation content in hepatic tissue compared to control, indicate prevailing of oxidative stress and alterations in fatty acid metabolism in these rats. Further, degenerative changes of hepatic cells in diabetic group are minimized to nearness in structure by administration of ginger as evinced by histopathological examination.
Conclusion: We summarize that the hypolipidemic and antioxidant compounds present in ginger may be useful in delaying the complicated effects of diabetes. This results also reveal that ginger possess hepatoprotective properties in diabetic cases.

PE401

Aqueous-Alcoholic Fraction of the Rhizome of Valeriana jatamansi Has Anti-Fibrotic Action

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Rhizomes of *Valeriana jatamansi* (family, *Valerianaceae*) have long been used in Indian subcontinent by the traditional healers for the treatment of various diseases. This study provides experimental evidence suggesting the therapeutic effect of the crude extract of rhizomes on rat liver fibrosis, and demonstrates its antiproliferative role. Crude extract (50% ethanolic) at a dose level of 800 mg/kg body weight was administered to rats to study the effect on biochemical and other markers of liver fibrosis. Administration of the extract for 9 weeks could bring down elevated the levels of biochemical markers of liver injury, and modulate several other biochemical responses. Morphology and hisopathological examination cooroborated with the biochemical changes, and indicated partial reversal of fibrosis. DPPH assay confirmed the antioxidant property of the extract, which is suggested to be due to -ionone, -sitosterol and other chemical constituents. Further, treatment could restore depleted glutathione level, inhibit lipid peroxidation, and inhibited elevated xanthine oxidase activity in fibrosis. The study also reports anti-tumour promotion activity of the extract as evident by a significant decrease in [^{3}H]-thymidine incorporation by hepatic DNA in extract treated rats. Results suggest that *V. jatamansi* extract has curative

effect and can partially reverse biochemical and histological changes associated with liver fibrosis.

PE402

Correlation of Leptin and Severity of Hepatic Fibrosis in Thai Patients with Chronic Hepatitis C

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Background: Leptin is a peptide hormone that mainly regulates food intake, energy expenditure and reproductive function. Leptin also releases from activated hepatic stellate cells and may have a role in regulation of fibrogenesis and inflammation. In human chronically infected by HCV, the role of leptin-associated fibrosis of the liver is still unclear. There is no data in Thai patients chronically infected by HCV regarding leptin level and its correlation with hepatic histology and fibrosis.The purpose of this study was to evaluate the relationship between leptin level and severity of liver fibrosis in Thai patients chronically infected by HCV.
Methods: Sixty-six patients (31 men, 35 women) with chronic HCV infection and liver biopsy was done within 3 months were enrolled. Fasting blood samples were obtained and serum leptin levels were measured by ELISA. BMI, blood sugar, liver function test, lipid profile, HCV RNA viral load and HCV genotype were also measured and related to histological findings.
Results: Mean serum leptin levels were significantly higher in women than in male. There was a significantly correlation between serum leptin and BMI ($r = 0.469$, $P < 0.001$). Leptin levels were not associated with hepatic fibrosis ($r = 0.166$, $P = 0.183$) and necroinflammation ($r = 0.203$, $P = 0.102$). Steatosis was significantly associated with severe necroinflammation ($r = 0.261$, $P = 0.034$), but not fibrosis ($r = 0.22$, $P = 0.076$).
Conclusions: These findings failed to demonstrate correlation of serum leptin and hepatic fibrosis in Thai patients chronically infected with HCV.

PE403

Insulin Resistance in Patients with Liver Cirrhosis

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Background and aim: Liver cirrhosis is one of the leading causes of mortality in our country as well as in our region. Even though deterioration of glucose metabolism and existence of insulin resistance in liver cirrhhosis has been well documented in many studies, it is still unclear how insulin resistance mechanism develops. The aim of the present study is to assess insulin resistance, cytokines and CRP levels in patients with liver cirrhosis and control subjects. In additon, we aimed to investigate the relation of insulin resistance in liver cirrhosis with such parameters as age, sex, etiology, Child-Pugh classification, spleen size, TNF-?, IL-1?, IL-2RES, IL-6, IL-8, IL-10, CRP and Hs-CRP.
Material and method: A total of 79 patients with cirrhosis of different etilogy (49 male, 30 female) were included into the study. As controls, 50 (23 male and 27 female) subjects were taken. The two groups were compared with each other in terms of glucose, insulin, C-peptid, HOMA-IR, TNF-?, IL-1?, IL-2RES, IL-6, IL-8, IL-10, CRP and Hs-CRP levels. In the second part of our study, the liver cirrhosis group was divided into two subgroups: Patients with HOMA-IR value >2.7 as insulin resistance positive, and those with HOMA-IR value >2.7 as insulin resistance negative. These two groups, i.e. , HOMA-IR positive and HOMA-IR negative, were compared in terms of age, sex, etiology, Child-Pugh classification, spleen size, TNF-?, IL-1?, IL-2RES, IL-6, IL-8, IL-10, CRP and Hs-CRP levels.
Results: In liver cirrhosis group, glucose, insulin, C-peptid, HOMA-IR, TNF-?, IL-2RES, IL-6, CRP and Hs-CRP levels were determined to be significantly higher than controls. Between patients with HOMA-IR positive and negative, however, statistically no significant difference was found in terms of age, sex, etiology, Child-Pugh classification, spleen size, TNF-?, IL-1?, IL-2RES, IL-6, IL-10, CRP and Hs-CRP levels, but IL-8 level was seen to be significantly low in patient HOMA-IR positive.
Conclusion: In patients with liver cirrhosis, the levels of glucose, insulin, C-peptid, HOMA-IR, TNF-?, IL-2RES, IL-6, CRP and Hs-CRP increase with respect to normal population. Determination of increased HOMA-IR level in liver cirrhosis supports the view that insulin resistance develops in liver cirrhosis as reported in related studies. In the study, it was also determined that the mechanism of insulin resistance development occurs independent of age, sex, etiology, Child-Pugh classification, spleen size, TNF-?, IL-1?, IL-2RES, IL-6, IL-10, CRP and Hs-CRP levels. The determination of statistically lower level of IL-8 in patients with HOMA-IR positive with respect to those with HOMA-IR negative does not indicate similarity with the studies carried out earlier.

Poster Exhibition – Metabolic and Genetic Disease Poster Session, Hall 5B

PE404

Histocompatibility Antigen in Relation to Hepatic Schistosomiasis

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Hepatic Schistosomiasis is one of the most prevalent chronic liver disease in Egypt.Great variation in disease severity occurs among infested individuals dueto the wide range of intensity and duration of tissue egg deposition.
Aim: to determine the association between hepatic Schistosomiasis and antigens of the HLA system.
Materials: 52 hepatic Schistosomiasis divided intoGroup I mild , Group II moderate ,Group III severe liver fibrosis. 10 patients active intestinal Schistosomiasis no hepatic involvement. 300 healthy controls.
Methods: clinical examination, ultrasonography, liver functiontests, viral markers for HBV and HCV, HlA testing by two stages lymphocyte microcytotoxicity technique.
Results: No significant association between active intestinal Schisto & HLA antigens.Significant association between HLA-AW 19 ($X2=19.593$, corrected $P= < 0.00115$, $RR=4.31$) and hepatic Schisto. (38.46%) compared to controls (12.67%). Similarly HLA-B5 significantly higher ($X2=31.219$,corrected $P= < 0.00023$,$RR-5.68$) in patients (48.08%) than in controls(14%)In group I HLA-B5 significantly increased in patients (60%)as compared to controls (14%) .
in group II HLA –B5 significantly higher in patients (45.46%)than controls (14%) also HLA-AW19 significantly higher (40.91%) in patients than controls (12.67%).in group III HLA-AW19 significantly increased in patients (46.67%) compared to controls.No significant association between HLA antigens and cases with HBV or HCV infection.
Conclusion: The significantly high association of HLA-AW19 and HLA-B5 in patients with hepatic Schistosomiasis as compared to normal controlstogether with the lack of any association with active intestinal Schisto . Antigens predispose to liver affection.Individuals possessing HLA-AW19 appear to be more prone to severeform of liver disease

PE405

Characterization of ATP8B1 Mutations and a Hot Linked Mutation Found in Chinese Children with Progressive Intrahepatic Cholestasis and Low GGT

L.Y. Liu[1], X.H. Wang[1], Q.R. Zhu[1], J.S. Wang[1]
[1] *Children's hospital of Fudan University*

Background: ATP8B1 mutation is one of the factors that result in cholestasis and progress to chronic liver disease, but has never been reported in the Mainland China before. The aim of this study was to elucidate the role of ATP8B1 mutation in Mainland Chinese patients with progressive intrahepatic cholostasis and low GGT.
Methods: 24 children who presented with progressive intrahepatic cholostasis and low GGT were admitted in a tertiary pediatric hospital in eastern China. ABCB11 gene was analyzed firstly to exclude BSEP deficiency. Afterwards, all the encoding exons and their flanking areas of ATP8B1 gene were sequenced in the remaining 19 patients in whom only one or no mutations of ABCB11 were found.
Results: 10 mutations of ATP8B1 gene were found in 9 patients. I694N had been reported in Taiwanese patients with PFIC1, and the others were novel. P209T and IVS6+5T＞G were linkage and found in 4 of 9 patients, including 2 homozygote and 2 heterozygote. Liver biopsy had been performed in 6 patients with ATP8B1 mutations and 5 with ABCB11

mutations. Variety portal fibrosis was showed in 2 patients with ATP8B1 mutations and 4 patients with ABCB11 mutations. Giant cell transformation was detected in one patient with ATP8B1 mutations and 4 patients with ABCB11 mutations.
Conclusion: ATP8B1 gene mutations play an important role in Chinese patients with progressive intrahepatic cholestasis and low GGT. The linked mutation P209T and IVS6+5T>G is a hot mutation. Phenotype may be helpful in differentiating FIC1- from BSEP-related disease.

PE406
The Diagnostic Value of Morning Urine Copper to Zinc Ratio in Wilson's Disease Children
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[1] *Children's Hospital of Fudan University*

Objectives: To compare the diagnostic value of morning urine copper to zinc (Copper/Zinc) ratio and 24 hour urinary copper excretion in Wilson's disease (WD) children.
Methods: Morning urine and 24 hour urine were collected from 96 patients over three years age who were hospitalized in a tertiary pediatric liver service. Each patient was re-evaluated according to WD Scoring system, and was assigned to one of the three groups: WD, suspecting WD, and non-WD. 24, 6, and 64 cases were assigned to WD, suspecting WD, and non-WD respectively. Urine copper and zinc concentration was determined simultaneously by using Inductively Coupled Plasma Mass Spectrometry.
Results: The morning urine copper/zinc ratio and 24hr urinary copper excretion correlated well ($r=0.758$, $P < 0.001$). The median of morning urine copper/zinc ratio, 24hr urine copper/zinc ratio, 24h copper excretion, and 24h zinc urinary excretion were 0.370, 0.394, 87.1 and 398.7 in WD group, and 0.051, 0.061, 24.2 and 358.9 in the non-WD group respectively. The differences of morning urine copper/zinc ratio, 24hr urine copper/zinc ratio, and 24h copper excretion were significant (Z-value -6.502, -6.020 and -6.208 respectively, all P values < 0.000). By using cutoff values of 0.17, 50.8, and 0.12 for morning urine copper/zinc ratio, 24hr urine copper/zinc ratio, 24h copper excretion, the sensitivity and specificity were 86.4% and 92.2%, 90.9% and 93.7%, and 86.4% and 85.9% respectively.
Conclusion: Morning urine Copper/Zinc ratio could be used as a good replacement of 24hr urinary copper excretion for diagnosing WD.

PE407
Role of Swimming Exercise in the Alterations of Free Radical Scavenging Enzymes and Oxidative Stress Markers during Aging
T.W. Shen [1], C.C. Yang [1], M.F. Hsu [1], H.T. Lin [1], T.H. Lu [1], J.P. Lee [1], K. Mallikarjuna[1], C.H. Kuo [1]
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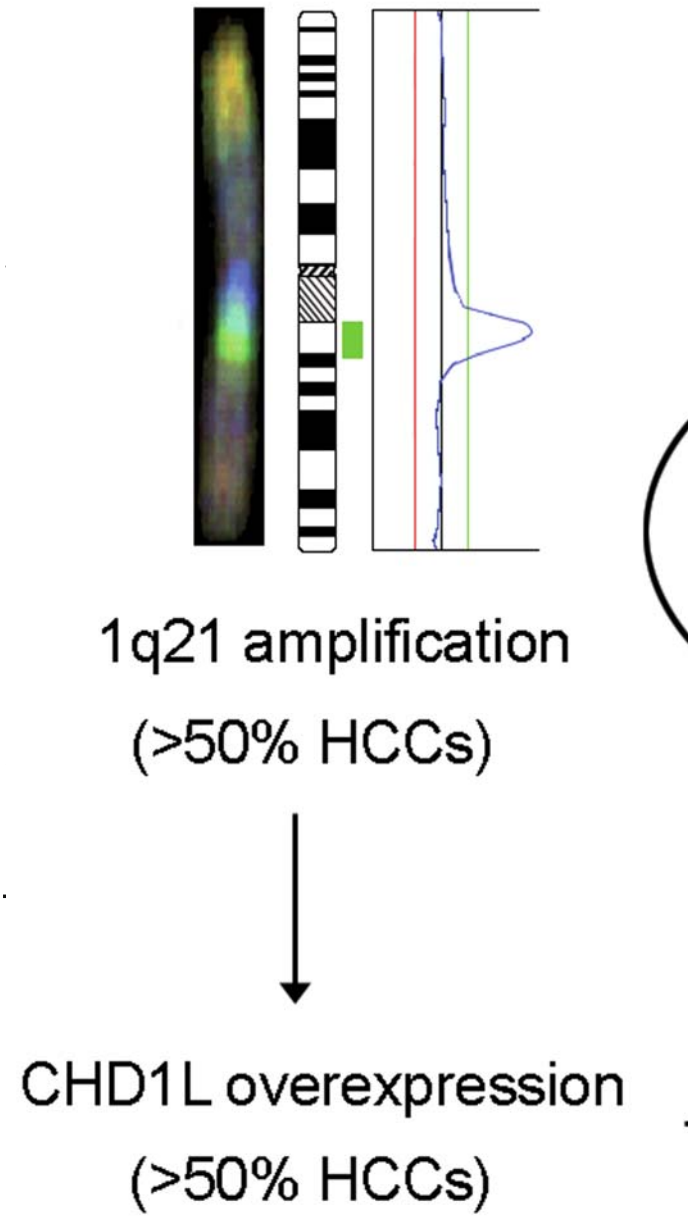
Background/aim: Accumulation of oxidative damage to proteins, lipids and mitochondria could increase with advancing of age. The current study was aimed to test the hypothesis that swimming exercise training could revert the age dependent oxidative damages in liver.
Methods: Sprague-Dawley rats of young (3 months) and old (12 months) were divided into four groups; young control (n=5), young exercise (n=5), old control (n=5) and old exercise (n=5). 90 minutes of swimming exercise was given to the exercise group for a period of two weeks.
Results: The estimated antioxidant enzyme activities including, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px) and glutathione reductase (GR) were decreased with age and significantly ($p<0.05$) increased with exercise training. However, elevated protein carbonyls and MDA levels were noticed in old animals, which indicate that old liver had greater accumulated oxidative damages. The significant drop in protein carbonyl content and increase in mitochondrial succinate dehydrogenase (SDH) activity was observed with response to swim training in old rats.
Conclusions: This data implied that swim exercise training could revert the oxidative damages in liver. This was also proven by enhanced antioxidant enzyme status with response to exercise training in old rats. To sum-up these results it is cleared that age induced detrimental effects to the liver might be reversed by regular swimming exercise training in old rats.



PE410
Induced Expression of Pd-1 in Lymphocytes by Hepatoma and the Function Study
J. Chen[1], X.J. Wu[1], Y. Wang [1], M. Yu[1], N.L. Zhang[1], Q.Q. Wang [1]
[1] *Peking University First Hospital*

Background: PD-1（Programmed cell death-1）is a member of CD28 family. It is expressed on stimulated T cells, B cells and monocytes. Recently studies demonstrated that interaction of PD-1 with its ligands (PD-L1 and PD-L2) can inhibit the function of T cell. The PD-1/PD- pathway plays a critical role in regulating T cell activation and tolerance in viral infection disease, tumor and autoimmune disease.

Methods: HepG2 or HepG2.2.15 were co-cultured with Jurkat cells, with blocking test by adding anti-PD-1 antibody. The PD-1 expression was detected by flow cytometry (FCM); Cytokines in culture supernatant in blocking groups and controls were measured by enzyme-labeled immunosorbent assay (ELISA); Cytotoxic test of T cells were measured by methyl thiazolyl tetrazolium (MTT).
Results: The PD-1 expression on Jurkat cells was induced by Hepatoma cells, the expression rate were 16.17±6.5% (by HepG2) and 17.43±6.8% (by HepG2 2.2.15), respectively. The cytokines IL-2 level (202.9±53.0 pg/ml), INF-γ level (88.6±4.6 pg/ml) and IL-10 level (63.7±13.4 pg/ml) in culture supernatant of blocking groups were significant higher than that of controls (IL-2, 102.9±53 pg/ml, INF-γ, 39.3±4.2 pg/ml and IL-10, 34.6±13.7 pg/ml, respectively. $p < 0.05$). The cytotoxic test (OD value) was markedly higher in blocking group (0.29±0.06) than that of control group (19±0.09, $p<0.05$) .
Conclusion: The PD-1 expression on lymphocytes can be induced by Hepatoma cells, and cytokines expression and cytotoxic test were recovered by blocking PD-1/PD-L1 interaction.

PE411

Changes in Hedgehog Pathway on Liver Regeneration after Partial Hepatectomy in Rat

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Background: Hedgehog (Hh) pathway is well known as a positive regulator for tissue construction(during development) and reconstruction (in adults). Our aim to observe the expression change of Hh pathway on rat hepatic regeneration .
Materials and methods: Adult male Sprague–Dawley rats underwent approximately 70% partial hepatectomy (PH) or sham operation (SO). Liver specimens were collected at 2, 6, 12, 24, 36, 48, 72, and 168h after PH or SO. Hedgehog expression was determined in mRNA level by RT-QPCR as well as in protein levels via immunohistochemical staining and western-blotting.
Results: SO treatment did not induce remarkable changes in hedgehog expression; however, the level of transcript for hedgehog was significantly upregulated after PH. We found Sonic hedgehog(Shh)and Glioblastoma (GLi1-3) mRNA expression in the regenerating liver arrive at its peak at as early as 24 h and returned to its physiologyical level 168 h later. It is similar to the change of proteins (Shh and Gli1) .As seen from immunohistochemistry experiments; SHH protein was expressed uniquely in regenerating hepatocytes. Similarly, PH induced over expression for Shh protein occurred from 12 h with a peak level at 36 h after surgery. But Gli protein mainly located in nucleus and no significantly changes in the phrase of liver regeneration.
Conclusion: Hedgehog pathway may play a role in the activation of hepatic proliferation during liver regeneration induced by physiological stress or pathological states, such as PH.

PE412

Suppressive Effects of Genomic Imprinted Gene PEG10 on Hydrogen Peroxide induced Apoptosis in L02 cells

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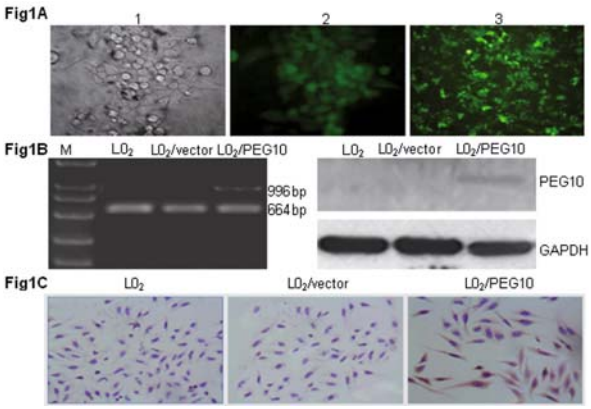
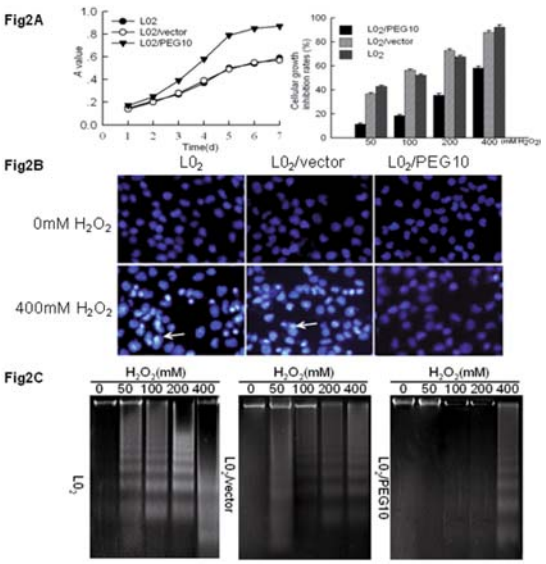
Background: To investigate whether PEG10, an imprinted gene with an active paternal but silent maternal allele, was involved in hydrogen peroxide (H_2O_2) induced cellular apoptosis.
Methods: PEG10 gene was stable transfected into $L0_2$. Cellular gene expression was determined by RT-PCR, Western blot and immunocytochemistry. Cell proliferation was analyzed by MTT. After treatment with different concentrations (50–400 mM) of H_2O_2, cell proliferation inhibition rate was measured by MTT. Morphological changes of apoptotic cells were determined by Hoechst33342 staining, DNA fragmentation was observed by agarose gel electrophoresis.
Results: PEG10 was expressed in $L0_2$/PEG10 (Fig.1). PEG10 accelerated the growth of $L0_2$. After treatment with 400mM H_2O_2 for 24 h, the inhibitory rate of $L0_2$/PEG10 cells was 32.5%; the chromosomal condensation and ladder-like DNA fragmentation were not observed (Fig.2).
Conclusions: Over-expression of PEG10 can significantly promot $L0_2$ proliferation and ameliorate apoptosis-inducing effects of H_2O_2 on $L0_2$.





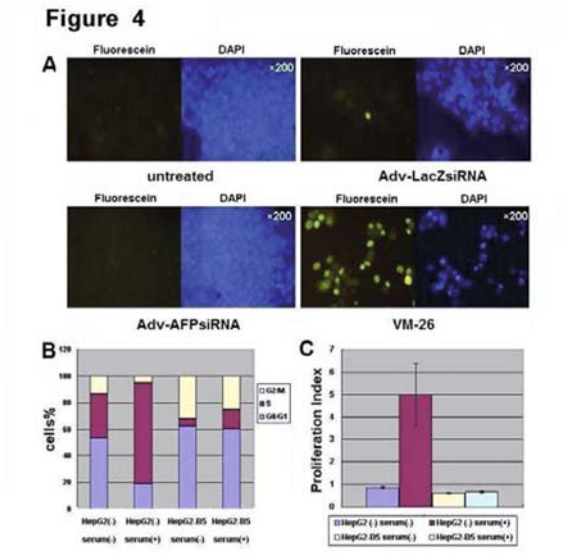
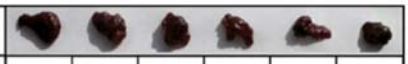
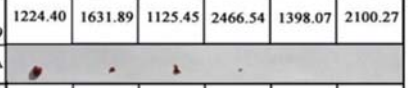
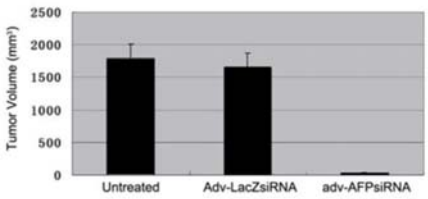


Figure 5

A

untreated						
tumor volume mm³ 1787.74±221.81	2499.27	2176.81	1949.41	1816.14	1416.59	1018.2
Adv-LacZsiRNA						
tumor volume mm³ 1657.77±215.19	1224.40	1631.89	1125.45	2466.54	1398.07	2100.27
Adv-AFPsiRNA						
tumor volume mm³ 22.28±11.53	65.25	13.65	50.00	4.80	0.00	0.00

B



PE413

Mechanism of Endogenous AFP Regulating the Growth of Hepatoma Cells

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We determined how AFP modulates the proliferation of hepatoma cells. A recombinant adenovirus expressing siRNA against AFP (Adv-AFPsiRNA) was created and found that it reduced expression of AFP specifically in hepatoma cells, and markedly inhibited the proliferation of hepatoma cells in vitro. Local treatment using Adv-AFPsiRNA caused significant repression of the growth of hepatoma derived HepG2 cells in xenograft in nude mice. Knockdown of AFP resulted in an obvious delay in the G1/S transition of cell cycle, but did not affect apoptosis in HepG2 cells, as analyzed by flow cytometry and TUNEL assay. Also, differential expressions of some genes related to the cell cycle, including SKP2, Cyclin D1, Csk and EBAG9 were identified by microarray and RT-PCR in HepG2 cells and HepG2 cells with knocked down AFP. These results suggest that endogenous AFP is a critical determinant of the growth of hepatoma cells.

PE414

A Pilot Study To Assess The Feasibility, Safety And Efficacy Of G-CSF Induced Mobilization Of CD 34+ Peripheral Blood Stem Cells In Patients With Cirrhosis Of Liver

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Hematopoietic stem cell (CD 34+) therapy can improve liver function in patients with cirrhosis. These cells can be mobilized into peripheral blood using Granulocyte colony stimulating factor (GCSF). This study was undertaken to assess feasibility and safety and of GCSF induced CD 34+ cell mobilization and its impact on liver function in patients with cirrhosis.

Patients with liver cirrhosis (Cryptogenic or alcoholic with 6m abstinence) with CPT > 7 and ≤ 12, and splenic diameter < 17 cm were included. GCSF injection was given for 5 days (5mcg/kg/dose). Baseline & day-6 CD 34+ counts in peripheral blood were done by flow cytometry. Follow up was weekly for 4 weeks and then monthly. CPT was compared at baseline and 6 months.

9 Patients (median age 51 y, range 33-64 y, 8 males; etiology: 6 alcohol, 3 cryptogenic; median CPT 10, range 8-12) were included. CD 34 + cell counts at baseline and day 6 were 2(0-3) and 15 (13-41) respectively (median, range). Side effects were fever in 8, allergic reaction in 1 and increase in splenic size in 1 (excluded). In follow up, 3 patients died (1, 3 & 4m after therapy, 1 after OLT), 1 lost to follow-up. 4 patients showed improvement in CPT (11- 8, 10- 7, 9- 6, 10-7) at 6-month follow-up.

GCSF treatment is safe and yields adequate CD 34+ cells in peripheral blood. In short term it results in improvement in liver function in patients with cirrhosis

PE415

Molecular cloning and Transcriptional analysis of KCTD9 gene promoter

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Aim: Our previous work has shown that high expression of KCTD9, a potassium channel associated gene, correlated with the disease severity of patients with severe chronic hepatitis B(SCHB). To further understand the gene transcription and regulation, KCTD9 promoter was cloned and gene transcription was studied.

Methods: A full length of isolated promoter and series of 5' truncated promoter of KCTD9 gene was subcloned into the luciferase report vector pGL2-basic to form the promoter-report constructs. The KCTD9 promoter-report construct upstream of the luciferase report gene was cotransfected with constructs expressing HBV X,C and S protein respectively or stimulated with cytokines (IL-2, IFNγ and TNFα) in 293 T cells to investigate KCTD9 gene regulation upon both viral factors and host cytokines.

Result: A 759bp KCTD9 segment upstream of ATG translation start site was evidenced to contain potential regulative domains. An important regulation site located between -268bp and -81bp upstream of ATG translation start site. Based upon the luciferase activity assay, IL-2 was able to upregulate the transcription of KCTD9 whereas there was no effect from neither HBV viral proteins nor IFNγ and TNFα.

Conclusion: Here we first successfully cloned the full length promoter of KCTD9. IL-2 significantly enhanced the transcription of KCTD9, a gene which has been shown to be involved in T cell activation and disease severity of SCHB from our group. This work was supported by NSFC(30571643, 30672380, 30700702); National Key Basic Research Program of China(2005CB522901, 2007CB512900）

PE416

The Correlation of Hepatic Apoptotic Markers and Histology and Their Predictive Role in Estimating the Response to Therapy in Chronic Hepatitis C

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Background: The treatment in chronic hepatitis C virus (HCV) is not highly effective, and cost, duration, and side effects are challenging. Predicting favorable factors of response to treatment would make it possible to give it only responsive patients. Recent studies report more conclusive results about the role of apoptosis in inflammation and fibrosis seen in chronic viral hepatitis.

Hepatocyte damage in HCV is mediated by cytotoxic T-cells. Apoptosis primarily developed by the interaction between Fas antigen on hepatocyte and Fas ligand on T-cell corresponds to a main mechanism for hepatocyte damage.

Methods: In this study, we aimed to detect any relationship between apoptotic markers (Fas, Fas ligand, Fas-associated death domain, caspases 3,8, and 9, insitu apoptosis) in liver biopsy taken before the treatment and response to the treatment of interferon+ribavirin. Additionally, any relationship between these parameters and the other ones predicting the response to therapy including ALT level, viral load, genotype, and gender were studied.

Results: The study includes the patients in 4 centers managing chronic HCV infection. All parameters were studied in 180 patients. Study results revealed

that histological activity index is correlated with CD95 staining density, caspase 8 intensiveness, and portal and parenchymal Fas ligand scores. Fibrosis is also seen to be correlated with the same parameters. Apoptotic parameters of the responsive cases were not significantly different from unresponsive ones.
Conclusion: Apoptotic parameters studied in the liver tissue is associated with inflammation and fibrosis, however these parameters may not predict the response to the treatment.

PE417
Construction of The Mirna Expression Plasmids of Human fgl2, Fas and TNFRI Genes and Their Effects In Vitro
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Objective: This study was designed to explore the opportunity of microRNA interference technique in the inhibitory application of human fgl2, human Fas and TNFR1 expression.
Methods: The eukaryotic expression plasmids of human fgl2, Fas and TNFRI genes were constructed and have successfully expressed hfgl2, hFas and hTNFRI protein. miRNA expression plasmids of hfgl2, hFas and hTNFRI complimentary to the sequence responsible for hfgl2, hFas and hTNFRI respectively were also constructed, meanwhile an irrelevant miRNA plasmid was used as control. By respective cotransfection of p-hfgl2miRNA and pcDNA3.1-hfgl2, p-hFasmiRNA and pcDNA3.0-hFas, p- hTNFRI miRNA and pcDNA3.0- hTNFRI expression construct into 293T cells, the inhibition of hfgl2, hFas and hTNFRI expression were analyzed by quatitative real time PCR and western blot.
Results: The experiments showed the significantly inhibitory effect of p-hfgl2miRNA on hfgl2, p-hFasmiRNA on hFas and p- hTNFRI miRNA on hTNFRI expression at 48h post-transfection both at RNA level and at protein level, as well in 293T cell lines the inhibitory efficiency reached as high as 89.3% for hfgl2, 87.5% for hFas and 80% for hTNFRI, respectively.
Conclusions: The study demonstrated the constructs of p-hfgl2miRNA, p-hFasmiRNA and p- hTNFRI miRNA successfully interfered their target genes expression in vitro, which provides the foundation for further investigation of these constructs' application in vivo and further more as a therapeutic strategy for a targeting intervention in the diseases which the gene fgl2, Fas and TNFRI contribute to. This work was supported by NSFC30571643, 30672380, 30700702;2005CB522901, 2007CB512900

PE418
Influence of the ID2 on the Anti-Tumor Activity of Histone Deacetylase Inhibitor in Hepatocellular Carcinoma Cells
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Background: Our recent study revealed that levels of the *Inhibitor of DNA binding/differentiation 2* (*ID2*) were associated with the progression of HCV-related hepatocellular carcinoma (HCC) and can affect susceptibility of HCC cells to histone deacetylase (HDAC) inhibitors. We here aimed to investigate how and whether *ID2* expression affected on the anti-tumor activity of sodium butyrate (NaB), one of HDAC inhibitors.
Methods: Two HCC cell lines, HLE and HuH-7, were used for gene targeting experiments. The *ID2* over-expressing and knockdown cells were subjected to MTS assay to evaluate the susceptibility to NaB. Time-course of the expressional change of *Bcl-2* and *Bcl-xL* genes after NaB administration was measured by real-time RT-PCR.
Result: Upregulation and downregulation of *ID2* levels in HCC cells resulted in decreased and increased susceptibility to NaB, respectively. We observed that after NaB administration, the *ID2* expression was induced gently, the *Bcl-2* expression was greatly increased immediately, and the *Bcl-xL* expression was decreased to less than half once and then recovered. These increase and recovery of the expression of anti-apoptotic genes were inhibited in the *ID2* knockdown cells. In the *ID2* overexpressing cells, the *Bcl-2* expression was more upregulated than mock-transfected cells.
Conclusion: In HCC cells, *ID2* influences the susceptibility to the HDAC inhibitor by regulating the expression of anti-apoptotic genes caused by the HDAC inhibitor stimulus. We suggest that *ID2* could serve as a fascinating marker predictive of response to HDAC inhibitors.

