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Postgraduate Courses

C-1
ENDOSCOPIC RETRAGRADE CHOLANGIO-PANCREATOGRAPHY IN ADVANCED CIRRHOSIS LIVER DISEASE WITH COAGULOPATHY

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Endoscopic Retrograde Cholangio Pancreatography (ERCP) is a very effective method in dealing with pancreatobiliary disorder, in making the diagnosis as well as therapeutic action. Gallstone is the most common problem in pancreatobiliary disease is gallstone, and it's also proven to be more common in cirrhosis liver compare to general population, with incidence of 7.5% to 38%. It was accepted that symptomatic gallstone should be treated. But in patients with cirrhosis liver might be dealing a difficult condition, since cirrhosis especially advanced class (Child's class C) had many complication especially coagulopathy and immunocompromize situation and might be increasing the risk of bleeding or infection. In deciding what procedure will be use to treat this disease, we must consider that the procedure us is not creating so many damage or adhesion in abdominal cavity, since patient might be a candidate for transplantation, and a minimally invasive procedure is preferable.
Therapeutic ERCP is accepted as the recommended procedure to deal with pancreatobiliary disease. The most important process in doing therapeutic ERCP is to get a save access to CBD. In cirrhosis patients especially in advanced stage, Endoscopic sphincteroplasty or endoscopic papillary balloon dilation (EPBD) is more save compare to endoscopic sphincterotomy (EST) especially in hemorrhagic related procedure with incidence of 0% compare to 30% respectively. For choledocholithiasis after EPBD extraction stone can be done directly for stone with diameter < 12mm. Stones > 12mm in diameter need the use of lithotriptor. Asymptomatic cholelithisis in cirrhosis liver shoud be monitor closely. For symptomatic cholelithiasis in compensated cirrhosis best treated by cholecystectomy, preferable using laparoscopy cholecystectomy. But in advanced state, EPBD followed by stent placement through the cystic duct to duodenum seems a good treatment option, while waiting for the definitive treatment i.e. Cholecystectomy or transplantation after the lifer function and general condition of the patients is getting better.
Conclusion: EPBD seems a save tool in getting access to CBD followed by therapeutic ERCP, lithotripsy or stent placement in treating symptomatic gallstone with advanced cirrhosis liver. The use of stent placement to the cystic duct.

C-2
Treatment of esophagogastric varices

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Many years ago, surgical procedures such as esophageal transection or distal splenorenal shunting were the only treatments for esophagogastric varices. In the 1970s, interventional radiology (IVR) procedures such as transportal obliteration, left gastric artery embolization, and partial splenic artery embolization (PSE) were introduced, improving the survival of patients with esophagogastric varices. PSE is a supplemental treatment to prolong the obliteration of the veins feeding and/or draining the varices. In the 1980s, endoscopic treatment, endoscopic injection sclerotherapy (EIS), and endoscopic variceal ligation (EVL), further contributed to improved survival.
The overall incidence of bleeding from gastric varices is lower than that from esophageal varices. The initial episodes of bleeding from esophageal varices or gastric varices without prior treatment may be at least partly triggered by a violation of the mucosal barrier overlying the varices. This is especially likely in the case of varices of the fundus.
Bleeding from gastric varices has been successfully treated by endoscopic modalities. Once the bleeding from the gastric varices is stabilized, endoscopic treatment and/or IVR should be performed to eradicate the varices completely. In view of the high rate of hemostasis achieved among bleeding gastric varices, treatment should be administered in selective cases. Among untreated cases, steps to prevent gastric mucosal injury confer very important protection against gastric variceal bleeding.
Most patients with esophageal varices treated endoscopically required follow-up treatment for recurrent varices. Proper management of recurrent esophageal varices can significantly improve patients' quality of life. Recently, we have performed EVL at 2-mo (bi-monthly) intervals for the management of esophageal varices. Longer intervals between treatment sessions resulted in a higher rate of total eradication and lower rates of recurrence and additional treatment.

C-3
LIVER CIRRHOSIS: 2D, CDUS AND 3D-4D ULTRASOUND FINDINGS

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Liver cirrhosis is caused by hepatocellular death and resulting fibrosis and regeneration.
Surface nodularity can easily be detected sonographically and is a reliable sign of liver cirrhosis, particularly in the presence of ascites.
In liver cirrhosis, hepatocellular death results in scarring which making the portal venous pressure increases and portal hypertension will occur.
On 2D-B mode US there will be an enlargement of the portal vein, ascites and splenomegaly.
Detection pf portosystemic collaterals is relatively sensitive and is the most specific sign of portal hypertension.
Detection of hepatofugal flow and portal thrombosis in the portal vein is another relatively specific sign of portal hypertension although its occurs in more advanced cases.
All above mentioned signs of liver cirrhosis can be detected by means of Color Doppler Ultrasound and more information can be achieve from the 3D-4D ultrasound examination.

C-4

Quantitative diagnostic value of contrast enhanced ultrasound in liver cirrhosis

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Objective: Non-invasive diagnosis of cirrhosis by transit-time analysis of Levovist has been reported. The aim of this study is to investigate the quantitative diagnostic value of the other contrast agent, SonoVue in liver cirrhosis.
Materials and Methods: Total 145 patients were enrolled in our study, including 118 cases with hepatitis history and 27 cases with neither liver disease history nor clinical signs. Liver samples were achieved by biopsy or operation. Histological were assessed according to Knodell scoring system. Contrast agent Sonovue was used. The hepatic artery, hepatic vein, portal vein and liver parenchyma arrival time and peak time after the contrast agent injection were observed. The time-acoustic intensity curves were analyzed by an image and cineloop display and quantification software package.
Results: The number of patients in fibrosis stage 0, 1, 2, 3 and 4 were 27, 24, 21, 40, 33. The arrival time and peak time of hepatic artery and the peak time of portal vein were not significantly different in different fibrosis stage patients. The arrival time of portal vein was significantly different between S0 and S1, 2, 3, 4. The arrival time of hepatic vein was significantly different between S0 and S3, 4, while no difference between S0 and S1. The peak enhancement of liver parenchyma were markedly different between S0 and S4, while no difference between S0, S1, S2 and S3. By receiver operating curve analysis (ROC), the sensitivity to distinguish fibrosis stage 4 (cirrhosis) from stage 0 (no fibrosis) was 79% and specificity was 85.2% if the cut-off value of arrival time of hepatic vein less than 23 seconds and the sensitivity was 55.6%, specificity was 100.0% if the cut-off value of the peak time of liver parenchyma less than 27 seconds.
Conclusion: Our study suggests that the using of ultrasound contrast agents has potential as a non-invasive diagnostic modality for cirrhosis.
Keywords: Ultrasonography, contrast agent, liver cirrhosis

C-5

Ethanol Ablation of Hepatocellular Carcinoma Sized up to 5 cm by Using A Multi-pronged Injection Needle with Single Treatment Session

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Objective: To investigate the treatment efficacy of ethanol ablation (EA) in patients with hepatocellular carcinoma (HCC) sized up tp 5 cm by using a multi-pronged injection needle with single treatment session.
Methods: The study was performed with approval of the ethic committee, and written informed consent was obtained for all patients. From August, 2004, to October, 2006, 100 patients with primary or recurrent HCC 5 cm or less in size were treated with EA by using a multi-pronged injection needle. Single tumors were seen in 85 patients, and 2 or 3 nodules seen in 15 patients. Primary HCC was observed in 57 patients and recurrent tumors were in 43 patients. Follow-up ranged from 3 to 28 months (mean, 15 months ± 6). Patients were observed for progression of the treated tumors and for appearance of new lesions in the liver. Risk factors to the local effectiveness, disease-free survival and overall survival were assessed with Chi-square test, univariate and multivariate analysis.
Results: Mean treatment session was 1.1. Primary effectiveness rate was 94% and was significantly related to tumor stage (P = .008) (≤ 3 cm, 100%; 3.1-5.0 cm, 87%), tumor pattern (P = .017) (encapsulated, 97%; noncapsulated, 81%), and existence of portal hypertension (P = .017). At the end of follow-up, local tumor progression rate was 12%. The 1-, and 2-year disease-free survival (DFS) rates in patients with primary or recurrent HCC were 81% and 62%, 47% and 36%, respectively. The independent predictors of DFS were tumor location (P = .0018), and occurrence of complication (P = .0016). The 1-, and 2-year overall survival (OS) rates in patients with primary or recurrent HCC were 96% and 82%, 84% and 46%, respectively. The independent predictors of OS were alpha-fetoprotein level (P = .0032), and recurrence (P = .0000) in all patients, and primary effectiveness rate (P = .003) in patients with primary tumors. Complication rate was 7%. No ablation-related death was observed.
Conclusions: The use of a multi-pronged injection needle may improve treatment efficacy of EA of HCC up to 5 cm in diameter within less sessions.

C-6

Current diagnostic status and criteria of hepatocellular carcinoma using contrast enhanced ultrasound in China

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Objectives: To identify enhancing phases of cirrhotic liver and enhancement patterns of hepatocellular carcinoma (HCC) using contrast enhanced ultrasound (CEUS) and SonoVue.
Materials and Methods: CEUS were performed in 253 HCC of 206 patients with cirrhosis. The enhancing start times for hepatic artery, portal vein, and liver parenchyma and peak parenchymal enhancing time after contrast injection were recorded. Enhancing time and patterns of HCC were also analyzed. The diagnostic value of CEUS for HCC was evaluated.
Results: CEUS process was divided into four phases after contrast injection: arterial phase begins when hepatic artery shows enhancement (5.8-18.4 seconds), portal venous phase begins when portal vein shows enhancement (8.7-23.8 seconds), parenchymal phase begins when parenchymal enhancement reaches peak (17.6-38.1 seconds), and delayed phase (180-360 seconds). In 253 HCC, 238 (94.1%) lesions showed arterial enhancement with 58.5% homogeneous and 35.6% heterogeneous enhancement. Fifteen (5.9%) lesions showed portal venous enhancement. There were 84.6% (214 lesions) HCC washed out within portal venous or parenchymal phase, 11.1% (28 lesions) in delayed phase and 4.3% (11 lesions) showed no contrast wash out. There were 53.4% HCC showed basket-like feeding vessels or tortuous vessels inside the tumor in arterial phase. “Fast-in and fast-out” and “fast-in and slow-out” patterns were seen in 91.7% HCC, and 2.4% were

"fast-in and no-out". Atypical patterns of "slow-in and fast-out" and "slow-in and slow or no-out" were seen in 5.9% HCC.Conclusion: The dynamic vascular features of HCC could be clearly depicted using the newly defined vascular phases. CEUS diagnostic criteria of HCC is proposed based on enhancing timings, enhancing and wash out patterns of the lesions.

Keywords: contrast enhanced ultrasound, hepatocellular carcinoma, liver cirrhosis, vascular phase

C-7

Interventional Ultrasound in Chronic Liver Diseases: What Should We Know?

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There are two basic interventional ultrasound (US) procedures for liver diseases, namely percutaneous biopsies of hepatic masses and aspiration or drainage of fluid collections. Ultrasound-guided biopsies can be performed as fine-needle aspiration biopsy (FNAB) for cytopathology, or as core biopsy, which yields cylinders of tissue for histopathologic analysis. Whereas US-guided aspiration for fluid collections can be used for diagnostic Gram-stain and culture, or for therapeutic decompression. Usually, FNABs are performed using "skinny" (20-22-gauge) needles, whereas 18-gauge needles are required for core biopsies. The vast majority of fluid collections can be drained with 8-French self-retaining pigtail catheters or aspirated (sometimes repeatedly) with 18-gauge needles.

Preparation for an US-guided intervention includes discussion of the indications, the risks and benefits of, as well as the necessity for performing the procedure. Appropriate medical and surgical back-up must be planned, and post-procedure care must be determined. Written informed consent must be provided, antibiotic coverage for possible infected collection must be ordered, and the patient's coagulation profile must be determined. The coagulation parameters need to be assessed include reviewed patient's history for bleeding risks, such as anticoagulant use or hepatocellular disease, prothrombin time (PT), international normalized ratio (INR), partial thromboplastin time (PTT), and platelet count. An INR > 2.0, PT > 1.5 times normal, or platelet count < 50,000/μL is a contraindication for most procedures, but can be corrected temporarily to allow the intervention.

The major complications of percutaneous interventions are hemorrhage, infection, sepsis, solid organ injury, bowel perforation, and pneumothorax, with the rate of about 0.06-0.6% for skinny needle to 3-4% for catheter drainage. Tumor seeding of the needle tract is rare for small needle, however, the usage of large probes such as in percutaneous thermal ablation (radiofrequency, microwave, laser) of hepatocellular carcinoma (HCC) and hepatic colorectal cancer metastases are associated with tumor seeding of the tracts in about 2-3% of patients.

The US-guided percutaneous procedures of the liver, among others, are (1) FNABs and core biopsies for primary and metastatic tumors; (2) Drainage or aspiration of abscesses and other fluid collections; (3) Injection sclerotherapy of hepatic cysts; (4) Ethanol injection (PEIT) of HCC and hepatic metastases; and (5) Radiofrequency (RFA), microwave and laser ablation of primary (HCC) or secondary liver tumors.

With regard to its safety, all of percutaneous procedures should be approached with extreme caution. FNAB of hepatic carcinoid metastases can precipitate carcinoid crisis characterized by profound hypotension. Since most (typical) hemangiomas can be characterized no-invasively with cross-sectional imaging, obtaining specimens for cytology or histology is unnecessary and may risking severe hemorrhage. In case of echinococcal cysts, percutaneous aspiration and drainage is quite controversial.

In summary, US-guided interventions in liver diseases are safe and beneficial for diagnostic as well as therapeutic percutaneous procedures.

Meet the Expert

MTE-1

Cancer is a systems disease characterized by cell growth abnormality of defined tissues or organs

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From our recent data of a genome-wide large scale cDNA transfection assay of 30,000 cDNA clones with low abundance in human hepatoma cells and mouse fibroblast, 8,237 cDNA clones from 3,806 gene possessed the ability in stimulating or inhibiting the cell growth. Among them, 2,836 genes have been identified as known genes (1). Unexpectedly, we found more than 600 genes were related to systems regulation, including metabolic/redox, immune response, ion channels or small molecule transporters/exchangers and neural transmitter receptors. Particularly, the neuron related genes and ion channels or small molecule transporters are ignored in current cancer biology based on the century-old concept that cancer is a disease of abnormal cell growth (Wan DF et al, PNAS 101:15724-15729, 2004, Gu JR and Yang SL, Natl. Med. J. China 85:505-507, 2005).

Based on our concept, we further examined the expression profiles of these genes in human liver cancer versus non-cancerous liver tissues (Qin WX, to be published). The preliminary data indicated that a number of neural transmitter/receptor related genes, ion channels did express in these non-neural cells of parenchyma organ and cancer, and some of these molecules exhibited their differential expression pattern. These results further support that cancer is not simply a disease of local tissue or organ. Instead, cancer is a systems disease characterized by abnormality of cell growth of a defined tissue or organ.

MTE-2

Study on the Expression of Toll-Like Receptor 3 (Tlr3) on Dendritic Cells Derived from Peripheral Blood Monocyte of Chronic Hepatitis B Patients

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Background: In the center of innate immune response, Toll like receptors (TLR) are the significant pathogen-associated molecular pattern (PAMP), and they bridge to the adaptive immune. The changes of expression of TLRs, which are on dendritic cells (DC), will induce the abnormal function of DC, and further result in the chronic and sustained infection. TLRs are known of 11 family members, however, it is still uncertain which type of TLR is recognized for the PAMP of the hepatitis B virus (HBV) infection.

Objective: To investigate the expression of Toll-like receptor 3 (TLR3) on DCs derived from peripheral blood mononuclear cells (PBMC) of chronic hepatitis B (CHB) patients and to explore the mechanism of HBV sustained infection.

Patients and Methods: Twenty CHB patients were randomly screened in the study, and ten healthy persons were as controls. The monocytes isolated from peripheral blood of candidates were incubated with rhGM-CSF and rhIL-4 to induce the DCs generation and proliferation. Then the phenotypes (HLA-DR, CD80, CD86, CD83) of immature and mature DCs (mDC) were characterized by flow cytometer. Furthermore, the expression of TLR3 on mDCs and immature DCs (imDC) were determined by Western blot analysis and flow cytometry.

Results: 1. The expression of CD80, CD86, HLA-DR and CD83 (expressed as a positive ratio) on DCs of control group was significantly higher on the 7th day than that on the 5th day ($P<0.001$). However, no difference was noted in the CHB patients group ($P>0.05$). 2. The expression of TLR3 on imDC of control group was significantly higher than that of CHB groups ($P<0.001$), but no difference were showed on mDC between control and CHB group ($P>0.05$). 3. The expression of TLR3 on imDC was significantly higher than that on mDC in control group ($P<0.001$), however, no significant difference was revealed on imDC and that on mDC in CHB group ($P>0.05$).

Conclusions: The expression of TLR3 on peripheral DCs of CHB patients were significant decreased than that of healthy persons. The changes of TLR3 expression had a influence on DCs phenotypes and their functions, which might be one of the important mechanisms of HBV sustained infection.

Keywords: Chronic Hepatitis B, patients, Dendritic cells, Toll like receptor 3, expression.

MTE-3

Managemant of Gastro-esophageal Variceal Bleeding

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Gastro-esophageal variceal bleeding is a major and life threatened complication in patients with cirrhosis. It is one of the leading causes of death in cirrhotic patients. Upper endoscopy is the gold standard for the diagnosis of varices. Any patient with newly diagnosed cirrhosis should undergo endoscopy to make sure if there is gastroesophageal varices and its size. If varices absent, then follow up endoscopy will be done every 2-3 years, however, if there are only small varices without red sign, follow up could be perform every 1-2 years. Up to now, little evidence shows beta-blocker could prevent the occurance of varices and prevent the varices from small developing to medium varices.

Three steps will be included in managemant of gastro-esophageal variceal bleeding, i.e. prevention of first variceal bleeding; emergency management of acute variceal hemorrhage and prevention of recurrent variceal bleeding.

Prevention of first variceal bleeding: Variceal hemorrhage is more likely in patients with hepatic venous pressure gradient (HVPG) above 12 mmHg. The risk of variceal bleeding is increasing with the severity of liver disease (Child-Pugh claasification), variceal size (d>5mm), and presence of red sign on varices. The result of meta-analysis showed that non-selective beta-blocker, such as propranolol or nadolol is effective for prevention of first variceal hemorrhage. However, 15% of patients have contraindications and 16-20% intolerance to non-selective beta-blocker. Endoscopy variceal ligation (EVL) is alternative therapy. Compared to beta-blocker, EVL shows a slight benefit in reducing first variceal bleeding without a difference in mortality (1b; A).

Emergency management of acute variceal hemorrhage: Resuscitative measures should be instituted, including transfusion, keep airway. In the case of a patient with cirrhosis and varices, Octreotide or somatostatin can be administrated during the

resuscitative process while an endoscopy is being made. It could be continued for next 2-5 days when the risk of rebleeding is highest (1a;A).Endoscopy should be performed within 12 hours from admission. If the suspected variceal bleeding is confirmed, endoscopic therapy should be performed. 90% active hemorrhage will be controlled by endoscopic variceal sclerotherapy (EVS). EVL is preferred when bleeding stopped, because it seems to have better effect and less side-effect than EVS. Balloon tamponade can acutely control variceal bleeding in whom pharmacologic and endoscopic therapies failed, but it should not last for 6 hours.

Antibiotics significantly reduce bacterial infection, variceal rebleeding and mortality in cirrhotic patients with acute variceal bleeding, so that it become standard methods to be administrated 1a, A

Urgent portosystemic shunt surgery has a high mortality and morbidity, particularly in Child-Pugh C patients. There it will be reserved for Child A patients. TIPS as a salvage therapy performed for the decompensated patients failed from pharmacologic and endoscopic therapy or for the acute bleeding from gastric varices.

Prevention of Recurrent variceal bleeding: Both pharmacologic and endoscopic therapies decrease the risk of rebleeding. The combination a non-selected beta-blocker plus EVL is better than beta-blocker alone, but no difference was found in mortality rate. TIPS should be considered in Child B or C patients failed both pharmacologic and endoscopic therapies and as a bridge for liver transplantation. Surgical shunt can be considered in Child A patients.

MTE-4

NEONATAL CHOLESTASIS: HISTOLOGICAL STUDY

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Cholestasis was a condition result from hepatocellular or biliary dysfungcion may also present as jaundice. Cholestasis was divide as two term there were obstructive and non obstructive chlestasis. Obstructive cholestasis was a mechanical obstruction in large bile duct outside the liver or within the porta hepatic (extra hepatic cholestasis). Non obstructive condition called intra hepatic cholestasis is a bile secretory failure caused by a mechanism located within the anatomical confines of the liver.

This study was a preliminary report of histopathological study in neonatal cholestasis.The morphologic features of extra hepatic and intra hepatic chlestasis some time difficult to differentiate and almost of the cases already progress to cirrhosis.

Keyword: cholestasis, neonatal, histopathology

MTE-5

Stop-gap Treatment with Vasoactive drugs for Acute Gastroesophageal Variceal Bleeding

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Gastro-esophageal variceal (GEV) bleeding is a major and dread complication of portal hypertension resulting from liver cirrhosis (LC). GEV bleeding occurs in 25-35% of patients with LC and accounts for 80-90% of bleeding episode in these patients. It's associated with more substantial morbidity, high mortality and high hospital costs. GEV bleeding is typically an acute emergency clinical event. Up to 30% of initial bleeding episodes are potentially fatal and 60% of survivors have recurrent bleeding.

Management of patients with GEV bleeding includes the prevention of first bleeding, the control of active bleeding, and the prevention of complication and the prevention of recurrent bleeding. Many therapeutics options for control active bleeding are available, consists of pharmacologic therapy, balloon tamponade, therapeutic endoscopy (sclerotherapy and ligation), TIPS and emergency surgery.

The vasoactive drugs (vasopressin and its analogue, somatostatin and its analogue) have been used as 'stop-gap treatment' to control active bleeding and prevention of early re-bleeding. The critical advantage of vasoactive drugs for treatment of acute GEV bleeding is that they can be administered early, easy procedure and do not require special technical expertise. It's especially more important in health services without endoscopic facility or with endoscopic facility but early endoscopic procedure can not be done. Vasoactive drug should be used as first line therapy for patients with probable variceal bleeding.

The current recommendation for control acute GEV bleeding is combination of two approaches, starting vasoactive drug early (ideally at admission and during the hospital transfer, even if active bleeding is only suspected) and performing endoscopic variceal ligation after initial resuscitation.

This article will review the new evidence from clinical trials and meta-analysis regarding the role and the advantages of various vasoactive drugs for controlling active GEV bleeding.

MTE-6

A randomized control trial of bi-monthly versus bi-weekly endoscopic variceal ligation of esophageal varices

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Endoscopic variceal ligation (EVL) is a safe and simple procedure now being used on a widening scale. Yet most patients who undergo endoscopic treatment for esophageal varices eventually require additional treatment for recurrent varices. In this study, we investigated and compared the efficacy and long-term results of EVL performed in three treatments with a total of sixteen O-rings at two different intervals; bi-weekly (once every two weeks: the conventional interval) and bi-monthly (once every two months). A total of 63 patients with esophageal varices were randomly assigned to groups receiving bi-weekly or bi-monthly EVL treatment. Optimal medical therapy was assessed by one medical doctor who was unaware of the patients' treatment assignments. Three parameters of treatment outcome were evaluated: the rate of recurrence, rate of additional treatment, and overall survival. The overall rates of variceal recurrence and additional treatment were both higher in the bi-weekly group than in the bi-monthly group ($P < 0.001$). In conclusion, EVL performed for the treatment of esophageal varices at bi-monthly intervals brought about better results than the same treatment performed at bi-weekly intervals. The treatments intercalated by

the longer interval obtained a higher total eradication rate, lower recurrence rate, and lower rate of additional treatment.

MTE-7

Natural History of HBV Infection Related to Genotype in Asia

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Today hepatitis B has become a major global health problem due to high rate of morbidity and mortality. Around 400 million people are estimated to be persistently infected with hepatitis B virus (HBV) and Asia hosts three-quarters of these people. About 5 to 10% of adults and 95% children infected by hepatitis B virus more than six months develop to an advance liver disease, ranging from cirrhosis to hepatocellular carcinoma (HCC).

The studies about HBV have increased over the years. Based on the diversities in HBV DNA sequence the HBV strains have been classified into eight genotypes (genotypes A to H). The knowledge of the genotypes has become more important in epidemiological field, and moreover in clinical fields as it considered to be chronic liver disease, also the response to antiviral therapies.

These genotypes are distributed all over the world and have a distinct geographical distribution and ethnic association. Overall, genotype D is the most common genotype worldwide. In Europe, genotype A and D are commonly found while genotypes A, D and E are predominant in Africa. Genotypes B and C are mostly found in patients infected with HBV in Asia.

The genotypes implies in the progression of the disease. Genotype B, associated with slower progression of liver disease, spontaneous HBeAg seroconversion at young age and less development of HCC compared with genotype C. Although having slower progression rate than genotype C, the end result of cirrhosis and hepatocellular carcinoma may be similar. Furthermore, Sugauchi et al. reported that HBV strains in the same genotype may differ in capacity to influence the progressivity of liver disease. Subgroup Ba of genotype B, which is recombinant with genotrype C is found predominantly in Southeast Asian countries and appears to have more detrimental effects than subgroup Bj.

MTE-8

Advances in HBV Genotype Studies

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Hepatitis B virus (HBV) is a genetically divergent virus. Based on the genomic sequence differences by at least 8%, eight genotypes have been identified, designated as genotypes A-H. Recently, HBV genotypes have been further classified into at least 24 subgenotypes (genomic sequences differ by at least 4%). Both genotypes and subgenotypes show clear geographic distribution. The recombinant strains of different genotypes have also been identified.

Methods: developed for HBV genotyping include sequencing, primer-specific PCR, PCR-RFLP, INNO-LiPA reverse phase membrane hybridization, pre-S2 mAb EIA. In the last year, several new methods have appeared, including flow-through reverse dot blot, oligonucleotide chip, improved multiplex-PCR, real-time PCR and two step melting curve analysis, and PCR-invader assay.

Data: concerning the clinical relevance are less clear but it seems that in Europe, the genotype A has a higher HBeAg clearance rate and a better outcome. In Asia, genotype B is associated with a lower serum HBV DNA level, an early HBeAg clearance, an easy success of prevention of mother-to-infant transmission by vaccination and with less development of cirrhosis and HCC compared to those of genotype C.

Regarding: anti-viral therapy response, it has been reported that HBV genotype was an important predictor of response to pegylated interferon treatment for chronic hepatitis B. Both retrospective and prospective studies on the response to pegylated interferon treatment indicate that HBV genotypes C and D are more difficult to treat than genotypes A and B.

Knowledge: on HBV genotype so far suggests that further diagnosis, prevention and therapeutic strategies may require stratification according to genotypes

MTE-9

Toll-like receptor 4 siRNA attenuates LPS-induced secretion of inflammatory cytokines and chemokines by macrophages

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Toll-like receptor 4 (TLR4) is critical for activation of macrophages by Lipopolysaccharide (LPS). In this study, we investigated the silencing effects of TLR4-specific 21-nt small interfering RNAs (siRNA) on TLR4 expression in RAW264.7 cells. It was found that treatment with TLR4 siRNA down-regulated the TLR4 mRNA and protein expression in macrophage RAW264.7 cells, and reduced the sensitivity of the cells to LPS stimulation. Our findings also demonstrate that treatment with TLR4 siRNA significantly decreased the tumor necrosis factor-a (TNF-a) and macrophage inflammatory protein 2 (MIP-2) expression induced by LPS. TLR4 siRNA treatment also impaired the signalling of mitogen-activated protein kinases (MAPK) induced by LPS in RAW264.7 cells. These data suggest that inhibition of TLR4 expression by TLR4 siRNA may be therapeutically beneficial in controlling the overall responses of immune cells to LPS.