PE419
The role of Zinc Finger Protein 146 in Liver Cancer
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[1] The Chinese University of Hong Kong, [2] Croucher Laboratory for Human Genomics

Background/aims: The aim of this research project is the characterization of a Krüppel zinc finger protein, zinc Finger Protein 146 (ZNF146) using hepatocellular carcinoma as a disease model. Zinc finger protein 146 (ZNF146), also named as Only Zinc Fingers protein (OZF), is a 33kDa nuclear zinc finger protein consisting solely of ten C2H2 zinc finger motifs of the Krüppel type. Like most of Krüppel proteins, it is assumed to be the transcription factor and involved in the regulation of gene expression. The ZNF146 gene is amplified in 15-25% of pancreatic carcinomas and overexpressed in more than half of the tumors including liver cancer. It is thus proposed that overexpression of the ZNF146 may contribute to the development or progression of hepatocellular carcinoma.
Methods: We used flow cytometry, microarray, green fluorescent recombinant protein, RT-PCR site-directed mutagenesis, and transfection to study the effect of expression of ZNF146.
Results: Our results shown that ZNF146 was over-expressed in two human HCC cell lines HepG2 and Hep3B. Expression profiles of ZNF146 over-expressing shown that genes related to the p53 tumor suppressor activity or DNA damage, repair response and control were deregulated upon overexpression of ZNF146.
Conclusions: ZNF146 is possibly involved in liver carcinogenesis by affecting DNA repair and cell cycle control upon induced DNA damage.

PE420
Study on Antiviral Effects on Hepatitis B Virus with the Recombinant Adenovirus Admxa In Vitro
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Background: There is no specific treatment on Hepatitis B now. MxA is the main effective protein of IFNα/β. The recombinant adenovirus plasmid carrying human MxA gene is constructed to investigate the anti-HBV effects with the recombinant adenovirus AdMxA in vitro.
Methods: (1) Constructing the recombinant adenovirus plasmid carryting human MxA gene and (2) the levels of MxA mRNA were detected by RT-PCR and the tites of HBsAg and HBeAg were detected by ELASE after HepG2.2.15 cells were transfected by 1 MOI or 5 MOI of recombinant adenovirus AdMxA.
Results: The levels of MxA mRNA in HepG2.2.15 cells transfected with recombinant adenovirus AdMxA were increased significantly. The titers of HBsAg and HBeAg in HepG2.2.15 cells transfected with recombinant adenovirus AdMxA were lower significantly than those in HepG2.2.15 cells without recombinant adenovirus AdMxA (both $P<0.05$), but there is no difference between 1 MOI and 5 MOI groups($P>0.05$).
Conclusions: It indicates that the replication and expression of HBV in HepG2.2.15 cells can be inhibited after the recombinant adenovirus AdMxA transfected. It may be an effective way of gene therapy of HBV infection with recombinant adenovirus AdMxA.

PE421
Establishment of a Real-Time Monitoring System for Kinetic Characterization of RNA-Cleaving Dnazyme
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Background: In the present study, we reported the establishment of a real-time monitor system for directly observing the catalytic, kinetic characteristics of DNAzyme 10-23 in vitro cleavage on the target RNA

molecules as well as for rapid, accurate, high-throughout evaluation of varied DNAzymes on their counterpart RNA molecules.
Methods: DNAzyme named Dz-HCV-9 specific to hepatitis C virus (HCV) ORF AUG were designed and synthesized. Dz-HCV-Mis-9 with mismatched substrate-recognition domains, Dz-HCV-Mut-9 with mutant catalytic domains, antisense oligonucleotide ASON and nonsense oligonucleotide NSON were synthesized respectively as controls. A chimeric oligonucleotide of 29nt containing both RNA and DNA bases was designed and synthesized as the substrate: 5' FAM-GT AGACCGUGCACCAUGAGCACGAAUCCT-BHQ 3', corresponding to the330—354 nt (underline) of HCV genome(gi: 329873) The reporter FAM/BHQ was incorporated at the 5' and 3' end, respectively. Under simulated physiological conditions (37℃), kinetic characterization of RNA-cleaving DNAzyme was analyzed in a real-time way. Factors that influencing DNAzyme cleavage were analyzed.
Results: Dz-HCV-9 specific to HCV ORF AUG could cleave target RNA at A•U site, a continuous change of fluorescence intensity was monitored. While the control oligonucleotides couldn't cleave RNA, there were no change of fluorescence intensity. Factors that influencing DNAzyme cleavage concluded different substrate-recognition domain, Mg^{2+}concentration and pH.
Conclusion: A real-time monitoring system for kinetic characterization of RNA-cleaving DNAzyme was successfully established in the first time.

PE422

The Study on the Apoptosis of Hepatoma Cells Synergeticly Induced By Plasmid-Mediated Anti-Angiogenesis and Immunopotentiation Therapy

P.Y. Li[1], Q. Zhang[1], Y. Chang[1], J.S. Lin[1], D.A. Tian[1]
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Background: Angiogenesis is improtant to hepatoma and decreasing of host immunity promotes the development of tumor. We want to study the effect and mechanism of apoptosis of mice implanted hepatoma cells induced by eukaryotic plasmid-mediated anti-angiogenesis and immmunopotentiation therapy.
Methods: Mouse endostatin eukaryotic plasmid (pSecES) and mouse IL-12 (interleukin 12) eukaryotic plasmid (pmIL-12) were extracted and purified from E. coli. H22 hepatoma cells were inoculated into the leg muscle of mice, which was divided into four groups and injected with pSecES, pmIL-12, pSecES+pmIL-12 or pcDNA3.1 naked plasmid DNA respectively into implantation sites repeatedly. Tumor formation and its weight was evaluated. Tumor microvessel density, tumor infiltrating lymphocytes and apoptosis of tumor cells were assayed by CD31 staining, HE staining and TUNEL assay respectively.
Results: Inoculated mice received pSecES, pmIL-12 injection formed tumor slowly with less microvessel density, more tumor infiltrating lymphocytes in the latter and more tumor apoptosis cells in both groups compared with pcDNA3.1 injection. There were much more tumor apoptosis cells in pSecES+pmIL-12 group (19.9±5.5 per 400× microscope field，P<0.05) than any other single plasmid injection group (400× microscope field: pSecES 11.3±4.1, pmIL-12 14.6±3.2, pcDNA3.1 1.4±1.3).
Conclusion: Tumor cells of implanted hepatoma in mice could be synergeticly induced to apoptosis by eukaryotic plasmid-mediated anti-angiogenesis and immunotherapy through inhibiting tumor angiogenesis and promoting tumor lymphocytes to infiltrate, by which mice implanted hepatoma was inhibited.

PE423

Activation of Canonical Wnt Signaling Pathway Promotes Proliferation and Self-Renewal of Rat Hepatic Oval Cell Line WB-F344 In Vitro

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Aim: To investigate the effect of activation of canonical Wnt signaling pathway on the proliferation and differentiation of hepatic oval cells i*n vitro*.
Methods: WB-F344 cells were treated with recombinant Wnt3a (20, 40, 80, 160, 200 ng/mL) in a serum-free medium for 24 h. Cell proliferation was measured by Brdu incorporation analysis, untreated WB-F344 cells were taken as controls. After treatment with Wnt3a (160ng/mL) for 24 h, subcellular localization and protein expression of β-catenin in WB-F344 cells treated and untreated with Wnt3a were examined by immunofluorescence staining and Western-blot analysis. CyclinD1 mRNA expression was determined by semi-quantitative reverse-transcript polymerase chain reaction (RT-PCR). mRNA levels of some phenotypic markers (AFP, CK-19, ALB) and two hepatic nuclear factors (HNF-4, HNF-6) were measured by RT-PCR. Expressions of CK-19 and AFP protein were detected by Western-blot analysis.
Results: Wnt3a promoted proliferation of WB-F344 cells. Stimulation of WB-F344 cells with recombinant Wnt3a resulted in accumulation of the transcriptional activator β-catenin, together with its translocation into the nuclei, and up-regulated typical Wnt target gene cyclinD1. After 3 d of Wnt3a treatment in the absence of serum, WB-F344 cells retained their bipotential to express several specific phenotypic markers of hepatocytes and cholangiocytes, such as AFP, CK-19 following activation of the canonical Wnt signaling pathway.
Conclusion: The canonical Wnt signaling pathway promotes proliferation and self-renewal of rat hepatic oval cells.

PE424

The effect of doxorubicin on endogenous Bid in hepatocellular carcinoma cells containing HBx

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Background: Hepatocellular carcinoma (HCC) is a major malignant tumor worldwide and the effectiveness of its non-surgical therapeutics remains poor. There are several causative agents that trigger the paradox of HCC, and hepatitis B x (HBx) protein is one of them. The HBx plays dual roles of pro- and anti- apoptosis. A BH3 domain-only molecule Bid possesses bi-functions in the regulation of apoptosis. Previously, our group suggested that the introduction of HBx in HCC would decrease the expression of Bid, and Bid would activate S phase checkpoint under etoposide-induced DNA damage in HCC cells. Here we would like to investigate the effect of doxorubicin (Dox), which generated double-stranded break of DNA, on Bid in the Chang Liver cells (CL) transfected with HBx mutants.
Method:
Cell Lines
4 stable cell lines were established and used for the experiment: HBx (CL with full length HBx); HBx/50 (CL with the first 50 a.a. of HBx); HBx/51 (CL with 51 a.a. to 154 a.a. of HBx) and CL (CL with the empty vector pcDNA3.1).
MTT Cytotoxicity Assay
Determination of cell death for each cell line under various dosages of Dox was done by MTT assay.
Immunoblotting
The expression level of Bid and other pro- and anti-apoptotic proteins were detected by immunoblotting.
Results: HBx/51 showed the most sensitive towards Dox treatment, and truncated Bid (tBid) was also only detected in this cell line. The level of Bax was also increased in HBx/51 cells.
Conclusions: The carboxy-terminal of HBx may enhance the processing of Bid into tBid, which may contribute to increased sensitivity of the cell towards the Dox treatment.
Acknowledgement: This study was carried out in the Cancer Center in CUHK, and supported by the Research Grants Council of the Hong Kong Special Administrative Region (RGC project CUHK 4534/06M).

PE425

Oxysterol Induce Hepatic Cells Senescence

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Reactive oxygen species (ROS) are known as main mediators of cellular senescence and organism aging. ROS and oxysterols (7-ketocholesterol (7K) and 7 betahydrossicholesterol) are increased in chronic liver diseases. 7K is one of the most studied oxysterol, whereas, 5'6-secosterol (5'6S) is a newly discovered molecule and derives from ozonolysis of cholesterol. Unfortunately up to now, the few studies on the role of oxysterols on hepatic

cell homeostasis were performed with concentrations of oxysterol ($3x10^{-5}$-10^{-4}M) faraway from the physiological and/or pathological one (0.2 and $2x10^{-7}$M). In our study, we asked the effects of oxysterols (7K and 5'6S) on hepatoma cell lines homeostasis. To this purpose we used concentrations similar to those described in physiological or pathological conditions. Sub-physiological (10^{-9}M) to pathological (10^{-7}M) oxysterol (7K and 5'6S) concentrations were used to stimulate HepG2 cells.
A surprising pro-proliferative effect of 5'6S at sub-physiological (10^{-9}M) concentration was observed. This behaviour was confirmed by the synergic increase of ERK1/2 levels. FACS analysis revealed an early progression of cells in S phase at the lowest concentration of 5'6S, while all the remaining concentrations of the two studied oxysterols induced a weakly accumulation of cells in G2/M phase. Apoptosis was absent at all concentration used, except for the highest one (10^{-5}M). At this point we asked if cells didn't undergo apoptosis but acquired a senescent profile. Effectively, both 7K and 5'6S, at all concentration used (except for 10^{-9}M), induced cell senescence (revealed by SA-ß-gal staining and SIRT1 and p21 over-expression).
In conclusion the two oxysterols analyzed have different and in same case opposite effects on hepatocellular line. The main effect is surely the senescence induction, but it is important to highlight the proproliferative effects of 5'6 secosterol at low concentration.

PE426
Mortalin Inhibits p53-dependent Apoptosis in Hepatocellular Carcinoma
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[1] *Hong Kong University*

Mortalin, a member of HSP70 family protein, has been shown to play an important role in hepatocellular carcinoma (HCC). It has been reported that mortalin is binding to the C-terminal of p53, which acts as a safety guard and is a commonly mutated gene in HCC. In this study mortalin was silenced by specific shRNA in PLC/PRF/5, a HCC cell line constitutively expressing p53ser249, and normal liver cells MIHA, and we found that suppression of mortalin can selectively trigger the mitochondria mediated apoptosis pathway by p53 dependent way in PLC cells. Tunel staining positive cells were only found in the PLC cells mortalin knockdown group, and apoptosis associated protein, such as p53, Bax, Bcl-xl, cleaved-caspase 3, have been screened by western blot after transfection. Quantitative-PCR data also showed that p53 mRNA level are upregulated about 2 folds in mortalin knockdown group compared with the control groups in liver tumor cells. Two p53 inhibitors, PFT-α and PFT-μ, which can reverse this apoptosis was applied to demonstrate p53 dependent way. In summary, knockdown mortalin can selectively kill liver cancer cells through reactive apoptosis by sensitizing mutant p53 in PLC cells, but had no effect on normal cells. The clinical application of this study suggested that motalin specific shRNA might be a potential anti-cancer drug for HCC.

Poster Exhibition – NAFLD & Alcoholic Liver Disease
Poster Session, Hall 5B

PE427
Characteristics of Patients with NAFLD in Bangladesh
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[1] *Bangabandhu Sheikh Mujib Medical University,* [2] *Rajshahi Medical College Hospital*

Background: NAFLD can proceed to NASH and are at risk of cirrhosis and HCC. Aim was to study profile of Bangladeshi NAFLD patients.
Methods: 52 patients with NAFLD were included. Of them 59.6% were males and 40.4% females. Patients were between 12-60 years of age. They presented with dull right upper abdominal ache and/or incidental detection of raised ALT/AST and/or fatty liver on ultrasonography. All tested negative for hepatitis B and C. None had history of alcohol. All underwent per-cutaneous liver biopsy for histopathology. They were also tested for DM, dyslipidaemia, insulin resistance, hypothyroidism and hepatitis C. Their BMI and BP were recorded.
Results: 88.5% had NASH. 63.0% of them were males and rest 37.0% females. 11.5% had NAFL. Of them 50% each were males and females. Majority had NASH. 47.8% were obese and 41.3% had dyslipidaemia. 28.3% had hypertension, 28.3% insulin resistance and 13% were diabetics. 6.5% had hypothyroidism. None had hepatitis C. ALT was raised in 72% and AST in 40%. Although all patients with NASH did not have elevated ALT, it was raised in majority, contrary to AST, which was normal in most.
Conclusion: Majority NASH patients in Bangladesh are obese. Other leading causes of NASH include dyslipidaemia, hypertension and insulin resistance. Some NASH also had diabetes and hypothyroidism. This study also reveals that elevated ALT in patients with NAFLD is suggestive of fibrosis, although normal serum ALT does not exclude NASH. The study further suggests that ALT is superior to AST in predicting NASH.

PE428
Correlations of Laparoscopy with Histology and Laboratory Studies in Patients with Non-alcoholic fatty liver disease
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Background: Non-alcoholic fatty liver disease is prevalent in obese patients. Liver biopsy remains the best diagnostic tool for confirmation. We tried to find out the correlations of laparoscopic parameters with histology and laboratory data. Besides, we also evaluated the effectiveness of laparoscopy in liver disease diagnosis.
Methods: In the period of one year and five months,126 morbidly obese patients submitted to laparoscopic bariatric surgeries at our institutions were prospectively studied.
Results: Laparoscopic parameters of significant correlations with histologic steatosis, inflammation and fibrosis were summarized in Table 1. Besides, important parameters with relationships to laboratory data were summarized in Table 2.
Conclusion: In addition to histology and laboratory studies, laparoscopic inspection of the abdominal cavity provides important and additional information, which contributes to the final diagnosis of non-alcoholic fatty liver disease and detection of possible pathology in patients.

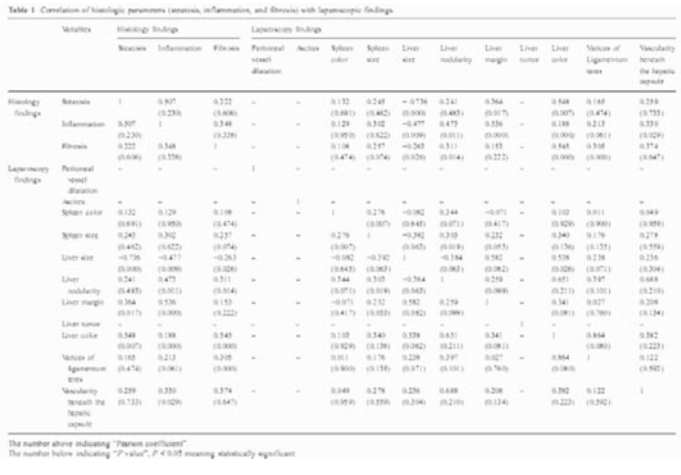

Table 2 Correlation of laboratory data with laparoscopic findings

Variables	Ascites	Spleen color	Spleen size	Liver size	Liver surface nodularity	Liver surface nodularity type	Liver margin	Liver tumor	Liver color	Liver surface fibrosis	Varices of Ligamentum teres
Albumin	–	0.017	0.079	−0.255	0.044	0.602	−0.207	–	0.119	−0.203	0.025
		(0.851)	(0.376)	(0.004)	(0.622)	(0.050)	(0.019)		(0.183)	(0.021)	(0.775)
T-protein	–	−0.125	−0.067	−0.174	0.059	−0.182	−0.056	–	0.270	−0.044	0.006
		(0.158)	(0.452)	(0.049)	(0.507)	(0.593)	(0.529)		(0.102)	(0.623)	(0.947)
AST	–	−0.049	0.171	−0.304	0.073	−0.090	−0.086	–	0.162	0.060	0.008
		(0.584)	(0.053)	(0.000)	(0.412)	(0.793)	(0.331)		(0.069)	(0.496)	(0.932)
ALT	–	−0.042	0.137	−0.323	0.073	0.120	−0.138	–	0.177	−0.091	−0.008
		(0.640)	(0.122)	(0.000)	(0.412)	(0.726)	(0.119)		(0.047)	(0.305)	(0.924)
ALP	–	0.095	0.707	−0.316	0.577	0.014	−0.577	–	0.000	0.949	0.163
		(0.284)	(0.182)	(0.604)	(0.308)	(0.877)	(0.308)		(1.000)	(0.014)	(0.066)
γ-GT	–	−0.058	0.222	−0.315	0.117	−0.414	0.224	–	0.280	−0.037	−0.173
		(0.579)	(0.032)	(0.002)	(0.265)	(0.268)	(0.031)		(0.007)	(0.727)	(0.098)
Blood glucose	–	0.116	0.222	−0.113	0.238	−0.030	−0.053	–	0.041	0.037	0.201
		(0.189)	(0.012)	(0.202)	(0.006)	(0.930)	(0.549)		(0.650)	(0.673)	(0.223)
HbA1c	–	0.108	0.119	0.009	0.097	0.030	−0.091	–	−0.064	−0.124	0.073
		(0.222)	(0.181)	(0.922)	(0.275)	(0.930)	(0.305)		(0.475)	(0.163)	(0.414)
C-peptide	–	−0.063	0.051	−0.255	0.101	−0.060	−0.145	–	0.119	0.082	−0.137
		(0.482)	(0.576)	(0.004)	(0.264)	(0.861)	(0.107)		(0.188)	(0.366)	(0.128)
Insulin	–	−0.097	0.091	−0.140	0.024	0.120	−0.073	–	0.163	0.034	−0.128
		(0.275)	(0.307)	(0.115)	(0.784)	(0.726)	(0.410)		(0.068)	(0.699)	(0.150)
HOMA-IR	–	−0.107	0.160	−0.287	0.127	−0.181	−0.126	–	0.286	0.472	0.080
		(0.226)	(0.070)	(0.061)	(0.153)	(0.594)	(0.155)		(0.074)	(0.121)	(0.365)
CHO	–	−0.128	−0.164	0.026	−0.091	0.000	−0.082	–	−0.020	−0.117	−0.105
		(0.148)	(0.063)	(0.768)	(0.305)	(1.000)	(0.354)		(0.820)	(0.185)	(0.235)
TG	–	0.002	−0.051	−0.127	0.103	0.120	0.007	–	−0.014	0.088	−0.044
		(0.979)	(0.563)	(0.151)	(0.245)	(0.726)	(0.939)		(0.874)	(0.319)	(0.622)
HDL-C	–	−0.045	0.052	0.020	−0.048	0.332	−0.110	–	0.056	−0.047	0.049
		(0.612)	(0.555)	(0.820)	(0.591)	(0.318)	(0.213)		(0.528)	(0.596)	(0.582)
UA	–	−0.021	−0.003	−0.053	−0.049	0.719	−0.124	–	0.050	−0.195	−0.008
		(0.810)	(0.973)	(0.550)	(0.583)	(0.063)	(0.162)		(0.579)	(0.127)	(0.932)
PTH	–	0.095	−0.014	−0.126	−0.065	0.099	−0.022	–	0.244	0.090	−0.058
		(0.286)	(0.913)	(0.321)	(0.609)	(0.266)	(0.863)		(0.052)	(0.480)	(0.649)
WBC	–	−0.051	−0.042	−0.048	−0.019	−0.240	−0.076	–	0.012	−0.088	−0.187
		(0.566)	(0.636)	(0.591)	(0.828)	(0.478)	(0.393)		(0.896)	(0.324)	(0.134)
Hb	–	0.123	0.116	−0.147	0.106	0.150	−0.066	–	0.051	0.158	−0.008
		(0.163)	(0.190)	(0.097)	(0.230)	(0.660)	(0.454)		(0.571)	(0.073)	(0.924)
MCV	–	0.091	0.062	0.085	0.019	−0.179	0.026	–	−0.133	0.137	0.056
		(0.303)	(0.484)	(0.340)	(0.831)	(0.598)	(0.772)		(0.135)	(0.121)	(0.531)
Ca	–	0.167	−0.248	−0.042	−0.105	0.109	−0.089	–	0.159	−0.198	−0.036
		(0.058)	(0.145)	(0.735)	(0.369)	(0.223)	(0.477)		(0.203)	(0.111)	(0.774)
CRP	–	0.125	0.140	−0.108	0.052	−0.359	−0.079	–	0.103	0.057	−0.104
		(0.160)	(0.116)	(0.224)	(0.560)	(0.279)	(0.375)		(0.251)	(0.520)	(0.243)

The number above indicating "Spearson coefficient"
The number below indicating "*P* value", *P*<0.05 meaning statistically significant

PE429

NAFLD Index: A Simple Screening Tool Reflecting Nonalcoholic Fatty Liver Disease in the Korean Population

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Background: To optimize management of nonalcoholic fatty liver disease (NAFLD), a simple screening tool is necessary. In this study, we aimed to devise a simple index that reflects the presence of NAFLD in the Korean population.

Methods: A cross-sectional study was conducted on 10,724 health check-up subjects at a healthcare center (5,362 cases with NAFLD versus age- and sex-matched controls). Study subjects were randomly assigned to a derivation cohort or a validation cohort. An index reflecting the presence of NAFLD was derived in the derivation cohort and validated in the validation cohort.

Results: Multivariable analysis indicated that body-mass index (BMI), serum alanine aminotransferase (ALT) to serum aspartate aminotransferase (AST) ratio, sex, and the presence of diabetes mellitus were independent predictors of NAFLD. Using these variables, a formula was derived using a linear regression model: NAFLD index (NAFLDI) = 8×ALT/AST ratio +BMI (+3, if female; +2, if diabetes mellitus). NAFLDI had an area under receiver-operating curve of 0.812 (95% confidence interval, 0.801–0.824). At a value <31.0, NAFLDI ruled out NAFLD with a sensitivity of 89.0% and a negative likelihood ratio of 0.22, and at a value >36.0, NAFLDI detected NAFLD with a specificity of 91.2% and a positive likelihood ratio of 5.42. In the validation cohort, the predictive power of NAFLDI was maintained at similar levels.

Conclusion: NAFLDI was a simple, efficient screening tool for NAFLD that could be utilized for selecting individuals for liver ultrasonography and for determining the need for lifestyle modifications.

PE430

The Role of Insulin Resistance, Adipokine and Cytokine pro-inflammatory in Non-Alcoholic Fatty Liver Disease

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Background: Non-alcoholic fatty liver disease (NAFLD) is a benign disease during 5-10 years period, with 67%-59% survival. NAFLD can progress to fibrosis, cirrhotic and cancer of the liver. The etiopathogenesis of NAFLD is still unknown, however genetic and environment factors are predicted.

Objective: To know the role of insulin resistance, adipokine and cytokine pro-inflammatory on NAFLD.

Methods: The cross sectional study was performed on General Check-up population at Dr. Sardjito General Hospital Yogyakarta, Indonesia. The study was begun from January 2007 until November 2007 at Internal Medicine outpatient Department. Inclusion criteria: adult, alcohol consumtion ≤20g/day, metabolic syndrome patients, and healthy subjects. Exclusion criteria: The diseases with increasing liver enzymes (HBV, HCV, ischemic hepatitis, congestive liver), a "bright liver" on ultrasound examination (malnutrition, rapid weight decreased, post gut surgery on obesity patients, and drug induced). Based on liver ultrasound subjects were devided into steatosis group and non-steatosis group. Data were analyzed by t-test and non-parametrical test.

Results: 101 subjects that were enrolled the study 61 steatosis (60.4%) and 40 non-steatosis (39.6%) and the subjects who completed cytokine and adipokine examination were 48 steatosis and 30 non-steatosis. There were significantly different on HOMA –IR and adiponectin level in steatosis group (HOMA-IR 3.367±4.901 vs. 1.430±1.889, p=0.019; adiponectin 4.049±1.929 vs. 7.034±3.777, p=0.000). There were not significantly different on TNF-α, IL-6, leptin and visfatin level (p>0.05).

Conlusions: There were significantly different on HOMA-IR and adiponectin level in NAFLD patients compared non-NAFLD patients.

PE431

Prevalence and Clinical Features of Non-Alcoholic Steatohepatitis (NASH) Among Patients with Non-Alcoholic Fatty Liver Disease (NAFLD)

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Aim: Since NASH could progress to liver cirrhosis and hepatocellular carcinoma, it is important to correctly diagnose between NASH and Simple steatosis (SS). The aim of this study was to determine the prevalence of NASH among NAFLD patients and to clarify differences in clinical features between NASH and SS.

Subjects and Methods: Thirty-one patients with NAFLD showing abnormalities in serum transaminase (AST and /or ALT >40 IU/l) were enrolled (sex: male 11, female 20; mean age: 49.5 yrs, mean body mass index: 29.3), after obtaining informed consent. Differential diagnosis between NASH and SS was performed histologically according to the Matteoni classification and clinical features were compared.

Results: Among the patients with NAFLD, 81% and 19% were diagnosed with SS and NASH, respectively. No significant differences in the sex, mean age and BMI were seen between NASH and SS groups. The levels of AST, ALT, homeostasis model assessment-insulin resistance (HOMA-IR) and hyaluronic acid were significantly elevated in NASH patients compared to SS patients. No significant differences in serum levels of adiponectin, as well as the rates of occurrence of diabetes, hypertension and hyperlipidemia were observed between the two groups.

Conclusion: The prevalence of NASH in NAFLD patients was about 20%. NASH patients showed higher levels of serum transaminase, HOMA-IR and hyaluronic acid, compared to SS patients. A large-scale biochemical study is required to accurately diagnose NASH patients and confirm these results.

PE432

Evaluation of the Efficacy of Two Simple Noninvasive Fibrosis Markers in Korean NAFLD Patients: a Cross-Sectional Study in a Single Center

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Background/aims: Hepatic fibrosis is associated with poor prognosis in non-alcoholic fatty liver disease (NAFLD). Recently, many non-invasive fibrosis markers have been studied to overcome the limitations of liver biopsy. Among them, BARD score and Guha's simple panel are easy to use in clinical practice. In this study, we evaluated the efficacy of BARD score and Guha's simple panel as a noninvasive fibrosis marker in Korean NAFLD patients.
Methods: Data from 79 patients with biopsy-proven NAFLD in Seoul National University Hospital from 2000 to 2007 were used. BARD score and Guha's simple panel were calculated by using clinical and biochemical data and were compared with the histological fibrosis stages.
Results: Stage 0 fibrosis were found in 67 patients, stage 1 in 4, stage 2 in 2, stage 3 in 1 and stage 4 in 5. The relationship between fibrosis stage and BARD score ($\rho = 0.43$, $p < 0.001$) was statistically significant. All patients with advanced fibrosis (stage 3-4) had BARD score greater than 2. Mean values from original Guha's simple panel for no fibrosis were not different between the patients with and without fibrosis. However, after adjusting coefficients by logistic regression analysis, the differences in mean values became statistical significant ($p < 0.001$).
Conclusions: Our data suggest that Bard score may be effective for detecting high risk patients for advanced fibrosis, and modification of coefficients within the Guha's simple panel may be needed to use as a fibrosis marker in Asian NAFLD patients.

PE433

NASH Profile: A Combination of Intercellular Adhesion Molecule - 1, Adiponectin And Type IV Collagen, to Detect Non - Alcoholic Steato Hepatitis (NASH), among Patients Having Non - Alcoholic Fatty Liver Disease (NAFLD)

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Background: Non-Alcoholic Fatty Liver Disease (NAFLD) covers a spectrum of liver diseases from simple fatty infiltration to progressive fibrosis. Non-Alcoholic Steato Hepatitis (NASH) is a severe form of NAFLD and progresses to the end stage of liver disease. It is becoming the leading cause for referral to liver clinics in most areas. The prevalence of NAFLD in Indian population is estimated around 7 – 13%. The NAFLD has the potential to progress to hepatocellular carcinoma or liver failure, both events that ultimately lead to early death.
Aim: To evaluate the combination of Inter Cellular Adhesion Molecule – 1 (ICAM - 1), Adiponectin and Type-IV collagen, a new biomarker profile for NASH in patients with NAFLD.
Methods: 76 patients with NAFLD and age & sex matched 68 normal healthy individuals as controls were selected for this study. Levels of Serum ICAM – 1, Adiponectin, Type-IV collagen, lipid profile and liver function test parameters were estimated in patients and compared with controls.
Results: Serum ICAM – 1 & Type – IV collagen levels were significantly increased in patients with NASH among the NAFLD patients compared to controls. The Serum Adiponectin levels were significantly reduced in patients with NASH among the NAFLD patients compared to controls. Compared to liver function test parameters and lipid profile levels, NASH profile has got positive negative predictive value among the NAFLD patients.
Conclusion: In patients with NAFLD, NASH profile Test - a simple, non – invasive and reliable to predict the presence or absence of NASH.