MTE-10

Both regulatory T cells and inhibitory receptors impair CD8+ T cell responses in chronically HBV-infected patients

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Chronic hepatitis B causes a significant morbidity and mortality worldwide. However, the reason why antigen-specific T-cell immune response is impaired in patients with chronic hepatitis B has not yet been fully elucidated. Here, my team, together with other labs, has recently demonstrated that endogenous factors like regulatory T cells and inhibitory receptors (PD-1/PD-L1) contribute to the impairment of virus-specific T cell responses in

chronic viral infection.
FoxP3$^+$ regulatory T cells (Treg) have been shown to maintain immune tolerance against self and foreign Ags, but their role in HBV-infected or HBV-associated liver cancer patients has not been well-defined. To address this issues, we investigated the characteristics of Treg in both PBMC and liver-infiltrating lymphocytes from patients with acute (AHB), chronic hepatitis B (CHB) and hepatocellular carcinoma (HCC), respectively. We demonstrated that in chronic severe hepatitis B patients, the frequencies of Treg in both PBMC and liver-infiltrating lymphocytes were significantly increased and there was a dramatic increase of FoxP3$^+$-cell and inflammatory cell infiltration in the liver compared with healthy controls. In CHB patients, circulating Treg frequency significantly correlates with serum viral load. In acute hepatitis B patients, circulating Treg frequency was initially low and with time, the profile reversed to exhibit an increased number of circulating Treg in the convalescent phase and restored to normal levels upon resolution. In PBMC taken from infected patients, depletion of Treg led to an increase of IFN-γ production by HBV-Ag-stimulated PBMC. In addition, Treg were capable of suppressing proliferation of autologous PBMC mediated by HBV Ags, which probably reflects the generation of HBV-Ag-specific Treg in circulation and in the liver of HBV-infected patients. Together, our findings suggest that Treg play an active role not only in modulating effectors of immune response to HBV infection, but also in influencing the disease prognosis in patients with hepatitis B (Journal of Immunology, 2006, 177:739-747).
Subsequently, we also found circulating Treg frequency was significantly increased and correlated with disease progression in HCC patients. An abundant accumulation of Treg concurrent with significantly reduced infiltration of CD8$^+$ T cells was found in tumor regions compared with non-tumor regions. Expression of granzyme A, B and perforin was dramatically decreased in tumor-infiltrating CD8$^+$T cells. Furthermore, Treg of HCC patients inhibited proliferation, activation, degranulation, and production of granzyme A, B and perforin of CD8$^+$ T cells induced by anti-CD3/CD28 antibodies. Importantly, increased quantity of circulating Treg was associated with high mortality and reduced survival time of HCC patients. Therefore, increased Treg may impair effector function of CD8+ T cells, promote disease progression and represent both a potential prognostic marker and a therapeutic target for HBV-related HCC individuals (Gastroenterology 2007, 132:2328-2339).
Furthermore, in order to investigate whether the increased B7-H1 expression on dendritic cells (DCs) mediates T-cell tolerance in CHB patients, we examined B7-H1 expression on circulating myeloid dendritic cells (mDCs) in CHB patients and healthy subjects. We found that B7-H1 expression is significantly up-regulated on circulating mDCs of CHB patients compared to healthy individuals. B7-H1 upregulation was significantly correlated with an elevation of serum alanine aminotransaminase levels and plasma viral load. In addition, in vitro both IFN-α and IFN-γ could strongly stimulate mDCs to express B7-H1. More importantly, elevated B7-H1 expression is also closely associated with suppression of T-cell immune function. In vitro blockade of B7-H1 signaling could not only down-regulate interleukin (IL)-10, up-regulate IL-12 production by mDCs but also enhance mDC-mediated allostimulatory capacity and cytokine production of T cells. Blockade of B7-H1 signaling could improve HBcAg-pulsed monocyte-derived DCs-induced interferon (IFN)-γ production by autologous HBV-specific T cells. These new findings suggested that chronic inflammation may contribute to B7-H1 upregulation on mDCs in CHB patients, which potentially cause defective HBV-specific T-cell function and viral persistence (Journal of Immunology, 2007, 178:6634-6641).
In conclusion, our findings demonstrate that both increased Treg and B7-H1/PD-1 inhibitory receptors contribute to the impairment of T-cell immune response in chronically HBV-infected as well as HBV-associated liver cancer patients, which make us get more insight into understanding the pathogenesis and clinical significance of T-cell immune dysfunction in chronic HBV infection.

MTE-11

SEQUENCE ANALYSIS OF HEPATITIS B VIRUS REVERSE TRANSCRIPTASE IN TREATMENT NAIVE PATIENTS

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The reverse transcriptase (RT) of HBV is the target of nucleot(s)ide analogue antiviral drug and RT mutations can lead to treatment failure. The aim of this study is to investigate whether there are primarily existed nucleot(s)ide analogues related mutants in treatment naive chronic hepatitis B patients and its prevalences and to construct a RT sequence database in treatment naive patients for further studies of HBV. Serum samples were obtained from 342 treatment naïve patients infected chronically with HBV from 5 provinces of China from year 2005 to 2006. By amplifying and sequencing the HBV RT region, we analyzed the mutation status. Genotyping and subgenotyping base on sequence results. Logistic regression was used to test correlation, two sides tested. Gene trees are constructed based on genetic distance and deep sequence analysis was performed. Among these patients, 36.3% are genotype B (B2: 88.7%) which is the main strain in south region, 63.7% are genotype C (C2: 92.2%), and one genotype D. The average age of those infected with genotype B is 32.5, and 37.3 for genotype C. Nucleot(s)ide analogue resistance related mutants are detected in all 5 regions, mostly presented as heterozygosis, but dominant mutant strains do exist. M204V/I dominant mutant ratio is 1.8%, L180M+ M204V/I is 1.2%, A181T/V is 0.6%, one Shanghai sample got L180M+ M204V/I +V84M mutant, the rest nucleot(s)ide analogue related dominant mutants account for 9.3%, the total nucleot(s)ide analogue related heterozygosis mutant rate is 37.7%. The bases usage in RT region differs at the mono- and di-nucleotides levels and thymidine dominated. Primarily existed mutant strains do exist in treatment naïf chronic hepatitis B patients and could be the cause of primary or secondary treatment failure. These characteristics of RT sequences obtained by deep sequence analysis in treatment naive patients implied that HBV may take advantages of the host hepatocyte replication mechanism, which need to be confirmed by further study. The database we constructed will be helpful in the future study of HBV including its infection course, in vivo evolution and clinical antiviral agent target design for preventing drug resistant.

MTE-12

Regulation of HBV transcription and replication --- looking the target for anti-HBV drug discovery

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HBV has a 3.2-kb partially double-stranded DNA genome. In the nucleus, the viral genome is converted into covalently closed circular DNA that is transcribed to produce the 3.5-, 2.4-, 2.1- and 0.7-kb HBV transcripts. The 3.5-kb pregenomic RNA serves as the substrate for reverse transcription and is converted into the 3.2-kb partially double-stranded genomic DNA inside the viral capsid in the cytoplasm of the hepatocytes. Therefore, the regulation of the transcription of the pregenomic RNA is a critical step in the viral life cycle. Various ubiquitous and liver-enriched transcription factors have been shown to modulate the level of RNA synthesis from the core promoter.

Hepatotropism is a prominent feature of hepatitis B virus (HBV) infection. Cell lines of non-hepatic origin do not independently support HBV replication hepatic origin. In our study, a new HBV nonhepatoma cell replication system has been developed where pregenomic RNA synthesis and consequently HBV replication are controlled by the ectopic expression of liver-enriched transcription factors. We show that the nuclear hormone receptors, hepatocyte nuclear factor 4 (HNF4) or retinoid X receptor α (RXRα) plus peroxisome proliferator-activated receptor α(PPARα), support HBV replication in non-hepatic cells by controlling pregenomic RNA synthesis, indicating these liver-enriched transcription factors control a unique molecular switch restricting viral tropism and probably represent a major determinant governing the hepatotropism of HBV. In contrast, hepatocyte nuclear factor 3 (HNF3) inhibits nuclear hormone receptor mediated viral replication both in cell culture system and in the HBV transgenic mouse model. Further study demonstrated that the N-terminal transcriptional activation domain of HNF3βis important for the inhibition role of HNF3 and hepatitis B e antigen (HBeAg) encoded by the precore RNA mediates part of the inhibition of viral replication by HNF3. Our studies also showed that mutation of each individual HNF3 site in the HBV promoters does not obviously affect the inhibition effect of HNF3 on HBV replication, indicating that inhibition of HBV replication by HNF3 is not mediated through a single HNF3 site in the HBV genome. It is possible that HNF3 inhibition of HBV replication involves the interaction of multiple HNF3 sites or the indirect effects on HBV transcription. Therefore, this replication system has identified roles for these liver-enriched transcription factors in controlling HBV transcription and replication, and also provided new targets for anti-viral drug development.

We showed recently that HBx has augmentation effects on HBV transcription and replication. The C-terminal two thirds (aa. 51-154), which contains the transactivation domain, is required for this function of HBx and the N-terminal one third (aa. 1-50) is not required. Using the alanine scanning mutagenesis strategy, we demonstrated that the regions between amino acids 52 to 65 and 88 to 154 are important for the augmentation function of HBx in HBV replication. With the luciferase reporter gene analysis, we found that the transactivation and coactivation activities of HBx are coincide well with its augmentation function in HBV transcription and replication. These results suggest that HBx has an important role in stimulating HBV transcription and replication, and the transcriptional transactivation function of HBx may be critical for its augmentation effect on HBV replication. Therefore, proteins that antagonize the tansactivation function of HBx may be potential negative regulators of HBV replication.

MTE-13

Treatment of hepatic cysts with percutaneous injection of acetic acid

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Objectives: To evaluate the safety and efficacy of acetic acid vs. ethanol as sclerosant for treatment of hepatic cysts by percutaneous aspiration and injection.

Methods: From October 2002 to May 2006, a total of 195 patients with hepatic cysts were enrolled in this study. 165 patients (405 cysts) were treated with percutaneous aspiration (or drainage) and acetic acid injection, including 89 patients with solitary cysts and 76 patients with polycysts. 117 of 405 cysts were large than 9cm in diameter. 30 patients (56 cysts) were treated using ethanol as sclerosant, 16 patients with a single cyst, and 14 patients with multiple cysts, 21 cysts being above 9cm in diameter. Under ultrasound guidance with a Chiba-needle the target cyst was punctured after local anesthesia. The cyst content was aspirated before injecting sclerosant. Tube was placed if the cyst diameter being above 9cm. Acetic acid or ethanol was injected when the cyst content was completely drained. The density of acetic acid was adjusted for inter-communicated cysts. The 1 and 3 years follow-up were conducted by ultrasound. The criterion for curative was defined as the cyst was disappeared completely or the cyst was high echo. The criterion for effective was the cyst decreased half or more than its original diameter size and asymptomatic. The cyst with no change or decreased less than half of its original diameter size was considered as treatment failure.

Results: 1 year after treatment, 75 patients treated by acetic acid were followed up. 52 patients were found cysts vanished, 19 patients were defined as treatment effective, and 4 patients were considered as treatment failure. While 18 patients were followed up in ethanol injection group, 3 patients were found cysts vanished, 8 patients were defined as treatment effective, and 7 patients were considered as treatment failure. 3 year after treatment, 38 patients treated by acetic acid were followed up. 25 patients were found cysts vanished, 11 patients were considered as treatment effective, and 2 patients were considered as treatment failure. 12 patients were followed up in ethanol injection group, 3 patients were found cysts vanished, 5 patients were considered as treatment effective, and 4 patients were considered as treatment failure.

Conclusions: Compared with injection of ethanol treatment of hepatic cysts by percutaneous injection of acetic acid shows higher rate of cysts vanishing, lower rate of relapse, and easy performing.

MTE-14

ENDOSCOPIC TREATMENT IN BILIARY STRICTURE

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Jaundice can be caused by extrahepatic cholestasis, such as biliary stones, papillary tumor/carcinoma, biliary stricture, cholangiocarcinoma, pancreatic cancer, Klatskin's tumor etc. The etiology of biliary stricture are infection (cholangitis), malignancy (cholangiocarcinoma, pancreatic cancer etc), and cancer metastases (breast cancer, lymphoma etc). The diagnosis of etiology can be made by ultrasound, Abdominal CT-scan, Magnetic Cholangio Pancreatography (MRCP) or Endoscopic Cholangio Pancreatography (ERCP) or Percutaneous Transhepatic Cholangiography (PTC). The treatment of biliary stricture can be supportive, pharmacologic, biliary drainage or surgical option. The biliary drainage can be done by therapeutic endoscopic retrograde cholangiography (ERC), percutaneous transhepatic biliary drainage (PTBD) or Cholecystostomy. The therapeutic ERC which can be done for biliary strictures are biliary dilatation, biliary stenting, placing the nasobiliary drainage (nbd) tube. The supportive treatment for biliary stricture includes liver diet, normalization of vital sign, water and electrolyte maintenance, education about the disease. The pharmacologic treatments are chenodeoxy cholic acid, ursodeoxy cholic acid, antibiotics for biliary infection/cholangitis. There are two kind of biliary stents, plastic stent and self expandable metal stent. Biliary stenting can be done with endoscopic retrograde cholangiography. Firstly we insert the guide wire into the CBD through the stricture, and then insert the stent into the bilary duct. The stent must be placed from the biliary duct above the stricture until the biliary duct below the stricture, outside the papilla vateri. Then take out the guidewire so the bile can go through into the duodenum. Placing of nasobiliary drainage (nbd) must be done with endoscopic retrograde cholangiography. Firstly we insert the guide wire into the CBD through the stricture, and then insert the nbd into the biliary duct above the stricture. The distal end of nbd must be placed into the nasal similarly with the placing of nasogastric tube. Then withdraw the guide wire, so the bile can come out via the nbd. If the stricture is very severe, there is no change to insert the guidewire passing through the biliary stricture, so we have to do biliary dilatation first. The biliary dilatation can be done with biliary balloon dilators or biliary. After the biliary stent, we can perform the biliary stenting or placing the nasobiliary drainage tube. The plastic biliary stent must be change with a new one every 2 - 3 months, because of the chance of biliary clogging. The self expandable metal stent must be placed life time for biliary malignancies.

Keywords: bilary stricture, biliary dilatation, biliary stenting, nasobiliary drainage

MTE-15

Prevention of upper gastrointestinal bleeding by Fuzheng Huayu Capsule in cirrhotic patients

Lieming Xue, Jie Gu

Background: To assess the role of Fuzheng Huayu Capsule in upper gastrointestinal bleeding prevention.
Methods: 146 patients with post-hepatitis B cirrhosis without previous bleeding were assigned into 2 layers. In the layer of small esophageal varices, 29 patients were randomized to Fuzheng Huayu Capsule group (FHC group) and 27 to placebo group. In the layer of medium and large esophageal varices, patients were divided into FHC group (30 patients), propranolol group (30 patients), and the combination of FHC and propranolol group(F&P group, 30 patients). The treatment with administration of medicine in relevant group was for 2 years.
Results: In small varices layer, there was 1 patient with bleeding in FHC group and 5 in placebo group during 2 years. The cumulative probability of being free of upper gastrointestinal bleeding (CPBFUGB) was higher in FHC group (96.3%) than in placebo group (77.01%; $P < 0.05$). The percentages of esophageal varices to disappearance, no change, and to medium or large were 53.33%, 33.33% and 13.33 in FHC group but 11.11%, 33.33% and 55.55% in placebo group. The difference was obviously in 2 groups ($P < 0.05$). In medium or large varices layer, CPBFUGB in FHC group (76.13%) and F&P group (87.55%) were higher than in propranolol group (56.99%, $P < 0.05$). The cumulative survival in FHC group was higher than in propranolol group (90.22% vs. 70.92%, $P < 0.05$).
Conclusions: Fuzheng Huayu Capsule could effectively decrease the happen of upper gastrointestinal bleeding in cirrhotic patients, and improve survival of cirrhotic patients with medium and large varices.

MTE-16

PORTAL HYPERTENSION: Miliary liver tuberculosis as a cause of profuse hematemesis-melena / Case report

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We report a case of hematemesis-melena. The spleen had a very large tuberculosis/tuberculoma, spread the liver as miliary portal tuberculosis.
That, then, caused portal hypertension and the patient had then profuse hematemesis-melena.
So, miliary spread of liver tuberculosis from the spleen can caused portal hypertension and end up in profuse hematemesis-melena.

State of the Art Lecture

STAL-1

Prevalence and Prevention of Hepatitis B in China

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Hepatitis B is a serious disease in China, among the global HBV carriers and deaths attributed to Hepatitis B, over one-third occur in China.

Data from national sero-survey conducted in 1992 showed that 32% of HBV chronic carriers acquired HBV infection during perinatal period, 65% in early childhood and 5% in adolescent and adulthood. Four sero-surveys were conducted in 1979, 1992, 2000 and 2006. the HBsAg carrier rates in children under 15 years significantly declined after HBV vaccination, and maintained almost the same between the groups above 20 years age. Hepatitis B was designated by the Ministry of Health (MOH) China as one of the four high priorities for infectious disease control in 2005. Hepatitis B control plan (2006-2010) was published by MOH in 2006. The goal is 1% HBV carrier rate among children <5 years by 2010. Since 1992, China has recommended the routine infant hepatitis B immunization with the schedule of 0, 1, 6 months to prevent perinatal transmission of hepatitis B virus (HBV) using domestically produced hepatitis B vaccines. The ultimate integration of HBV vaccine into the Expanded Programme Immunization (EPI) has strated since 2002. The HBV vaccine coverage in infants under 12 months of age was 88.5% for urban areas and 62.7% for rural areas, respectively. The ultimate integration of HBV vaccine into EPI started since 2002 in China. HBV vaccine is provided free to all infants, except the user fee. Free of charge for HepB vaccine started in 2005 according to the new immunization regulation in March 2005. HBV vaccination has led to reduction in morbidity and mortality of hepatitis B in the vaccinated group. The prevalence of HBsAg in general population decreased from 9.75% in 1992 down to 6.97% in 2006.

STAL-2

Therapeutic Options of HCC

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Etiology: Approximately 34,000 patients died of hepatocellular carcinoma last year in Japan. Of these, 11% and 83% of the patients with the cancer were positive for HBV and for HCV, respectively. This indicates that 94% of our patients with hepatocellular carcinoma are currently infected with either of two hepatitis viruses. In contrast, only 3% (1.5% for HBV and 1.5% for HCV) of general population are infected with the viruses.

Natural Course: Our follow-up study indicates that there is difference between B-viral and C-viral disease to develop into hepatocellular carcinoma, e.g., C-viral hepatocellular carcinoma often develop with the background of advanced fibrosis and/or cirrhosis, whereas B-viral HCC sometimes without. Therefore, surgical resection or complete ablation of nodules not necessary leads to complete cure of hepatocellular carcinoma, especially in C-viral HCCs.

Our Treatment Strategy: In fact, our experience of more than 5000 patients treated by PEIT (Percutaneous Ethanol Injection Therapy), PMCT (Percutaneous Microwave Coagulation Therapy) and recent RFA (Radio Frequency Ablation), indicates frequent recurrence. It is clear that you need the treatment both for backgrounds and tumor nodules. Otherwise, the recurrence of cancer from background (cirrhotic nodules) could reach 80% within 5 years.

Strategy of ours is to treat cancer nodules by PEIT, PMCT and RFA. Approximately 85% of our patients who are admitted to our Department of Gastroenterology, University of Tokyo, were treated with one of the above percutaneous methods.

Recently, we have completed a prospective controlled study of PEIT and RFA (Gastroenterology 2005;129:122-130). In that study, the RFA treated patients' survival were significantly better than those of PEIT. Thus, majority of the patients are now treated by RFA, resulting in 3000 cases so far and only exceptionally cases are treated by PEIT.

Recurrence: However, there are several problems. The biggest is the recurrence from cirrhotic background. Treatment for the backgrounds are basically to cure cirrhosis or advanced fibrosis. We have indicated that eradication of HCV by interferon eventually induces the resolution of fibrosis (Ann Intern Med 2000;132:517-524) . In fact, this reduction of the fibrosis due to the interferon treatment were related to decrease of incidence of hepatocellular carcinoma (Ann Intern Med 1999;131:174-181). We initiated a prospective controlled study for the patients who had hepatocellular carcinoma, treated by percutaneous injection therapy and interferon. The result indicates that 21 patients treated by ablation and interferon which induced good response, 5-year survival were 83%, compatible with liver transplantation (Ann Intern Med 2003;138:299-306).

Advanced HCC: We still have many patients suffering from advanced hepatocellular carcinoma, especially with portal vein tumor invasion (PVI) who usually live only for 6 months. The combination of 5-FU and Interferon was given to more than 300 patients with 17% of CR (Complete Response) (Cancer 2006;106:1990-1997). Furthermore, we have experience on "Molecular Targeting Drugs" on fairly advanced cases. I may present some of the data in this lecture.

STAL-3

Autoimmune liver diseases in China

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Autoimmune liver diseases including autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) are increasingly reported in world medical literature, but generally believed, at least in China as "western diseases" involving predominantly Caucasian peoples. However, as the awareness and understanding of this group of diseases has being steadily improved among Chinese hepatologists, more and more such cases has been diagnosed and a number of large series published in Chinese literature. For example, as one of the major centers with special interest in autoimmune liver diseases in China we diagnosed and managed more than hundred cases of PBC and more 20 cases of AIH and some cases of PSC in the last 5 years.

To observe the clinical manifestation and biochemical response to immunosuppressive therapy in Chinese patients of AIH, we

followed 31cases of probable or definite cases of autoimmune hepatitis assessed by IAIHG scoring system. We found that: 1). Autoimmune hepatitis occurred mainly in women, characterized by elevated serum aminotransferase, hypergammglobulinemia, and circulating autoantibodies. 2). Prednisone alone or combined with azathioprine can relieve symptoms and improve laboratory abnormalities very effectively.

PBC has been recognized as a chronic intrahepatic cholestatic liver disease in Western countries for a half century. For decades, in China and other Asian countries, PBC had been less well recognized and less reported. In recent years, however, more than 1000 hundred cases of PBC have been reported in the mainland China. As in western countries, in China PBC is predominantly affects women, with a peak age of about 50 years. The earlier series was consisted of mainly older late stage cases which had not been correctly diagnosed until very late stage of the disease. Recent series comprised of more earlier and even asymptomatic cases who has been accidentally identified at routine health check or workup for other medical reasons. In our institutel around 200 cases of PBC have been diagnosed in the last 8 years. All the patients were either hospitalized or out-patients at Beijing Friendship Hospital from January, 1991 to August, 2007. The diagnosis of PBC was made according to the 2000 Practice Guidelines of AASLD. Therefore, we conclusion, PBC in China is probably much more common thant we thought before, and the clinical characteristics as well as the biochemical response to UDCA are similar to that reported in western literature.

Sponsored Symposium

SS-1

Optimizing Long-Term Treatment Success Roadmap

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An international group of experienced hepatologists and virologists conducted a single-day workshop to review the management of patients with chronic hepatitis B receiving treatment with oral nucleosides or nucleotides. Guidelines regarding on-treatment management were reviewed. On-treatment monitoring strategies to define early virologic responses that might be predictive of better outcomes and a reduced risk of viral resistance were proposed.

This treatment plan, labeled the “roadmap concept”, recommends monitoring of serum HBV DNA to identify outcomes of therapy. The recommendations that the panel proposed are based on a review of published data showing a definite relationship between serum HBV DNA levels and disease outcomes. From their analysis, the panel identified specific HBV DNA levels that could serve as indicators of treatment response and predictors of patient outcomes. The roadmap recommends that serum HBV DNA levels be tested at 12 weeks into treatment to be sure that patients are responding to the therapy. Then, serum HBV DNA should be tested again at 24 weeks, when the physician should classify the patient’s response as complete, partial, or inadequate, based on the specific HBV DNA level. Primary treatment failure was defined as a reduction of serum HBV DNA by less than 1 log10 IU/mL from baseline at week 12. Measurement of the level of serum HBV DNA level at week 24 was considered essential to characterize virologic responses as complete, partial, or inadequate. Complete virologic response was defined as negative HBV DNA by a sensitive assay (<60 IU/mL or <300 copies/mL); partial virologic response as HBV DNA levels <2,000 IU/mL (4 log10 copies/mL), and inadequate virologic response as HBV DNA levels ≥2,000 IU/mL (4 log10 copies/mL).

Strategies are proposed for managing patients in each of these categories, depending in part on the rapidity with which HBV DNA suppression is achieved and the emergence of genotypic mutations that reduce the effectiveness of a specific drug. Using this roadmap approach, physicians now have a way to monitor their patients on HBV therapy, individualize the treatment, and achieve better results for their patients than ever before. Future studies of the utility of the roadmap concept in improving outcomes of chronic hepatitis B are warranted.

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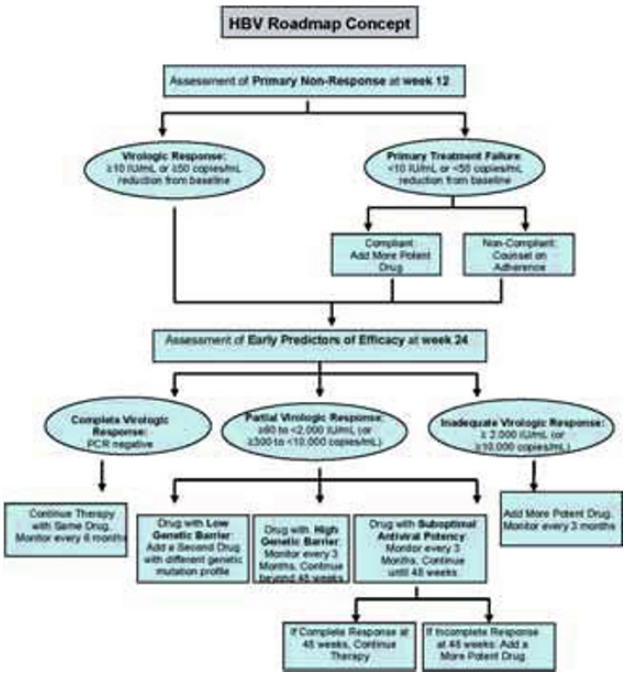

SS-2

Combination Therapy for Those Who Failed Response to HBV Therapy

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A number of guidelines or consensus on the management of chronic hepatitis B have been published and updated. All of them emphasize the importance of monitoring HBV DNA in patients on antiviral treatment. However, only the updated 2007 American Association for the Study of Liver Diseases practice guideline provides relatively detailed description of on-treatment management. This new guideline recommends that patients who have less than a 2-log10 IU/mL decrease from baseline of HBV DNA after at least 6 months of treatment should be switched to or adds on another approved NA therapy. This recommendation reflects the concept of Roadmap which is emerging in the recent years.

Therefore, using rescue therapy for patients at clinical breakthrough with sequential monotherapy is no longer considered appropriate. The current strategy for early control/delay of resistance is to rescue the suboptimal responders at week 24 or 48 with “add on” and rescue of patients at virologic breakthrough with “add on”. Maybe the future strategies for prevention/delay of drug resistance is to use de novo combination therapy in selected patients with high risk of resistance and reliable to flare.

Lastly, the roadmap concept is based mainly on clinical evidence derived from nucleas(t)ide analogs trials. Therefore, it is not applicable directly to other clinical scenario such as to interferon-based therapy.

SS-3

The Importance of Resistance Profile in Hep-B Management: A Perspective from Japan Data

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HBV was discovered in 1964 and HBV suppression by treatment started in late 1970 by Dr. Greenberg using Interferon. However, until 1998 when Dr. CL Lai reported one year experience of Lamivudine in New Engl J Med, the treatment of HBV has not become common practice. That time, I wrote critical comment on this article by Editorial in New Engl J Med. Because the majority of the patients treated had infection more than thirty years or sometimes even fifty years. And only one year suppression is not obviously sufficient to change the natural course of HBV infection. Subsequently, very high resistance rate was noted in the Lamivudine treatment and long-term efficacy was blurred. In our previous in vitro study, a new drug, Entecavir, showed more than thousand times stronger potency than Lamivudine. Entecavir was now launched in many Asian countries. And experience of three to four years of use was gathered and Entecavir seems so far very safe and potential suppressor of HBV replication. Now the question is raised how long it can continue to suppress HBV before the emergence of HBV resistant mutant. In my talk, I will compare the potency and durability of Entecavir and emergency of Entecavir resistant strains. We know envision the use of these drugs for longer than five years. I personally feel if these drugs can suppress longer than ten years, probably the natural course of HBV infection could be drastically changed in the majority of HBV carriers.

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Symposia

S-1
HIV and HBV coinfection

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As hepatitis B virus (HBV) and HIV share ways of transmission, co-infection has become a frequent health problem among the HIV/AIDS patients, approximately 10% of HIV individuals have chronic hepatitis B, as evidenced by the detection of HBsAg in the serum persisting for a minimum of 6 months which is higher prevalence of HBV infection than in general population. The natural history of HBV is known to be complicated by HIV coinfection, with a higher rate of chronic hepatitis, greater levels of HBV replication and lower incidences of spontaneous loss of HBeAg or HBsAg. Additionally, the incidence of cirrhosis and mortality attributable to liver disease are significantly increased when HBV infection is complicated by HIV infection. HBV DNA levels are usually high in HIV/HBV coinfected patients, which is an independent risk factor for HCC. Some study indicated that HBV coinfected patients may be at increasing risk for progression to end stage liver disease and HCC compared with HCV coinfected or HIV mono-infected individuals. HBV coinfection is an important cause of morbidity and mortality in an era of effective HIV therapy. Different hypothesis can be raised. First, HBV itself could explain this excess of liver-related mortality in HIV-infected subjects because of its worsened natural course and a less-vigorous immune response against HBV, as reflected by lower level of liver transaminases and increased incidence of cirrhosis. Second, several studies performed have shown a higher incidence of severe forms of hepatotoxicity caused by antiretroviral drugs, Third, immune reconstitution induced by HAART could trigger a more severe inflammatory response against HBV and accelerate liver disease.

The goals of anti-HBV therapy for HBV coinfected patients are to reduce HBV related morbidity and mortality. Surrogate endpoints include sustained suppression of HBV DNA, prevention of liver disease progression, and clearance of HBeAg. Lowering HBV DNA levels is critical for long-term survival of HIV/HBV coinfected patients. The lamivudine(150 mg twice daily), adefovir dipivoxil (10 mg daily), Tenofovir (300 mg daily), Emtricitabine (200 mg once daily) and interferon (standard or pegylated interferon α2a) may be useful in suppressing HBV replication with HAART regimen but should be used in combination. Recent clinical trial showed that long-term treatment of HIV/HBV-coinfected patients with adefovir and concomitant antiretroviral treatment can effectively lower the HBV viral load and normalize ALT levels while maintaining an acceptable safety profile.