PE434

Lipid Peroxidation and Cytokines in Patients with Nonalcoholic Fatty Liver Disease (NAFLD)

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Background/Aim: Oxidative stress and cytokines plays an important role in the pathogenesis of nonalcoholic fatty liver disease (NAFLD). Aim of study was to assess lipid peroxidation, serum levels of transforming growth factor-β (TGF-β) and tumor necrosis factor-α (TNF-α) in patients with NAFLD and compare it with patients of chronic viral hepatitis (CVH) and healthy controls (HC).
Methods: Lipid peroxidation was studied by estimating plasma malondialdehyde (MDA) levels as per the methodology described by Buege and Aust and TGF-β & TNF- α levels were measured by ELISA kits (Ray Biotech, USA, & Diaclone, UK) in the stored sera in 10 biopsy proven patients with NAFLD (M: 4, F: 6, Mean age: 41.7 ± 11.0 yrs), 15 patients with CVH (M:14, F:1, Mean age: 33.7 ± 11.4 yrs) and 5 HC (M:5, Mean age: 25.2 ± 2.7 yrs).
Results: There was no difference in mean plasma MDA levels amongst patients with NAFLD (17.28 ± 3.6 mol/L), CVH (15.29 ± 2.3 mol/L) and HC (16.79 ± 1.2 mol/L). Serum TGF- β levels between NAFLD (0.56 ± 0.41 ng/mL) and CVH (0.52 ± 0.25 ng/mL) patients and HC (0.58 ± 0.57 ng/mL) were also comparable. Though patients with CVH (17.2 ± 27.0 pg/mL) and NAFLD (7.5 ± 6.3 pg/mL) had higher levels of TNF–α than HC (5.5 ± 1.1 pg/mL), the difference was not significant statistically.
Conclusion: Lipid peroxidation, TGF-β and TNF-α need to be studied in a larger number of patients with NAFLD.

PE435

Surrogate Markers of Nonalcoholic Fatty Liver Disease (NAFLD) are Increased in Patients with Cryptogenic Cirrhosis and Cryptogenic Hepatocellular Carcinoma.

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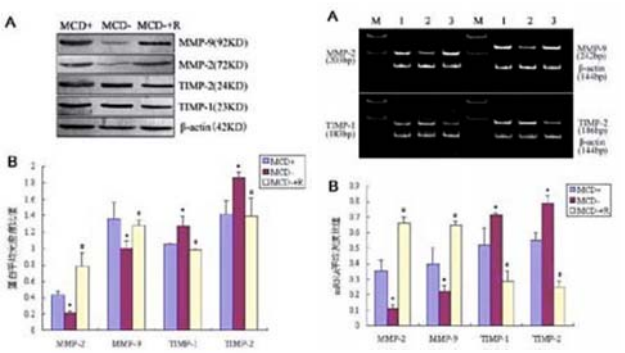
Background/Aim: Burnt out nonalcoholic fatty liver disease (NAFLD) may be responsible for cirrhosis and hepatocellular carcinoma (HCC) in the absence of other causes. Aim of this study was to evaluate the surrogate markers of NAFLD in patients with cryptogenic cirrhosis (CC) and cryptogenic HCC (CHCC).
Methods: Sixty five patients with CC and 31 patients with CHCC were analyzed for the presence of abnormal body mass index (BMI) and type 2 diabetes mellitus (DM). Other metabolic abnormalities were assessed in all patients with CC and 24 patients with CHCC. Patients with CC or CHCC were negative for all possible etiologies. Results of CC were compared with 20 patients with virus related cirrhosis (VCC). Anthropometry and diabetes mellitus in CHCC were compared with 87 patients and other abnormalities with 15 patients with virus related HCC (VHCC).
Results: Mean BMI was higher in patients with CC (26.06±5.96 kg/m^2) in comparison to VCC (23.13±2.72 kg/m^2) ($p = 0.038$). Higher number of patients with CC had abnormal waist (58.8% Vs 30% p= 0.029), type 2 diabetes mellitus (39.6% Vs10% $p = 0.028$) and lower serum high density lipoproteins (HDL) (53.5% Vs 5%, p=0.0003) in comparison to VCC. There was no difference in mean BMI, abnormal HDL, triglycerides and hypertension amongst patients with CHCC and VHCC. Patients with CHCC had higher prevalence of type 2 diabetes mellitus in comparison to VHCC (32.2% Vs 16% p =0.05).
Conclusion: Patients with cryptogenic cirrhosis and cryptogenic HCC have higher prevalence of surrogate markers of NAFLD.



PE436

Effect of Insulin Sensitizing Agents (ISA) on Hepatic "Protein C" and Paraoxonase m-RNA Expression in Rats with Fatty Liver

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Background: Previous studies reported increase in serum protein C and decrease in serum paraoxonase levels in patients with non alcoholic fatty liver diseases (NAFLD).
Aim: 1) Determine whether there is a relationship between NAFLD, Protein C and Paraoxonase levels in quiescent and in regenerating rats fatty liver 2) determine the effect of ISA on hepatic "protein C" and paraoxonase mRNA.
Methods: Forty-eight SD rats were treated with fructose enriched diet (FED), or FED with Metformin (2 mg/Kg/d), FED with Rosiglitazone (3 mg/Kg/d), or the combination of both drugs for 5 wks. 30% PHX was performed at WK 5. Protein C, paraoxonase mRNA expressions, lipids, MDA were measured before and 24 hours after PHX.
Results: Hepatic "protein C" mRNA was higher in rats with fatty liver than control rats (+105%, $p<0.01$) whereas hepatic paraoxonase mRNA was lower in rats with fatty liver than control rats (-28%, $p<0.005$). Hepatic protein C and paraoxonase mRNA increased in rats with fatty liver in regeneration (+116%,
$p< 0.01$, and +15%, $p<0.01$ respectively). The combination of metformin and rosiglitazone decreased hepatic protein C expression at 24 hours after PHX by -170% ($p<0.001$) and increase paraoxonase mRNA by +50% ($p<0.01$). Serum paraoxonase correlates with serum protein C ($r=-0.2$), MDA ($r=0.4$), TG ($r=-0.23$).
Conclusion: Hepatic "protein C" mRNA levels are high at baseline, up regulated during liver regeneration and decrease after treatment with (ISA) whereas hepatic paraoxonase mRNA levels are low at baseline, up regulated during liver regeneration and increase after treatment with ISA.

PE437

Effect of PPARγ Targeted Agonist on Expression Of MMP And TIMP In Nutritional Fibrosis And Steatohepatitis In Mice

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Objective: To study the effect of rosiglitazone on expression of matrix metalloproteinase (MMP), tissue inhibitor of metalloproteinase (TIMP) in fibrosing nonalchoholic steatohepatitis.
Methods: C57BL6/J mice were fed with MCD diet to induce hepatic fibrosis and rosiglitazone was given in treated group. Effect of rosiglitazone was assessed by comparison of the severity of hepatic fibrosis in liver sections, expression of MMP-2/9, TIMP-1/2 mRNA and protein detected by RT-PCR and Western blot respectively.
Results At week 8, fibrosing NASH models showed severe hepatic steatosis, infiltration of inflammation and fibrosis, which is associated with down-regulated MMP-2/9 mRNA and protein, up-regulated TIMP-1/2 mRNA and protein. Rosiglitazone significantly reduced MCD-induced fibrosis by induced MMP-2/9 expression and reduced TIMP-1/2 expression by activating PPARγ.
Conclusions The present study provides evidence for the protective role of rosiglitazone in improving nutritional fibrosing steatohepatitis. Rosiglitazone may ameliorate hepatic fibrosis by activating PPARγ, which can up-regulate MMP and suppress TIMP expression.

PE438

Association of Phosphatidylethanolamine N-methyltransferase Gene G175A Single Nucleotide Polymorphism with Nonalcoholic Fatty Liver Disease

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Aim: To investigate the relation of phosphatidylethanolamine N-methyltransferase（PEMT） gene G175A single nucleotide polymorphism (SNP) with the susceptibility to nonalcoholic fatty liver disease（NAFLD）.
Methods：The genotypes and allele frequencies of PEMT exon 8 SNP G175A were analyzed by using PCR-RFLP in 51 NAFLD patients and 50 controls.
Results: The G to A variation of the PEMT gene G175A SNP was significantly higher in NAFLD group compared with controls. The frequencies of GG，GA and AA genotypes were 58.8%、39.2% and 2.0% in NAFLD and 78.0%、22.0% and 0.0% in controls ($P=0.038$). The A allele of the PEMT gene was significantly more frequent in NAFLD group (21.6%) than that (1.0%) in controls（$P=0.042$）.There were significant differences in serum levels of cholesterol, triglyceride, HDL-C and LDL-C between GG and GA/AA genotypes（$P <0.05$）.
Conclusion：People with PEMT gene G175A SNP were more susceptible to develop NAFLD

PE439

Change of Arginase Ⅱ in the Progress of Non-Alcoholic Steatohepatitis in Rats

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Background: Non-alcoholic steatohepatitis (NASH) is a type of non-alcoholic fatty liver disease (NAFLD), and may progress to hepatic fibrosis and cirrhosis. The pathogenesis of NASH remains unclear. The aim of this study was to explore the arginase Ⅱ change in the progress of steatohepatitis in rats.
Methods: Male SD rats weighing 70-80g were obtained. Twenty animals were randomly divided into two groups. In the model group, five animals were fed with high lipid forage that includes 3% cholesterol and 20% lard for 6 weeks, five were fed for 12 weeks, while the control group ate normal foods. The animals were sacrificed after 6 weeks. The animals were sacrificed after 6 weeks and 12 weeks. Liver and blood serum were collected while the serum levels of ALT, AST, TG and TC were measured. The pathology of liver was observed by HE staining. Western blot was used to investigate the expression of arginase in control and model group.
Results: Vacuolization were observed extensively in hepatic cells in the model group after 6 weeks and 12 weeks of high-fat diet. It is demonstrated that rats fed with high-cholesterol food are indeed fatty liver models. Western blot showed that the level of arginase II increase in the liver of model group rats as compared to the control group. Furthermore, the level of arginase was higher in liver samples obtained from model rats that were 12 weeks on a fat diet as compared to rats that were only 6 weeks on the same diets.
Conclusion: The level of arginase II was altered in the progress of non-alcoholic steatohepatitis in rats suggesting that arginase II is putative biomarkers and may represent new targets in the development of therapeutic strategies against fatty liver disease，hepatic fibrosis and cirrhosis.

PE440

The Ethanolic Extract of Fructus Schisandrae Chinensis Decreased Hepatic Triglyceride Level in Mice Fed with a High Fat/Cholesterol Diet

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Effects of the ethanolic extract of Fructus Schisandrae Chinensis (EtFSC) on serum and liver lipid contents were investigated in mice fed with normal diet

or high fat/cholesterol diet for 8 or 15 days. Single dose of EtFSC (1 or 5 g/kg/day, i.g.) increased the serum triglyceride (TG) level (40 and 142%, respectively), but decreased hepatic total cholesterol (TC) level (15 and 16%, respectively) in normal mice. The hypertriglyceridemia produced by EtFSC was suppressed by the co-administration of fenofibrate. The induction of hypercholesterolemia by high fat/cholesterol diet caused significant increases in serum and hepatic TC levels (up to 165%) and hepatic TG levels (up to 528%) in mice. EtFSC treatment (1 or 5 g/kg/day for 7 days, i.g.) significantly decreased the mouse hepatic TG level (by 35%) and slightly increased the hepatic index (by 8%). Whereas fenofibrate treatment (0.1 g/kg/day for 7 days, i.g.) significantly lowered the hepatic TG level (by 61%), it significantly elevated the hepatic index (by 77%) in hypercholesterolemic mice. The results indicate that EtFSC treatment can invariably decrease hepatic TG in hypercholesterolemic mice, suggesting its potential use for fatty liver treatment.

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PE441

The Influence of Multiple Gene Polymorphisms in the Susceptibility of Non-Alcoholic Fatty Liver Disease (NAFLD)

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Aim: To investigate the influence of multiple gene polymorphisms in the susceptibility of NAFLD.

Methods: The data of single nucleotide polymorphisms (SNPs) in 201 NAFLD patients，who had at least one of the genetic variations at the sites of TNF-α-238, adiponectin -45 and leptin-2548 were analyzed. The genotypes were determined by using PCR-RFLP. Our previous studies showed that the variations of these sites increased the susceptibility of NAFLD.

Results: The prevalence of NAFLD in adiponectin variation alone group (n=45) was 35.6%; in TNF-αalone group (n=33) 42.4%; in leptin alone group (n=54) 35.2% ($p>0.05$). In comparison with the above groups with single SNP, the prevalence of the groups with two gene variations of TNF-αplus adiponectin (57.9%, n=19) increased significantly ($p<0.05$). However the prevalence of other two groups i.e. adiponectin plus leptin (34.6%, n=26) and TNF-αplus leptin (40.0%, n=15) did not differed significantly from those of groups with single SNP ($p>0.05$). The prevalence in the group with three gene variations (55.6%) differed significantly from all ($p<0.05$) except that of TNF-αplus adiponectin group ($p>0.05$). The metabolic features of the NAFLD patients in the 7 groups mentioned above were not different significantly ($p>0.05$).

Conclusion: NAFLD is a polygenic disease. Multiple gene polymorphisms may, but not always, increase the susceptibility of NAFLD.

PE442

Study on Clinical and Pathological Characteristic in Hbeag Negative Chronic Hepatitis B Patients with Nonalcoholic Fatty Liver Disease

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Background: To investigate clinical pathological characteristic in HBeAg negative Chronic hepatitis B (CHB) patients with nonalcoholic fatty liver disease (NAFLD).

Methods: We measured fasting blood glucose, insulin, triglyceride, cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST) in HBeAg negative chronic hepatitis B (CHB) patients with nonalcoholic fatty liver disease (NAFLD). And we detected Hepatitis B Virus marker, HBV-DNA, counted body mass index, insulin resistance index and observed pathological characteristic. All these patients with diagnosis were confirmed by clinical and pathological evidence.

Result : The body mass index, homeostatic model assessment (HOMA) of insulin resistance, fasting blood glucose, insulin, triglycerides, cholesterol, were significantly higher in HBeAg negative chronic hepatitis B (CHB) patients with nonalcoholic fatty liver disease (NAFLD) than HBeAg negative chronic hepatitis B patients. But the alanine aminotransferase (ALT), aspartate aminotransferase (AST), HBV DNA levels were significantly lower in HBeAg negative CHB patients with NAFLD than in HBeAg negative chronic hepatitis B patients. Histologic features in HBeAg negative chronic hepatitis B(CHB) patients with nonalcoholic fatty liver disease (NAFLD) are in zone 3 predominate macrovesicular steatosis and mild inflammatory infiltrate in portal region.

Conclusion: The HBeAg negative chronic hepatitis B (CHB) patients with nonalcoholic fatty liver disease, whose hepatic steatosis changes are mainly caused by the metabolic factors. To carry out liver biopsy selectively for the patients with HBeAg negative chronic hepatitis B having metabolic factors, which is helpful for early diagnosis in HBeAg negative chronic hepatitis B (CHB) patients with nonalcoholic fatty liver disease (NAFLD).

PE443

Effect of Cordyceps Sinensis on Hepatocyte Apoptosis in Experimental NFALD Model of Rats and Possible Mechanisms

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Aims: To investigate the preventive effect of Cordyceps sinensis and its possible mechanism on apoptosis of NAFLD.

Methods: Rats were randomly divided into basic diet group (B group), pathologic group (NASH group) and cordyceps sinensis group(CS group).The latter two groups were administered with high-fat diet to establish NAFLD animal models. CS group were treated with CS at the 9th week after high fat diet. Rats were sacrificed at the end of the 18th week. Biochemical examination were used to detect superoxide dismutase (SOD) of liver tissue. Hepatocyte apoptosis was assessed in each group using the TUNEL assay and immunohistochemistry for activated Bax、Bcl-2、Caspase-3 and NF-kB P65.

Results: (1) Compated with the B group, severe hepatosteatosis, inflammative necrosis and local fibrigenisis were showed in liver of NFSH group. SOD lever was significantly decreased ($P<0.01$) and TUNEL-positive cells were significantly increased ($P<0.01$). Immuunohistochemistry test demonstrated active Bax、Caspase-3was increased ($P<0.01$) while no apparent change was observed in Bcl-2. (2) In CS group, only diffusive steatosis but not inflammation or fibrosis was found. SOD lever was increased than that of NASH group ($P<0.05$). TUNEL-positive cells and active Bax、Caspase-3 were significantly decreased ($P<0.05$ $P<0.01$) that those of NASH group. Bcl-2 and NF-kB P65 were increased ($P<0.01$) than those of NASH group.

Conclusions: Hepatocyte apoptosis is a prominent feature of NAFLD. Cordyceps sinensis may be useful as an antiapoptosis theraphy in this syndrome through increasing activity of SOD, decreasing express of Bax and increasing express of Bcl-2 and NF-kB P65.

PE444

A Meta-Analysis on the Efficacy of Thiazolidinediones among Patients with Non-Alcoholic Steatohepatitis

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Background: Non-alcoholic steatohepatitis (NASH) is a leading cause of chronic liver disease. Insulin-sensitizing , anti-inflammatory and anti-fibrotic effect of thiazolidinediones support their use in the treatment of NASH. We aimed to evaluate the efficacy of thiazolidinediones in the treatment of NASH.

Methods: We have identified randomised clinical trials, evaluating the efficacy of thiazolidinediones versus placebo in NASH, through MEDLINE, EMBASE, AMI, Cochrane Central Register of Controlled trials. Data were abstracted from each study and disagreements were resolved by consensus. Dichotomous outcomes were reported as relative risk with 95% confidence interval based on fixed-effects model.

Results: We included three trials, two evaluating pioglitazone and another rosiglitazone. A total of 171 patients were involved in the analysis. Thiazolidinediones was noted to improve liver function tests. It was effective in the reduction of steatosis among patients with NASH (RR 0.67, 95% CI 0.52-0.87). It was found to be beneficial in improving ballooning necrosis (RR 0.79, 95% CI 0.66-0.95). It was also found to improve lobular

inflammation (RR 0.72, 95% CI 0.56-0.92). Finally, it was noted to have a trend towards benefit in reducing hepatic fibrosis (RR 0.92, 95% CI 0.77-1.09).
Conclusion: Thiazolidinediones may be beneficial in reducing steatosis, lobular inflammation, and ballooning necrosis among patients with NASH. And it has a trend towards benefit in reducing hepatic fibrosis.

PE445

Waist to Stature Ratio is More Strongly Associated with Nonalcoholic Fatty Liver Disease (NAFLD) Risk than Waist Circumference [WC]

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Introduction: NAFLD has emerged as the numero uno liver disorder in both the developed and the developing countries. Studies on NAFLD give greater stress on waist circumference [WC] than BMI as a marker of central obesity without any hard evidence to support this. The present study was conducted to study the utility of waist versus waist/stature ratio [WSR] as a marker of central obesity with reference to NAFLD.
Material and Methods: 38 subjects without fatty liver [FL] on ultrasound [US], and 66 patients with FL on US were subjected to anthropometric measurements to compare waist circumference [WC] with WSR as markers of obesity. Statistical calculations were made by using SPSS software [version 10].
Results: In subjects without fatty liver, increase [>90 cm for males and >80 cm for females] in WC was seen in only 3 of 38 subjects [7.9%], while in fatty liver patients, WC was increased in 41 of 66 [62.1%] subjects. On the contrary, an increased WSR [0.52] was seen in only 4 of 38 [10.5%] non-fatty subjects, and 53 of 66 [80.3%] patients with FL. Besides when BMI was correlated with WC and WSR in subjects with and without FL, in both group of patients, BMI correlated with both WC and WSR with significance at 0.001 level.
Conclusion: Waist/stature ratio WSR is more strongly associated with fatty liver risk than waist circumference [WC]. A WSR cut-off value of 0.52 might be appropriate as an indicator of central obesity/risk factor for NAFLD.

PE446

The Effects of Fat Loss on ALT Abnormalities in Japanese Patients with Non-Alcoholic Fatty Liver Disease

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Background: It is well known that the weight reduction is effective for ALT normalization in patients with non-alcoholic fatty liver disease (NAFLD).
The necessary condition for ALT normalization is still unclear. To clarify the necessary and sufficient condition for ALT normalization, we investigated the effects of body fat decrease in NAFLD patients by body composition analyzer.
Methods: Forty-six NAFLD patients (23 male, 23 female, mean age 49.8±12.9 years old) with abnormal ALT levels were evaluated. The volume of skeletal muscle, body fat and BMR were examined by using the body composition analyzer (In Body 720; Biospace Co. Ltd., Tokyo Japan). All patients were received an individualized diet consultation by dietician every 4 weeks for 6 months. Daily energy was BMR (basal metabolic rate) x1.2 kcal and protein was 1.0-1.2g per ideal body weight.
Result: Twenty-eight of 46 patients (60.9%) were achieved normal ALT level. In ALT normalized group, the body weight and fat loss were 3.6±2.3 kg, 3.0±1.5kg (2.8±1.7 %body fat) respectively. On the other hand, in cases with ALT remained abnormal level, the body weight and fat loss were 0.5±1.5kg, 0.4±1.6kg (0.5±1.6 %body fat).
Conclusion: Our results demonstrate that the fat loss of 3 kilograms or more was necessary to normalize ALT level in NAFLD patients.

PE447

Familial Clustering of Non Alcoholic Fatty Liver Disease: Does Insulin Resistance Holds the Key?

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Background : NAFLD is often clustered within families and the causes include both genetic and environmental factors. Family studies done thus far have been limited by small sample size. To examine the familial patterns , we performed a prospective study to see (a) Whether NAFLD is more common in first degree relatives (b) Genetically determined risk factors associated for clustering.
Methods: First degree relatives of histologically confirmed NAFLD patients and spouses (controls) were included after excluding other causes of fatty liver. Those having raised transaminases >3 months or sonographic examination consistent with fatty liver, had undergone liver biopsy for histological confirmation. They were divided into three groups.
Group I Patients
Group II First degree relatives
Group III Spouses
Results: NAFLD was more prevalent among first degree relatives then spouses (37% and 17%, p<0.01). Anthropometric measurements, systolic and diastolic blood pressure, lipid profile and liver function tests were comparable in three groups. HOMA-R was similar in Group I and II (p=0.073), but was significantly different in Group I and III (p= 0.0001) and Group II and III (p=0.0001) respectively. Metabolic syndrome was present in >70% of patients and were comparable in three groups except for fasting glucose > 110, which was present in 76%, 77% and 57% of patients in group I, II and III respectively. Majority (>50%) of our patients among groups I, II and III were having only steatosis while NASH was present in 20%, 13% and 14% of patients.

PE448

Nonalcoholic Fatty Liver Disease Associated with Normal ALT Values: A Clinicopathological Study

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Background: Normal levels of alanine aminotransaminase (ALT) have been demonstrated in NAFLD patients. ALT levels are also modulated by age, gender, BMI, fasting glucose, and serum triglyceride levels. We performed a prospective study of patients with histologically confirmed NAFLD and having ALT < 1.5 times and compared them with those having raised ALT to determine (a) clinico-pathologic features of NAFLD patients with normal ALT (b) to observe any differences between them.
Methods: Patients with fatty liver on sonography had under gone biopsy for histological confirmation after excluding other causes of fatty liver. Participants were divided into two groups
(a) Those having ALT > 1.5 times normal (n=97)
(b) Those having normal ALT (n=47)
Results: Mean age was comparable with slight male predominance. There were significant differences in anthropometric measurements like BMI (p=0.0001) and WHR (0.90±3.57 and 0.88±3.23, p=0.0071). Mean BP, lipid profile, fasting glucose, insulin, and HOMA R were comparable. There were significant differences in both mean AST (50.2±5 and 37.4±3.21, p=0.0001) and ALT (104±7.29 and 69.9±11.5, p=0.0001) levels. Metabolic syndrome was present in >75% of patients and Individual components were comparable except for increased waist circumference which was significantly more in those with raised ALT (78.35% and 44.68%, p<0.001). Majority of our patients were having only steatosis, while NASH was present in (27.82% and 8.5%, p<0.05) of patients.
Conclusion: NAFLD can exist in patients with normal ALT values. Although more work is needed to determine who should be screened for NAFLD and how such individuals should be evaluated, this study is a step toward the identification and characterization of NAFLD patients with normal ALT. We can suggest that patients having metabolic syndrome or insulin resistance, despite having normal ALT, should be screened for NAFLD. Also ALT values should be adjusted for variables like BMI to appropriately screen NAFLD patients.

PE449

Evaluation of Patterns of TCM Therapy on NAFLD Based on Cluster, Factor and Logistic Regression Analysis

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Background: Scientific evidence has demonstrated that Traditional Chinese Medical (TCM) approaches and products can be beneficial for managing Non-alcoholic Fatty Disease (NAFLD), but few rigorous criteria of patterns of TCM therapy are available to guide practitioners in deciding the CAM interventions.
Objectives: To evaluate criteria of patterns of TCM therapy for the management of NAFLD identified by biomedicine.
Methods: literature research, clinical epidemiological investigation and mathematical statistics were employed to make information collecting tables and to establish database. Descriptive analysis, factor analysis, and cluster analysis were involved.
Results: (1) Thirteen patterns of TCM therapy were differentiated. (2) Information collecting table of TCM therapy for NAFLD was constructed. (3) Public factors were obtained after factor analysis in 246 cases with NAFLD and five criteria of patterns, Patterns of Mucus Dampness Hindering the Lungs (*Tan-Shi-Nei-Zu*) (59 cases), Patterns of Dampness and Heat Collecting in the Interior (*Shi-Re-Nei-Yun*) (54 cases), Patterns of Constrained Liver and Deficient Spleen (*Gan-Yu-Pi-Xu*) (53 cases), Patterns of Deficient Spleen Yang and Kidney Yang（*Pi shen yang xu*）(45 cases), Patterns of Stagnant Qi and Congealed Blood (*Qi Zhi Xue Yu*)(35 cases) were established in frequency analysis. (4) The models of binary logistic regression of each pattern were obtained.
Conclusions: This could provide a reliable basis for facilitating potential practitioners being interested in integrating TCM therapy into their operations.

Poster Exhibition – NAFLD, DILD & Alcoholic Liver Disease
Poster Session, Hall 5B

PE450
Association of serum uric acid level with nonalcoholic fatty liver disease: a cross-sectional study
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Background/Aim: Serum uric acid level has been suggested to be associated with factors that contribute to the metabolic syndrome. The aim of this study was to investigate the association of serum uric acid level with nonalcoholic fatty liver disease (NAFLD).
Methods: A cross-sectional study was performed among the employees of Zhenhai Refining & Chemical Company Ltd., Ningbo, China.
Results: The study included 8925 subjects (6008 men) with a mean age of 43 years. The prevalence rate of NAFLD and hyperuricemia was 11.78% and 14.71%, respectively. NAFLD patients had significantly higher level of serum uric acid than controls (370.3 ± 86.6 vs. 321.1 ± 82.6 μmol/L; $P < 0.001$). The prevalence rate of NAFLD was significantly higher in the subjects with hyperuricemia than those without hyperuricemia (24.75% vs. 9.54%; $P < 0.001$), and the prevalence rate increased along with serum uric acid levels (P value for trend < 0.001). Multiple regression analysis showed that hyperuricemia was associated with increased risk for NAFLD (odds ratio [OR]: 1.291, 95% confidence interval [CI]: 1.067 – 1.564; $P < 0.001$).
Conclusion: Serum uric acid level is significantly associated with NAFLD, and increased serum uric acid level is an independent risk factor for NAFLD.

PE451
Up-regulation of Hepatocyte Metabolism Enzymes, Pro-inflammatory Cytokines and Cirrhosis-related Genes Precedes Steatosis in the Early Development of Alcoholic Liver Diseases
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Background: Development of fatty liver is believed to be an early and reversible consequence of excessive alcohol consumption. However, the cellular and molecular events in the early development of alcoholic liver diseases (ALD) and the contributory effects of a high fat diet are not fully understood.
Methods: This study was designed to quantify specific enzymatic and cytokinetic activity as well as the development of hepatic steatosis in a rat model of alchohol-induced liver injury without high fat diet.
Results: Ethanol-fed rats exhibited high blood ethanol levels (0.85±0.31%) and significant increases in serum ALT (67.7± 13.4 unit/L), AST (136.3± 60.2 unit/L), and ALP (400±108.9 unit/L) when compared with control rats ($p<0.01$, respectively). Histopathological examination found unevenly raised Knodell scores (5.33±1.15 in the ethanol-fed livers vs. 0.33±0.58 in control), which were characterized by scattered hepatocyte ballooning, portal inflammation and collagen fiber deposition. However, typical steatosis lesions were absent. qPCR demonstrated up-regulation of genes in the ethanol-fed livers, including hepatocyte metabolism enzymes/receptor (ADH1, $P<0.05$; cytochrome P450 2E1, CYP2E1, $P<0.05$; GSTA2, $P<0.01$; PPAR α, $P<0.05$), and genes coding for pro-inflammatory cytokines (IL-1β, $p<0.01$ vs. control livers; TNF- $p<0.05$; TGF-β, $p<0.05$; RANTES $P<0.05$), ECM components and proteinases (collagen-1, $P<0.01$; SMA, $p<0.01$; MMP-9, $P<0.05$ and TIMP-1, $P<0.05$).
Conclusion: Chronic administration of ethanol to rats without high fat diet productively induces alcohol hepatitis in the absence of fatty liver, suggesting that alcohol hepatitis may precede steatosis in the development of ALD.

PE452
Effects of Extracorporeal Liver Support MARS on Serum Cytokines in Acute-on-chronic Liver Failure versus Standard Medical Therapy
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Background: The aim of the present study was to evaluate the changes of several cytokines associated with inflammatory liver disease and liver regeneration by Molecular Adsorbent Recirculating System (MARS) in 15 ACLF patients versus 15 patients treated with Medical Standard Therapy (SMT) that presented alcoholic liver disease etiology and similar Model End-stage Liver Disease (MELD).
Methods: *MARS Group:* Fifteen (10 male and 5 female) patients were treated with MARS® (Gambro). Five patients were excluded by study.The number of MARS applications was about 9, the length of applications was about 10h. *SMT Group*: Fifteen patients (10 male and 5 female) were treated medical standard therapy such as prophylaxis against bacterial infections, albumin and fresh plamsa and *judicious* use of diuretics. Three patients were excluded by the study. The patients were valued during 30 days from inclusion with a survival follow up a three months.
Results: *MARS Group:* we observed a significant changes in levels of IL-6($p<0.01$), IL-1($p<0.002$), IL-8($p<0.04$) and TNF-alfa ($p<0.03$) in association with improvement of hepatic growth factor ($p<0.001$). The patient's survival at three months was 50%. *SMT Group:* we observed only a significant changes in IL-1($p<0.01$) and TNF-alfa ($p<0.2$). The patient's survival at three months was 33%.
Conclusion: The MARS liver support device has corrective effects on disturbed pathophysiology of ACLF and may be used to enhance spontaneous recovery or as bridge to transplant.

PE453
A Study of Protective Effect of Centella Asiatica in 1-methyl-4phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced Liver Injury
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Background: Centella asiatica has been used for centuries as a medicinal herb for wound healing, memory enhancement, cancer, vitality, respiratory ailments, psoriasis and eczema, revitalizing connective tissue, burn and scar treatment, skin infections, arthritis, rheumatism, periodontal disease, varicose veins, hypertension, sedative, anti-stress, anti-anxiety, aphrodisiac, and as immune booster.

Aim: This study was conducted to evaluate the hepatoprotective effects of the *Centella asiatica* extract in 1-methyl-4phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced liver injury in rats.
Methods: Sprague Dawley rats were treated with alcohol extract of *Centella asiatica* orally in two doses (20 and 40 mg/kg/day) for 3 months along with intraperitoneal injection of MPTP (1 ml/kg). Biochemical parameters such as serum total protein, albumin and marker enzymes were estimated. Histopathological studies of liver were also carried out to confirm the biochemical changes.
Results & Discussion: MPTP -induced hepatotoxic effects were evident by a significant ($p < 0.05$) increase in the serum marker enzymes and a decrease in the total serum protein and albumin. Administration of extract of *Centella asiatica* effectively inhibited these changes in a dose-dependent manner; maximum effect was with 40 mg/kg. Histopathological examination of liver tissue corroborated well with the biochemical changes. Hepatic steatosis, hydropic degeneration and necrosis were observed in MPTP-treated group, while there was a significant reduction in these changes in the treatment group.
Conclusion: *Centella asiatica* extract exhibited hepatoprotective action against MPTP induced liver injury.

PE454

Liver Contents of Free Amino Acids after Pyrazinamide Treatment

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Further optimization of tuberculosis chemotherapy requires a comprehensive evaluation of the effects of antitubercular drugs on metabolic processes in organism.
Wistar albino male rats, body weight (b.w.) of 160–200 g, were divided into three groups: group I received pyrazinamide *per os* at a dose of 1000 mg/kg b.w./day, whereas group II received a dose of 2000 mg/kg b.w./day, in both groups it was given for 60 days; the control group was composed of intact animals. The contents of free amino acids were determined using an amino acid analyzer AAA-881 (Czech Republic).
The study of the effects of pyrazinamide administered in different doses on the liver contents of free amino acids showed the largest number of changes at a dose of 1000 mg/kg b.w./day. The content of free amino acids at the level of 16 amino acids and total sum of amino acids significantly differed from controls. Part of these changes could be regarded as compensatory answer of organism to this drug action. Further pyrazinamide dose increasing caused exhaustion of liver adaptive possibilities.
The study of the influence of pyrazinamide on liver contents of free amino acids allows to fully estimate the effects of this substance on metabolic processes in this organ. Moreover, the effect of pyrazinamide on the majority of free amino acids in the liver is dose-dependent.

PE455

The Diversity of Chemotherapy Induced Hepatitis between Lymphoma Patients in HBV And HCV Carrier

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Background: Taiwan is an endemic area of HBV and HCV infection, chemotherapy for lymphoma patients who has been HBV infection, may induce serious clinical sequela due to reactivation of HBV. This study want to clarify the difference of the chemotherapy induced hepatitis between HBV and HCV carrier in lymphoma patients.
Methods: From July, 2003 to July 2006, 537 non-hepatocellular carcinoma patients were enrolled, 49 (12.5%) cases were lymphoma, in these lymphoma patients, 24(48.9%) cases have been HBV infected, and 22 (44.9%) cases have no HBV or HCV infected. 3 (0.6%) cases have been infected with HCV. All patients received chemotherapy with the regimen of CHOP or R-CHOP. Liver function , viral markers, HBV DNA, HCV RNA were checked before and after chemotherapy.
Results: Hepatitis happened in 16 (32.7%) lymphoma patients, 11 (45.8%) cases were in HBV infected patients, 3 (12%) cases were in non-HBV infected patients, 2 cases of HCV infected patients suffered from hepatitis. HBV infected hepatitis patients HBV DNA elevated more than 2 Log as before chemotherapy. Non of the HCV infected patient has elevated of HCV RNA after chemotherapy. The mortality rate in HBV infected patient is 33%. No mortality in HCV infected patients after chemotherapy.
Conclusions:

1. High rate of HBV reactivation and mortality in chemotherapeutic lymphoma patients who has been HBV infected.
2. Screening of HBV viral markers among candidates for cancer chemotherapy is mandatory, especially in lymphoma patients.
3. Large number and prospect study for chemotherapy induced hepatitis in HCV carrier are needed.

PE456

Epidemiological Investigation of Alcoholic Liver Disease and Analysis of Relevant Factors in North-East China

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Background: Excessive drinking leads to social, psychological, physical and other problems. This study investigated the epidemiology of ALD and analyses the associated risk factors.
Methods: From 6,043 residents 3,815 blood samples were collected. Alcohol consumption and the impact of alcohol on liver function, blood lipids, blood pressure and BMI and MCV have been evaluated.
Results: The drinking rate and average daily alcohol intake was 35.0% and 36.97±48.76g respectively. The total alcohol intake was 297.90±506.52kg and the average drinking age was 19.21±11.34 years. The average γ-GT, AST, ALT, MCV, Chol, TG, LDL-c, HDL-c and BP increased gradually with increase in alcohol intake. The population ALD prevalence was 3.98%. The prevalence of ALD among the drinking population and the alcoholic population was 11.76% and 44.17% respectively.
Conclusion: Chol, γ-GT, AST, ALT, and MCV were highly correlated with daily alcohol intake which closely related to the occurrence of ALD.

Table 1. Comparison of different factors among the five groups of population

	Prevalence of hypertension	The rate of abnormal liver function(%)	The rate of dyslipidemia (%)	The rate of abnormal BMI(%)	The rate of abnormal MCV(%)
Drinking group	24.1	25.4	32.7	52.3	42.9
Non-drinking group	23.5	8.3	25.7	45.9	28.4
X^2	0.166	205.199	20.311	14.099	80.169
P	0.684	<0.001	<0.001	<0.001	<0.001
ALD group	39.5	82.9	57.9	61.8	61.2
Alcohol group	27.1	38.1	34.5	41.4	50.3
The control group	23.5	8.6	26.4	46.1	28.0
X^2	18.033	727.527	69.089	15.278	102.169
P	<0.001	<0.001	<0.001	<0.001	<0.001

PE457

Polyenephosphatidylcholine Prevents Alcoholic Liver Disease in Pparalpha-Null Mice through Attenuation of Increases in Oxidative Stress

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Background: Alcoholic liver disease (ALD) is one of the leading causes of cirrhosis and yet efficient therapeutic strategies are lacking. Polyenephosphatidylcholine (PPC), a major component of essential phospholipids, prevented alcoholic liver fibrosis in baboons. However, its precise mechanism remains uncertain. We examined the effects of PPC on ALD using peroxisome proliferator-activated receptor (Ppara)-null mice treated with an ethanol-containing diet, which showed pathological features similar to human ALD.
Methods: Male Ppara-null mice were pair-fed a Lieber-DeCarli control or 4% ethanol-containing diet with or without PPC at a clinically comparable dose (30 mg/kg/day) for 6 months.

Results: PPC significantly reduced hepatocyte damage, hepatitis, and hepatic fibrosis, but did not affect steatosis. Phosphorylation of apoptosis signal-regulating kinase 1, p38 mitogen-activated protein kinase, and protein kinase C, as well as activation of nuclear factor-kappa B, were markedly suppressed by PPC. These effects were likely a consequence of decreased oxidative stress through down-regulation of reactive oxygen species (ROS)-generating enzymes, including cytochrome P450 2E1, acyl-CoA oxidase, and NADPH oxidases, in addition to restoration of ethanol-induced increases in Toll-like receptor 4 and CD14. PPC also decreased the pro-apoptotic proteins Bax and truncated Bid, thus inactivating mitochondrial permeability transition. Furthermore, PPC suppressed overexpression of transforming growth factor- 1 and hepatic stellate cell activation, which retarded hepatic fibrogenesis.
Conclusion: PPC exhibited anti-inflammatory, anti-apoptotic, and anti-fibrotic effects on ALD as a result of inhibition of alcohol-induced ROS production.

PE458

Clinical Features of 19 Acute Toxic Hepatitis Patients by Dyctamnus Dasycapus: Single Center Clinical Experience

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Background: *Dysctamnus dasycarpus* has used for the promotion of health in South Korea. But, there were rare a report concerning the hepatotoxicity. We report cilinical features of liver injury by *Dysctamnus dasycarpus.*
Method: Eighteen patients diagnosed as acute toxic hepatitis by *Dysctamnus dasycarpus* in Chungnam national university hospital between January 2005 and Arpil 2008 was enrolled. Toxic hepatitis was diagnosed by RUCAM score (≥4). The medical records were reviewed, retrospectively.
Result: Eleven patients (61%) were female and the mean age was 53.5. Most common symptom was jaundice. Initial laboratory findings were as follows(mean value): WBC 6126/uL, Hemoglobin 13.4 g/dL, Platelet 212×10^3/L,ALT 1375IU/L, total bilirubin 11.3 mg/dL, alkaline phosphatase 159 U/L, GGT 244U/L, prothrombin time(INR) 1.1. The mean hospitalization was 21.5days. Peak laboratory findings were as follows: ALT 1382IU/L, total bilirubin 15mg/dL. Recovery time of each biochemical finding was as follows: ALT 37days, total bilirubin 39.4 days. Recovery rates of ALT and total bilirubin were 27.8% and 38.9%, 89.9% and 89.9% at 4 weeks, 8 weeks, respectively. The main biochemical pattern of hepatotoxicity was hepatocellar (72.2%) type. Prednisolone was prescribed in six patients. Progressive anemia and thrombocytopenia were detected in one patient diagnosed as pure red cell aplasia. Other one patient had prolonged jaundice (117 days). But, all patients had recovered without sequelae.
Conclusion: In South Korea, Liver injury by *Dysctamnus dasycarpus* was more frequent in women. The main pattern of hepatotoxicity was hepatocelluar type. Most patients had prolonged icteric phase and hospitalization. Patients were recovered by supportive management after drug cessation or prednisolone therapy.

PE459

Three Cases of Toxic Hepatitis Resulting after Dictamnus Albus Intake

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In Korea, traditional medicine that is based on the use of herbal medicine developed from a long time ago. However, clinical study of the herbal medicine is not conducted in a structured manner. We report three cases of toxic hepatitis caused by the intake of Dictamnus Albus. The first patient, a 44 year old woman was admitted due to nausea after ingestion of liquor containing Dictamnus albus for 2 months. Total bilirubin was 2.55 mg/dL AST/ALT 774/1,424 IU/L on admission. Liver biopsy observed hepatocyte necrosis and cholestasis. The elevated bilirubin and transaminase returned to normal 2 weeks later after cessation of Dictamnus albus. The second patient, a 64 year old man was admitted due to jaundice after ingestion of boiling Dictamnus albus for 3 months. Total bilirubin was 11.37 mg/dL AST/ALT 2,010/2,522 IU/L on admission. Liver biopsy observed pericellular fibrosis and necrosis. The bilirubin decreased slowly compared to the transaminase and normalized 3 months later after cessation of Dictamnus albus. The third patient, a 48 year old man was admitted due to jaundice after ingestion of liquor containing Dictamnus ablus for 1 month. Total bilirubin was 12.8 mg/dL AST/ALT 1,097/1,869 IU/L The hepatocyte necrosis was observed by liver biopsy. The elevated bilirubin and transaminase levels normalized 1 month later after cessation of Dictamnus albus. All patients had negative viral markers and non-specific ultrasonographic findings. The above mentioned three cases demonstrate that liver may have been damaged by Dictamnus albus, which indicated clinical characteristics.

PE460

Systematic evaluation of suspected Chinese Medicine Induced Liver Injury (CMILI) by a Multidisciplinary Approach

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Background/Aims: CMILI poses a diagnostic challenge as no tests are available to confirm the causality. The aims of this study were 1) to evaluate clinical features and patterns of CMILI and 2) to assess the likelihood of causality among patients with liver impairment and exposure to Chinese Medicine (CM) by a multidisciplinary approach.
Method: Between 5/2005 and 8/2007, patients who had liver derangement and CM or proprietary CM exposure within six months managed in the United Christian Hospital were studied. Clinical features and the CM were reviewed by a multidisciplinary team involving a hepatologist, a toxicologist and CM experts. Literature search of relevant herbs in Chinese and western journals were performed. CM samples or residue were sent to toxicology laboratory for analysis to look for any toxic constituents, adulterant or contaminant. The likelihood of causality was ranked by various experts independently and disagreements were settled by a consensus meeting.
Results: There were forty-six cases of suspected CMILI, nineteen cases with alternative causes of liver diseases were excluded. Twenty-seven cases of CMILI proceeded to detailed analysis. Median age of patients was 51 (21-76) with female predominance. The median duration of CM exposure to presentation was 20 (1-150) days. Majority of them (82%) had hepatocellular liver injury pattern. One case of adulteration with NSAID and erroneous substitution of herb was identified respectively Causality were classified as unlikely, possible, probable and highly probable in 3, 12, 8 and 3 patients respectively.
Conclusion: A multidisciplinary approach allows systemic evaluation of suspected CMILI.

PE461

A Histopathological Study of Increased Hepatotoxicity after Co-Administration of Imatinib and Acetaminophen in a Preclinical Mouse Model

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Background: Imatinib, a selective tyrosine kinase inhibitor, exhibits drug interactions with other drugs that are metabolised via the cytochrome P450 pathway. Acetaminophen, a widely used analgesic and anti-pyretic drug is also metabolised via P450 pathway. This study aimed to evaluate the nature of hepatotoxicity after co-administration of imatinib and acetaminophen in a preclinical mouse model.
Methods: Four groups of male ICR mice (30-35g) were used. The mice were administered either saline solution orally, imatinib 100 mg/kg orally (control), acetaminophen 700 mg/kg intraperitoneally (positive control) or co-administered imatinib 100 mg/kg and IP acetaminophen 700 mg/kg (study group). The mice (n=4 per group) were fasted overnight, dosed respectively and sacrificed at pre-determined time intervals of 15, 30 minutes, 1, 2, 4, 9 and 12 hours and liver samples obtained by dissection. H&E stained liver sections (3µm thick) were histopathologically analysed.
Results: The liver samples showed reversible cell damage like feathery degeneration, microvesicular fatty change, sinusoidal congestion and pyknosis, with both imatinib and acetaminophen, administered separately.

The damage increased gradually with time, peaked at 2 hours and then resolved completely by 6 hours. Liver samples showed irreversible damage (cytolysis, karyolysis and karyorrhexis) when both drugs were administered concurrently, the damage increased with time and had not resolved after 12 hours duration.
Conclusion: Co-administration of acetaminophen and imatinib increased the hepatoxicity caused by acetaminophen and imatinib to become irreversible. This may be due to the fact that both drugs are metabolised by the cytochrome P450 pathway in the liver.

PE462

Role of Polymorphic Status of NAT2 and CYP2E1 Gene in Predicting Antituberculosis Drug- Induced Hepatitis in patients of New Delhi, India

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Background: A higher risk of Antituberculosis drug (ATT) induced hepatotoxicity has been reported in Indian subcontinent compared to the western counterparts. Slow acetylator genotype of N-acetyltransferase2 (NAT2) and cI genotype of Cytochrome P4502E1 (CYP2E1) gene are two known risk factors associated with this disease. CYP2E1 gene encodes a rifampicin inducible enzyme which increases hepatotoxicity. Therefore slow acetylation of isoniazid and simultaneous use of rifampicin may augment the toxicity of isoniazid.
Objectives: To analyze the allelic distribution of NAT2 and CYP2E1 gene in patients of pulmonary tuberculosis who developed ATT induced hepatitis
Materials and Methods: The study included cases of pulmonary tuberculosis (190) and ATT induced hepatitis (95). Polymorphism of NAT2 and CYP2E1 gene was studied by PCR-RFLP method in both these groups.
Results: Occurrence of ATT hepatotoxicity was 17.89%. There was a higher prevalence of slow acetylator genotype particularly NAT2*5/*7 and NAT2*6/*7 in patients with hepatotoxicity compared to patients without hepatotoxicity (72.09% vs 44.2%, P value < 0.05). No association of CYP2E1 RsaI polymorphism could be considered with ATT hepatotoxicity. However, DraI C/D genotype of CYP2E1 appears as a risk factor for predicting the occurrence of antituberculosis drug induced hepatitis (OR 5.06, P value < 0.05).
Conclusion: The study demonstrates that patients with slow acetylator genotype particularly NAT2*5/*7 and NAT2*6/*7 and heterozygous mutant C/D genotype of CYP2E1 gene are predisposed to develop antituberculosis drug induced hepatotoxicity. Regular monitoring of clinical and biochemical profile may be considered in these patients when they receive antituberculosis treatment.

PE463

Evaluate 27 Definite Cases of Drug-induced Liver Injury with Liver Biopsies by Clinical Diagnostic Scales

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Background: Drug-induced liver injury is the most common adverse drug reaction. We often use two kinds of diagnostic scales to evaluate suspected patients. However, we still can't diagnose accurately without the direct drugs history and the pathological evidence.
Methods: Twenty-seven drug-induced liver injury cases with liver biopsies from 2001 to 2008 were reviewed retrospectively by Maria and Japanese scale.
Result: There were 11.1% of cases with increasing eosinophils. Herbs (29.63%) were the most common suspected drug and unknown drugs intake history (14.81%) were described in these cases. The high possibility and possibility were 25.93%, 29.63% by Maria scale and 85.19%, 3.7% by Japanese scale, respectively (P=0.015).
Conclusions: Japanese scale seems more sensitive than Maria scale in these cases. However, there are still some definite cases ignored as low possibility due to absence of obvious drug using history. Early treatment and suspected drugs prohibition interferes the outcomes of the two diagnosis systems and lead to a false result. It is still a clinical challenge without strong drug using history or pathological evidence of liver biopsies to diagnose the drug-induced liver injury quickly and accurately.

PE464

Methamphetamine Induced Liver Remodeling Via Inhibited Activities of Anti-Oxidant Enzymes

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Background: Previous study suggested that oxidative stress may be an important mediator of methamphetamine-mediated tissue injury. The study was to examine the mechanism of antioxidant activity and methamphetamine-mediated liver injury.
Materials and Methods: The 25 days old male Sprague-Dawley rats were subcutaneous injected daily with methamphetamine (10 mg/kg body weight) for 15, 30, 60 and 120 days. Control group received equal volumes of vehicle. The liver tissues were extracted to measure the activities of SOD, catalase, glutathion reductase (GR), and glutathione peroxidase (GPx), and the level of glutathione. Western blot were used to measure the expression of Rho and phosphor-ezrin-radixin-moesin (p-ERM).
Results: Compared with vehicle group, treated with methamphetamine for 15 and 30 days, the activities of liver SOD, GPx, and catalase were significantly decreased. In 60 and 120 days group, the activities of antioxidant enzymes of methamphetamine-treated liver was not different from that of vehicle group. The levels of glutathione production also had the same trend. The activities of GPx and catalase on vehicle group gradually reduced following the days of treatment. However, administration of methamphetamine resulted to a lower activity of catalase through the treated days. There was no difference on the activity of GR between vehicle and methamphetamine group. The expression of Rho and p-ERM were also increased by methamphetamine treated for 30 days.
Conclusion: These results suggested the methamphetamine lead to liver remodeling via decreased antioxidant activity. Finally, the situation of mechanism needs taking in advantage discussion.

PE465

Polysaccharides of Radix Sophorae Tonkinensis Reduce Liver Damage with Preventive Treatment and Increase the Injuried Liver Damage

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Background: To observe intervening effects of preventive and theraptical treatment of Radix Sophorae Tonkinensis's polysaccharides(RSTP) on alpha-naphthylisotheganate(ANIT)-induced cholestasis in mice.
Methods: Kunming mice intoxicated with ANIT 50mg/Kg orally and treated with RSTP 50mg/Kg for 7 days before ANIT exposure and for 2 days after ANIT exposure respectively, the general condition,mortality rate and serum ALT activity are obeverated.
Result: It was found that by preventive treatment the general condition and mortality rate were improved, serum ALT activity reduced.By therapeutic treatment,the general condition deteriorated,mortality rate and serum ALT activity increased.
Conclusion: The preventive treatment of RSTP reduce the liver damage due to increasing the anti-stress ability such as the antioxidant capacity,its therapeutic treatment increase the injuried liver damage due to increasing the non-specific immune response and aggregating the preexisting liver inflammation.
*This project was supported by grants from Shanghai Municipal Education Commission under High School High-Tech Characteristic Development Programme (NO SMEC Finance (2005) 81)

PE466

Effects of Polyphenolic Acids From Salvia Miltiorrhiza on Serum ALT Activity of Mice with Alpha-Naphthylisotheganate (ANIT)-Induced Cholestasis

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Background: The product's instruction pointed out that in some patients polyphenolic acids' salt from Salvia Miltiorrhiza(PPAS-SM) may lead to a temporary increase in serum ALT activity.So we observe effects of PPAS-SM on alpha-naphthylisotheganate(ANIT)-induced cholestasis in mice.
Methods: 24 hours after intoxicated with ANIT 50mg/Kg orally, Kunming mice were treated with PPAS-SM 50, 25,10mg/Kg/days for 2 days orally, then serum ALT activity was measured.
Result: All doses of PPAS-SM led to rise of serum ALT activity in mice, most obvious in group of high dose.But the general situation and mortality rate did not increase significantly.
Conclusion: PPAS-SM lead to rise of serum ALT activity in mice with damaged liver.The auther suggests as a double-edged sword,the antioxidant PPAS-SM may have a prooxidative effect in some condition too.
*This project was supported by grants from Shanghai Municipal Education Commission under High School High-Tech Characteristic Development Programme (NO SMEC Finance (2005) 81)

PE467
Serum TNF-Alpha? Does It Correlate With Severity of Chronic Porta Systemic Encephalopathy in Alcoholic Cirrhosis
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Introduction: Hepatic encephalopathy, a complex neuropsychiatric syndrome secondary to acute liver failure, chronic parenchymal liver disease or portal-systemic shunting, may possibly develop through mediators of endotoxin and tumor necrosis factor-alpha (TNF-). Several studies have shown that serum levels of (TNF-) are significantly elevated in patients with acute and chronic liver diseases, where these elevations are independent of the etiology of the underlying disease. It has been shown that plasma levels of TNF- correlate with the severity of hepatic encephalopathy (HE) in fulminant hepatic failure. However, still there is very few published data regarding the relationship between serum levels of TNF- and the presence or severity of HE in patients with chronic liver failure.
Methods: The aim of this study is to determine the relationship between serum levels of TNF- and clinical grades of HE in patients with chronic liver failure. This prospective study included 149 consecutive male patients with alcoholic cirrhosis in various clinical grades of HE (according to West Haven criterion). Detailed clinical, biochemical and sonographic examination was done in all patients. Circulating levels of TNF- was measured using solid-phase ELISA.
Results: The mean±SEM values of serum TNF- at presentation in patients with MHE (n=37), grade 1 (n=17), grade 2 (n=41), grade 3 (n=44), and grade 4 (n=10) were 6.2±0.4, 9.5±0.6, 15±0.7, 26.3±1.7, and 46±5.9 pg/ml, respectively. Significant Positive correlation was found between serum levels of TNF- and severity of HE (Correlation Coefficient = 0.7).
Conclusion: From the present study we can suggest that there is significant relationship between TNF- and HE in patients with alcoholic cirrhosis and it could be involved in its pathogenesis.

Poster Exhibition – Other Viral Hepatitis
Poster Session, Hall 5B

PE468
Clincal Features of Acute Renal Failure Associated with Hepatitis A Virus Infection
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Background: Acute hepatitis A (AHA) is one of the most common infectious diseases and usually a self-limiting disease. Although extrahepatic manifestations are not common, a few cases associated with acute renal failure (ARF) have been reported.
Methods: We reviewed clinical features of AHA patients complicated with ARF (group A) and compared with non-complicated AHA patients (group B). Medical records of 191 patients with AHA were reviewed between January 2003 and December 2007. We experienced 11 patients (5.8%) with ARF associated AHA.
Result: There were no differences between group A and group B in sex ratio and age. The peak value of ALT (median: 6133 IU/L vs 1685 IU/L, p<0.001), Alkaline phosphatase (median: 235 IU/L vs 201 IU/L, p=0.03), prothrombin time (INR, median 1.72 vs 1.09, p<0.001) was significantly higher in group A than B. Nine patients (81.8%) recovered completely with hemodialysis (6 patients, 66.7%) and only conservative management (3 patients, 33.3%), while 1 patient underwent liver transplantation and 1 patient died due to fulminant hepatic failure. There were 4 patients who underwent kidney biopsy. Two patients were diagnosed as acute tubular necrosis and 2 patient as acute interstitial nephritis and IgA nephropathy.
Conclusion: AHA patients with ARF had higher ALT and more prolonged prothrombin time. The prognoses were poorer than those without ARF. However, ARF patients with nonfulminant AHA had a good prognosis with a proper treatment and should not be confused with hepatorenal syndrome.

PE469
A Study on Hepatitis E Virus (HEV) Infection in Animals and Human in Suburbs of Beijing
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Background/Aims: To investigate the HEV infection among different animals and people with special profession, and to analyse the genotype of HEV isolated in this study.
Methods: Serum and fecal samples were collected from various animals and people with special profession in the south suburbs of Beijing. HEV antigen and anti-HEV antibody were detected by DAS-ELISA. HEV RNA was extracted from fecal samples and amplified by RT-nPCR. The nucleotide sequence homology and phylogenetics of HEV strains isolated from swine were analysed.
Results: The anti-HEV antibody positive rate of adult swine, cow, sheep and younger swine were 98.23% (222/226), 29.35% (54/184), 9.80% (20/204) and 60.73% (99/164), respectively. The HEV antigen positive rates of adult swine, cow, sheep and younger swine were 2.65% (6/226), 4.35% (8/184), 1.45% (3/207) and 9.75% (16/164), respectively. The HEV antigen and anti-HEV antibody positive rate of professional group was 0.40% (1/247) and 42.51% (105/247) respectively. The HEV RNA positive rate of fecal samples from younger swine was 22.89 %(19/83). 16 of 19 samples were HEV RNA positive by PCR with primers of HEV ORF1 and ORF2. The sequence analysis of the 16 samples showed that there were 2 groups designated as BJ-1 (11/16) and BJ-2 (5/16). The nucleotide homology of BJ-1 and BJ-2 was 99%. Phylogenetic analysis of HEV ORF2 indicated that both of them belonged to genotype 4d.
Conclusion: Phylogenetic analysis of HEV ORF2 indicated that HEV isolated in the south suburbs of Beijing belonged to genotype 4d.

PE470
Hepatitis B-Delta Virus Co-Infection in Belgium: Preliminary Data of the BASL HDV Registry
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Hepatitis Delta virus is a subviral satellite requiring hepatitis B virus to propagate, usually leading to severe, chronic liver disease. As data on epidemiology and management practice of HDV infection in Belgium are lacking, a retrospective and prospective, multi-centric questionnaire-based registry is performed in 2008. Results of 32 patients are reported.

Active hepatitis B replication is defined as HBeAg + or HBV DNA > 2000 IU/mL HBeAg being negative. Fibrosis was scored according to the Metavir system. ALT levels were characterized as being normal, < 2 X normal, and > 2 x normal.

Conclusions:

1. HDV-HBV co-infection presents mostly as moderate to advanced liver disease.
2. Over 1/5 of patients show active HBV replication.
3. A majority of patients were infected outside Belgium.
4. A majority of patients have received or are receiving treatment for HBV and/or HDV.

Currently, the effect of pegylated interferon on HDV replication is being evaluated.

Variable	Unit	Value						
Gender, male	n(%), n=32	25/32(78.1)						
Ethnic origin	n(%), n=32	Caucasian 16(50.0)	Black African 11(34.4)	Oriental 3(9.4)	Turkish 2(6.2)			
HBV mode of transmission	n (%), n=32	Intravenous drug use 7 (21.9)	Sexual contact 2 (6.3)	Other/ unknown 23 (71.8)				
HDV mode of transmission	n (%), n=32	7 (21.9)	1 (3.1)	24 (75.0)				
Age	mean (range)	Value 37.94 (19-68)						
HBeAg+	n (%), n=32	6 (18.7)						
HBeAg-, HBV DNA >2000 IU/mL	n (%), n=32	1 (3.1)						
HCV coinfection	n (%), n=32	8 (25.0)						
HIV coinfection	n (%), n=32	0 (0)						
ALT	n (%), n=32	N 4 (12.5)	N-2N 13 (40.6)	>2N 15 (46.9)				
Biopsy, Metavir fibrosis	n=26	F0-F1 6 (23.1)	F2-F3 15 (57.7)	F4 5 (19.2)				
		Interferon	Peg interferon	Lamivudine	Adefovir	Pegylated interferon + adefovir	Pegylated interferon + ribavirine	No treatment
Treatment	n (%), n=22	5 (22.7)	12 (54.5)	2(9.0)	1 (4.5)	1 (4.5)	1 (4.5)	5/32 (28.2)
Outcome	n (%), n=32	Liver transplant 2 (6.3)	Death 2 (6.3)					

PE471

Full-Genome Nucleotide Sequence and Analysis of a Chinese Swine Hepatitis E Virus Isolate of Genotype 4 Identified in Guangxi Zhuang Autonomous Region： Evidence of zoonotic risk from swine to human in South China

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Background: Hepatitis E Virus is one of the leading causes of the enteric transmitted acute hepatitis. It is of great importance to provide convincing evidence of full-genome HEV sequence comparisons to prove hepatitis E as a zoonosis.

Methods: The overlapping fragments of HEV isolate swGX40 were amplified with reverse-transcription nested polymerase chain reaction (RT-nPCR)，and the 5’ and 3’ ends of viral genome were amplified with rapid amplification of cDNA ends (RACE). The PCR products were cloned and sequenced. The phylogenetic analysis of swGX40 was performed.

Result: The genome of swGX40 consisted of 7,233 nucleotides, excluding the poly (A) tail of 36 residues. The genome contained three open-reading frames (ORFs), ORF-1 encoding 1705 amino acids, ORF-2 encoding 674 amino acids and ORF-3 encoding 114 amino acids. The full-length genomic sequencing showed that swGX40 strain shared similarity with all known HEV genotype 1, 2 and 3 isolates by 73.4% to 76.5%, and with an identity of 83.1% to 91.2% among genotype 4 HEV isolates, and a high nucleotide identity as 94% with Chinese Guangxi human strain LZ-105.

Conclusion: The swine HEV strain swGX40 was phylogenetically close to the human HEV strain LZ-105, both from the same region in South China. Therefore it was concluded that HEV sub-genotype 4B might have existed in South China at least for 6 years and now it was prevalent both in local human and swine, which also strongly supported the zoonosis hypothesis of hepatitis E.

PE472

Severity of Acute Hepatitis and Outcome in Patients with Dengue fever at a Tertiary Care Center

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Background: Liver injury due to dengue infection is not uncommon. Acute liver injury is a severe complicating factor in dengue, predisposing to life-threatening hemorrhage, DIC and encephalopathy.

Objective: To compare the outcome (length of stay, mortality, complications) between patients of Dengue who have mild/moderate v/s severe acute hepatitis (*Mild- Moderate Acute Hepatitis*: SGPT 23-300 dl, *Severe Acute hepatitis*: SGPT > 300 dl)

Methods: An analytical crossectional study, at AKUH in 2005-7. All patients (≥ 14 yrs age) admitted with diagnosis of DF, DHF or DSS were included.

Results: 699 patients were enrolled. 86 % (604) patients had DF. Mean SGPT was 194.87 ± 351.93; 71 %(496) had mild to moderate hepatitis, 14.7 %(103) had severe hepatitis.Mean SGOT was 436.76 ± 987, Mean T.Bil was 1.52 ± 2.59, Mean GGT was 149.65± 161.44 and ALK.Phos 118.47 ± 18. Mean length of stay (LOS) in patients with mild/moderate hepatitis was 3.63 days v 4.3 days in those with severe hepatitis (P* 0.002). Mortality was 33.3 %(6) in mild/moderate hepatitis v 66.7%(12) in severe hepatitis group(p value <0.001). Complications between mild/moderate and Severe hepatitis were; Bleeding 30% v 70% (P value < 0.001), Renal failure (RF) 1.6% v 8% (P* 0.002), Acalculus cholecystitis 66.7% v 33.3 %(P value 0.047) and encephalopathy 64.1% v 38.9% (P* 0.02), ARDS 66% v 33 %(P* 0.425), Shock 75% v 25% (P*0.4)

Conclusion: Severe hepatitis (SGPT>300mg /dl) in Dengue is associated with prolonged LOS, mortality, bleeding and RF.