End Stage of Liver Disease (ESLD) among HBV and HIV coinfected patients is managed same as HIV-seronegative patients. IFN is contraindicated in ESLD, but limited data indicate that lamivudine and adefovir (and probably tenofovir) can be safely used. Liver transplantation has been successfully performed among selected patients with HBV and HIV-1 coinfection.

S-2
HIV and Hepatitis C Virus Co-infection

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HIV prevalence is a global public-health challenge. Hepatitis C virus (HCV) infection is frequently encountered in HIV-infected patients because of the same routes of transmission. Among those HIV-infected patients with a high exposure to blood and blood products, such as intravenous drug users and haemophyliacs, co-infection with HCV is ranging from 50% to over 90%. HCV is found in 83.6% of HIV-positive former paid blood donors and 93.6% of HIV-positive intravenous drug users in China.

We conducted a prospective multicenter study to evaluate the efficacy and safety of Chinese generic antiretroviral drugs. One hundred and ninety-eight treatment-naïve HIV/AIDS patients were enrolled and randomized to three regimens: AZT/ddI/NVP, D4T/3TC/NVP, and AZT/3TC/NVP. 3TC was trade-mark formulation, and the other 4 drugs were Chinese generic ones. Patients were followed up at the end of 1, 3, 6, 9 and 12 months.

From 175 patients whose data on HCV antibody before HAART initiation were available, HCV co-infection was recorded in 58 patients (58/175, 33.1%). But HCV co-infection was found not to influence the efficacy of HAART. There were no significant differences in changes in both viral load (P=0.611) and CD4+T cell count (P=0.162) from baseline between the HIV+HCV+ and HIV+HCV- groups at week 52. Hepatotoxicity occurred in a total of 58 patients (58/175, 33.1%), in which 26 cases (44.8%, 26/58) came from HIV+HCV+ group, while 32 cases (27.4%, 32/117) from the HIV+HCV- individuals. There was a significant increase in the probability of developing liver damage in HCV co-infected individuals (44.8% vs 27.4%, P=0.002) during one year treatment.

In conclusion, HCV co-infeciton may cause significantly higher prevalence of hepatotoxicity during HAART. HCV co-infection impact the management of HIV infection, strategies to treat HIV/HCV co-infection are urgently needed for HIV-infected individuals.

S-3
LAPAROSCOPIC COMMON BILE DUCT EXPLORATION (LCBDE)

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Since Laparoscopic Cholecystectomy was done for the first time by Philippe Mouret (France,1987) the development of minimally invasive surgery in hepatobilliary system have been progressing, followed by Berci, Phillips (USA,1991) which done LCBDE successfully later on.

Indications of LCBDE: 1).Abnormal intra operatif cholangiogram, 2).Unsuccessful attempts at endoscopic stone extraction for large/occluding stones, 3).Intra hepatic stones.

Contraindications: 1).Inability of the surgeons to perform the necessary maneuvers, 2).Absent of indication, 3)Instability of the patient, 4).Local condition in the porta hepatic that would made exploration hazardous, 5).Diameter of cystic duct <4mm (transcystic procedure) or diameter CBD <6mm

(transcholedochal).
Three mayor options in management cholelithiasis with CBD stone: 1).Open Cholecystectomy + CBD Exploration, 2).Endoscopic Sphincterotomy and Stone Extraction + Laparoscopic Cholecystectomy (2 Stages) 3).Laparoscopic Cholecystectomy + LCBDE (1 Stage).
Treatment of choice based on: 1).Patient safety consideration, time efficiency, cost effectiveness, 2).Surgeons competency, 3).ERCP Facilities, 4).Availability and preparedness of supporting instruments/equipments.
The techniques of LCBDE: 1).Transcystic Approach (Transcystic LCBDE), 2).Anterior Choledochotomy (Transcholedocal LCBDE).
LCBDE in Jakarta was done between August 1998 – December 2006 : 76 patients (Male:23, Female:53), Mean Age:54 yrs, Mean Operation Time:3.5 hrs, Mean Hospital Stay:5.5 days, Conversion Rate:7 (9.2%) with various causal of: Impacted Stones:3, Masive Adhesion (Anatomical Reason):2, Instruments Failure:2.
Result of operations: Retained Stone:1 (1.3%), Morbidity:9 (11.8%) with Subphrenic Abscess:2, T-tube Insertion Leakage:1, Respiratory Tract Infection:1, Urinary Tract Infection:1, Superficial Wound Infection:4, Mortality :0.
Conclusion: 1).LCBDE will become an important alternative choice in treatment of CBD Stone in the near future, especially in the failure of ERCP/Endoscopic Stone Extraction, 2).LCBDE as a minimally invasive procedures has the advantages with high success rate, low morbidity and mortality rate and faster post operative period recovery, 3).LCBDE need more training properly and more learning curve.

S-4

Effect of plasma exchange before liver transplantation on the operation and prognosis of patients with chronic severe hepatitis: a report of 70 cases

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Objective: To observe and investigate the efficacy of plasma exchange (PE) before liver transplantation on the operation and prognosis in chronic severe hepatitis patients.
Methods: Consecutive clinical data of 70 patients with severe hepatitis undergoing orthotopic liver transplantation were analyzed retrospectively. The patients were allocated to two groups based on plasma exchange or not: plasma exchange group (PE group) and a control group without PE. The MELD scores were not significantly different between 2 groups. The operating time, volume of blood loss, volume of blood infusion, the process of recovery, the complications post operation and the survival rate were observed and compared.
Result: Among 70 cases, one-month survival rate was 85.71%, one-year survival rate was 78.69%. The volume of blood loss, volume of blood infusion and the operating time were remarkably lower in the plasma exchange group than in the control group. Consciousness, digestive system recovered more early in the plasma exchange group than in the control group. There were no significant difference between the two groups of complications post operation and the survival rate.
Conclusions: The application of plasma exchange before liver transplantation on patients with chronic severe hepatitis is beneficial to the operation procedure and the recovery post operation. But PE can not reduce the complications around the operation and can not improve the survival rate in chronic severe hepatitis patients underwent liver transplantation.
Keyword: Plasma exchange; Chronic severe hepatitis; Liver transplantation; prognosis

S-5

Ethical and Legislative Perspectives on Liver Transplantation in Mainland China

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Brief introduction of organ transplantation in China: As we all know, China has the largest population in the world. Accompanied by the fast development of economy, science, technology in the recent two decades, the demand of health care increased and medical technology developed quickly. Organ transplantation is getting more extensive applications in China.
In the past two years (2004, 2005), around 8000 cases of kidney transplantation were performed each year and the 1 to 5 years survival rate was 95.4%, 92.1%, 89.3%, 80.2%, 72.7%, respectively. As for heart transplantation, more than 100 cases were performed each year. Dozens of pulmonary, combined heart-pulmonary, liver-kidney, pancrease-kidney transplantation were also reported.
Liver transplantation in China: As far as the liver transplantation is concerned, the evolution of the liver transplant in China could be classified into initiative period (1978-1983) and developing period (1993-present). Following the first human liver transplantation in 1978, it has been accepted as an effective therapeutic modality for end stage liver disease. The number of liver transplantation is blooming in recent years. The survival rate of 1, 3, 5 and 10 years was 80.5%, 70.7%, 65.9% and 60.7% in total 6783 cases of liver transplantation. The most common diagnoses in patients undergoing liver transplant are hepatitis B or/and C, cirrhosis and hepatocellular carcinoma for adults and biliary atresia for Children. The percentage of benign and malignant diseases is almost the same. Certainly, the recipient survival rate of benign disease is much higher than that of malignant disease (1, 3 and 5 years survival rate was 83% vs 77%, 79% vs 59%, 74% vs 55%, respectively). For HCC patients, the 1, 3 and 5 years survival rate of those within Milan criteria was 83.6%, 70.0% and 65.0%, while the survival rate of those beyond Milan criteria was 72.8%, 50.2% and 49.1%, respectively. The TNM stage of HCC and MELD score could also affect the result of liver transplantation. Whether the operation was performed in urgent situation or selectively had no influence on the survival rate of patients.
Now, use of living donor has been gradually increased. Heroic conduct to donate a partial liver to other person is highly respected by society. At present, most of living related donors are genetically connected to the recipients, such as parents, siblings or children etc.
Legislation of Liver Transplantation in China: The Chinese government pays much attention to the legislation of organ transplantation. As early as in 1995, "the Human Organ Transplant Ordinance" was first enacted by the ministry of health together with other related ministries to prohibit commercial dealings in human organs intended for transplant, restrict the

transplant of human organ between living persons.
Mandated by State Council, Ministry of Health launched "Interim Provision on the Administration of Clinical Application of Human transplant Techniques" entered into effect on July 1st 2006. The document states: Only medical facilities and physicians attaining a certified level can perform human organ transplantation; Organ transplantations will be monitored and supervised by The Organ Transplantation Technique Clinical Application and Ethics Committee; The medical facility should report and register the category, number and result of the organ transplantation within a specific time.
Chinese government has attached great importance to the promulgation of legislation on organ transplant. State Council has drafted the first version of "Organ Transplantation Act" which is now open for discussion in relevant sectors before the final version is completed. The Chinese legislation on organ transplant will follow the international recognized legislative principles with the characteristics of the statute of organ transplant in the context of Chinese socio-cultural reality, what that framework should be, will continue to be the subject of much discussion, debate and legislative attention.
Conclusion: Organ transplant is a newly-born frontier of medical science in China. Various attempts are being made to formulate more applicable codes and policies to guide our transplant practice. However, there are still many obstacles in organ transplantation. For example, there is lack of information for common people regarding the concept of brain death. Given China's large land area, huge population, disparity of regions and less-developed economic situation, communicating public awareness of such policy is a tough task. Nevertheless, we are confident in achieving our goals in near future, moral support and understanding from the international communities will be of great importance and appreciation.

S-6
CHOICE OF IMAGING IN BILIARY OBSTRUCTIONS MSCT VS MRCP
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In patient with suspected biliary obstructions, accurate and early diagnosis is crucial to selecting the appropriate therapeutic management.
They are many imaging techniques may be used to evaluate the biliary tree, including Ultrasonography, Multislice CT scan, MRI and MRCP, ERCP and PTC.
The ultrasonography is used as first screen of examination, but they have a limited value in the evaluation of the main biliary tract The sensitivity is 20-80 % depending on the series, technique of examinations and operator dependent.
With the multi slice CT scan we can correctly asses the level of the bile duct obstruction, allow accurate diagnosis of the causes of the obstruction and characterize the suspected lesions of the liver or the pancreas. The most causes of the biliary obstruction is gall stone, with familiarity of the diagnostic pitfall to detect gall bladder stone at CT examination, we can accurately confirmed the diagnosis. The sensitivity of CT scan to detect stone = 39-90% and the specificity 73-92%.
MRCP is used since 1991 in conjunction with MRI examination and can accurately determine the status of the biliary ductal system by identifying the exact location ,extent of the obstruction and the severity of duct dilatation .MRCP tolerate well in most patients and does not requires any contrast injection. Familiarity with the using of sequences and the diagnostic pitfalls we can accurately determined the diagnosis. MRCP in the diagnosis of stone have a high sensitivity (81-100%) and specificity =85-100%.
MSCT and MRI imaging have a high accuracy to identify the cause of the biliary obstruction, define the tumor margins and determine the stage of the disease. With MRCP there is an additional value for the anatomical information to determine the site of the obstruction.

S-7
Biliary Cast Syndrome after Orthotopic Liver Transplantation: Prophylaxis and Treatment
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Objectives: We want to identify clinical features associated with blilary cast formation, study the prophylaxis on BCS of meliorated portal flush strategy in quick donor harvest, and review treatment with choledochoscope.
Methods: To test our hypothesis, we compared the incidence of BCS in two groups of adults undergoing OLT using different types of portal vein preservation solution in the donor: group 1(n=65) University of Wisconsin (UW) solution, group 2 (n=72) hypertonic citrate adenine (HCA) solution combined with UW solution. All donors in both groups received additional aorta flushing with HCA solution. All OLT were performed between Jan 2005 and Dec 2006 in our center (Liver transplantation center of the general hospital of Chinese People's Armed Police Forces) by the same surgeon (Dr. LIU Zhen-Wen). Patient records were reviewed retrospectively to identify patients who developed casts and the value of choledochoscope on coping with BCS. We focused our attention on collecting data associated with ischemia, rejection, immunosuppression, infection and cast-directed management.
Results: 12.4% (17/137) recipients developed BCS in the first 6 months after OLT. The incidence of BCS in group 1 is 20% (13 of 65 patients), compared to 5.56% in group 2 (4 of 72 patients). There were no significant differences in the following factors between group 1 and group 2: donor and recipient age, incidence of multiple vessels in donor liver, indications of OLT, post-OLT peak aspartate aminotransferase level, immunosuppression use, acute cellular rejection. Interestingly, cold ischemia time (CIT) was longer in group 2, which had less incidence of BCS although no remarkable difference is noted. Casts were successfully treated by choledochoscope providing favorable prognosis.
Conclusions: BCS are likely to develop in an inadequate portal vein perfusion environment. Combined preservation solution (HCA in aorta, HCA & UW in portal vein) might protect against BCS formation. Choledochoscope cast extraction might achieve favorable results and should be attempted before surgical therapy.