PE473

Acute Viral Hepatitis A in HBV carrier: Possible Suppressive Effect on HBV Replication

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Background: Hepatitis B virus (HBV) replication in chronic carrier may be affected by acute hepatitis A virus (HAV) superinfection by bystander effect. This study aimed to evaluate the clinical characteristics of patients with acute HAV superinfection in chronic hepatitis B and to investigated whether acute HAV infection might suppress HBV replication in them.

Methods: A total of 606 patients with acute hepatitis A (AHA) were analyzed retrospectively. Seventeen patients had AHA chronic HBV infection concomitantly. They are compared with the age- and gender-matched control group

Results: There were no significant differences of demographic features and laboratory parameters such as peak serum ALT, total bilirubin and creatinine between 2 groups. However, peak AST was higher in superinfected group than control group (median: 2,000 IU/L vs 731 IU/L, p=0.035,). Additionally, the peak serum albumin levels, prothrombin time and platelet counts were lower in superinfected group than control group (median: 3.0 mg/dL vs 3.3 mg/dL, p=0.02, 51.8 % vs 87.2 %, p=0.027 and 103 x 10^3/mm^3 vs 165 x 10^3/mm^3, p<0.001, respectively). Of superinfected group, 9 patients were followed over 6 months after resolution of AHA. Interestingly, serum HBV-DNA levels decreased significantly over 3 months following resolution of AHA, then rebounded subsequently (median: -1.89, -1.85, -0.38, 0.58 and 1.10 $\log_{10}$ copies/ml at 1, 3, 6, 12 and 24 months, respectively).

Conclusions: Acute HAV super-infection may suppress HBV-DNA replication in chronic HBV carriers and chronic hepatitis B, although the suppressive effect did not seem to sustain longer than 3 months.

PE474

Seroprevalence of IgG Anti-HAV in Hospital Employees Less Than 40 Years Old

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Background/ Aims: Hepatitis A is an acute infectious disease that is transmitted by fecal-oral root. Because the incidence of hepatitis A has been increased in Gwangju and Chonnam province of Korea recently, hepatitis A patients in Chonnam National University Hospital employees had been increased. So we investigated the seroprevalence of IgG anti-HAV in hospital empolyees less than 40 years old.
Methods: We analysed seroprevalence of anti-HAV IgG from 1,002 hospital employees (men: 190, women: 812) who are less than 40 years old, working in the Chonnam National University Hospital. The age group was divided by 5 years; 21-25 years old 199 (19.9%), 26-30 years old 426 (42.5%), 31-35 years old 215 (21.5%), 36-40 years 162 (16.1%)
Results: Overall seropositive rate of IgG anti-HAV was 32.8% (329/1002). Seropositive rate of men was 40.5% (77/190) and that of women was 31.0% (252/812). Seropositive rates of each age group were 1.5% (3/197) in 21-25 years old, 21.4% (91/425) in 26-30 years old, 41.5% (88/212) in 31-35 years old, 78.6% (132/168) in 36-40 years old. Seropositivity rate of the high risk group (doctors, nurses, technicians) was 28.9% (234/809).
Conclusions: Seropositive rate of IgG anti-HAV was the lowest in early twenties of hospital employees and it was below 50% in early thirties. Therefore hepatitis A vaccination may be warranted in the hospital empolyees less than the early forth decade.

PE475

Clinical Significance of Anti-Nuclear Antibody in Patients with Acute Hepatitis A

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Background/aims: Although anti-nuclear antibody (ANA) is positive in many cases of acute hepatitis A, the clinical significance is still unclear. This study was performed to evaluate the clinical significance of ANA in patients with acute hepatitis A.
Methods: Patients with acute hepatitis A who admitted at our hospital between September 2007 and August 2008 were enrolled. Positive ANA was defined as ANA titer 1:80.
Results: One-hundred twenty-six patients with acute hepatitis A were enrolled (mean age, 30 years; men, 71 [56.3%]). Serum ALT and bilirubin at admission were 2,979 1,711 IU/L and 3.9 2.4 mg/dL, respectively. These levels were elevated up to 3,397 1,789 IU/L and 6.8 3.7 mg/dL, respectively. ANA was positive in 81 patients (64.3%). Age, duration from peak-ALT day, duration from peak-bilirubin day, ALT level, and peak-bilirubin level were not different between ANA(-) patients and ANA(+) patients. In the while, sex, duration from symptom-onset day, and bilirubin level, and peak-ALT level were significantly different. In 51 (62%) of 81 patients with positive ANA, ANA was followed after 1 month and ANA became negative in 38 patients (74.5%). Among 13 patients with positive ANA after 1 month, titer decreased from the baseline in 7 patients, showed no interval change in 4, and increased in 2.
Conclusions: Positive ANA result is not rare in patients with acute hepatitis A. It is considered that ANA transiently appear during the course of acute hepatitis A and then, disappear with the improvement of acute hepatitis.

PE476

Analysis of Acute Hepatitis A Occurred in Cheonan City Area in Korea on 2008: Two Center Experience

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Aim: This year, big outbreak of acute hepatitis A occurred in Korea. The symptoms and clinical course seemed to be more severe than past. We aimed to analyze the characteristics of acute hepatitis A patients occurred on 2008 year and compared with previous 4 years patients.
Patients and Methods: We analyzed acute hepatitis A patients who have admitted on Dankook university hospital and Soonchunhyang university hospital located on Cheonan city in Korea. The admission period was from January 2004 from August 2008. We compared the clinical data between them.
Results: Total 445 acute hepatitis A patients admitted during 5 years. 180 patients of them (40.4%) admitted on 2008. The patients were increased as time goes on-2004(31), 2005(41), 2006(89), 2007(107). The clinical data such as sex, admission period, AST, ALT, total bilirubin, prothrombin time, CRP, ALT normalization time did not show difference. Just WBC and GTP were higher on 2008 group. The older age patients were more on 2008 group. The patients admitted mainly on April, May, June, July (84%) on 2008 while admitted even on past years.
Conclusion: Acute hepatitis A ptients is increasing. It is occurring in older age people and mainly on specific period. The more concern to prevention should be needed.

PE477

Phylogenetic Analysis of Hepatitis A Virus 5' Non-translated Region, Non-structural Proteins 2B and 2C in Sera from Patients with Hepatitis A of Various Severities

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Background: We analyzed the 5' non-translated region (5'NTR), non-structural proteins 2B and 2C of hepatitis A virus (HAV) genome, whose mutations have previously been shown to be important for enhanced replication in cell culture systems, in order to align all of our data and examine whether genomic differences in HAV are responsible for the range of clinical severities.
Methods: Our accumulated HAV strains of 5'NTR (nt 200 and 500), entire 2B and 2C from 25 Japanese patients with sporadic hepatitis A, consisting of 7 patients with fulminant hepatitis (FH), 5 with severe acute hepatitis (AHs), and 13 with self-limited acute hepatitis (AH), in whom the sequences of all 3 regions were available, were subjected to phylogenetic analysis.
Results: FH patients had fewer nucleotide substitutions in 5'NTR, had a tendency to have more amino acid (aa) substitutions in 2B, and had fewer aa substitutions in 2C, than AH patients. Four FH and 2 AHs with higher viral replication were located in the near parts of the phylogenetic trees, indicating the association between the severity of hepatitis A and genomic variations in 5'NTR, 2B and 2C of HAV.
Conclusions: Our study suggests that genetic variations in some parts of HAV might cooperatively influence replication of the virus, and thereby affect virulence. Viral factors should be considered and examined when discussing the mechanisms responsible for the severity of hepatitis A.

PE478

Clinical Features of Acute Viral Hepatitis A in Daejeon and Its Surrounding Area of South Korea

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Aims: The incidence of acute viral hepatitis A in adults is increasing very much in South Korea, 2008. The aim of this study was to the clinical features and course in Daejoen and its surrounding area.
Methods: Forty seven patients admitted as acute viral hepatitis A in Chungnam national university hospital between January 2008 and June 2008 were enrolled. The medical records were reviewed, retrospectively.
Results: The mean age was 30.5. Common occupations were company employee and studuents. Most common symptom was jaundice. Presumptive infection sources were raw fish or shellfish and raw meat. Initial laboratory findings were as follows(mean value): WBC 6126/uL, Hemoglobin 13.4g/dL, Platelet 212×10^3/L, AST 2268IU/L, ALT 2755IU/L, total bilirubin 5.2mg/dL, alkaline phosphatase 207U/L, GGT 379U/L, prothrombin time(INR) 1.2. Hospitalization was 21.5days. Peak laboratory findings were as follows: ALT 3181IU/L, total bilirubin 8.8mg/dL. Leukopenia (<4000/uL) and thrombocjtopenia ($<10\times10^5$/L) were ocurred in sixteen and six patients, respectively. Recovery time of each biochemical finding was as follows: ALT 20.2 days, total bilirubin 26 days. Recovery rates of ALTand total bilirubin were 74.4% and 74%, 88.5% and 92% at 4 weeks, 8 weeks after diagnosis, respectively. Prolonged jaundice (115days) was detected in one patient. All patients were recovered by supportive management.
Conclusions: In South Korea, acute viral hepatitis A was more prevalent in young adults, recenlty. Presumptive infectious sources were raw fish or

shellfsh and raw meat. If it can not change the food style that many Korean enjoy raw seafood, vaccination for adults must be considered to prevent it.

PE479

IgG Anti-HAV Sero-prevalence in the Years of 2000s in Korea

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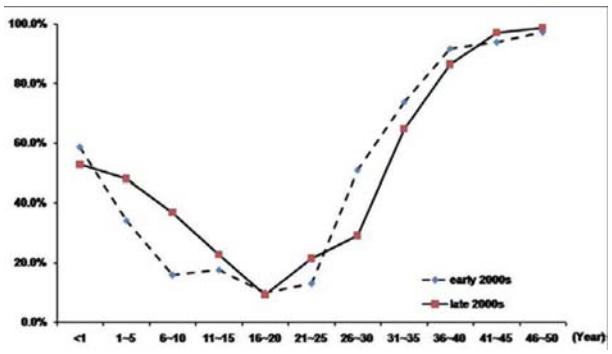
Background/Aims: To investigate the sero-positive rates of IgG anti-HAV according to various age groups in the early 2000s (the years 2001~05) and late 2000s (2006~08) in Korea.
Methods: IgG anti-HAV was measured in a total of 3905 subjects under the age of 50, who visited Hanyang University Seoul and Guri Hospitals between January 2001 and May 2008.
Results: Fig. 1 shows the relatively low positive rates of the antibody in ages of 11 to 30 and the lowest rates of 9.9% and 9.2% in the age group of 16 to 20, following the ages of 21 to 25 with rates of 12.9% and 21.3% in the early 2000s and late 2000s, respectively.
Conclusion: The recent decreased positive rates of IgG anti-HAV, esp. in ages of 11 to 30 in 2000s were compatible with the recent increased incidence of acute hepatitis A in these ages in Korea.



PE480

Acute Pancreatitis in Acute Viral Hepatitis

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Aim: The coincidence of viral hepatitis and acute pancreatitis is well described. This study was done to find out the frequency of pancreatic involvement in the course of acute viral hepatitis in Nepali population.
Methods: Consecutive patients of acute viral hepatitis presenting with severe abdominal pain between January 2005 to June 2008 to find out the prevalence of acute pancreatitis were studied in this prospective study. Patients with history of significant alcohol consumption and gall stones in ultrasound examination were excluded. Acute viral hepatitis was diagnosed clinically, liver function test, ultrasound examination and confirmed by viral serology. Pancreatitis was diagnosed by clinical presentation, biochemistry, ultrasound examination and CT scan.
Results: We studied serologically confirmed 218 patients with acute viral hepatitis. Severe abdominal pain was present in 23 patients. Sixteen patients (7.3%) were diagnosed to have acute pancreatitis. The patient were between 8-36 years of age with M:F ratio of 2.2:1. The pancreatitis was mild in 10 and severe in 6 patients. The etiology of pancreatitis was hepatitis E virus in 12 and hepatitis A virus in 4 patients. One patient died of complications secondary to shock. All other recovered from both pancreatitis and hepatitis on conservative treatment.
Conclusion: Acute pancreatitis occurred in 7.3% of patients with acute viral hepatitis. Incidental cholelithiasis and probably biliary sludge are the other cause of severe abdominal pain in the patient of viral acute viral hepatitis. If diagnosed on time it recovers with conservative management.

PE481

Safety and Immunogenicity of a New Inactivated Hepatitis A Vaccine (Vero Cell): A Randomized Control Trial

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Objective: To assess the safety and immunogenicity of a new inactivated hepatitis A vaccine (Vero Cell).
Methods: 1507 subjects were selected in Gongcheng city of Guangxi Zhuang Autonomous Region, and the clinical trail was carried out according to the random, double-blind and parallel principle from January to August, 2005. After vaccination by 0, 6 schedule, adverse events of the subjects were observed, the seroeonversion rate and geometric mean titer (GMT) were tested by the competitive inhibition ELISA.
Results: After immunization, the systemic and local reaction rates of adults were 8.80% and2.67%, which was no significantly statistical difference compared with control group, 12.41%and 4.41%; while the rates of children were 10.60and 2.28%%, and no significant statistical difference compared with control group, 10.71%and2.86%. One month after first dose of vaccination, the seroconversion rates of children and adults were 88.2% and 93.8%, and one month after second dose of vaccination, the rates were all 100%, the GMTs of children and adults were 16447mIU/m1 and 8555mIU/ml, which was significant statistical difference in children compared with control group, 1946 mIU/ml and 5881 mIU/ml, respectively.
Conclusion: The new inactivated hepatitis A vaccine(Vero Cell) has the same result in safety compared with the imported vaccine, and the seroconversion rates was 100% by 0, 6 schedule, with highly antibody titer.

PE482

Hepatitis A Virus Proteins 3C and 3BC Have Inhibitory Effects on Translation and Are Possible Antiviral Targets

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Background: Some viruses encode proteins that affect their cap-independent internal ribosomal entry site (IRES)-mediated translation and their replication. It was recently reported that hepatitis A virus (HAV) proteases interact with intracellular dsRNA-induced retinoic acid-inducible gene (RIG-I)-mediated signaling, but it remained unknown whether HAV proteins have any effects on HAV IRES-independent translation. In this study, we investigated the effects of 7 HAV non-structural proteins on their IRES-mediated translation using a reporter assay.
Methods: The bicistronic reporter constructs, termed pSV40-HM175-IRES, pSV40-A1-IRES, pSV40-A2-IRES, pSV40-F1-IRES, and pSV40-F2-IRES, contain the SV40 promoter that controls the expression of a bicistronic message coding for renilla and firefly luciferases separated by HAV IRES, and are derived from strain HM175, acute convalescent hepatitis clones A1, A2, fulminant hepatitis clones F1, F2, respectively. Human hepatoma cell lines were co-transfected with pSV40-HAV-IRES and each HAV protein-expression vector. Luciferase activity was determined 48 h after transfection.
Results: Renilla luciferase activities mediated by cap-dependent translation in cells co-transfected with 3C- and 3BC-expression vectors were suppressed. Firefly luciferase activities of HM175-IRES-dependent translation were also suppressed by 3C and 3BC. 3C and 3BC also suppressed patient-derived HAV IRES-dependent translation. The effect of 3BC was generally stronger than that of 3C.
Conclusions: HAV proteins 3C and 3BC have an inhibitory effect on HAV-IRES functions, suggesting their potential as antiviral targets.

PE483

Characteristics of Hepatitis Delta in Northern California

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Background: To assess characteristics of patients with hepatitis delta in northern California.
Methods: 55 patients who were positive for HBsAg and hepatitis D virus (HDV) antibody were included.
Result: There is male dominance, with 43 (78%) patients out of 55 male and 12 (22%) out of 55 patients female. The country of origin for the patients was predominantly United States (60%) but there were also 5 (9%) patients of Chinese origin and 3 (5%) patients of Vietnamese origin. The remaining

were from other countries within Asia, Africa, Middle East, and Eastern Europe. Patients of a wide age range were affected by hepatitis delta (mean age 46.0, median 47.0, range 19-79). 18 (40%) of 45 were co-infected with HCV. Hepatitis B virus (HBV) DNA was detectable in 43 (78%) patients and negative in 8 (15%) patients.

All hepatitis delta patients were extracted from a prior study conducted by this collaboration. There were 1,191 chronic HBV carriers. 18 (1.51%) were HBV/ HCV/HDV infected. 32 (58%) of 55 patients carried a diagnosis of cirrhosis compared to 262 (22%) of 1191 chronic HBV patients. 13 (72%) HCV co-infected patients had evidence of cirrhosis while 4 (22%) patients did not.

Conclusion: Individuals with HBV/HDV co-infection have higher rates of cirrhosis. Individuals with HBV/HCV/HDV infection have rates of cirrhosis significantly higher than individuals with either chronic HBV infection or HBV/HDV co-infection. Testing for HDV should be performed in all patients, especially those with advanced liver disease or high risk behavior.

PE484

Hepatitis E Infection: Predictors of Mortality in Pregnant Females

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Background/Aims: In males and non pregnant females Hepatitis E virus(HEV) infection is often self limited and has low mortality, but in pregnancy mortality increases significantly. The aim of this study is to identify predictors of mortality in pregnant females with HEV infection.

Methods: Medical records of all acute HEV patients were reviewed from January 2000-June 2007.Diagnosis was based on clinical presentation, liver function tests and positive HEV IgM results. Outcome and predictors of mortality in pregnant females with HEV were analyzed.

Results: Overall 347 patients were admitted with HEV infection. Out of 173(49.8%) females, 66(38.1%) were pregnant. Mortality in pregnant females was 21.2 %(14/66). Predictors of mortality on admission in pregnant females found to be statistically significant on univariate analysis were age, Total bilirubin, SGPT (ALT), PT, fulminant hepatic failure and number of readmissions. Mean age, T.bilirubin and PT in alive vs. mortality group was 25±4.7 vs. 27± 6.5 years, 6.36±4.3 vs. 9±4.4 mg/dl and 23.5±18.7 vs. 38.1±32.9 secs, respectively. However on multivariate logistic regression analysis, predictors of mortality were age p =0.03, AOR: 1.21; 95%CI [1.02-1.44], T.bilirubin p=0.009, AOR: 1.46; 95%CI [1.10-1.95] and PT p=0.04, AOR: 1.03; 95%CI [1.00-1.06].

For each 5 years rise in age, 5secs rise in PT and 3mg/dl rise in T.bilirubin the mortality would be increased to 2.6,1.2,3.1 times respectively.

Parity and trimester of pregnancy was not associated with poor outcome.

Conclusion: Independent predictors of mortality were age of the patient, higher values of total Bilirubin and PT on admission.

PE485

Need of Esophago-Gastro-Duoenoscopy in Patients with Acute Hepatitis

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Background/Aims: Patients with acute hepatitis commonly complain of upper gastrointestinal symptoms such as nausea, epigastric soreness, discomfort or pain. However it is unclear if the symptoms are related to acute liver injury itself or newly developed significant gastrointestinal disease. The aims of this study were to investigate the incidence and associated factors of significant upper gastrointestinal disease in patients with acute hepatitis.

Methods: Medical records of 328 patients admitted at Department of Gastroenterology and Hepatology, Korea University Ansan Hospital due to acute hepatitis from March 2006 to August 2008 were reviewed. 128 patients had moderate to severe upper gastrointestinal symptoms and underwent esophago-gastro-duoenoscopy. Regardless of size, active stage ulcers with/without hemorrhage on stomach or duodenum were considered to be significant endoscopic findings.

Result: Among 128 patients, who underwent esophago-gastro-duoenoscopy, 94 patients (73.4%) had acute viral hepatitis and 34 patients (26.5%) had toxic hepatitis. Twenty three of 128 patients (17.9%) had significant endoscopic findings. Clinical characteristics were compared between the patients with significant endoscopic findings (group A) and without such findings (group B). Peak AST and ALT level were higher in group A (p<0.01). There were no statistical differences in age, gender, comorbidity, and etiology of acute hepatitis between group A and group B

Conclusion: Significant endoscopic findings were found in considerable proportion of patients with acute hepatitis. Severity of acute liver injury was associated with significant upper gastrointestinal endoscopic findings. In patients with severe acute hepatitis who complain of upper gastrointestinal symptom, esophago-gastro-duoenoscopy should be performed.

PE486

The Role of Hepatitis E Virus Testing in Etiology-Obscure Acute Liver Injury

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Background: In Japan, hepatitis E virus (HEV) testing is not allowed as routine one. To study the role of HEV testing, we checked 22 sera of the patients diagnosed as etiology-obscure acute liver injury.

Methods: We have seen 54 cases of acute liver injury from January 2004 through December 2007 in our hospital and 25 cases of them were etiology-obscure. In 25 cases, 22 were retrospectively tested for HEV-IgM, HEV-IgA and HEV-RNA (RT-PCR) by direct sequence method on stored sera taken at the time of presentation.

Result: Two of 22 cases (9.1%) were positive for both HEV-IgM and HEV-IgA and one case was positive for HEV-RNA. In 54 cases of acute liver injury, the cause of virus was 31 cases (57.4%) and unknown was 8 cases (14.8%). HEV was occupied in 3.7% in all cases and 6.5% in the cases caused by virus. One of the two cases had been misdiagnosed as “drug induced hepatitis”. HEV of genotype 3 was detected in one case and its nucleotide sequences of HEV showed quite a high degree of similarity to the reported one at closed city in the same year.

Conclusion: HEV is not rare in Japan and the HEV testing can reverse the diagnosis of acute liver injury. HEV testing sould be used as routine one for acute liver injury.

PE487

Association of Progesterone Receptor Gene with Hepatitis E Disease Severity in Pregnancy

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Background/Aims: Incidence of Fulminant Hepatic failure (FHF) in Hepatitis E is high in pregnancy particularly during 3rd trimester when there is an altered status of hormone and immunity. Progesterone receptor (PR) up regulation provides fetal protection via immunosuppression but lower immune status in pregnancy may add to the disease severity. Till now, no data is available whether PR can play any role in Hepatitis E disease severity during pregnancy. PROGINS, a haplotype of PR consisting of 320-bp insertion in intron G together with point mutations in exons 4 and 5 is associated with increased stability and higher transcriptional activity. The aim of the study is to analyze PR mutation (PROGINS) and m RNA expression in hepatitis E virus infected pregnant women with AVH and FHF.

Methods: A total of 68 AVH and 32 FHF cases were studied. Blood and placental tissue were collected from the Medicine and Gynecology wards of LNJP hospital, New Delhi. Cases were screened for acute viral markers by commercially available ELISA kit. Extraction of DNA from blood and RNA from placental tissue was done by Qiagen kit. Mutation in PR was detected by PCR-RFLP. Semiquantitative rt-pcr for PR expression was performed in placental tissue using beta-actin as internal control.

Results: PR mutation (PROGINS) was significantly more in FHF compared to AVH (28.1% vs 10.3%, P value<0.05). Protein expression was found higher in PROGINS carriers.

Conclusion: Progesterone receptor mutation (PROGINS) may have a role in the Hepatitis E disease severity in pregnant women.

PE488

Detection of the Hepatitis E Virus in the Livers of Slaughtered Swine

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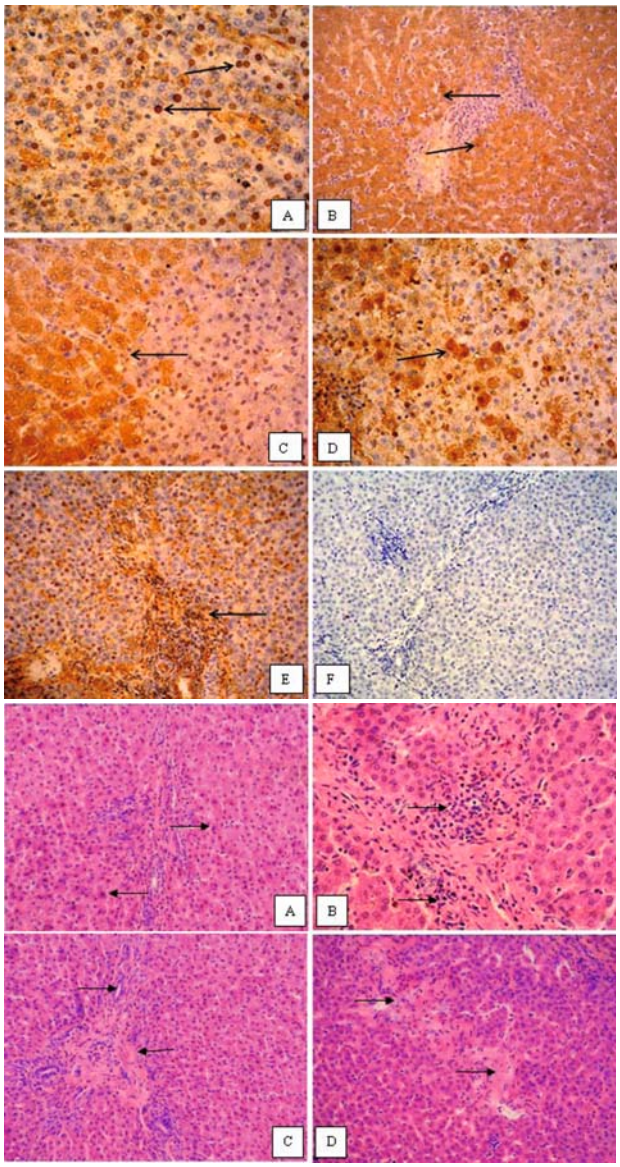
Background: Hepatitis E is a zoonosis and swine is the principal animal host. Accumulating research results revealed that commercial pig livers are contaminated by infectious HEV. This study investigated the infection status of HEV among 581 swine livers collected across China.
Methods: liver sample were paraform-glutaral fixed, paraffin-embedded, sectioned and immunohistochemical stained, and positive samples were selected for histological analysis and RT-PCR detection.
Result: Positive rate of HEV Immunohistochemistry ranged from 90% to 100% (Fig. 1). Hepatocyte degeneration, scattered singled karyopyknosis, lymphocytic infiltrate, hyperplasia of bile canaliculus at the portal area and fibrous connective tissue hyperplasia been observed during histological analysis (Fig. 2), and two genotype 4 HEV which closely related to many strain isolated from patients with sporadic acute hepatitis been detected.
Conclusion: Additional public-health concerns might be placed on pork safety and the risk of HEV infection via the consumption of undercooked pork products.



PE489

A Clinical Analysis of 110 Patients with Sporadic Viral Hepatitis E

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Objective: To investigate the clinical features of sporadic hepatitis E.
Methods: To analyze 110 patients with hepatitis E retrospectively.
Results: The hepatitis E was predominantly sporadic, some patients superinfected with other viral hepatitis, especially hepatitis B. In the old patients, jaundice lasted longer and the length of stay was longer, the incidence of complication was higher than the young men. The incidence of complication in the superinfected group was higher than the simple infection. The transaminase in the simple infection group was obviously raise than superinfected with liver cirrohsis.
Conclusion: The patients infected with hepatitis E of young men were frequently. Jaundice lasted long in the old patients, the incidence of complication was higher in the superinfected men and the old men.

Poster Exhibition – Portal Hypertension and Cirrhosis Poster Session, Hall 5B

PE490

Risk Factors for Early Recurrence of Esophageal Varices after Endoscopic Variceal Ligation and Endoscopic Injection Sclerotherapy

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Aim: Esophageal varices (EV) recurs frequently after endoscopic variceal ligation (EVL) or endoscopic injection sclerotherapy (EIS). We retrospectively investigated risk factors for early recurrence of EV after endoscopic treatment.
Methods: We treated 110 patients with EV, who had no past history of EV, at Ehime Prefectural Central Hospital from October 2005 to June 2008. Of those, 78 (71%) were observed for at least 2 months after treatment and enrolled. We divided them into rupture cases at initial endoscopic treatment [(bleeding group; n=25 (32%)], and cases with preventive EVL or EIS performed [preventive group; n=53 (68%)]. All received periodic upper endoscopy examinations to confirm recurrence or no recurrence of EV.
Results: Recurrence of EV occurred in 18 of all subjects and the average period after treatment was 6.5±3.0 months. The recurrence rate was significantly higher in the bleeding group (11/25) as compared to the preventive group (7/53) (P=0.0026). There was a significant relationship between recurrence of EV and hepatic reserve function (Child-Pugh A+B, C; 11/64, 7/14 respectively; P=0.0083). In logistic multi-variant analysis, EV rupture at initial treatment and Child-Pugh C were risk factors for recurrence. In contrast, age, sex, hepatocellular carcinoma, portal tumor thrombosis, continuous alcohol consumption, therapeutic modality (EVL or EIS), number of treatment sessions, and operator experience did not have a significant relationship with recurrence.
Conclusion: In cases with EV rupture at initial treatment or Child-Pugh C, the risk for early recurrence must be considered and patients carefully observed in follow-up examinations.

PE491

Endoscopic Cyanoacrylate Injection: Less Oil for Less Ectopic Embolism

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Background and Aim: Endoscopic injection sclerotherapy with N-butyl-2-cyanoacrylate (NBCA, histoacryl) has been reported to be effective for hemostasis of bleeding gastric varices, but occasionally the gel flows to other organs and causes ectopic embolism. The present study aimed to determine whether less amount of iodized oil preload in NBCA injection helps in decreasing ectopic embolism.
Methods: From January 1997 to April 2006, 2 different methods of endoscopic NBCA injection, “Sandwich method” and “modified Sandwich method” (in which iodized oil preload was minimized), were applied on 635

GV cases, to evaluate if decrease of iodized oil preload resulted in less ectopic embolism.
Results: Altogether 5 cases of ectopic embolism occurred in the whole group (0.8%), including 3 cases of splenic infarction, 1 case of transient paralysis and 1 case of minor infarction of the lung. The modified Sandwich method showed some superiority over original method in decreasing ectopic embolism (0/276 vs. 5/359, p=0.049). Less cough during procedure was also found with the modified method (3/276 vs. 18/359, p=0.006).
Conclusions: Less amount of iodized oil preload in endoscopic NBCA injection is beneficial to decrease ectopic embolism.

PE492

Hepatic Venous Pressure Gradient can Predict the Development of Hepatocellular Carcinoma and Hyponatremia in the Decompensated Cirrhosis

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Background: Portal hypertension is closely associated with serious complications of liver cirrhosis which contribute to bad prognosis. Hepatocellular carcinoma (HCC) and low serum sodium (SNa) are manifestations of end-stage liver disease (ESLD) and are associated with poor survival in decompensated cirrhosis patients. Therefore, we aimed to determine the relationship between hepatic venous pressure gradient (HVPG) and the development of HCC or low SNa in decompensated alcoholic cirrhosis patients.
Methods: Child-Pugh scores, MELD scores, and HVPG at baseline, and the development of low SNa (SNa <130 mEq/L) or HCC during follow-up were analyzed prospectively in 170 patients with decompensated alcoholic liver cirrhosis. The predictive values of different risk factors for the progression to the ESLD were investigated by multivariate analysis and the Kaplan-Meier method
Results: Twenty-four patients developed HCC during the follow-up period. In the multivariate analysis, only baseline HVPG>15mmHg was an independent predictive factor for the development of HCC (relative risk (RR)=1.128, $P<0.05$). Those with HVPG >15 mmHg showed a significantly shorter time for the development of HCC on Kaplan-Meier analysis. Twenty patients developed low SNa during follow-up. Initial HVPG was also an independent predictive value for the development of low SNa in the multivariate analysis (RR=1.169, $P<0.05$). Those with HVPG>15 mmHg also showed significantly shorter times for the development of low SNa on Kaplan-Meier analysis.
Conclusions: In decompensated alcoholic cirrhosis, HVPG may be a useful predictive factor for the development of HCC and low SNa, both of which are characteristic of ESLD and poor prognosis.

PE493

The Effectiveness of the Treatment of Octreotide on Chylous Ascites after Liver Cirrhosis

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Background: Octreotide is a crucial drug used for treating patients with chylous ascites; however, there have been few reports related to octreotide that are being used in cirrhotic patients. Thus, this thesis is designed to determine the effects of octreotide on patients with chylous ascites after liver cirrhosis.
Methods: Eight patients were diagnosed with chylous ascites, on the basis of laboratory findings on ascites samples, between January 2003 and May 2008. Octreotide was given to the six patients, while the remaining two were treated as a control. All patients had persistent peritonea drainage with the quantity and quality of the drainage fluid observed once every other day. All the necessary care was individually given to the patients during the therapy.
Results: All patients properly received combined therapy including low fat and sodium diet, and diuretic and peritoneal drainage. The volume of the peritoneal drainage was reduced to zero in one of the six patients who received octreotide therapy, while the other five had the drainage volumes decreased from 2000 ml to 50 ml with a clear appearance and negative qualitative analysis of chyle. For those two patients who did not receive octreotide therapy, the conditions of peritoneal drainage seldom changed both from the qualitative and quantitative aspects.
Conclusion: Octreotide, along with combined therapy, can rapidly relieve portal hypertension and reduce fat absorption from intestinal mucosa. It appears to be an effective therapy available for the treatment of chylous ascites caused by liver cirrhosis.

PE494

Frequency of Portal Hypertensive Gastropathy and its non-invasive predictors in patients with Viral Cirrhosis

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Background: portal hypertensive gastropathy (PHG) is found in 65% of patients with cirrhosis and account for 10-60% of bleeding episodes.
Aims and Objectives: To study the frequency of PHG in patients with cirrhosis due to viral etiology and its correlation with different non-invasive markers of bleeding.
Methods: Medical record of all patients with cirrhosis due to hepatitis B and C who underwent for screening EGD for varices in last 2 years was reviewed. PHG was defined endoscopically by using McCormack classification. Noninvasive markers such as spleen/platelets ratio, MELD score and Child score of all the patients who underwent for EGD were recorded.
Results: Out of 360 patients 226(62.77%) were males. Out of 300(83.3%) patients who had PHG, 136(45.3%), 93 (31%) and 71(23.7%) had mild, intermediate and severe PHG respectively. Higher proportion of esophageal varices (89.7%) was present among those who have PHG ($P<0.001$).196(65.3%) with PHG has child score of ≥7. MELD score >15 and ≤ 15 were seen in 32.3% and 67.7% of patients with PHG, respectively. Platelet/spleen ratio was 916.08± 400 in patients with PHG as compared to 1476.83± 898.70 in patients without it ($p<0.001$). On multivariate analysis Child score of ≥ 7 (OR 7.16, $p<0.001$), MELD score>15 (OR13.61, $p<0.001$), EV(OR 9.78, $p<0.001$) and platelet/spleen ratio≤ 900(OR 2.65, $p=0.001$) were found as significant predictors of severe PHG.
Conclusion: The frequency of PHG is high in viral cirrhosis patients. MELD score>15, Child score≥7 and spleen/platelets ratio≤ 900 can be used as noninvasive predictors of severe PHG.

PE495

Factors Predicting the Presence of Oesophageal Varices in Patients with Advanced Liver Disease - A 12-Month Retrospective Review

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Background: Patients with advanced liver disease are recommended to undergo endoscopic surveillance to detect/treat large oesophageal varices. Some reviews postulated clinical, biochemical and radiological indices that correlate with presence of large oesophageal varices. We aim to identify clinical, laboratory and radiological predictors of large oesophageal varices on endoscopy.
Methods: Retrospective analysis of cirrhotics undergoing surveillance endoscopy was undertaken assessing for oesophageal varices. Clinical, biochemical and radiological indices were analysed.
Results: 81 cirrhotics underwent surveillance endoscopy during the study. Childs Pugh Scoring (CPS) to assess prognosis of liver disease showed CPS A(58%), CPS B(27%) and CPS C(14%). 68% were male; mean age 53.9years.
Comparison between patients with small (Grade 0-1) and large (Grade 2-4) oesophageal varices showed statistically significant differences on univariate analysis in age (53.5yrs vs 55yrs; p=0.03), Bilirubin (14umol/L vs 23umol/L; p=0.002), Albumin (42g/L vs 35g/L; $p<0.001$), INR (1.1 vs 1.2; p=0.01), CPS (5.0 vs 7.0; $p<0.001$), Platelet count (136x10E9/L vs 75x10E9/L; $p<0.001$) and spleen size (12.2cm vs 15.4cm; p=0.002). Significant factors on multivariate analysis were Albumin (p=0.003) and Platelet count (p=0.026). Best cut-off predictors of large varices were Platelet count <105x10E9/L ($p<0.001$, OR 4.73(95% CI: 1.95-11.50)) and Albumin <38g/L ($p<0.001$, OR 4.8(95%CI 2.27-10.30)).
Conclusion: In our cohort there were significant biechemical and radiological differences in differentiating patients with large varices (Grade 2-4) on surveillance endoscopy. Low platelet count <105x10E9/L and

albumin <38g/L were the best predictors of large varices. A model using these predictors in a validation cohort study is planned.

PE496

Acute Phase Protein Levels in Cirrhotic Patients with or Without Infection

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Background-Aim: Cirrhosis is associated with raised acute phase proteins (APP), irrespective of infection. It is, however, unclear whether their values differ significantly or whether a particular APP might be more indicative of infection, and these questions were addressed in our study.
Methods: We measured serum CRP, fibrinogen, ferritin, haptoglobin, β_2-microglobulin, C_3, C_4, and C_1 inhibitor in 88 consecutive, cirrhotic patients, on admission. All patients were investigated according to a standard protocol for infection. Child-Pugh scores (CPS) were calculated. Results of APP were expressed as means SEM and compared with the Mann-Whitney test.
Results: 19 (21,6%) patients, median age 60 years, (CPS: A=0; B=7; C=12), were diagnosed with infection (spontaneous bacterial peritonitis=7; pneumonia=5; septic shock=4; extensive cellulitis=1; Listeria Monocytogenes meningitis=1; viral infection=1), while 69 (78%) patients, median age 59 years, (CPS: A=25; B=28; C=16), showed no infection. Although most APP values were raised, there was no statistically significant difference between patients with or without infection, or among different CPS groups, except for CRP, which was significantly more raised in patients with infection ($p<0.01$). This difference remained even after CPS A cases in the non-infection group were excluded from analysis.
Interpretation: A significantly raised CRP in cirrhosis would seem to be independent of CPS staging and should prompt a thorough work up to exclude infection. By contrast, the discriminating power of all other APP in the face of possible infection is negligible. The predictive value of CRP towards infection is under investigation prospectively.

PE497

Endoscopic Treatment of Rectal Varices

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Background and Aim: Recent advances in diagnostic and therapeutic options continue to evolve in the field of portal hypertension and important technical developments have been made to control life-threatening variceal bleeding. Gastro-esophageal varices are the most common site of variceal bleeding. Although bleeding from ectopic varices such as duodenal, jejunal, ileal, colonic, and rectal varices is less common, it can also cause life-threatening problem, which is often difficult to diagnose and treat successfully. Here we present a novel endoscopic approach for hemorrhagic rectal varices using endoscopic injection sclerotherapy with ligation (EISL).
Patients and Methods: In 2000-2008, we performed endoscopic treatment in 215 patients with portal hypertensive varices. Among those, four cases of hemorrhagic rectal varices were treated with the combined EVL and sclerosing technique. The etiology of portal hypertension included oen idiopathic portal hypertension and three HCV cirrhosis. All patients had a history of prior abdominal surgery or endoscopic treatment for gastro-esophageal varices.
Results: Hemostasis was obtained easily by the EVL initially. Furthermore, to avoid recurrent bleeding, the patients underwent endoscopic varicerography injection sclerotherapy (EVIS) using 5% ethanolamine oleate with iopamidol and the feeding vein was sclerosed successfully with no major complication occurred during the entire course of the treatment.
Conclusions: It is important to recognize the possibility of ectopic varices as a cause of gastro-intestinal haemorrhage especially in patients with a history of variceal therapy or abdominal surgery. The EISL technique is useful to control the initial and recurrent bleeding from rectal varices.

PE498

Laparoscopic Splenectomy Reverses Thrombocytopenia in Patients with Portal Hypertension

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Aim: Interferon (IFN) therapy is a powerful treatment for HCV-related hepatitis and is known to decrease the incidence of progression of hepatocellular carcinoma (HCC). However, thrombocytopenia is a common side effect of IFN treatment, often leads to discontinuance without insufficient therapeutic effect. In this study, we investigated the efficacy and safety of laparoscopic splenectomy (↻ →) in reversing thrombocytopenia in patients with hepatitis C cirrhosis and portal hypertension.
Patients and Methods: Out of 41 patients who underwent LS in our department during Aug 2003 and December 2007, 13 patients associated with portal hypertension. Among these patients, three patients had HCC, and they were simultaneously underwent partial hepatectomy after splenectomy. Platelet count, operative time, blood loss, complications and length of stay were calculated.
Results: Thirteen patients underwent laparoscopic splenectomy; their mean age was 59 years (range 20 to 68 years). Six patients were Child's class A and seven patients were class B. Mean operative time was 178 minutes (range 97 to 255 minutes). Blood loss was little, and none required transfusion with packed red cells. A hand-assisted laparoscopic technique was used in four cases (30.8%).
Average length of stay was 12.7 days. There have been no major complications during follow-up. Platelet counts improved from a preoperative mean of 62000/ul (44000 to 108000) to 273000/ul (126000 to 469000) postoperatively. Six patients are ongoing IFN treatment without remarkable thrombocytopenia.
Conclusion: Laparoscopic splenectomy is safe and in patients with portal hypertension and thrombocytopenia. It may allows these patients by reversing thrombocytopenia.

PE499

Effects of Acetyl-L-Carnitine in Cirrhotic Patients with Hepatic Encephalopathy

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Background: Hepatic encephalopathy (HE) is a significant cause of mortality in advanced cirrhosis patients. L-acyl-carnitine has been suggested as an alternative treatment for patients with HE patients. To assess the clinical efficacy of acetyl-L-carnitine in the treatment of hepatic encephalopathy in cirrhotic patient, especially in diminishing the recurrence and reduction serum ammonia level.
Methods: We performed a randomized placebo-controlled, cross-over study. We administered acetyl-L-carnitine to group 1 during 3 months first then placebo during later 3 months, and administering acetyl-L-carnitine to group 2 alternatively.
Results: Between January 2008 and February 2008, thirty two selected cirrhotic patients were enrolled in this study. Following randomization, the patients were divided into two groups (group 1=14, group 2=18). During administering acetyl-L-carnitine period, serum ammonia level was decreased significantly in both groups significantly (p=0.005, vs. p=0.001 respectively). However, during administering placebo period, serum ammonia level changes were not significant. In group 1, the first recurrence cases of hepatic encephalopathy were more than group 2(group 1=5, group 2=2), and the first recurrences were occurred during first 3 months in all groups.
Conclusion: Our study demonstrates that acetyl-L-carnitine administration reduced serum ammonia level, but not definitely diminishing the recurrence of hepatic encephalopathy.

PE500

Impaired Natriuresis in Non-Azotemic Cirrhotic Patients with Ascites According to MELD Score

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Sodium (Na^+) and water retention are the most common abnormalities in cirrhotic patients and the magnitude varies from patients to patients.

Aim: To assess the relationship between the MELD score and urinary excretion of Na+ in non-azotemic cirrhotic patients.
Methods: Fifty four cirrhotic patients with ascites and normal serum creatinine (<1.5 mg/ml) were admitted and placed on a low sodium diet (4g/day), while all diuretics were withdrawn for 3 days. The electrolytes (Na^+, K^+, Na^+/ K^+) were measured in a random urine and both the volume and Na^+ concentration of urine collected for 8 h after administration of furosemide 80 mg i.v. were determined.
Results: Table.
Conclusions: The MELD score was significantly correlated with the degree of impairment of urinary Na+ excretion. The ratio of Na^+/K^+ in a random urine specimen and furosemide-induced Na+ excretion reflect the degree of impaired natriuresis in non-azotemic cirrhotic patients with ascites.

PE501

HVPG Does Not Correlate with the Presence and the Severity of Portal Hypertensive Gastropathy in Patients with Liver Cirrhosis

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Background: Portal hypertensive gastropathy (PHG) is common finding in patients with liver cirrhosis and portal hypertension. Despite portal hypertension remains the crucial trigger for the development of PHG, the relationship between portal hypertension and PHG has not been widely investigated.
Methods: Fifty-three cirrhotic patients (48 males, mean age 51 years) who were performed hepatic vein catheterization between November 2006 and August 2008 were prospectively included in this study. The degree of PHG was assessed according to the Third Baveno International Consensus Workshop, and classified three degrees as no, mild and severe. The hepatic venous pressure gradient (HVPG=WHVP-FHVP) measurements were performed by triplicate in each case, and results were given as arithmetic means of the three determinations.
Result: HVPG values did not differ between the patients without PHG (13.28±4.72 mmHg) and those with PHG (14.91±3.84, p=0.187), nor between those with mild (15.31±3.69 mmHg) or severe PHG (14.27±4.12mmHg, p=0.323). The degree of PHG and HVPG did not differ regarding the etiology of the cirrhosis(p=1.0, p=0.085) nor regarding the Child Pugh classification(p=0.085, p=0.738). No correlations were found between the degree of PHG and Child Pugh score, age, with or without ascites, albumin, bilirubin, creatinine, MELD score and the degree of gastroesophageal varices.
Conclusions: Our data show that the presence and the severity of PHG does not correlate with the degree of HVPG, and that correlate with esophageal varices in patients with liver cirrhosis.

PE502

Phlebosclerotic Colitis in a Cirrhotic Patient with Portal Hypertension: The First Case in Korea

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Introduction: Phlebosclerotic colitis is a rare form of ischemic colitis characterized by the thickening of the colonic wall due to fibrous degeneration of the submucosal layer and fibrotic sclerosis of the venous wall. There are a few reports those this entity might be related to portal hypertension with disturbed venous return from the colon and mesentery.
Case description: A 61-year old man with alcoholic liver cirrhosis presented with right lower abdominal pain/tenderness and bloody diarrhea. A colonoscopy revealed multiple circumferential ulcerations in the transverse colon and the scope could not get through the ascending colon due to luminal stenosis, showing histologic finding of ulcerative inflammation with inflammed granulation tissue. Abdominal computed tomography demonstrated liver cirrhosis with splenomegaly, multiple portosystemic venous collaterals, diffuse vascular engorgement and the wall thickening of right proximal to mid ascending colon with increased density in the surrounding fatty tissue. A follow-up colonoscopy performed one month later showed still remained multiple ulcerations in the transverse colon and could not further advance to ascending colon. Superior mesenteric angiography revealed no main branch occlusion but pooling at the venous phase on ascending colon. A right hemicolectomy was performed because of the colonic obstruction. Gross findings on operation showed thickening of the cecum and ascending colon. Microscopic examination showed fibrous thickening in the submucosa, abundant neurovascular bundles in the mesentery and several intravascular hyaline thrombi of the mesenteric vessels. Here we report the first case of early stage of phlebosclerotic colitis in a cirrhotic patient in Korea.

PE503

Detection of the Causative Pathogen Using the In-Situ Hybridization Kit in a Patient with Spontaneous Bacterial Peritonitis

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Spontaneous bacterial peritonitis (SBP) is one of the severe complications in advanced cirrhotic patients with a high mortality rate. Although a more rapid diagnosis should lead to the better survival, it takes several days to detect the causal bacteria from ascitic fluid cultures. Furthermore, despite the use of sensitive methods, ascitic fluid cultures were negative in more than 50% of patients with suggestive clinical manifestations of SBP. Therefore, diagnosis of SBP is based on the polymorphonuclear leucocytes (PMN) cell count in the ascitic fluid. The Hybrizep kit (Fuso Pharmaceutical Industries, Osaka, Japan) detects the DNA of bacteria that have been phagocytized in neutrophils and macrophages, using in-situ hybridization method within one day. Here we present a case of the patient for whom the Hybrizep kit was used to detect the causal pathogen of SBP.
A 76-year-old man had been admitted for the treatment of ascites and esophageal varices. One week after the admission, he complained abdominal pain and fever. Because the PMN cell count in ascites fulfilled the criteria of SBP (1141/mm^3), we started an empirical antibiotic therapy without waiting for a result of the culture, and his symptoms improved within a few days. On the following day of the onset, in situ hybridization showed the positive signals by the EK probe, which detected the genomeic DNA of E.coli species. However, the ascitic fluid culture was negative. This case suggested that the Hybrizep kit was useful for the rapid diagnosis of SBP with high sensitivity.

PE504

The Parameters of Doppler Ultrasonography Associated with Splenomegaly and Varices in Patients with Cirrhosis

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Background: It has not been known that the hemodynamic effect of a portal hypertension for splenomegaly or esophageal and gastric variceal formation. This study was performed to access the parameters of doppler ultrasonography associated with splenomegaly or varices in patients with cirrhosis.
Patients and Methods: From May 2007 to May 2008, 144 cirrhotic patients were performed the doppler ultrasonography. 91 of these patients were accessed the severity of varices endoscopically. The three dimensional volume of spleen was measured from a length, width and thickness on sonography.
Results: The splenic volume (415.2ml vs 505.6ml, p=0.048) and blood flow of main portal vein (12.6cm/s vs 15.1cm/s, p=0.012) were statistically significant different in alcoholic (38/144) and non-alcoholic (105/144) cirrhosis groups. The splenic volume (600.1ml vs 384.4ml, p=0.001), damping index (0.52 vs 0.38, p=0.024), and blood flow of main portal vein(12.5cm/s vs 15.7cm/s, p=0.006) were statistically significant different in esophageal variceal groups (55/91) and non-esophageal variceal groups(36/91). The only splenic volume (669.4 ml vs 461.7 ml, p=0.004) were statistically significant different in gastric variceal groups (24/90) and non-gastric variceal groups (66/90). The hemodynamic parameters

associated with splenic volume were damping index (r=0.213, p=0.022) and blood flow of portal vein (r=-0.314, p=0.001).
Conclusions: The splenomegaly in portal hypertension was more frequent in non-alcoholic groups, and associated with a damping index and a blood flow of portal vein. The measurement of blood flow of portal vein, damping index, and splenic volume by a doppler sonography can be helpful to predict the varices.

PE505
MicroRNA Expression Profile Analysis of Rat Hepatic Stellate Cell during in vitro Activation
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Background: To reveal the microRNA (miRNA) expression profile of the hepatic fibrosis inducing cells, rat hepatic stellate cells (HSCs), during *in vitro* activation.
Methods: The HSCs were isolated from male SD rats by *in situ* perfusion and density-gradient centrifugation. The quiescent and activated HSCs, which were harvested at day 2 and 14, respectively, were then subjected to immunocytochemical staining (desmin and α-SMA), Oil red O staining and quantitative RT-PCR (desmin, α-SMA, albumin, CD31, CD68 and cytokeratin-19). After extraction and labeling, the Hy3-labeled cellular RNA samples and Hy5-labeled reference pool RNA samples were mixed pair-wise and hybridized to the LNA mercury microarray. Differentially expressed miRNAs were filtered and randomly verified by stem–loop RT followed by quantitative PCR.
Results: Both the purity and the total activation of HSCs were validated. Global analysis of the miRNA expression profile based on quiescent and activated HSCs demonstrated 21 differentially expressed miRNAs. Among these, 12 miRNAs were up-regulated more than 2-fold in activated HSCs as compared to that in quiescent HSCs, while 9 miRNAs were less than the threshold level (0.5-fold) during the HSC activation. Furthermore, the expression of miR-16, 15b, 122, 138, 143 and 140 had been proved.
Conclusions: The culture-activation of HSCs may be related to the regulation of miRNAs. Twenty-one miRNAs may contribute the process.

PE506
Practical Significance of the Peripheral Blood Corpuscle Counts for Prediction of Hepatitis B Associated Cirrhosis
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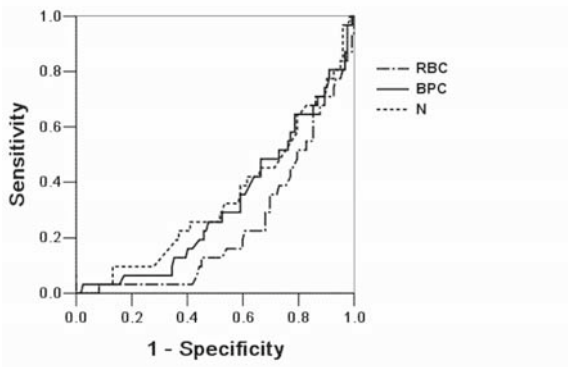
Objective: To explore the practical significance of the peripheral blood corpuscle counts for prediction of hepatitis B associated cirrhosis.
Methods: 122 and 31 male patients with chronic hepatitis B were pathologically diagnosed as non-cirrhosis and cirrhosis. Peripheral blood corpuscle counts were measured by Coulter Ac•T diff Hematology Analyzer.
Results: Red blood cell (RBC), platelet (PLT), neutrophil (N) counts in cirrhosis were significantly lower than those in non-cirrhosis; and lymphocyte, mid-cell counts were similar to those in non-cirrhosis. The areas under the ROC curves of RBC, PLT, N counts for prediction of cirrhosis were 0.24, 0.32, 0.34 respectively; according the optimal cut-off determined by the ROC curves, the sensitivity, specificity, positive predictive value, negative predictive value, accuracy of RBC, PLT, N counts for prediction of cirrhosis were 0.55-0.77, 0.59-0.71, 0.31-0.38, 0.86-0.92, 0.61-0.70.
Conclusion: RBC, PLT, N counts could be helpful of excluding hepatitis B associated cirrhosis.



PE507
Appraisement of Simple Non-invasive Models for Predicting Hepatitis B Associated Cirrhosis by ROC Curve Method
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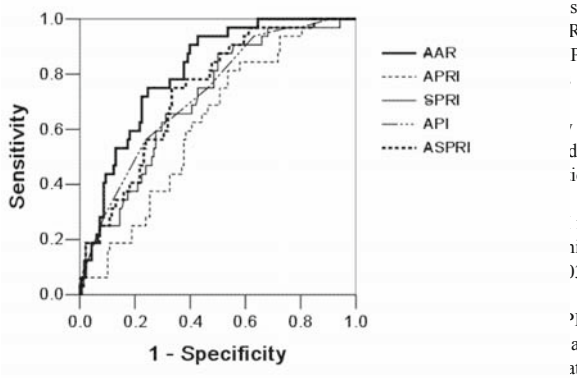

PE508
A Predictive Model for Cirrhosis Development in Patients with Chronic Hepatitis B Virus Infection
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Background/Aims: Only limited patients with chronic hepatitis B virus (HBV) infection will develop liver cirrhosis, and no effective methods to precisely predict ones who will develop cirrhosis. We try to establish a model to predict the patients with the risk of cirrhosis development basing on a clinical epidemiological factor survey.
Methods: Cirrhosis patients with HBV markers (case group) and asymptomatic HBsAg carriers (control group) were recruited and inquired by researchers with a specific designed questionnaire including 98 items. A multivariate Logistic regression analysis were conducted to establish a predictive model, in which two third patients selected randomly as model sample and another 1/3 patients as validating sample, key factors screened out as variables. The predictive performance of the model was evaluated.
Results: Total 272 patients enrolled in the study, males 77.2%, females 22.8%, average age 54.4. No differences existed in age compositions and sex ratios of patients between two groups (P=0.910~0.980). Recurrence of hepatitis B and other 8 factors entered into the model. The predictive performance of the model in model sample is as follows: sensitivity 94.7%, specificity 95.5%, accuracy 95.1%, and in validating sample: Sensitivity 93.5%, specificity 88.6%, accuracy 91.1%.
Conclusions: The established model with 9 key factors shows a good performance for prediction of cirrhosis development in patients with chronic hepatitis B infection.

PE509
Critical Flicker Frequency for Assessment of Recovery of Minimal Hepatic Encephalopathy Patients in Cirrhotics
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Background and Aims: Minimal hepatic encephalopathy (MHE) impairs quality of life and predicts overt encephalopathy in cirrhotics.We evaluated utility of critical flicker frequency (CFF) for recovery of MHE.
Patients and Methods: Consecutive 60 cirrhotic patients without overt encephalopathy {Child A, 26 (43%), Child B 20(34%), Child C 14 (23%)} were evaluated by psychometry (number connection tests A, B or figure connection tests A, B), P300 auditory event related potential (P300ERP),

venous ammonia and CFF at baseline and after one month of treatment with lactulose. MHE diagnosed by abnormal psychometry and/or P300ERP.Response defined by normalization of abnormal test parameters.
Results: MHE diagnosed in 35(58%) patients. Of 35 patients 26 (74%) had both abnormal psychometry and P300ERP whereas30 (86%) alone had abnormal psychometry, 31 (89%) had abnormal P300ERP.CFF was <39Hz in 28(80%) patients. MHE recovered in 55% with treatment and CFF >39Hz was seen in 22(69%) of 32 patients. CFF sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy before and after treatment is shown in table.
Conclusions: Critical flicker frequency is a simple and accurate test without any age or literacy dependence for the diagnosis and recovery of patients with MHE.

CFF	Psychometry		P300ERP		Psychometry+P300ERP	
	Pretreatment	Posttreatment	Pretreatment	Post treatment	Pretreatment	Post treatment
Sensitivity(%)	87.0	80.0	87.0	64.0	96.0	88.0
Specificity(%)	60.0	91.0	75.0	86.0	67.0	89.0
PPV(%)	93.0	80.0	96.0	70.0	89.0	70.0
NPV(%)	57.0	91.0	43.0	82.0	86.0	96.0
Diagnostic Accuaracy(%)	83.0	88.0	86.0	78.0	89.0	89.0

PE510

Risk Factors Associated With Multiple Complications after Endoscopic N-Butyl-2-Cyanoacrylate Injection for Varix Bleeding

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Background/Aims: Endoscopic injection of N-butyl-2-cyanoacrylate (Histoacryl) is an effective treatment of varix bleeding. But nontarget embolizations and septicemia are unwanted complications. We evaluate the risk factors for complications.
Methods: Thirty-three patients with esophageal or gastric varix bleeding received endoscopic Histoacryl therapies (54 procedures). Baseline varix size, CTP score were checked. Serum leukocyte, blood culture and body temperatures were repeated checked within one week after procedure. Average volume of Histoacryl per each session was 1.6 mL, and dilution volume ratio of Histoacryl/lipiodol was 1/1 or 1/2.
Results: Average of CTP score was 8.0 ± 1.7. Three cases of septicemia were correlated with CTP score rather than session frequency or injection volume. Two cases of systemic embolizations (pulmonary and splenic arterial embolism) were correlated with high lipiodol dilution ratio (1/2) and lipiodol volume rather than Histoacryl volume or CTP score.
Conclusion: CTP score, lipiodol volume and dilution ratio of Histoacryl/lipiodol were significant risk factors for complications.

PE511

Detection of Circulating Toll-Like Receptor 2 and 4 and CD4+CD25+ Regulatory T Cells in Patients with HBV-Related Liver Cirrhosis

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Background : To detect circulating $CD4^+CD25^+$ regulatory T cells and toll-like receptor(TLR)2 and TLR4 expression on the peripheral blood mononuclear cells (PBMCs) of patients with HBV-related liver cirrhosis (LC), and to explore the correlation between them.
Methods: PBMCs isolated from 14 LC patients , 21 chronic hepatitis B (CHB) patients and 16 normal controls(NC) were stained with fluorescent labeling anti-TLR2-PE, anti--TLR4-APC, anti--CD14-FITC monoclonal antibodies and anti-CD4-PerCP、anti-CD25-FITC、anti-CD127-PE. Samples were collected and detected of three-color immunofluo rescence by flow cytometry. Results: The expression of TLR2 and TLR4 were significantly up-regulated in patients with LC than those in the controls.The expression of TLR2 was significantly increased in patients with LC than those in patients with CHB, but there were no differences of TLR4 expression between LC and CHB.Treg/$CD4^+$ T cells were significantly increased in patients with CHB than those in patients with NC and LC, but there were no differences between LC and NC. There were no correlation between the expression of TLR2,TLR4 and Treg in patients with LC . The expression of TLR2 and TLR4 on PBMCs in patients with LC were positive correlation.The expression TLR4 and HBV DNA level were negative correlation in patients with LC.
Conclusion: The expression of TLR2 and TLR4 were up-regulated on PBMCs in patients with LC. It seems to be expression of TLR2 and TLR4 invovlved in the pathogenesis of LC.

PE512

Evaluation of 13C-Phenylalanine Breath Test for the Measurement of Hepatocyte Function in Patients with Chronic Liver Disease

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Background: The objective is to investigate whether the 13C-phenylalanine breath test(PBT) would be useful for the evaluation of hepatic function in patients with chronic hepatitis B, liver cirrhosis and minimal hepatic encephalopathy (MHE).
Methods: L-[1-13C] phenylalanine was administered orally in a dose of 100 mg to 80 patients with liver cirrhosis, 20 with chronic hepatitis B and 20 healthy subjects. The PBT was measured at 8 different time points (0, 10, 20, 30, 45, 60, 90, 120 min) to obtain the values of Delta over baseline, percentage 13CO2 exhalation rate and cumulative excretion (Cum). The relationships of the cumulative excretion with the 13C-%dose/h and blood biochemical parameters were investigated.
Results: The 13C dose h-1 at 20 and 30 min combined with the cumulative excretion at 60 and 120 min showed correlations with the chronic liver diseases, especially Child-Pugh score and MHE or not. And the data showed correlations with serum albumin， hemoglobin， platelet and Child-Pugh score. Prothrombin time, total and direct bilirubin were significantly increased, while serum albumin, hemoglobin and platelet, the cumulative excretion at 60 and 120 min values decreased by degrees in healthy controls, Child-Pugh A, B, and C patients (P<0.01). Similar results of PBT were in the patients with and without MHE, while only prothrombin time prolonged and total bilirubin increased (P<0.05).
Conclusions: The PBT can be used as a non-invasive assay to evaluate hepatic function in patients with liver cirrhosis and MHE. The %13C dose h-1 at 20 min, %13C dose h-1 at 30 min and cumulative excretion at 60 min may be the key value for determination at a single time-point.

PE513

Branched Chain Amino Acids in Improving Survival and Decreasing Risk of Liver Failure among Cirrhotic Patients: A Meta-Analysis

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Background: The state of a patient's nutritional status greatly affects disease outcome. Among cirrhotic patients, approximately 60-90% are in a state of protein-energy malnutrition. Hence, adequate nutritional support is essential to improve their general medical condition and long term prognosis. Several studies have shown than branched chain amino acids (BCAA) may be of benefit for this purpose. It is the aim of this study to evaluate the effectiveness of diet plus BCAA compared to diet alone in improving survival and in decreasing liver failure among cirrhotic patients.
Methods: Pubmed, Cochrane, and EMBASE search was done for articles which compared the clinical effects of BCAA supplementation versus diet alone among patients with liver cirrhosis. The following free-text terms and MESH words were used – "Branched chain amino acids", "amino acids, branched chain", "BCAA", "liver cirrhosis", "cirrhosis", "Randomized Controlled Trials'" and "Meta-analysis". After critical appraisal of the included studies, a random effects model using odds ratio was used to synthesize the results (RevMan 4.2).
Results: 3 RCTs were included for analysis with a total study population of 836. Combination of the studies showed a significant decrease in the risk of liver failure (OR 0.45, 95% CI 0.25-0.82, p=0.009) and a trend towards benefit in improving survival (OR 0.57, 95% CI 0.27-1.17, p=0.12).
Conclusions: The overall trend appears to show benefit in the use of Branched Chain Amino Acids for patients with cirrhosis with respect to liver failure and survival.