S-8

TREATMENT OF HEPATORENAL SYNDROME

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Hepatorenal syndrome (HRS) is a frequent complicationin patients with advanced cirrhosis and ascites. Characterized by an intense renal vasoconstriction which leads to very low renal perfusion and glomerular filtration rate (GRF).The renal ability to excrete sodium and free water is also severely reduced
Renal histology shows no significant lesions sufficient to justify the impairment in renal function. The annual incidence of HRS in patients with cirrhosis and ascites has been estimated as 8%
Criteria of diagnostic base on International Ascites Club's diagnostic criteria of HRS. There are two types of HRS: Type-1 HRS is characterized by a severe and rapidly progressive renal failure which has been defined as doubling of serum creatinine reaching a level greater than 2.5 mg/dl in less than 2 weeks. Type-2 HRS is characterized by a moderate and steady or slowly progressive renal failure (serum creatinine lower than 2.5 mg/dl).
Available treatments for type-1 HRS.
Liver transplantation is the treatment of choice of HRS, a recovery of renal function is noted, usually 48–72 h after transplantation. The long term survival of patients with HRS who undergo liver transplantation however is good, with a 3-year probability of survival of 60%. Treatment of type-1 HRS with vasoconstrictors and albumin increases survival and the number of patients reaching living transplantation and decreases early morbidity and mortality after surgery
Vasoconstrictors and albumin: The i.v. administration of vasoconstrictor agents (vasopressin, ornipressin, terlipressin, noradrenaline) or the combination of oral midodrine (an a-agonistic agent) and intravenous or subcutaneous octreotide during 1–3 weeks is an effective treatment of type-1 HRS. Terlipressin has been the most widely used vasoconstrictor agent in type-1HRS. It is very effective and is associated to low incidence of side effects.
Transjugular intrahepatic portacaval shunt (TIPS), Three pilot studies have evaluated TIPS in type-1 HRS. TIPS is effective in normalizing serum creatinine in a significant proportion of patients with cirrhosis and severe azotemia and is an alternative treatment of type-1 HRS.
Extracorporeal albumin dialysis (MARS).Three pilot studies including 29 patients (26 with type-1 HRS and 21 with alcoholic cirrhosis and/or severe acute alcoholic hepatitis) aimed at assessing MARS in patients with type-1 HRS. Since the end point of this trial was encephalopathy, no conclusion could be obtained in relation to survival.
Available treatments for type-2 HRS.
In patients with type-2 HRS the main clinical problem is refractory ascites, treatment of type-2 HRS should consider not only survival but also the control of ascites.
Transjugular intrahepatic portacaval shunt: Two pilot studies assessing TIPS in type-2 HRS. TIPS is therefore effective in reversing type-2 HRS, although more data on complication rate and survival are needed before advocating widespread use of this procedure.
Vasoconstrictors and albumin : Three pilot studies provided data on the effect of terlipressin plus albumin in 26 patients with type-2 HRS. The current state of knowledge on vasoconstrictor therapy in type-2 HRS is therefore very poor. It appears to be not as effective as in type-1 HRS due to the high rate of HRS recurrence.
Prevention HRS: Three randomized controlled studies in large series of patients have shown that HRS can be prevented in specific clinical settings. In the first study, the administration of albumin to patients type-1 HRS, it is markedly reduced the incidence of circulatory dysfunction and Hospital mortality rate. The second study, cirrhotic patients with a high risk of developing SBP and type-1 HRS. Primary prophylaxis of SBP using long-term oral norfloxacin a significant decrease in 1-year probability of development of SBP and type-1HRS and a significant increase in the 3-month and 1- year probability of survival. In the third study, the administration of the tumor necrosis factor inhibitor pentoxyfilline (400 mg 3 times a day) to patients with severe acute alcoholic hepatitis reduced the occurrence of HRS and the hospital mortality.
Conclusion: Transplantation liver is the choice treatment of hepatorenal syndrome, Treatment of type-1 HRS with vasoconstrictors and albumin increases survival and the number of patients reaching living transplantation and decreases early morbidity and mortality after surgery. Terlipressin has been the most widely used vasoconstrictor agent in type-1HRS, TIPS is therefore effective in reversing type-2 HRS
Keyword: HRS, Vasocontrictor and Albumin, Transplantation liver

S-9

CURRENT TREATMENT OF HEPATIC ENCEPHALOPATHY

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Hepatic encephalopathy (HE) is a neuropsychiatric disorder cause by central nervous system effects of toxins that accumulate in blood circulation because of the inability of the liver to detoxifying it. The clinical manifestation of HE include a spectrum of abnormality in cognition, attention, functional ability, personality, and intellect. The neuropsychiatric impairment associated with HE range from mild alteration of cognition and consciousness to coma. Other carachteristic of HE: neuromuscular symptoms, such as tremor, asterexis, hyperrefexia, and, in advanced cases, decerebrate posture.
The concept of intestinal-derived ammonia as the principle which contributes to the pathogenesis of HE, makes the direction of current therapeutic approaches is to reduce the bacterial production of ammonia and inhance its elimination. Non-absorbable disaccharides are first-line therapy for hepatic encephalopathy, but published clinical studies evaluating their safety and efficacy are limited. A meta-analysis of 22 randomized trials showed that the data's is insufficient to support or refuse the use of non-absorbable disaccharides.
Alternative therapies such as benzodiazepine receptor antagonists, branched-chain amino acids, and L-ornithine-L-aspartate also have limited clinical data supporting their use. L-ornithine-L-aspartate lowers serum ammonia levels by providing substarte which is essential for the intracellular metabolic conversion of ammonia to urea and glutamine. Results from clinical trial suggest that ornithine-aspartate reduces ammonia levels and provides therapeutic benefits in patients with chronic mild to moderate HE.

To reduce the number of ammonia producing bacteria in the colon, selective colon decontamination with antibiotic is recommended. Systemic antibiotics demonstrated its efficacy, but their widespread use is limited by its side effects. A minimally absorbed antibiotic, rifaximin, concentrates in the gastrointestinal tract and is excreted mostly unchanged in faeces. In the treatment of HE it appears to confer therapeutic benefits greater than those of placebo and non-absorbable disaccharides and at least comparable with those of systemic antibiotics.

S-10

Therapeutic analysis on 105 cases of hepatocellular carcinoma

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Background: Hepatocellular carcinoma remains the most important malignant disease in the Asia, including China.
Objectives: To investigate the survial rate and the complication of combination treatment with a predominance of resection for hepatocellular carcinoma.
Methods: Clinical records of 115 cases of hepatocellular carcinoma treated by resection from January 1998 to December 2002 were reviewed. The types of resection included trisegmentectomy, hemihepatectomy, lobectomy, segmentectomy and local hepatectomy. The hepatic arteriography was done after resection of 1-,6-,and 12 month. The patients without palpable evidence of recurrence were given the prophylactic chemotherapy, else they will be given seguential resection, radiofrequency ablation and Percutaneous ethoanol injection therapy.
Results: The total complication rate was 13.04%(15/115).The rates of postoperative bleeding, pleural effusion, hepatic failure, bile leakage and hemorrhage of upper digestive tract were 4.34%, 3.48%, 2.60%, 1.74% and 0.75%. The 1-,3-,5 and 7-year survial rates were 89.6%, 56.8%, 41.0% and 32.7%.
Conclusion: Liver resection combined with other nonoperation modalitise are idel ways to treat hepatocellular carcinoma at the present. The sruvial rate can be increased after hepatectomy by close obsecvation of postoperative state and comprehensive postoperative tecatment.

S-11

SURGICAL RESCUE FOR FAILURE ENDOSCOPIC THERAPY IN VARICEAL BLEEDING

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Esophageal varices bleeding are the common cause of Massive Upper GI Bleeding in Indonesia, mortality 70% in bleeding and cirrhotic patients during hospitalization. Cause of death due to deterioration of liver function.
Portal hypertension itself does not require treatment, but intervention is indicated when there are complications of bleeding such as hemorrhagic shock or deterioration of liver function.
The majority of patients are now manage successfully by medical, endoscopic and radiologic treatments, although surgery still has a distinct role for selected patients. The selection of their options needs to be tailored to the individual patient, including severity of any underlying liver disease, the local medical facilities and expertise available.
Liver transplantation can cure both the complications and the underlying liver disease, but this options of surgical treatment is not yet available in Indonesia.
In Bandung, if surgical treatment was indicated, devascularization is a procedure of choice, because it can be performed in any hospital by general surgeons and so far with acceptable morbidity and over all mortality less than 10%.
Surgical rescue means emergency or urgent life saving, so in the very urgent case surgical procedure should be as short as possible, and its goals are to stop bleeding, but with temporary result, such as just stapling the distal esophagus. In the center with liver transplantation facility, the choice for life saving intervention may be urgent TIPS application.
When the general condition of the patient permits, we prefer porto-azygos disconnection by esophago-gastric devascularization with/without distal esophagus or cardiac transection, as a procedure for life saving which expecting a long-term benefits with lower incidence of recurrent bleeding and mortality

S-12

Hepatitis C Research in China

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The milestones for HCV research in China are Prevalence of hepatitis C virus infection (1992-1995), Development of anti-HCV Kit (1991-1995), Improvement of anti-HCV Kit (1996-2000), Natural History of HCV infection (2001-2003), HCV Free core antigen EIA kit(2001-2003), Develop of Chronic Hepatitis C Guideline (2003-2004). According to the National Survey on Prevalence of hepatitis C virus infection during 1992-1995, the standardized rate of anti-HCV was 3.2%, therefore, 38.4 million patients in China at least. Since 1992, Ministry of Health of China developed a regulation which stated "Blood Donor must be screened by anti-HCV". After that, significant reduction of HCV infection among donor was obtained. Up to 2004-2005, anti-HCV could be found only 0.30%-0.93% by EIA and 0.11%-0.36% by RIBA. Most of genotype are genotype 1b and others are genotype 2a. Different investigation reported that the common of transmission included intravenous drug abuse, maternal to fetal or neonatal, sexual contact, household contact, tattooing, haemodialysis facilities and so on.
By prospective and cohort study, 1360 infected person were enrolled in natural history study from 7 provinces including Hebei(507), Beijing(245), Jiangsu(203), Shanxi(114), Inner Mongolia(96), Hunan(77), Shandong(68), Ganshu(50), and among them 693, male and 667, female. Their clinical manifestations were recorded and sera were detected for alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyltransferase (γ-GT) alkaline phosphatase (ALP) total bilirubin TBil direct bilirubin DBil total protein TP albumin ALB and α-fetoprotein (αFP), as well as virus markets. The ultrasound detecting was performed for examination of liver, gall bladder, spleen and pancreas. In virus markets, HCV RNA was detected with fluorogenic-quantitative polymerase-chain-reaction, HBsAg, anti HIV antibody and anti-HCV antibody, with enzyme-linked immuno-absorbed assay (EIA). It was found that 22-46 years

after infection, 77.74% detected for HCV RNA still had detectable HCV RNA in their blood and the infection had cleared spontaneously in 22.26%. Total 16.20% cases developed to cirrhosis at 2003 last visiting, including 2.63%, 8.60%, 13.70% and 19.64% for <20, 21~30, 31~40 and elder than 40 years old at infection respectively. 0.59% developed to hepatocellular carcinoma. Also HCV's role in China HCC was investigated by analysis of percentage of sole HCV infection among HCC patients from 1999 to 2006. gradually increasing of sole HCV infection percentage from 1999 to 2006 was found, from 2.50% to 12.77%. Among patients old than 50 yr. at infection, the during from infection-cirrhosis was 3 - 11 yrs, infection-HCC, 10- 14 yrs, and cirrhosis-HCC, 2 - 8 yrs. However, among the patients less than 50 yr. at infection, it took 18-51 yrs from infection to cirrhosis, 25 to 57 yrs, from infection to HCC, and 5 to 19 yrs from cirrhosis to HCC. The most common sign was fatigue, which presented among 27.71% patients, other signs included anorexia, liver pain, nausea and abdominal pain, a few of patients complained of arthralgia and diarrhea at present. Even among cirrhosis patients, no obvious clinical features were found. Abnormal ALT and/or AST was observed in 37.40% cases, most within 3ULN. Increased ALT presented three types as rapid increase then permanent normal, permanent abnormal and interval increase. Most patients remained anti-HCV antibodies against HCV core antigen, HVR, NS3, NS4 and NS5, some patients showed permanent sole anti-NS3, some patients showed permanent sole anti-core, in a few of patients were found that anti-NS3 disappeared after positive and permanent anti-HVR. Also 13 children obtained infection at infant from their mother were follow up for 10 years, only one child developed active hepatitis after infection and clear HCV RNA and anti-HCV after 7 and 8 years respectively. All others cleared HCV RNA within 60 months. No HCV RNA was detected again during 10 years follow up.

One phase II randomized, open-label and active controlled trial was performed by PEG-IFN alpha -2a in China. 208 patients with chronic hepatitis C were included and divided into two groups randomly, PEG-IFN alpha 2a group and IFN alpha 2a group respectively. There was no significant difference between two groups in pretreatment HCV RNA, HCV genotype and other clinical data. Sustained virological response rate in PEG-IFN alpha 2a group was significantly higher than that in IFN alpha 2a group (41.51% and 16.67% respectively). As the patients were divided to HCV genotype 1 and genotype non-1, the SVR rate of PEG IFN alpha 2a group was significantly higher than conventional IFN alpha 2a group (35.37%, 66.67% vs 14.47%, 21.74%). Patients with higher viral load had significant higher rate of virological response in PEG-IFN alpha 2a group than in conventional IFN alpha 2a group. However, there was no difference between two groups in the patients with low viral load. Similar side-effects were observed in both 2 groups and no severe side-effects developed.

S-13

Management of Bile Duct Injury during Operation

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Bile duct injury (BDI) increases about twice in the laparoscopy era. The risk factors were near similar on both approaches. Three broad categories tent to emerge: dangerous anatomy, pathology postoperative finding and dangerous surgery. The injury can be presented directly during operation or as a late complication. The severity frequently depends not only on the type of treatment, but also on the delay in recognition and initial attempts at treatment. The reconstruction it self depend on facilities and experience of the surgeon. In two years period 8 late cases and one early case were managed by our digestive team. T tube was inserted directly on the Strasberg type A through laparotomy approach. Endoscopic stent were performed on two types A&C. Two types B&D were repaired using internal stent or T tube through a laparotomy approach. Roux and Y reconstruction to hepatic duct was performed on 3 type E cases. Hepp-Couinaud reconstruction was performed on one Bismuth grade III which presented late with severe stricture. To conduct any operation safely on or near the biliary system , the surgeon should be familiar with the anatomy and its variations, the nature of pathologic processes that my causing harm and most important the surgeon own limitations and limitation of system with which they has to work. During operation injury definitive reconstruction is not mandatory, care the contamination and adequate drainage are a good strategy. Plant the definitive treatment in well prepared situation and by an expert surgeon.

S-14

Incident of Complication in Laparoscopic Cholecystectomy in Japan

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Biliary injury is severe complication in laparoscopic cholecystectomy. We experienced 5 patients (0.4%) with biliary injury during laparoscopic cholecystectomy from 1991 to 2003. We present the cases with biliary injury in video. Cholangiography during laparoscopic cholecystectomy is important to avoid bile duct injury.

S-15

BILIARY SURGERY IN ADVANCED LIVER CIRRHOSIS

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Most cirrhotic patients with gallstones remain asymptomatic and do not require surgical intervention. Surgical treatment in these patients has a high mortality, with most deaths in patients with Child's class C. Patients with Child's A and B cirrhosis have lower morbidity and mortality following surgery, although still higher than the general population.

The role of laparoscopic cholecystectomy in this patient population is being defined, should be weighed upon its benefits and disadvantages. For patients with Child's A and B cirrhosis, laparoscopic cholecystectomy is the procedure of choice (Friel CM et al. 1999).

Complications were more frequent in patients with ascites. Particular care should be taken in trocar placement in order to avoid venous collaterals, as they may be a source of major intraoperative bleeding.