PE514

Hydrogen Sulfide: Production and Decrease Intracellular Ca2+ through Activation KATP Channel in Activated Hepatic Stellate Cell

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Objective: To study the effects of hydrogen sulfide (H_2S) on the intracellular Ca^{2+} concentration and proliferation of hepatic stellate cells and the possible mechanisms.

Method: Activated rat hepatic stellate cells (HSC-T6) were used in this study. After loading of Ca^{2+} fluorescent probe, Fluo-3/AM, the change of fluorescence intensity (FI) of intracellular Ca^{2+} was dynamically scanned with LSCM.And the effects of different concentrations of NaSH, the H_2S 'donor', on the proliferation of HSC-T6 cells were observed using MTT colorimetric assay. HSC-T6 H2S production rate was detected by methylene blue spectrophotometry. HSC-T6 CSE mRNA was tested using RT-PCR.

Results: Low-concentration H_2S (100 μmol/l) significantly decreased the Ca^{2+} concentration in HSC-T6 cells (16.20±3.56 vs. 14.12±3.76, $P<0.05$), and promoted the cell proliferation (proliferation rate was 116%). Glibenclamide, blocker of K_{ATP} channels, can block the effects of H_2S. High-concentration H_2S (1 mmol/l) increased the Ca^{2+} concentration in HSC-T6 cells.HO-1 inductor and eNOS inhibitor had the tendency to suppress H_2S production rate in HSC-T6. Compared with the control group, DL-PPG(CSE inhibitor) can significantly suppress H_2S production rate.

Conclusions: Low-concentration H_2S decreases the intracellular Ca^{2+} concentration through activation of K_{ATP} channels on HSC-T6 cells, and it may promote the cell proliferation though the regulation of cell oxidative stress, which suggests that H_2S has dual effects on the mechanisms of cirrhotic portal hypertension.

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PE515

The Effect of Pioglitazone, a Specific Ligand of the Proxisome Prolifrator-Activated Receptor Gamma, on Ethanol-Induced Gastric Ulcers in Cirrhotic Rats: Role of Nitric Oxide

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Background: The proxisome prolifrator-activated receptor gamma (PPARγ) is a member of the nuclear hormone receptor superfamily that is involved in the control of inflammation, carcinogenesis and gastric ulcer. On the other hand, the frequency of gastrointestinal ulceration is higher in cirrhotic patients compared with the normal population. The present study was designed to investigate the effect of specific PPARγ ligand, pioglitazone, on the mucosal lesions induced by ethanol in cirrhotic rats and the possible involvement of nitric oxide in the pioglitazone effect.

Methods: Cirrhosis was induced by surgical ligation of bile duct and sham-operated rats served as controls. Both cirrhotic and sham rats were kept for 28 days after the operation. Different groups of sham and cirrhotic animals received saline, or 5, 10 or 15 mg/kg pioglitazone, daily during last 5 days of the fourth week after the surgery. Another 2 groups of BDL or 2 groups of sham rats received L-NAME, a non selective inhibitor of nitric oxide synthase, alone or along with 5 mg/kg pioglitazone for 5 days. On day 28, rats were killed 1 hour after ethanol administration and the area of gastric lesions was measured.

Results: The ethanol-induced gastric mucosal damage was significantly more sever in cirrhotic rats than sham-operated ones ($P < 0.001$). Pretreatment with pioglitazone dose dependently attenuated gastric lesions induced by ethanol in both sham and cirrhotic rats, but this effect was more significant in cirrhotic ones. Concurrent treatment of L-NAME and pioglitazone decreased the ulcer index in BDL rats more than the groups that received L-NAME or pioglitazone alone.

Conclusion: We conclude that chronic treatment with pioglitazone exerts a potent gastroprotective effect on the stomach ulcers of cirrhotic rats probably due to inhibition of nitric oxide synthase.

PE516

Inhibition of Phosphodiesterase 5 - a Novel Therapeutic Strategy for Portal Hypertension

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Introduction: The NO–cyclic GMP system is a key factor in the regulation of splanchnic and hepatic blood flow and may be a target for medical treatment of portal hypertension. Clinical data have shown that inhibitors of phosphodiesterase 5 (PDE5) lower portal pressure in cirrhotics.

Methods: We monitored in rats the effects of the PDE5 inhibitors vardenafil and sildenafil on systemic and hepatic hemodynamic parameters up to 60 minutes after the drug. The drugs were administered intravenously into the tail vein at 1 (group A), 10 (group B), and 100 μg/kg body weight (group C). 0.9% NaCl was the control. N = 7 for each group.

Results: The most prominent changes were observed in the vardenafil B group: Mean arterial and portal venous pressure decreased (-9%, -8%), as well as portal venous, hepatic arterial, and systemic vascular resistance (-31%, -30%, -12%). Portal venous and sinusoidal flow increased (+31%, +13%). In the vardenafil C and sildenafil B and C groups there was an increase of portal venous flow by 20-30%, an increase of sinusoidal flow by 12-30%, and a decrease of portal venous resistance by about 25%. There was a trend for reduction of portal venous pressure.

Conclusions: Vardenafil and sildenafil influence portal hemodynamics in the rat. Portal venous flow increases by 20-30%, portal venous resistance decreases by >25%. Dependent on the dose, portal venous pressure decreases significantly. These data yield further evidence that PDE5 inhibitors may be a novel therapeutic option for portal hypertension.

PE517

Lethal Complications of Portal Hypertension in Different Etiologic Groups of Liver Cirrhosis

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Introduction: Rupture of esophageal varicose resulting in posthemorrhagic anemia is a common life-threatening complication of liver cirrhosis. But it is not clear, why the other patients, having the same degree of sclerosis and histologic activity index, die from hepatocellular failure or other reasons.

Aims & Methods: 3713 autopsy cases performed in Lviv regional hospital in 2004-2007 were analyzed. Screening of slides with liver tissue allow to select 580 cases (15,6%) with cirrhosis (complete and incomplete), which are examined in order to evaluate the frequency of lethal portal hypertension complications in the different etiologic groups of liver cirrhosis.

Results: According to the etiologic factor the following groups of liver cirrhosis were examined: alcoholic disease (49,8%), viral hepatitis (7,8%), nonalcoholic steatohepatitis (14,8%), secondary biliary cirrhosis (2,9%), cardiac sclerosis (0,9%), combined lesions (11,9%) and cryptogenic cirrhosis (11,9%). Analysis shows that in 287 cases (49,5%) patients die from cirrhotic complications (hepatocellular failure, jaundice, portal hypertension) and only in 105 cases (18,3%) - from posthemorrhagic anemia caused by rupture of esophageal varicose. In the latter cases correlation between the etiologic types of cirrhosis is almost the same, as in the main group and only alcoholic lesions (60%) and biliary cirrhosis (6,7%) are more frequent.

Conclusion: Analysis shows that development of lethal complications of portal hypertension can not be explained only by etiologic factor. Probably additional stimuli are more important for morphogenetical variants of cirrhotic transformation.

PE518

Frequency of Esophageal Varices and its Non-invasive Predictors in Patients with Viral Cirrhosis

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Background: Screening Esophago-gastro-duodenoscopy (EGD) is recommended for detection of esophageal varices (EV) in patients with cirrhosis due to its high prevalence. Repeated EGD is unpleasant and therefore non-invasive markers can be used to diagnose EV.
Aims and Objectives: To study the frequency of EV in patients with cirrhosis due to viral etiology and its correlation with different non-invasive markers.
Methods: Medical record of all patients with cirrhosis due to hepatitis B and C who underwent screening EGD for varices in last 2 years was reviewed. EV were divided in two grades (small and large) as proposed in Consensus Development workshop. Noninvasive markers such as spleen/platelets ratio, MELD and Child Turcotte Pugh (CTP) scores of all patients were recorded.
Results: Out of 360 patients, 226 (62.77%) were males. Out of 269(74.7%) patients who had EV, 177(65.79%) had small and 92(34.2%) had large EV. 222(82.5%) patients with EV have CTP score of ≥7. MELD score >15 and ≤ 15 were seen in 38.2% and 61.7% of patients with EV, respectively. Platelet/spleen ratio was 867.46±495 in patients with EV as compared to 1325.28±865 in patients without it ($p<0.001$). On multivariate analysis CTP score of ≥7 (OR 2.06, $p<0.01$), MELD score >15 (OR1.63, $p<0.05$) and platelet/spleen ratio ≤900(OR 2.35, $p=0.005$) were found as significant predictors of large EV.
Conclusion: The frequency of EV is high in viral cirrhosis patients on screening EGD. MELD score>15, CTP score≥7 and spleen/platelets ratio ≤900 can be used as non-invasive predictors of large EV.

PE519

Treatment Outcome and Prognostic Factors of Spontaneous Bacterial Peritonitis and Culture Negative Neutrocytic Ascites in Patients with Hepatitis B Virus-Related Cirrhosis

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Background/Aims: Ascitic fluid infection (AFI) consists of spontaneous bacterial peritonitis (SBP) and culture negative neutrocytic ascites (CNNA). This study compared the characteristics of SBP and CNNA in patients with hepatitis B virus (HBV)-related cirrhosis and investigated treatment outcome and prognostic factors for them.
Methods: The study retrospectively analyzed 130 patients who were diagnosed as having AFI for the first time from January 1998 to January 2008. The end of follow-up was October 2008.
Results: The mean age of the patients was 53.3 years (88 men and 42 women). Thirty-seven (28.5%) patients had SBP while 91 (71.5%) had CNNA. Except the higher proportion of renal failure at admission in patients with SBP than CNNA (32.4% vs. 7.5%, P=0.001), no significant difference in the clinical and laboratory data related to liver and renal function was observed. Overall mortality during hospitalization was higher in patient with SBP than that of CNNA (16.2% vs. 4.3%, P=0.031). However, no independent predictor for in-hospital mortality was found on multivariate logistic regression analysis. For 120 patients (92.3%) who survived from the first episode of AFI, the only independent prognostic factor was Child-Pugh grade [median survival; 20.8 (range, 0.4–128.1) in Child-Pugh A vs. 4.7 (range, 0.1–33.7) months in Child-Pugh B; P<0.001, log-rank test], not the culture positivity of ascitic fluid (P=0.752, log-rank test).
Conclusions: SBP shows a higher mortality than CNNA at the first episode in patients with HBV-related cirrhosis. Independent prognostic factor after recovery from the first episode was Child-Pugh grade.

PE520

Beta-Blocker is as Effective as Endoscopic Variceal Ligation (EVL) in Secondary Prophylaxis of Variceal Bleeding in Patients with Extra-Hepatic Portal Vein Obstruction

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Background: Role of beta-blocker (BB) therapy in prevention of variceal-rebleeding in patients with non-cirrhotic-portal-hypertension is not clear.We compared EVLwith BB therapy in prevention of variceal rebleeding in patients with extra-hepatic-portal-vein-obstruction (EHPVO).
Methods: Consecutive patients of EHPVO, with history of variceal bleed,were randomized to receive either EVLor propranolol(BB).EVL was repeated every 2-weeks till varicial eradication.BB dose was titrated to achieve a resting heart-rate of 55bpm or a maximum dose 320mg/d or when side-effects began to appear.Primary end-points were rebleed and death.Secondary end-points were complications as a result of EVLor beta-blocker,variceal recurrence afterEVL,and decrease in variceal grade inBB limb.
Results: 71 patients (median age 14[range2-68] yrs, males65%) were included (EVL arm[n=37]and BB arm[n=34]. Median grade of varices was III(range II to IV).Gastric varices and portal hypertensive gastropathy were present in 28(39%) and 29(41%), respectively.Baseline characteristics were comparable.Mean sessions needed to eradicate the varices were 6±2and mean dose of BB used was166±72 mg/d.After a median follow-up was 12(range 4-30)months the rebleeding rates were similar in the two arms(EVL 5/37[14%] versus BB 3/34[9%]; p=0.712).The actuarial probability of remaining free of rebleed was similar in two arms.There were no deaths.In 14(38%) patients in the EVL arm there was variceal recurrence which needed additional sessions of EVL.In 14(41%) patients in BB arm there was reduction in variceal size.Side-effects due to therapy were minor and comparable in the two arms (EVL 5/37[14%] versus BB 2/34[6%];p=0.432).
Conclusions: Beta-blocker is as effective asEVL in secondary prophylaxis of variceal bleeding in patients with EHPVO.

PE521

Nitric Oxide Synthase Isoforms Play Distinct Roles in the Evolution of Hyperdynamic State in Endotoxemia Induced Portal Hypertension

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Background and Aims: Increased nitric oxide (NO) production is incriminated in the pathogenesis of arterial vasodilation and hyperdynamic circulatory state in non cirrhotic models of portal hypertension (PHT). We investigated the relative roles of constitutive NOS (eNOS) and inducible NOS (iNOS) isoforms in the development of rabbit models of endotoxemia induced portal hypertension (EIPHT)
Methods: EIPHT was induced by chronic injection of lipopolysaccharide via an indwelling cannula placed in the gastrosplenic vein of rabbit and maintained for 6 months. The concentration of NO, expression of NOS (eNOS and iNOS) mRNA and protein was measured in EIPHT and sham operated control animals.
Results: Rabbits with EIPHT compared with controls had raised portal pressure (in mmHg-14.34±1.78 vs 6.30±0.60;$p<0.05$;1mo; 14.91±0.56 vs 7.04±0.42; $p<0.05$, 3mo; 19.8±3.10, vs 10.2±4.80;$p<0.05$), arterial hypotension (in mmHg-65.40±3.2 vs 80.04±1.40, $p<0.05$, 1mo; 62.90±5.40 vs 76.05±2.60,$p<0.05$, 3mo; 65.85±2.50 vs 79.1±5.10, $p<0.05$,6mo), splenomegaly (in g-0.92±0.14 vs 0.60±0.13,1mo; 0.90±0.16 vs 0.62±0.04, 3mo; 0.97±0.12 vs 0.67±0.07, 6mo), normal liver functions and preserved hepatic architecture at 1,3 and 6 mo. Serum levels of NO_2 as well as the NO_3 were significantly elevated in EIPHT rabbits as compared to the controls. The expression of eNOS, at the level of mRNA, was significantly increased in EIPHT rabbits consistent with increased levels of expression of iNOS as compared to the controls. The eNOS but not iNOS protein expression was elevated in EIPHT than control rabbits.
Conclusion: Vascular dysfunction in the splanchnic circulation during the development of endotoxemia induced portal hypertension is predominantly characterized by eNOS and partly by iNOS gene up-regulation.

PE522

Increased Percentage of Memory Regulatory T Cells in Patients with Decompensated Liver Cirrhosis Contributed to the Immunocompromised Status by Shedding the Membranous TNFRII

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Background & Aim: Patients with decompensated liver cirrhosis (DLC) were regarded as immunocompromised, reflected by high incidence of bacterial infection. Paradoxically, the proinflammatory cytokine like TNF- increased significantly in patients with DLC even in the face of this immunocompromised status. On the other hand, regulatory T cell (Treg cell) is believed to play an important role in inhibiting immune responses, including innate immune responses like blockade of TNF- effect through soluble TNFRII. Here, we studied the role of Treg cells and TNFRII in patients with decompensated liver cirrhosis.
Patients and Methods: 33 healthy volunteers and 78 cirrhotic patients were enrolled. The percentage of Treg cells were enumerated by flow and serum levels of IL-10, TGF- and TNF- by ELISA.
Results: The percentage of Treg cells increased significantly in patients with DLC associated with increased serum levels of IL-10 and TGF- . In addition, these Treg cells were mainly memory type reflected as high CD45RO. Furthermore, the TNFRII expression increased significantly on these Treg cells of DLC. Interestingly, these membranous TNFRII on Treg cells could be shed-off. Lastly, we found the serum soluble TNFRII concentration increased significantly in patients with DLC when compared with normal volunteers.
Conclusion: Our results demonstrated memory Treg cells with high TNFRII expression increased significantly in patients with decompensated liver cirrhosis that could possibly blocked the biological effect of TNF- by shedding membranous TNFRII and contributed to the immunocompromized status of DLC.

PE523

Liver Stiffness Correlates with Portal Pressure among Indian Patients with Portal Hypertension

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Background: Portal pressure measured as hepatic venous pressure gradient (HVPG) correlates with severity of portal hypertension and the development of complications. HVPG measurement is invasive. Recently, liver stiffness measurement has been shown to correlate with liver biopsy and helps predict outcome in chronic liver disease patients. This study was conducted with the aim to study the correlation between portal pressure as measured by HVPG and liver stiffness as measured by fibroscan among patients with portal hypertension due to various causes.
Methods: Between August and September 2008, consecutive patients with portal hypertension were included and were subjected to HVPG measurement and fibroscan (Echosens, France).
Results: Of the 18 patients with portal hypertension, both HVPG and liver stiffness were measurable in 12[9 (75%) males; mean age 37.5(10.6) years]. The etiological distribution was HBV related cirrhosis in 3 patients, HCV cirrhosis in 3, cryptogenic cirrhosis in 2, alcoholic cirrhosis in 2, HBV and alcoholic cirrhosis in 1and primary extra-hepatic portal vein obstruction in1. The mean HVPG and liver stiffness of this group were 13.9 (5.1) mm hg and 26.6 (16.5) kPa respectively. There was a strong positive correlation between HVPG and liver stiffness [r = 0.708; p = 0.01].
Conclusions: Non-invasive measurement of liver stiffness correlates well with invasive measurement of portal pressure. Liver stiffness measurement could be used as a prognostic indicator to predict the severity of portal hypertension.

PE524

Portal Biliopathy in Extra-hepatic Portal Vein Obstruction: A Progressive Disease!

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Background: Portal biliopathy is a well known and serious complication of portal hypertension,especially in patients with extra-hepatic portal vein obstruction(EHPVO).Its natural history has not been well described.We studied the clinical presentation,extent of involvement and long-term natural history of portal biliopathy inEHPVOpatients.
Methods: Endoscopic retrograde cholangiography(ERC) was performed in patients ofEHPVO who had bled from varices and had achieved variceal eradication.Biliopathy was classified according to Sarin et al(1992):only extra-hepatic involvement(type 1);only intra-hepatic(type 2);both intra and extra-hepatic involvement(type 3a[left],3b[right]).A secondERC was performed after two or more years to assess the progression of the disease.
Results: 79 EHPVO patients(median age 20[range 5-62]yr, males 67%) were studied.History of present or previous jaundice was present in 24%,ascites 18% and pain 9%. On ERC,92% had portal biliopathy.The type of bile duct involvement was categorized as: type 3 b(51%) and type 1(42%).The pattern of involvement included indentations(49%) and dilatation and strictures(36%).20%of the patients had bile duct stone and 9% had history of cholangitis.The mdian bilirubin was1.1(range0.3-15.9) mg/dl and median serum alkaline phosphatase 171(range 42-617) IU/L.All patients were treated endoscopically by endoscopic stone extraction, dilations with/without stenting. 24(30%) patients underwent second ERC after a median interval of 21(range 1-111)months.The type of involvement progressed,75% patients developed type-3 involvement compared to54% at the baseline (p=ns).Indentations progressed to develop strictures, from46% to71%.The frequency of new bile duct stones per year was 4%(p= ns).
Conclusions: Portal biliopathy is very common in EHPVO, often remaining asymptomatic.However,it is slowly progressive leading to development of biliary strictures.Bile duct stone formation is also common.

PE525

Role of Rho-Rock Pathways Induced By Angiotensin II in Hepatic Stellate Cell Contraction

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Objective: To investigate the mechanisms of angiotonin II (AngII)-induced Ca (2+)-independent pathways mediated by Rho kinase in hepatic stellate cells (HSCs).
Methods: HSC-T6 cells were treated with 1 micromol/L of AngII, and the subsequent cell contraction was directly observed with silicone rubber membrane culture method. The cells with 10 micromol/L AngII treatment were examined for myosin light chain (MLC) phosphorylation level using Western blotting, and the effects of irbesartan (a specific inhibitor of AngII 1- receptor) and Y27632 (a Rho kinase inhibitor) on AngII-induced MLC phosphorylation were evaluated. RT-PCR was used to detect the expression of Rock2 in Ca(2+)- independent pathways mediated by Rho kinase.
Results: The silicone-rubber-membrane covered by AngII treated HSCs showed obvious wrinkles indicating the contraction of HSCs. AngII induced HSC time-dependent MLC phosphorylation changes, which peaked 15 min after the treatment followed by gradual reduction. Irbesartan or Y27632 treatment significantly lowered MLC phosphorylation level in AngII-induced cells ($P<0.01$). The mRNA expression of Rock2 increased significantly after AngII treatment ($P<0.01$), but decreased following subsequent irbesartan or Y27632 treatment.
Conclusion: AngII induces HSC contraction through Ca(2+)-independent pathways mediated by Rho kinase.

PE526

Comparative Efficacy and Safety of 10-Days versus 5-Days Treatment with Terlipressin in Bleeding Esophageal Varices

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Background: Various vasoactive drugs that reduce portal pressure are used in treatment of esophageal variceal bleeding alongwith endoscopic treatment. Terlipressin use decreases both, recurrent bleeding and mortality. It is given usually for 3-5 days, nevertheless there is very little data comparing different time periods. Our aim was to compare the efficacy and safety of 5-days versus 10 days of terlipressin treatment in bleeding esophageal varices.
Methods: Out of 15 patients who presented with variceal bleeding, 8 were randomized to receive terlipressin 2 mg 8 hrly, i.v. daily for first 5 days and placebo for next 5 days (Group A) and 7 to receive terlipressin 2 mg 8 hrly, i.v. daily for 10 days (Group B). Both groups were both age and sex matched.

Endpoints were rate of rebleeding and mortality till day 30 after inclusion and to see for any adverse events.
Results: The bleeding was stopped in all 15 patients (100%). Rebleeding till day 30 was observed in 4 (26%) patients (2 each in group A and B). Total 2 patients (13%) died (1 each in both groups) due to rebleeding. Transfusion needs were higher in group A (4.2±2.8 versus 2.3±2.1, p<.05). Serious adverse effects leading to treatment discontinuation were not seen in any patients in both groups.
Conclusion: Prolonging terlipressin treatment did not confer any significant decrease of mortality or bleeding recurrence. However transfusion requirements were significantly decreased in patients receiving prolonged treatment. Serious adverse effects leading to treatment discontinuation are rare.

Poster Exhibition – Miscellaneous
Poster Session, Hall 5B

PE527

Very High Frequency of the P.H1069Q Mutation in ATP7B Gene of Lithuanian Patients with Hepatic Presentation of Wilson's Disease

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Background: It is important to know the prevalence of *ATP7B* gene mutations of different geographical areas to justify the local screening strategies for Wilson disease (WD).
Materials: Eleven unrelated Lithuanian families, including 13 WD patients were tested. Genomic DNA was extracted from whole venous blood using a salt precipitation method. Firstly, semi-nested PCR technique was used to detect the c.3207C>A (p.H1069Q) mutation. Patients not homozygous for c.3207C>A (p.H1069Q) mutation were further analyzed. The 21 exons of the WD gene were amplified in a thermal cycler. Direct sequencing of the amplified PCR products was performed by cycle sequencing using fluorescent dye terminators in an automatic sequencer.
Results: Total of 13 WD patients (mean age 26.4 years; range 17-40; male/female, 3/10) presented with hepatic disorders and 16 their first degree relatives were studied. Some of WD patients in addition to hepatic symptoms have had extrahepatic disorders (haemolytic anaemia 3; Fanconi syndrome 1; neurophsychiatric and behavioural disorder 2). Twelve of 13 (92.3%) WD patients have had c.3207C>A (p.H1069Q) mutation, 6 of them in both chromosomes, 5 were presented as compound heterozygotes with additional c.3472 – 82delGGTTTAACCAT, c.3402delC or c.3122G>A (p.R1041Q) mutation. For one patient with liver cirrhosis and psychiatric disorder no mutations were found. Out of 16 first degree WD relatives 11 (68.7%) were heterozygous for c.3207C>A (p.H1069Q) mutation.
Conclusion: c.3207C>A (p.H1069Q) missense mutation is characteristic for Lithuanian WD patients. Even 92.3% of WD patients with hepatic presentation of the disease are homozygous or compound heterozygote for this mutation.

PE528

The Relationship between Glutamic-Pyruvic Transaminase (GPT) And High-Density Lipoprotein Cholesterol (HDL-C) Among Diabetic Patients In Taiwan

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Background: Diabetic dyslipidemia is a crucial problem of diabetic patients with inadequate control. We investigated the relationship between glutamic-pyruvic transaminase (GPT) and high-density lipoprotein cholesterol (HDL-C) in diabetic patients.
Methods: With informed consents, we recruited outpatients with diabetes at a hospital in rural area in Taiwan in 2004-2007. Anthropometric measures, blood tests and urine screening were examined in diabetic patients.
Results: Overall, there were 1241 diabetic patients aged 19-91 years enrolled in this study and 660 (53.2%) of them had low HDL-C. Diabetic patients with the highest quintile of GPT had higher average of body mass index (p<0.0001), diastolic blood pressure (p = 0.003), but lower average of HDL-C (p<0.0001) compared with diabetic patients with the lowest quintile of GPT. The prevalence of obesity (45.7% vs. 24.8%, p<0.0001) and low HDL-C (64.6% vs. 48.3%, p<0.0001) were higher in diabetic patients with highest quintile of GPT than in diabetic patients with lowest quintile of GPT. In the multivariate logistic regression, diabetic patients with highest quintile of GPT had higher odds ratio (OR) of low HDL-C compared with diabetic patients with lowest quintile of GPT (OR = 1.88, 95% confidence interval [CI] = 1.21-2.92). The corresponding OR of low HDL-C in patients aged 70 years and older was 3.30 (95% CI = 1.15-9.47).
Conclusion: High GPT is one of factors associated with low HDL-C in diabetic patients.

PE529

The Effect of Desferrioxamine as supplement to Cefotaxime in the Treatment of Spontaneous Bacterial Peritonitis

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Background: Oxidative damage lead to cell damage, organ dysfunction and death in sepsis. Desferrioxamine (DFX), an antioxidant iron Chelators. The aim was to assess the efficacy of Desferrioxamine supplemented to Cefotaxime in the treatment of Spontaneous Bacterial Peritonitis (SBP) in cirrhotic patients.
Methods: thirty patients divided into two groups: Group I (n=15) with SBP and receiving Cefotaxime (1g IV every12 hours) alone and Group II (n=15) with SBP receiving Cefotaxime (1g IV every 12 hours) with desferrioxamine (500mg IM twice daily).All patient were monitored for seven days, their vital organs were screened and their ascitic fluid was assessed completely including microbiological investigations.
Results: The concomitant administration of Desferrioxamine with Cefotaxime significantly at (p<0.001)and(p<0.01) improved the therapeutic outcome and the cure rate after 5 days of treatment as compared to patients using cefotaxime only.
Conclusions: Desferrioxamine can improve the therapeutic outcome by preventing iron-induced organ damage and inhibiting bacterial growth.

PE530

Septicemia Caused by Oligella Ureolytica in a Patient with Decompensated Cirrhosis

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Oligella ureolytica is a gram-negative, nonfermenting rod that is infrequently recovered from clinical specimens and is most commonly isolated from the urine of patients with chronic indwelling urinary catheters or other urinary drainage systems. Bacteremia due to this organism is an extraordinary finding. We describe here a case of *Oligella ureolytica* being detected in the blood of a patient with decompensated cirrhosis. A 51-year-old male man was admitted to hospital with 9-month duration of debility, poor appetite and abdominal distension. Decompensated cirrhosis was diagnosed based on clinical findings such as hepatic face, ascites, edema of lower limbs and icteric sclera. Laboratory results showed positive serum anti-HCV and high serum HCV RNA level. The patient received a therapeutic regimen of pegylated interferon alpha 2a plus ribavirin after being admitted to hospital. During hospital stay, a fever of 2-day duration with shivering occurred to the patient. Three blood cultures were drawn, which all grew *Oligella ureolytica* in pure culture. The organism was identified by the Viteck 2 Compact (Biomerieux, France). Additional tests for identification resulted positive for nitrate reduction and urea hydrolysis, strongly positive for phenylalaninedeaminase activity and showed no growth at 42.7C. Tests for nitrite reduction and motility resulted negative. The organism was resistant to amikacin, cefoperazone, levofloxacin, piperacillin/tazobactam, trimethoprimsulfamethoxazole, aztreonam, cefotaxime, piperacillin and was susceptible to gentamicin, imipenem, meropenem, and netilmicin. A 14-day of combined therapeutic regimen with cefminox and isepamicin was administered to the patient. Within 2 days, the patient became afebrile.

PE531

Endoscopic Ultrasound Guided Liver Biopsy: Feasibility and Efficacy in a Porcine Model

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Background: Endoscopic ultrasound (EUS) is often performed in patients with unexplained liver tests to assess the gallbladder, bile ducts and pancreas. An unremarkable EUS exam and negative hepatology workup often leads to a liver biopsy. EUS may provide histopathologic evaluation of the liver in these cases under direct, real-time visualization. Aim: To assess the feasibility and efficacy of EUS guided core biopsy of the liver in a porcine model.
Methods: Female pigs were used and live procedures were performed under general anesthesia. A linear echoendoscope was used and the liver identified endosonographically. Transgastric core biopsies of the liver were obtained with a 19 gauge Quick-Core ultrasound biopsy needle (Wilson-Cook) and sent for histopathologic evaluation. Live animals were euthanized at the end of the procedure and necropsy performed.
Results: Core biopsies of the liver biopsy were obtained in 4 animals (1 cadaver and 3 live anesthetized). A total of thirteen needle passes were made (mean 3.25; range 2 - 4 needle passes per animal) and a visible core of tissue obtained. The maximum length of liver tissue obtained was 10 mm and considered adequate for assessment as more than one such specimen could be obtained. Microscopic evaluation confirmed liver tissue. No complications were noted. Necropsy did not show any evidence of bleeding, perforation or damage to surrounding structures.
Conclusion: EUS-guided liver biopsy is feasible and can be performed at the time of routine echoendoscopic exam in select patients undergoing EUS examination for abnormal liver tests.

PE532

The Level of ALT, AST and PLT in Blood in the Normal Population of North-East China

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Background: As the common indexes, ALT, AST and PLT play an important role in disease diagnosis, treatment and prognosis. Many researchers suggested that there was inflammatory changes and fibrosis in chronic hepatitis B and C patients whose ALT level was persistently normal. A large sample investigation showed that the serum level of ALT in healthy persons is lower than the normal reference value. This study re-evaluated the normal serum level of ALT, AST and PLT.
Methods: 3815 people were enrolled in the study between Sep. and Oct. 2007. The platelet count and serum ALT and AST levels were measured. Frequencies, One-Sample Kolmogorov-Smirnov test and nonparametric tests were used to analyze the difference between age groups, male and female, glucose groups, cholesterol groups and triglyceride groups.
Result: In the five groups, there is significant difference in ALT and AST levels between male and female. In group 1, the ALT and AST levels showed a significant difference between different age groups, between different glucose groups and triglycide groups. In the three groups the PLT level is significantly different between male and female, and the serum level in male is higher than female. There is significant difference between different age groups
Conclusion: The serum levels of ALT, AST and PLT are all significantly different between male and femal. There is significant difference between different genders and age groups for PLT. The serum level of PLT is higher than the reference value.

PE533

Presence of JAK2V617F Mutation in Idiopathic Splanchnic Venous Thrombosis

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Background/aims: Myeloproliferative disorders (MPD) (like polycythemia vera, essential thrombocythemia and primary myelofibrosis) are responsible for 50% cases of hepatic venous thrombosis (HVT) and 35% of portal venous thrombosis (PVT) in western series. Latent form of MPD lacks the characteristic blood picture and may be classified as idiopathic thrombotic disorder. A point mutation at Val617Phe of Janus kinase 2 tyrosine kinase gene ($JAK2^{V617F}$ mutation) occurs in high proportion of the patients with MPD. This non-invasive test with high positive predictive value is now considered to be essential for diagnosis of various MPD. This test may be useful in diagnosing latent form of MPD in splanchnic venous thrombosis (SVT) {consisting of HVT and PVT}. There is no such data from India.
Methods: All the adult patients (more than 25 years of age) with diagnosis of idiopathic SVT were checked for presence of $JAK2^{V617F}$ mutation by allele specific polymerase chain reaction.
Results: In 19 patients with idiopathic SVT, HVT was present in 10 and PVT was present in 9 patients. $JAK2^{V617F}$ mutation was present in 11/ 19 (57%) patients of idiopathic SVT. $JAK2^{V617F}$ mutation was statistically more common in HVT {7/10 (70%) patients} than in PVT {4/9 (44%) patients}.
Conclusions: $JAK2^{V617F}$ mutation occurs in high frequency in patients with idiopathic SVT. All the idiopathic SVT must be screened for $JAK2^{V617F}$ mutation to detect latent MPD. $JAK2^{V617F}$ mutation seems to be more common in HVT than in PVT.