To avoid surgical complications, we have to know the problems

in liver cirrhotic patients, and how to correct these conditions, such as hepatic malnutrition, compromised liver function, persisting coagulopathy, engorged vascularization in the abdominal wall and cavity and the patients is immuno compromised.
An emergency open or laparoscopic cholecystectomy in cirrhotic portal hypertension patients not uncommonly culminates into a bloody disaster due to an intra or post-operative bleeding from congested gallbladder hepatic bed with large venous collaterals at the duodenohepatic ligaments. Stay away from the trouble, not to dissect near the engorged and rigid hepatic parenchyma, and the excessively vascular triangle of Calot. In this situation, in some cases, the procedure of choice is subtotal or partial cholecystectomy.
In such conditions, surgery in patients with liver cirrhosis whether elective or emergency can be safely performed if we can correct coagulopathy, maintaining metabolic support and correcting electrolyte imbalance, performing safety surgery and practicing good critical care

S-16

Cadaveric and Living donor Liver transplantation for acute on chronic hepatic failure patients caused by Hepatitis B: A preliminary report of 70 cases

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Objective: To summarize the experience of cadaveric and Living donor Liver transplantation for acute on chronic hepatic failure patients caused by Hepatitis B.
Methods: The clinical and follow-up data of 70 cases from June 2004 to June 2007 were analyzed retrospectively.
Results: All the 70 patients had Child C liver function, and their mean MELD score is (30±6.58). Before receiving Liver transplantation (Ltx), they suffered from several complications including abnormal renal function 47.1% (33/70), hepatic encephalopathy 38.6% (27/70), lungs infection and abdominal infection17.1% (12/70), hepatorenal syndrome 22.9% (16/70), as well as alimentary tract hemorrhage 15.7% (11/70). 47 patients totally underwent plasma phremsis, continuous hemofiltration and Molecular Absorbent Recirculating System (MARS) therapy 54 times. HBV active replication (HBV DNA positive) occurred in 68.6% of the patients (48/70). 11 patients died within 30 days after Ltx, and the perioperative mortality is 15.71%. Leading post-Ltx complications were lungs infection 41.4% (29/70), There were no primary liver nonfunction and blood vessel complications in all the patients. Biliary complication accounts for 12.8%,One-year survival is 75.5% (37/49). Lamivudine combined HBIG were used to prevent HBV recurrence, and there was no HBV graft reinfection and hepatitis B recurrence during a mean 18- month follow up period.
Conclusion: Acute on chronic hepatitis B patients waiting for Ltx are generally with severe damaged liver function, multiple-organ impairment and inner environment disturbance. Therefore much should be done to improve organ function so that better inner environment can be obtained before Ltx. While during Surgery, attention should be paid in the maintenance of coagulability and urine output and in the shrinking of operation time. Attention should also be paid to the intensive care of liver, lung and kidney functions, the appropriate living graft volume, the reasonable use of immunity depressants and the effective prophylaxis for acute lungs injury and secondary infections post-operatively. With sufficient efforts in all the aspects listed above, acute on chronic hepatitis B patients underwent Ltx could expect a satisfactory clinical outcome and a better quality of life.

S-17

N-glycomics changes in hepatocellular carcinoma patients with liver cirrhosis induced by hepatitis B virus

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** X.L and L.D contributed equally to this work.*

We evaluated the use of serum N-glycan fingerprinting as a tool for diagnosis of hepatocellular carcinoma (HCC) in patients with cirrhosis induced by hepatitis B virus. A group of 450 HBV-infected patients with liver fibrosis or cirrhosis with or without HCC were studied. HCC was diagnosed by AFP analysis, ultrasonography and/or computed tomography, and was studied histologically. N-glycan profiles of serum proteins were determined using DNA-sequencer based carbohydrate analytical profiling technology. In this study, we found that a branch alpha (1,3)-fucosylated triantennary glycan (NA3Fb) was more abundant in HCC patients than in cirrhosis patients, fibrosis patients and healthy blood donors, whereas a bisecting core bata(1,6)-fucosylated biantennary glycan (NA2FB) was elevated in cirrhosis patients. The concentration of these two glycans and the log ratio of peak9/peak7 (renamed as glycoHCCTest) was associated with tumor stage. Moreover, for screening HCC from cirrhosis patients showed that overall sensitivity and specificity of the GlycoHCCTest is very similar to that of AFP.
In conclusions: The present study indicates that a branch alpha (1, 3)-fucosylated glycan is associated with development of HCC. The serum N-glycan profile is a promising non-invasive method for detecting HCC in cirrhosis patients, and could be valuable supplement to AFP in diagnosis of HCC in HBV-infected liver cirrhosis patients. Its use for screening, follow-up and management of cirrhosis and HCC patients should be evaluated further.
Key words: HCC, liver cirrhosis, non-invasive, HBV, N-glycan, glycosylation, glycomics.

S-18

Non-Antiviral Treatment for Prevention of Hepatocellular Carcimona

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Hepatocellular carcinoma (HCC), accounts for 90% of all primary liver cancer, is the fifth most frequent malignancies worldwide. The most practical approach to better management of HCC is prevention. For most patients, HCC is a late complication of chronic liver disease. The major risk factors of HCC are chronic hepatitis B or C, accounting for 80%.

Primary preventive measures against HCC include universal vaccination against HBV. For persons who are already chronically infected, both non-antiviral treatments as well as antiviral therapies of chronic hepatitis and cirrhosis will reduce the incidence of HCC. The annual risk of developing HCC in patients with cirrhosis is 5%, and 90% of HCC patients are affected by cirrhosis.

Hepatocarcinogenesis is a multistep process, including inflammatory, regenerative, proliferative, and genetic mechanisms. Suppression of inflammation might inhibit HCC development in cirrhotic livers such as shown by herbal medicines as Stronger Neo-Minophagen C (glcyrrhizin) and Sho-saiko-to (TJ-9), as well as Ursodiol (UDCA) and Colchicine.

Hepatic damage due necroinflammatory process will be followed by hepatic fibrosis. Hepatic fibrosis is a common path leading to hepatic cirrhosis in chronic liver diseases. The reversal treatment of hepatic fibrosis or even cirrhosis could be accomplished by antifibrotic drugs which inhibit fibroblast proliferation, and delay the transport of procollagen and increases collagenase activity as shown by a Chinese herbal therapy, Compound 861.

In future, a combination of immunopreventive and chemopreventive therapies may a clue to the further advance of cancer prevention, and thereby the improvement of the prognosis of cirrhotic patients.

S-19

Antiviral Resistance in Chronic Hepatitis B

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The majority of patients with chronic HBV require long-term treatment. The major goals of antiviral therapy for hepatitis B patients are to suppress HBV replication and to induce a remission in liver disease activity. The development of drug resistance is a critical problem in the long-term management of these patients, as resistance puts patients at risk of liver disease progression. The consequences of drug resistance include the increase of viral load and the 'restart' of liver disease progression. Understanding the underlying mechanisms of resistance is essential. Careful patient monitoring for early recognition of emergent resistance will avoid potential complications by breakthrough infection.

Terminologies and definition: An effective antiviral treatment is defined as a minimum reduction in serum HBV DNA of 1 log10 IU/mL from the pre-treatment baseline, generally assessed within the first 3 months (Shaw et al, J Hepatology 2006; 44:593-606)

Several conditions describe manifestations of antiviral resistance:

Term	Definition
Primary treatment failure (nonresponse)	Inability of nucleoside/tide analogue treatment to reduce serum HBV DNA by ≥1 log10 IU/ml after the first 6 months of treatment
Secondary treatment failure (virologic breakthrough)	Increase in serum HBV DNA by ≥ 1 log10 above nadir on ≥ 2 occasions 1 month apart, while on treatment, after achieving initial response in a medication compliant patient
Biochemical breakthrough	Elevation in serum alanine aminotransferase (ALT) while on treatment, after achieving normalization in a medication compliant patient
Genotypic resistance	Detection of viral populations bearing amino acid substitutions in the reverse transcriptase region of the HBV genome that have been shown to confer resistance to antiviral drugs in phenotypic assay, during antiviral therapy. These mutations are usually detected in patients with virologic breakthrough but they can also be present in patients with persistent viremia and no virologic breakthrough.
Phenotypic resistance	Decreased susceptibility of an HBV polymerase to an antiviral treatment in vitro
Cross resistance	Decreased susceptibility to more than one antiviral drug conferred by the same amino acid substitution or combination of amino acid substitutions

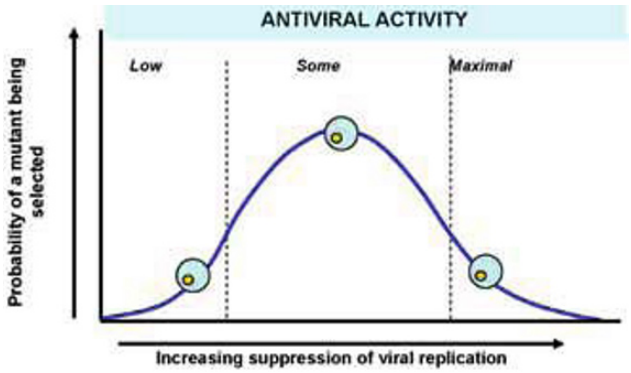
Lok et al. Hepatology 2007; 46:254-265

Mechanism of antiviral resistance: Two major determinants of antiviral resistance are: 1) the long half-life of HBV-infected cells containing viral cccDNA, and 2) the replication of HBV DNA via a reverse transcription phase lacking of correction system. In the presence of selective pressure (by antiviral or immune response), the fittest mutants which are less susceptible can escape and survive.

The incidence of antiviral resistance is associated with viral (pretreatment serum HBV DNA level, pre-existing antiviral-resistant mutations), host (immune status, pharmacodynamics, compliance), and treatment characteristics (potency, genetic barrier to resistance [number of mutations required to produce a marked decrease in susceptibility to the antiviral drug], and duration of treatment).

The probability of a mutation being selected during therapy depends on the ability of a drug to suppress viral replication. A drug with low antiviral activity does not exert substantial pressure on the virus. In this situation, the wild-type virus predominates and the chance of resistance is not high. On the other hand, maximal suppression of viral replication allows little opportunity for resistance to emerge, since mutagenesis is replication dependent. The use of an antiviral with modest antiviral activity and directed at a single target site would provide favourable replication space to the mutants, thus resulting in the highest probability of selecting drug resistance (Fig 1).

Figure 1: Probability of a mutant being selected during antiviral therapy with low, moderate and high activity (Locarnini2006; www.vidrl.org.au/ publications/ hep_updates.com)



Implications for Clinical Practice: Prevention and management of resistance could be approached from two sides: 1) The use of antivirals with potent activity that can exert complete suppression, and 2) The use of regimen with antiviral activity targeted at different sites.

Several points for clinical practice are:

- Thorough understanding of the molecular mechanism of HBV replication is the key to apply antivirals for HBV.
- The pattern and dynamics of HBV drug resistance are determined by mutational mechanisms, replication fitness, replication space, and selection pressure
- Continuous potent suppression of HBV replication below a threshold is necessary
- Close monitoring of HBV levels in patients undergoing treatment is important in developing a logical and successful approach to the treatment of HBV.

S-20

Management of Hep-C after HCC Resection

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Hepatitis B and C virus infection is a major cause of hepatocellular carcinoma (HCC) in Japan. I will present our data how we have tried to prevent HCC by treating hepatitis.

Treatment of acute hepatitis C by interferon was so successful. The effectiveness of interferon therapy against chronic hepatitis C virus infection was shown in many studies including ours.

In 1994, we set up a national surveillance program for HCC development among chronic hepatitis C patients and enrolled about 2,900 biopsy-proven cases (1). 2,400 of them received interferon treatment, showing a sustained virologic response rate of 33% on average. The risk of HCC was reduced by half among the interferon-treated patients as a whole, and down to one-fifth among sustained virologic responders (1). Even among the cirrhotic, the incidence of HCC was decreased by long term follow-up. We also confirmed histologically the resolution of cirrhosis following sustained virologic response and the calculated rate of fibrosis regression rate was 0.28 fibrosis stage per year (2). Similar strategy might be employed for hepatitis B virus infection.

Complete removal of HCC nodules was achieved by surgical resection. In our department of Medicine at University of Tokyo, more than 3,000 cases of HCC were treated by medical ablation. However, recurrence is frequent even after with curative treatment.

After the complete ablation of HCV-related HCC, we treated patients with interferon. Survival rates in sustained virologic responders were 78% at 5 years and 68% at 7 years. These results suggested that de novo occurrence of HCC was suppressed along with the resolution of liver fibrosis by antiviral treatment.

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S-21

Pre and Post-Transplantation Management of Chronic Hepatitis C

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An estimated 170 million people worldwide have chronic hepatitis C virus (HCV) infection. After the development of cirrhosis, the annual risk of clinical deterioration is 3.6% to 6%, the risk of hepatocellular carcinoma (HCC) 1.4% to 3.3%, and the risk of death 2.6% to 4%. Cirrhotics with hepatitis C who experience decompensation have a 5-year survival rate of only 50% without transplantation. Chronic hepatitis C with cirrhosis and/or HCC is the leading indication for liver transplantation in

most countries. Reinfection with HCV is virtually universal at the time of transplantation, and the rate of fibrosis is accelerated such that the median time to recurrent cirrhosis is less than a decade. Three patterns of recurrence are recognized: evolution over time to chronic hepatitis and cirrhosis (most common), an indolent course of reinfection over at least the first decade, and cholestatic hepatitis with early graft failure (infrequent). There are a number of conflicting reports in the literature regarding risk factors for poor outcomes after liver transplantation for chronic hepatitis C, but the factors most often cited include high pretransplant viral load (>1 million IU/mL), high post-transplant viral load (>10 million IU/mL), genotype 1b, early recurrence within months of transplant, older donor age (>40 to 50 years of age), cytomegalovirus infection, prolonged cold and warm ischemia times, non-white race, female gender and treatment of acute rejection. Use of corticosteroids boluses and antilymphocyte therapies are most consistently implicated as detrimental. There were some preliminary reports that live donor transplant recipients were at greater risk of recurrence compared with deceased donor recipients, but these observations have not been confirmed and remain uncertain.

The treatment of chronic hepatitis C has improved significantly since the early 1990's, with the sustained virologic response (SVR) rate increasing from approximately 10% with standard interferon to 50% to 60% with peginterferon plus ribavirin. The most common strategy currently in use following liver transplantation for chronic hepatitis C is protocol liver biopsies to make an early diagnosis of progressive disease, followed by antiviral therapy with peginterferon plus ribavirin as tolerated.

Pretransplant Management of Chronic Hepatitis C

Antiviral therapy for patients with chronic hepatitis C and compensated cirrhosis, decompensated cirrhosis, or patients on the waiting list for liver transplantation is evolving. Current data from existing clinical trials suggest that up to 41% of patients with genotype 1 HCV and 73% with genotypes 2 and 3 HCV with advanced fibrosis or early compensated cirrhosis can achieve SVR. Thus, therapy in well-compensated cirrhotics who lack evidence of clinical decompensation has become standard. However, response of cirrhotics to antiviral therapy declines with severity of liver disease and onset of decompensation. In the largest single center experience with treatment of decompensated cirrhotics in Colorado, SVR was achieved in only 13% of patients with genotype 1 but 50% of patients with genotypes 2 and 3. Reasons for low SVR in decompensated cirrhotics include high prevalence of genotype 1, inability to achieve full doses of interferon and ribavirin due to side effects and dose-limiting cytopenias, and risk of complications related to deteriorating liver function. Although SVR rates are low in decompensated cirrhotics, on-treatment clearance of HCV from blood occurs in approximately 30% of patients with genotype 1 and 80% with genotypes 2 and 3, raising the possibility of maintenance therapy as a potential strategy to either prolong the time to transplantation or render the patient negative at the time of transplantation. Three reports suggest that pretransplant clearance of HCV RNA from blood may reduce risk of post-transplant recurrence of hepatitis C.