PE534

A Comparative Study of Male vs. Female Upper G.I. Endoscopic Lesions in a Small G.I. Clinic in Rural India

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Background: Mucosal lesions are frequently observed.Gender differences are expected due to food habits, nature of job, mobility related to work, consumption of alcohol, tobacco etc.
Material and Methods: Procedure done in 1395(2007-2008) by endoscopist
Result: 1395 included, muscular inflammation 1096, 646(77.2%) M & 450(80.6%)F.& significant lesions 299, 191(22.8%) M & 108(90.4%) F .Hiatus 24, Complicated /uncomplicated hernia 9/5 (1.67%) in M & 7/3(1.79%) in F.Inflammatory nodule in 5 in duo 2 M & 2 F & stomach 1 M Esophageal stricture 7, 4 M & 3 F .Foreign body 5, 4 F &1 F.Ulcer(67) eso ulcer 7(.83%) M & 4 (0.71%)F. Gastric ulcer 6 (.71%) M & 6(1.07%) F & Duo ulcer 22(2.32%) M & 12(2.15%)F.Erosion 159 eso erosion 14(1.67%)M & 9 (1.61%) F & gastric erosion in 37 (4.4%) M & 19(3.4%) F& duo 48(5.73%) M & 32 (6.73%)F.Varices (48) eso varices 31 (4.3%) M &10(1.8%) F & Gastric varices 1 (.11%) M & 1(.11%) F .Growth (17)Eso growth 5 (.59%) M &1(.17%) F & Stomach growth 9(1.07%)M & 1(.17%) F & Laryngeal 1(.11%)M. Eso Monoliasis (7) 3(.35%) M & 4(.71%) F.Polyp (8) Eso polyp 4(.47%) M & 1(.17%) F & Gastric polyp 1(.11%)M & 1(.17%) F & Duo 1(.17%)F.
Conclusion: Gender differences in G.I. problems are expected due to - Different sex, harmone, Dietary, Stress, Mobility , Pregnancy etc..
Moniliasis and ulcers are more common in female.
Polyps , malignant lesions of oeso. & stomach, varices, gastric erosions are more common in male.

PE535

Complication of the Pyogenic Liver Abscess: Analysis of the Predictive Factors

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Background/Aims: Although the pyogenic liver abscess is a common intraabdominal inflammatory disease, this complications are not rare. However, reports dealing with this complications are not good enough and results are often variable. The aim of this study was to identify the predictive factors of complication in the pyogenic liver abscess.

Methods: 232 patients with confirmed pyogenic liver abscesses admitted from 1995 to 2007 in our institution were included. There were 145 men and 87 women ranging in age from 19 to 91 years. The medical records were reviewed for clinical, laboratory and radiographic characteristics.
Results: Among 232 patients, 81 (34.9%) experienced at least one complication. There were 67 pulmonary (pleural effusion, pneumonia, empyema) complications, 16 septic shock, 12 acute renal failure, 2 abscess rupture, 2 pseudomembranous colitis, and 2 pericardial effusion. The predictive factors for its complications were: systemic inflammatory response syndrome (SIRS, ≥2 factors), thrombocytopenia (≤80,000/mL), hypoalbuminemia (≤3.0g/dL), elevated AST or ALT (>200 IU/L), hyperbilirubinemia (> 2.0 mg/dL), *K. pneumonia*, air within abscess cavity ($p<0.05$).
Conclusions: The incidence of complications in the pyogenic liver abscess was 34.9%. The various predictive factors of complication should be monitored carefully. Further large scaled study should be warranted.

PE536

The Status and Significance of Hepatic Iron Deposition in the Korean Patients with Chronic Hepatitis C

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Background/Aims: Hepatic iron deposition is a common feature in chronic hepatitis C (CH-C), however, whether it could enhance the progression of fibrosis or not is controversial. The aim of this study was to evaluate the status and significance of hepatic iron deposition in the Korean patients with chronic hepatitis C.
Methods: Untreated, 78 CH-C patients who underwent liver biopsy were included. The hepatic iron was assessed by Scheuer's scoring system, and activity, fibrosis, and steatosis were scored by a pathologist in a blind manner to the clinical features. Clinical and laboratory data including serum iron indices, virological, biochemical results were analyzed to search for significant factors associated with hepatic iron deposition.
Results: Hepatic iron staining was positive in 26(33%). Among 26 patients with hepatic iron deposition, serum levels of ferritin (p=0.005) and α-fetoprotein (p=0.002), and body mass index(BMI) (p=0.039) were significantly elevated. There was no significant association between the degree of hepatic iron deposition and fibrosis stage (p=0.321), although elevated levels of serum hyaluronic acid (p=0.049), γ-Glutamyl transpeptidase (p=0.028), and prothrombin time (p=0.012) were associated with advanced fibrosis.
Conclusions: Hepatic iron deposition in Asian-Pacific CH-C patients seemed to be neither frequent nor related to hepatic fibrosis, but related to obesity. Therefore, phlebotomy might not commonly applicable to this area. Further studies on the pathogenic role of iron in CH-C in Asian-Pacific countries are warranted.

PE537

Human Hepatic Epithelial Progenitor cell transplantation to the patients with End stage Liver cirrhosis

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A late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture, necrosis of hepatocytes and the formation of regenerative nodules contributes to cirrhosis. Limitations like organ donors shortage, high cost, absence of proliferation in cultured hepatocytes, inherent risks of infection, rejection in xenogenic cells and other socio-economical complications emerges advanced regenerative Human hepatic stem cells(hHpSCs) transplantation. hHpSCs are located in the ductal plates in fetal and Canals of Hering in adult livers[Schmelzer et al.(2006)]. Hepatoblasts, in turn, give rise to the hepatocytic and biliary lineages, the hepatocytes and cholangiocytes[SchmelzerE etal(2006)].hHpSCs express CD326(EpCAM)marker. Scjelzer etal demonstrated that during embryogenesis 90% of the EpCAM positive cells had hepatoblast phenotype. In animal study, on transplantation of freshly isolated hHpSCs in SCID mice results in mature liver tissue expressing human-specific proteins. Recently, we(Aleem etal 2008)have shown clinical improvement in study in patients with Crigler-Najjar syndrome, Biliary atresia using hHpSCs infusion. In the present study we transplanted hepatic progenitors to five subjects of end stage liver cirrhosis with MELD score >30. hHpSCs were sorted using MACS with CD326 antibody microbeads and infused through hepatic artery via femoral artery catheterization, a safe procedure provided portal pressure to monitor cell infusion route in order to prevent vascular thrombosis. All the patients showed improvement clinical and functional biochemical parameters after first month of cell infusion. Ascites was decreased and changed Encephalopathy grade into normal level was observed. MELD score system falling to normal level from >30 to <22 after infusion.

PE538

Effects of Saikosaponinsd (Ssd) on Expression of C-Myc and PCNA in Experimental Hepatocarcinoma of Rats

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Objective: To study the possible mechanismsm of inhibiting tumor generation of saikosaponinsd (SSd) on rat hepatoma induced by diethylnitrosamine (DEN).
Methods: Ninety SD male rats were randomly divided into 5 group: normal control group、model control group and 3 different dosages（1.0,1.5 and2.0mg/kg）ssd intervention groups.Besides normal control group10, there were20 rats in other 4 groups. Model control group and intervention groups were traded with 0.2% DEN, In the meantime ,the intervention groups were administered intraperitoneally with ssd at the different doses once a day for 16 weeks.All rats were killed in the 18th week, then general conditions of rats were recorded, the serum ALT、AKP、*GGT*、AFU was detected and pathological examination was made. The expression of PCNA and c-myc were tested by immunohistochemistry.
Results: HE staining showed that rats were induced to hepatocellular carcinoma,The results of liver function in the 18th week displayed that ALT、AKP、*G*GT and AFU of all groups were increased than that of normal control group ($P < 0.01$), the 3（1.0,1.5 and2.0mg/kg）doses of SSd intervention groups can alleviate liver injury ($P<0.05$).The expression of PCNA and c-myc gene in the liver tissue of the ssd intervention groups were lower than those in the model ($P<0.05$).
Conclusion: SSd can inhibit development of hepatoma induced by DEN, possibly by down-regulating the expression of PCNA and c-myc protein.

PE539

Protective Efficacy of Polyenylphosphatidylcholine for Endotoxin-Induced Rat Liver Injury

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Background: To investigate the efficacy of polyenylphosphatidylcholine (PPC) for liver injury in a lethal endotoxic rat model.
Methods: 50 healthy male Wista rats were distributed into 4 randomized groups: Normal Blank (NS) and PPC Control (PPC), each 10; and Endotxin Injury Group (LPS) and PPC Protection Group (P+L), each 15. Lethal endotoxic shock was induced by single endotoxin (E.coli) 6mg/kg injection into abdominal cavity. PPC in 5% GS was given via tail vein at 1ml/100g (232.5mg/kg) 24h and 6h before endotoxin. Rats' behavior and 24h survival were recorded, venous blood taken for AST and ALT, liver preserved for HE staining and liver/body weight ratio（L/B）and liver wet/dry weight ratio (W/D) calculated. Intercellular adhesion molecule-1 (ICAM-1) expression in liver tissue was observed with 2-step immunohistochemistry assay.
Results: Rats of NS and PPC group demonstrated similar normal activity, histology and other characters ($P>0.05$), while LPS Group showed sag and less water-intak and severe inflammation in liver including inflammatory cell accumulation, parenchymal cells edema and tissue exudation. P+L Group turned tired but could drink water. P+L Group was between the two. Its

mortality was significantly lower than LPS Group (6.67% vs 46.67%, *P*=0.035), similar were other parameters such as L/B (4.09±0.28 vs 4.50±0.25, *P*=0.001), W/D (3.52±0.27 vs 3.84±0.18, *P*=0.004), AST (53.21±13.85 vs 85.25±18.91, *P*<0.001), ALT (157.71±32.63 vs 225.63±32.63, *P*=0.001) and tissue ICAM-1 positive expression rate (87.50% vs 35.71%, *P*=0.031).

Conclusion: PPC intravenous injection before endotoxin results in suppressed liver ICAM-1 expression, decreased edema, exudation and cell accumulation and therefore keep a relatively better liver function and lower mortality as well. Application of PPC in our rat endotoxin model was safe and reliable, suggesting its potential value in the treatment of sepsis which needs to be further investigated.

PE540

Co-Expression of Treg, Th17, DC and Ifnc Releasing Cells in Peripheral Blood Mononuclare Cells and Their Contribution to Chronic Hepatitis B Patients

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Background: How Treg and Th17 being regulated and effect from each other in CHB is unknown. Dendritic cells are believed to play an important role in the regulatory net work. A longitudinal study was carried out to investigate the correlation among Treg, Th17, IFN-gamma releasing cells and DCs.

Method: PBMCs of 8 active CHB patients under pyg-interferon treatment were analyzed for their Th17, Treg and pDC by flow cytometry. They were determined by CD4/IL-17 for Th-17, CD4/CD25/Foxp3 for Treg and CD123/CD86/CD14- for pDC. PBMC were collected every 4 weekly during the treatment until end of therapy (week 48) and every 12 weekly until the end of follow-up (week 72). ALT was quantified at every time of the PBMC collection. IFN-gamma release cells were analyzed by ELIspot to HBv-core and S Ag.

Results: In parallel with decline in ALT for the first 12 weeks, we found decline in both pDC (R=0.71, p=0.03) and ELIspot (R=0.65, P=0.03 for HBV-core Ag; R=0.48, P=0.05 for HBV-S Ag). Although there is trend that Th-17 decline with Treg decline, but they are not statistically significant differences in the same period. There is no significant difference between the SVP and non-SVP patients.

Conclusions: Under Pegyintron treatment, pDC, IFN-gamma change in the same trend of ALT during 12 weeks of treatment. It implied that pDC take regulatory effects on IFN-gamma releasing cells and be very tightly related to ALT. There wasn't a significant difference in both Treg and Th-17, which implies that Treg and Th17 might be of important cells in keeping the stability of the immune system.

PE541

MYD88 Dependent Signaling Pathway Behaves Different Functions between Nfkb and AP1 in Chronic Hepatitis Patients

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Background and aims: It was reported that most of TLRs behave their function through MYD88 dependent pathway, there still remains unclear in CHB. We first investigate the expression of TLRs related MYD88 dependent signaling molecules in PBMCs of different CHB patients.

Method: 96 CHB patients were divided into 5 groups according to their HBeAg, HBsAg and ALT. After the PBMCs were incubated with HBcAg, mRNA expression of MYD88 signaling molecules was tested by semi-quantative PCR. Th1/Th2 cytokines level in the culture medium was examined by FlowCytomix multiplex Assay and ELISA.

Results: Signal molecules mRNA level are shown in the Table 1 (** P<0.01, * P<0.05). TNFa, IL1, IL6 and IL8 were higher in group 1, 2 and 4 than those in group 5. IFNa was higher in group 5 than that in other groups. There are no significant difference in INFc, IL2, and IL4. There was a positive correlation between TNF and MYD88 in group 2, TNF and NFkB in group1 and 2.

Conclusions: TRIF and AP1 are the most important molecules in TLRs mediated antiviral immunity, whereas MYD88 and NFkB take more effect in pro-inflammatory response.

Group	Determine	MYD88	TRIF	TRAF6	AP1	IRF3	NFkB
1	HBsAg+/HBeAg+/ALT-normal	4.21±2.33	0.41±0.36**	1.05±0.35	0.65±0.83*	1.15±0.33	4.69±4.03
2	HBsAg+/HBeAg+/ALT-high	2.75±1.57	0.27±0.18**	1.07±0.23	0.44±0.50*	0.92±0.42	6.44±6.42
3	HBsAg+/HBeAg-/ALT-normal	3.15±2.34	0.42±0.36**	1.08±0.34*	0.04±0.05**	0.88±0.41	1.91±1.56*
4	HBsAg+/HBeAg-/ALT-high	2.01±1.33*	0.44±0.39**	1.24±0.23	0.73±0.64*	0.09±0.26*	1.62±1.39*
5	HBsAg-/HBeAg-/ALT-normal	0.91±0.28**	6.58±6.17	1.26±0.20	1.57±1.58	1.14±0.44	0.17±0.09*

PE542

Identification of Single Nucleotide Polymorphisms (SNPs) in the human Alpha-fetoprotein (AFP) gene

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Background: Alpha Fetoprotein (AFP) is a well-recognized tumor marker for HCC; elevated level of AFP is found in at least 70% of HCC. Other liver diseases such as cirrhosis and chronic hepatitis are also related with an elevated level of AFP. The regulation of *AFP* gene expression has been relatively less studied although the gene has been suggested to play a role in HCC development. In this study, we tried to identify genetic variations in *AFP* gene and analyze its effect on serum AFP level and possible HCC progression.

Methods: Direct DNA sequencing was carried out to sequence *AFP* promoter and 500 bp upstream and downstream of *AFP* coding regions in DNA samples isolated from 99 HCC subjects and 105 controls respectively. For each samples serum AFP levels were determined using commercially available ELISA Kits.

Results: A total of 30 SNPs were detected in the *AFP* genomic region analyzed, including 29 known SNPs and one novel SNP. Among the identified SNPs, the C>G nucleotide change in the position -250 bp upstream of AFP transcriptional start site showed a significant association with HCC ($p < 0.05$) and a decrease in AFP gene expression level.

Conclusion: Our preliminary results indicated a possible association between serum AFP expression and -205G allele. The identified SNP is located in *AFP* promoter region with possible binding sites for known transcription factors, such as TFIID, COUP, APF and NFIII.

PE543

Effects of Simulated Weightlessness on Tissue Structure and the AR and HSP70 Expression in Testicle of Rat

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-30°tail-suspension (TS) rats were used as the model to simulate the physiological effects of weightlessness. Thirty-two Wistar male rats were randomly divided into 4 groups: control for 7d (7d CON), 14d CON, TS for 7 d (TS7d) and TS14d. Histopathological changes of testicle of the rat were observed by HE stain. Localization and expression of AR and HSP70 in testicle of rat were observed comparatively by means of immuno-histochemistry, and the density of AR and HSP70 immunoreactivety in four groups were compared.

Results: Obvious pathological lesions presented in testicle of TS7d and TS14d rat. Germinal epithelium irregularity and malformed spermatozoa were found in seminiferous tubules. Degeneration and necrosis of Germinal epithelium appeared in testicle of TS7d and TS14d rat. AR immunoreactive

cell density in the TS7d and TS14d groups were significantly decreased compared with the in-phase normal control groups ($P < 0.01$). While HSP70 immunoreactive cell density in the TS7d and TS14d rats were significantly increased than those of control rats($P < 0.01$), and in testicular interstice or extracellular there were very strong eHSP70 immunoreactive positive staining signals. The results indicate that ground simulated weightlessness induced by 7d-14d tail-suspension in rats can lead to the serious injury , depressed expression of AR and enhanced expression of HSP70 in testicle.

PE544

Treatment of Chronic Hepatitis B (CHB) Patients with Normal Alanine Aminotransferase Level Using Nucleoside Analogues: A Preliminary Study with Results at 1 Year

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Background: Chronic hepatitis B (CHB) patients with high serum HBV-DNA and normal serum alanine aminotransferase (ALT) levels might be considered for treatment if histopathological findings show fibrosis stage 2 or more. However, to our knowledge there is no recommendation with regard to the therapeutic agents for this group of patients.

Objective: This study was aimed to evaluate the efficacy of nucleoside analogues (entecavir or telbivudine) in treating chronic hepatitis B patients with high serum HBV-DNA and normal serum ALT levels.

Patients and method: This was an open-label study in CHB patients with high level serum HBV-DNA levels between January 2007 and October 2008. Patients were included if they showed normal serum alanine aminotransferase (ALT) level at two measurements within a 3-month interval and had fibrosis stage ≥ 2 on liver biopsy specimens. Patients were treated with entecavir 0.5 mg/day or telbivudine 600 mg/day. The primary endpoint was the reduction or undetectable of serum HBV-DNA at 24 week and 48 week of treatment, while the secondary endpoint was hepatitis B e antigen (HBeAg) seroconversion.

Results: During a 2-year period, 37 CHB patients with high level serum HBV-DNA with normal ALT two times with 3 months interval underwent a liver biopsy. Twenty-eight (75.7%) of 37 pts showed fibrosis stage ≥ 2 on histological findings (Metavir score). Twelve of these 28 patients received nucleoside analogues, 7 (58.3%) of them were men. Patients' median age was 42 (range: 24-52) years. There were 5 patients with stage-2, 6 patients with stage-3 and 1 patient with stage-4 fibrosis. Eleven (91.7%) patients had genotype B virus. At baseline, the mean serum ALT level was 32 ± 11.8 U/L and mean HBV-DNA level was 2.48×10^6 IU/mL, ranging from 1.23×10^3 to 2.4×10^7 IU/mL. Six patients received entecavir and the other six received telbivudine therapy. Undetectable HBV-DNA was achieved by 9 (75.0%) patients at week-24 and 2 (16.7%) patients at week-48 of treatment. One patient who had the highest HBV-DNA level had viral load reduction to 1.6×10^4 IU/mL at week-48 of treatment. Two out of 5 patients with positive HBeAg achieved HBeAg seroconversion at week-48 of treatment.

PE545

Identification of Downstream Targets of Homeoprotein Six1 in Hepatocellular Carcinoma

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We previously demonstrated that overexpression of homeoprotein Six1 in hepatocellular carcinoma (HCC) patents is associated with venous infiltration, later pathologic tumor metastasis (pTNM) stage and poor overall survival rate. Moreover, down-regulation of Six1 expression in metastatic HCC cell line MHCC97L resulted in suppression of its in vitro and in vivo proliferation ability and metastatic potential. In this study, we identified the downstream targets of Six1 by cDNA microarray approach aiming to understand its regulation mechanism in HCC. We established a stable transfectant MHCC97L-shSix1 carrying Six1 specific shRNA plasmid that exhibited down-regulation of Six1 expression to about 40% of the control MHCC97L-Control cell line. cDNA microarray was employed to compare the expression profiles of MHCC97L-Control and MHCC97L-shSix1 cells. From that, 28 down-regulated and 24 up-regulated genes with known functions were identified in MHCC97L-shSix1. The functions of these target genes are involved in diverse biological and oncogenic activities. The expression of five down-regulated genes YWHAH, MAPKAP, CD46, CAMK2N1 and PGRMC1 in HCC patients were analyzed by SYBR Green real-time semi-quantitative RT-PCR. The result showed that YWHAH and CD46 were overexpressed in 73% and 76% respectively in liver tumor tissues of HCC patients compared with nontumor tissues. Overexpression of YWHAH mRNA in tumor tissues of HCC patients was significantly associated with Six1 mRNA overexpression, suggesting that YWHAH may be a downstream target of Six1. Our study suggested that homeoprotein Six1 can transcriptionally activate a various genes that may contribute to tumorigenesis and metastasis of HCC.

Conclusion: This preliminary study has shown that nucleoside analogues might be considered in the treatment for chronic hepatitis B patients with high serum HBV-DNA and normal serum aminotransferases levels.

PE546

Occult Hepatitis B Virus Reinfection after Liver Transplantation despite Nucleoside Analogues Prophylaxis

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Background and Aim: Clearance of serum hepatitis B surface antigen (HBsAg) in patients with chronic hepatitis B virus (HBV) infection can be achieved after liver transplantation with nucleoside analogues prophylaxis. Despite the absence of any serologic marker of HBV recurrence, however, it remains unknown whether there is occult reinfection in the liver graft. We aimed to detect and quantify the presence of intrahepatic HBV DNA in the liver grafts of patients who remain seronegative for HBsAg for more than 1 year after liver transplantation.

Materials and Methods: Liver biopsy and blood samples were obtained from 31 patients who had been receiving nucleoside analogue prophylaxis alone and remained persistently seronegative for HBsAg for at least 1 year (median 44.5 months, range 13.6 to 126.4 months) after liver transplantation for chronic hepatitis B. Quantitative polymerase chain reaction was performed to detect and quantify total and covalently-closed circular (ccc) HBV DNA in the liver (lowest detection limit, 10 copies/mL), serum and PBMC. Direct sequencing was used for HBV quasispecies screening.

Results: Liver biopsy was performed and intrahepatic HBV DNA as measured by quantitative real-time PCR was detectable in 26 of 31 recipients. Donors anti-HBc status before liver transplant was significantly related to the presence of intrahepatic HBV DNA in the recipient's study biopsy (p=0.038). Donor intrahepatic HBV cccDNA levels correlated with recipient post-liver transplant intrahepatic HBV cccDNA levels (p=0.004). Hepatitis B virus sequencing results and phylogenetic analysis revealed that HBV reinfection in two recipients were of donor origin, four recipients were of recipient origin and four recipients were of both donor and recipient origins.

Conclusions: Our findings demonstrate the presence of occult HBV reinfection with persistence of HBV DNA in liver allografts despite long term nucleoside analogue prophylaxis after liver transplantation, suggesting the need to continue indefinite antiviral therapy. The use of liver grafts from anti-HBc-positive donors might increase the risk of occult HBV reinfection. Both donor and recipient HBV DNA could contribute to occult HBV reinfection in liver transplant recipients.

PE547

Noninvasive Assessment of Liver Fibrosis by Combination of Serum Aminotransferase/platelet Ratio Index (APRI) and Hyaluronic Acid in Chronic Hepatitis B Virus Infection

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Aim: To construct one noninvasive assessment model consisting of routine laboratory data to predict both significant fibrosis and cirrhosis among patients with chronic hepatitis B(CHB).

Methods: We have retrospective analyzed 137 consecutive patients with chronic hepatitis B who underwent percutaneous liver biopsy. We calculated sensitivity, specificity, positive predictive value(PPV), and negative predictive value(NPV) of an APRI ≥ 1.5 in combination with different Hyaluronic acid(HA) cut-off points

Results: This study showed that APRI correlate with fibrosis stage in HBV

patients. The APRI of ≥1.5 in combination with a cut-off HA of >300 ng/ml can best detect patients with moderate to severe fibrosis (stages 2-4). It has a PPV of 93.7%. Also, for patients without moderate to severe fibrosis, the test is hardly ever positive (specificity of 98.9%). But the APRI of <1.5 in combination with different HA as cut-off points is not possible to detect patients with no or mild fibrosis.
Conclusion: The APRI of ≥1.5 in combination with HA >300 ng/ml as cut-off points to predict patients with moderate to severe fibrosis (stages 2-4) is an easy and accurate method.

	ETV 0.5mg n=118	ETV 1mg n=41	Total Group n=159
Baseline HBV DNA*	6.4±1.7	6.1±1.7	6.3±1.7
Median follow-up (mth)	10 [3-23]	13 [3-31]	11 [3-31]
HBV DNA decline*	4.2±1.7	3.4±1.9	4.0±1.8
HBV DNA < 80 IU/mL	85/118 (72%)	23/41 (56%)	108/159 (68%)
Virologic breakthrough	2/118 (2%)	6/41 (15%)	8/159 (5%)
Genotypic resistance	0/118 (0%)	4/41 (10%)	4/159 (3%)
ALT normalization	66/92 (72%)	16/26 (65%)	82/118 (69%)
HBeAg loss	5/38 (13%)	2/30 (7%)	7/68 (10%)
HBsAg loss	0/118 (0%)	0/41 (0%)	0/159 (0%)

* $\log_{10}$ IU/mL

PE549
Outcome of patients with gastro-oesophageal bleeding in a tertiary center
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Objectives: To determine the rebleeding rate, mortality and long term survival in cirrhotic patients presented with acute gastro-oesophageal variceal bleeding.
Method: This is a retrospective review of adult patients who were admitted to our hospital with the diagnosis of acute gastro-oesophageal variceal bleeding for the first time regardless of their underlying causes for cirrhosis. The study period was from January 2000- October 2008. Data were collected from our hospital computer system and records.
Results: A total of 172 patients were included in this study, with 122 male and 55 female. Their mean age was 61.9. The initial failure rate in endoscopic haemostasis was 15.1%. The 5- day and 6-week mortality rates were 11.8% and 21.9 %, respectively. Poor Child's grading, multiple columns of oesophageal varices, high grade of varices, failed initial endoscopic haemostasis, presence of inoperable HCC, low platelet count on admission, and short duration from index bleed to rebleed were factors associating with increased risk of 6-week mortality ($p < 0.05$). Mean duration from index bleed to first rebleed was 15.1 months. Poor Child's grading and presence of inoperable HCC were associated with both early or multiple rebleed ($p < 0.05$). Overall, 37.2% of our patients developed rebleed before their variceal eradication. 5-year survival in patients with Child's A, B and C were 65%, 22%, and 10%, respectively (Log rank test p 0.000).
Conclusion: Although endoscopic haemostasis is an effective treatment modality; rebleeding is still commonly seen among patients with poor Child's grading and inoperable HCC. This will result in significant bleeding-related death and poor overall survival. Further advancement in treatment strategies for this group of patients are required to improve their outcome and prognosis.

PE550
Efficacy of Short Course of Terlipressin in Acute Variceal Bleed
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Objectives: Terlipressin is used in esophageal variceal bleed (EVB) along with Endoscopic Band Ligation (EBL) for 3days (UC). Due to its high cost, it was stopped <3days (SC) who could not afford & were stable after achieving hemostasis with EBL. We retrospectively assessed the efficacy of SC Vs UC of Terlipressin for control of EVB and length of stay.
Methods: Patients with EVB who had achieved hemostatsis with EBL from Jan 2004-Dec 2005 were included. All were managed on standard protocol on hospital variceal bleeding pathway. The course of Terlipressin as SC or UC was based on patient's inability to afford the cost of hospitalization and Terlipressin. The Efficacy of Terlipressin in the control of EVB was defined based on Baveno III criteria.
Results: Total of 117 patients were admitted during the study period. Out of them, 66 received UC & 51 SC of Terlipressin. The base line characteristics were comparable except younger age in SC. There were 2 re-bleed (3%) in UC and 1 (2%) in SC Terlipressin group. The length of stay was shorter in SC group. (2.47±0.57 vs 6.15±2.92 days).
Conclusions: SC seems as effective as UC Terlipressin in the control of EVB after initial control of hemostatsis with EBL and may reduces the length of hospital stay. RCTs are needed to assess this as all stable patients may not need to continue Terlipressin for 72 hours.

PE551
A Simple Model for Death Prediction of Hospitalized Patients with Esophageal Varices Bleeding From Cirrhosis Based On Conventional Laboratory Results
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Background/Aims: To analyze the relationship between conventional laboratory results and death risk in patients with esophageal varices bleeding due to cirrhosis (CEVB), and establish a simple model for timely predicting death rsik of the patients.
Methods: The medical documents of CEVB patients were reviewed retrospectively and the data were collected. Univariate and multivariate Logistic regressions were performed, in which the discharged results (survival or death) as dependent variable and the results of liver function, kidney function, serum electrolytes and blood cell analysis as independent variables. The multivariate regression equation was as the model for the prediction of patient outcome and its predictive performance was evaluated.
Results: In univariate regression, the significant positive variables for death outcome were DBIL, AKP, K, WBC and PLT, and the significant negative variables were TP, AP, A/G, Na, Cl^- and Ca^{2+}. The variables entered the multivariate regression are ALT, TBIL, DBIL, GP, A/G, Cr, Na^+, Cl^-, Ca^{2+}, WBC, Hb, PLT. The sensitivity, specificity and accuracy of the regression model for predicting death of CEVB patients were 97.1%, 95.1% and 95.8%.
Conclusions: The liver function, kidney function, serum electrolytes and blood cell analysis are generally independent factors for CEVB patient death risk, especially DBIL, A/G and Ca^{2+}. The established model shows a excellent predictive performance.

PE552
An Imbalance in Plasma Amino Acids of Advaced Cirrhotic Patients Impairs the Maturation Of Dendritic Cells Via Mtor/S6K Signaling Pathway
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Background: We have demonstrated that extracellular branched-chain amino acids (BCAAs), especially valine, regulate the maturation and function of monocyte-derived dendritic cells (J Immunol. 179: 2007). However, it is not clear whether an imbalance in plasma amino acids of advaced cirrhotic patients influence the function of dendritic cells (DCs).
Methods: We used human PBMCs and CD1c+DCs in this study. We made two mediums: a serum free culture medium consistent with the average concentration of the plasma amino acids from a healthy volunteer (n=100) was defined as the healthy control medium (HCM); whereas that from advanced cirrhotic patients (n=50) was defined as the advanced cirrhotic

medium (ACM). We stimulated PBMCs or DCs under HCM and ACM, and evaluated the function.
Results: After adding the stimulants under HCM, the CD83 and CD86 expression of DCs from cirrhotic patients (LC) were lower than those from healthy contorols (HC). In both HC and LC, the CD83 and CD86 expression of DCs stimulated under ACM was lower than that under HCM. The IL-12 production in ACM was lower than that in HCM. The expression of CD98, which is related to amino acid transport, was not different between HCM and ACM. However, DCs cultured in ACM expressed lower levels of phospho-p70 S6K than those cultured in HCM. Finally, we ascertained that the IFN gamma production by PBMCs was significantly decreased under ACM.
Conclusions: An imbalance in plasma amino acids of advanced cirrhotic patients suppresses the maturation of DCs via mTOR/S6K signaling pathway.