Post-transplant Management of Chronic Hepatitis C

If HCV infection is not eradicated prior to transplantation, reinfection occurs in essentially 100% of patients. The rate of disease progression is variable, but approximately 25% will develop recurrent cirrhosis within 5 years of transplantation. The treatment strategies differ in terms of the timing of the intervention: 1) prophylactic therapy, starting at time of transplantation; 2) preemptive therapy, starting in the early post-transplant period; and 3) treatment of established, often progressive histological disease. The latter approach has been the most commonly used. However, well-controlled studies of antiviral therapy for recurrent hepatitis C after liver transplantation are lacking to provide solid evidence to support this approach. On the other hand, this strategy appears reasonable pending further data.

The treatment of recurrent HCV disease is focused primarily on treatment of recurrent histological disease with ≥stage 2 hepatic fibrosis. Reported SVR rates in interferon monotherapy studies, including peginterferon monotherapy, are <20%. Combination standard interferon and ribavirin is associated with slightly higher rates of response (SVR rates = 20% to 30%), and the limited data with peginterferon plus ribavirin report SVR rates of 30% to 45%. Thus combination therapy with peginterferon plus ribavirin is the treatment of choice. Though large-scale and controlled studies are lacking, use of peginterferon plus ribavirin would appear to be the treatment of choice although the optimal duration of therapy is unknown. Strategies to improve tolerability are needed, as this would be predicted to increase response rates. The role of maintenance therapy is unknown. Fortunately, the use of interferon or peginterferon has only rarely been associated with precipitation of acute cellular rejection or chronic ductopenic rejection. Finally, this is a patient population in which new antiviral agents, with improved efficacy and tolerability are urgently needed.

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Table1. SVR in Patients with Decompensated Cirrhosis

Author (Ref)	Total No.	Treatment	ETR	SVR	RNA (-) Post-LT
Everson (5)[1]	124 (110)	I-2b+R, PI-2b+R, LADR Genotype 1 Genotype non-1	46% 13% 50%	24%	12 (26%)
Forns (28)	30	I-2b+R, Pre-LT	30%	20%	6 (20%)
Thomas (29)[2]	20	I-2b, Pre-LT	60%	20%	4 (20%)
Crippin (27)	15	I-2b, I-2b+R	33%	0%	0 (0%)

Abbreviations: LT: liver transplantation; SVR: sustained virologic response; I-2b: interferon alfa-2b; R: ribavirin; wk: weeks; PI-2b: peginterferon alfa-2b. SVR was defined as either the standard definition of SVR or HCV RNA negative after transplantation or at last follow-up.
[1]Metavir scores of 3 or 4 (110 had Metavir 4); in other 3 studies, all patients Metavir 4.
[2]Although there were 27 patients reported, only 20 who received antiviral therapy are shown. Seven patients were excluded from treatment due to platelet count <50,000/μl.

Table2. Management Options for Liver Transplant Recipients at Risk for Recurrent HCV

Timing/Type	Definition
Prophylactic	Initiated at the time of transplantation and continued post-transplantation with the goal of preventing recurrent infection
Preemptive	Initiated early in the post transplant period (typically within first 8 weeks) before onset of biochemical and histological disease
Recurrent Disease	Initiated only after biochemical and histologically evidence of recurrent (and typically progressive) disease

Table3. Preemptive Treatment of HCV in Liver Transplant Recipients

Author Year	Study Type	N	Treatment Regimen	Time to Rx (wk)	SVR	Histologic Response	Dose Reduction or D/C
Singh 1998	RCT	12 treated 12 control	IFN, 3MU tiw x 6 mo vs. no Rx	2	0% both groups	No difference in severity	50%
Sheiner 1998	RCT	35 IFN 46 No Rx	IFN 3MU tiw X 6 mo vs. no Rx	3	17% IFN; 5% no Rx	Fewer with recurrence at 1 & 2 yr in IFN gp	28% d/c
Mazzaferro 2001	UC	36	IFN 3MU tiw + RBV 10mg/kg/d for 12 mo	3	33%	Normal biopsy in virologic responders	47%
Sugawara 2004	RCT* LDLT only	23	IFN (3 MU 6 MU tiw) + RBV (600 mg/d)	4	39%	Scores lower in responders	57%
Shergill 2005	RCT*	47	IFN or PEG-IFN alone vs. IFN or PEG-IFN + RBV	≤6 wk	18% with combo, 5% with IFN mono	NA	85% dose reductions 37% d/c
Chalasani 2005	RCT	26 treated 28 control	Peg-IFN a-2a 180 ug X 48 wk	≤3 wk	8% vs 0%	No statistical difference	32% d/c

RCT=randomized controlled trial; UC=uncontrolled; d/c= discontinuation
*2 different treatment arms

Table4. Controlled Studies of Treatment of Recurrent HCV Disease in Liver Transplant Recipients

Author	Treatment	Time to LT to Rx (Mo)	W/D N (%)	ETR N (%)	SVR N (%)
Interferon and Ribavirin					
Samuel 2003	IFN 3 MU tiw + RBV 1000-1200 mg/d x 48 wk (n=28) vs. untreated (n=27)	54	12 (43)	9 (23) vs. 0% controls	6 (21) treated vs. 0% controls
Peginterferon					
Chalasani 2005	PEG alfa-2a 180 ug x 48 wk (n=33), vs. untreated (n=32)	6-60	10 (30)	9 (27) vs. 0% controls	4 (12) treated vs. 0% controls

S-22

Immune Responses to Antiviral and Immunomodulatory Treatment for Chronic Hepatitis B

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Background/Aim: In this pilot study, we evaluated the effect of Thymosin-alpha 1 (TA1) on the secretion of Th1 cell related cytokines IL-2, IFN-γ, TNF-β and that of Th2 cell related cytokines IL-4, IL-6, IL-10 in the patients with chronic hepatitis B.
Method: Total 19 cases enrolled in Phase II clinical trial accepted TA1 therapy. A three-color flow cytometry was used to detect cytokines secreted by both of Th1 cell and Th2 cell secretion before treatment, week 13, 21, 37, 52 and the serum HBV DNA level, liver function and other serum markers were detected at the same time.
Results: In all patients treated with TA1, the cytokines secreted by both Th1 and Th2 were significantly increased and significantly higher that that in control group ($p<0.05$). However,

there was no relevance among the levels of cytokines, ALT level and HBV DNA. After 12 weeks treatment, in the patients who achieved complete virological response, various cytokines levels were significantly increased than that of control group (P<0.05). However, only the levels of Il-4 and Il-6 were significantly increased in the patients who achieved partial response and no significant increase of cytokines were observed in the patients with no virological response. The similar results were shown after 24 weeks of treatment and furthermore the cytokines levels in patients with complete response were higher than that at week 13 during treatment (P<0.001). However, in the patients with partial response, only IL-6 level was significantly increased. These results indicated that the secretion of Th2 cells was associated with the virological response to antiviral therapy with TA1. In all patients treated with TA1, no association was shown between AST and various cytokines levels at week 13. However, levels of IL-2, TNF, and IL-10 were observed to be positively correlated with AST level. Before treatment, Th2 cell cytokine secretion of IL-10 was related with HBV DNA level but no relevance seen at week 13 of treatment. In all patients who achieved complete biochemistry response, the IL-2, TNF, IL-6 and IL-10 level were significantly increased than baseline.

Conclusion: The results showed that immune regulator with TA1 can increase the Th1/Th2 cytokine secretion in the patients with chronic hepatitis B. The cytokines secreted by Th1 and Th2 cells were not associated with ALT and HBV DNA levels, but was independently related with AST level.

Keywords: chronic hepatitis B; Thymosin-alpha 1; Th1/Th2; cytokines

S-23

Advances in the noninvasive diagnosis hepatic fibrosis

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Hepatic fibrosis is a reversible wound healing response characterized by accumulation of extracellular matrix. Fundamental features of hepatic fibrosis are similar regardless of the origin of injury, and closely resemble the scarring response in other organs. Accurate assessment of the extent of fibrosis is essential to guide management and predict prognosis in patients with chronic liver injury. Histologic assessment of a liver biopsy specimen remains the "gold standard" for quantifying fibrosis. However, it is invasive with possible complications, costly and prone to sampling errors. It was reported that biopsy failure was more than 7 times more common than diagnostic failure of markers. Several semi-quantitative morphologic methods have been described which evaluate extracellular matrix in biopsy specimens stained with hematoxylin & eosin, or connective tissue stains such as Masson's Trichrome, reticulin silver impregnation, or Van Gieson. Semiquantitative methods include the Knodell score, METAVIR score, Ishak score and Scheuer classification and others. There has been considerable effort to identify some markers as noninvasive measures of hepatic fibrosis, these markers include serum markers, related liver functions, and FibroTest, Forns Index, APRI Index(AST to platelet ratio Index), FP Index(fibrosis probability), Zeng Index, and glycomics technology. In addition, transient elastography (FibroScan) and magnetic resonance elastography have been reported to diagnose and evaluate hepatic fibrosis and showed to be superior to some serum markers. These noninvasive diagnostic methods of liver fibrosis have recently been proposed as substitutes for liver biopsy but their reported accuracy was around 80%. Recently, some studies showed that the combination of serum markers with Fibroscan and other indexs may increase accuracy, sensitivity, specificity and predictive value of hepatic fibrosis, and may reduce but not substitute the need for liver biopsy.

S-24

Intrahepatic HBV DNA as a predictor of antivirus treatment efficacy in HBeAg-positive chronic hepatitis B patients

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Background: The role of intrahepatic HBV DNA on antiviral treatment for chronic hapetitis B patients is not known detailedly.

Objective: To evaluate the effect of antiviral agents on intrahepatic HBV DNA in HBeAg-positive chronic hepatitis B patients.

Methods: Seventy-one patients received treatment with lamivudine or interferon alpha (IFN-α2b) or sequential therapy with lamivudine-IFN-α2b for 48 wk. All subjects were followed up for 24 wk. Serum and intrahepatic HBV DNA were measured quantitatively by PCR. HBV genotypes were analyzed by PCR-RFLP.

Results: At the end of treatment, the mean values of Knodell score, serum HBV DNA level, intrahepatic HBV DNA level, and serum ALT level in all the 71 patients declined significantly (P<0.05). HBeAg seroconversion occurred in 17 out of the 71 patients. There was no significant difference in above mentioned parameters between HBeAg seroconversion group and HBeAg positive group before treatment (P>0.05), except for the baseline intrahepatic HBV DNA levels (5.6±1.2) log10 and (6.3±0.8) log 10, respectively (P=0.02). After treatment, HBeAg seroconversion group had better improvement than HBeAg positive group. The mean intrahepatic HBV DNA decreased to (4.1±0.8) log10 in seroconversion group (P=0.0124), and to (5.1±1.5) log 10 (P=0.0872) in HBeAg positive group. 20 patients presented undetectable serum HBV DNA levels at the end of treatment, 15 patients with serum HBV DNA level more than 5 log10, serum HBV DNA levels at the range from 3 to 4.9 log10 were shown in 36 patients. There was no significantly difference in the baseline parameters among three groups p 0.05, except that the intrahepatic HBV DNA level in serum HBV DNA undetectable group was obviously lower than that of other tow groups p = 0.00142. After treatment, no significantly improvement was seen in serum HBV DNA level more than 5log group. Mean of intrahepatic HBV DNA reduced from (6.3±0.8) log10 to(4.6±1.3) log10 (p=0.0074) in the patients with serum HBV DNA levels at the range from 3 log10 to 4.9 log10, and from 5.3±1.2 log 10 to 4.1±0.9 log 10(p=0.0256) in the patients with serum HBV DNA undetectable levels. The intrahepatic HBV DNA load was less than 5 log10 in 38 patients at the end of treatment, and higher than 5 log10 in 33 patients (P<0.05). The difference was not statistically significant in the baseline parameters in two groups. After treatment, compared with the patients with intrahepatic HBV DNA load greater than 5 log10, greater improvement was seen in patients with intrahepatic HBV

DNA load less than 5 log10. In the follow-up period of 24-week 16 out of 50 patients with therapy response at the end of therapy achieved virological sustained response, and 24 patients presented virological rebound. The means of intrahepatic and serum HBV DNA loads, Histology and ALT in the patients with virological sustained response were similar to that of patients with virological rebound before and after treatment p 0.05. HBV genotype C accounted for 85.9% (n=61), and genotype B for 14.1% (n=10). The mean intrahepatic HBV DNA loads in genotype C patients before and after treatment were (6.1±0.9) log10 and (4.9±1.4) log10 ($P<0.05$), and (5.6±1.5) log10 and (4.7±1.2) log10 in genotype B patients, respectively ($P>0.05$). There was no statistically significant difference in serum intrahepatic HBV DNA load and ALT level between the two groups at the end of treatment and in any of the parameters measured after 24 wk of treatment ($P>0.05$), the sustained virological response rate and ALT normalization rate were similar.

Conclusion: Intrahepatic HBV DNA can be effectively lowered by antiviral agents. It is a significant marker for monitoring antivirus treatment, low intrahepatic HBV DNA level may achieve better efficacy of antivirus treatment, loss of intrahepatic HBV DNA might be taken as the optimal endpoint of antiviral treatment. HBV genotypes (B and C) have no influence on intrahepatic HBV DNA load and the efficacy of antiviral therapy.

S-25

Fulminant Hepatic Failure: from Basic Science to Therapeutic Intervention

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Fulminant hepatic failure is defined by the sudden onset of severe liver injury accompanied by hepatic encephalopathy in an individual who previously had no evidence of liver disease. This disease causes multi-organ failure and is associated with a high mortality. The most frequently recognised caused of fulminant or subfulminant hepatic failure is viral hepatitis. In China, there are increasing cases of severe acute on chronic hepatitis B (AOC) which eventually leads to hepatic liver failure. Data is now emerging to support the hypothesis that irrespective of the aetiology of fulminant hepatic failure, the host's immune response (including production of proinflamatory cytokines and mediators) contributes to microcirculatory disturbances that result in hypoxic injury and cell death (apoptosis/necrosis). Impairment of the scavenger function of the reticuloendothelial cell system further contributes to reduced hepatic blood flow and ischaemic necrosis. An increased understanding of the molecular pathogenesis of fulminant hepatic failure now enables new molecular therapeutic modalities to be tested. It is clear that, given the complexity of this multi-dimensional disorder, the challenge is to provide a rational basis for the treatment of patients with fulminant hepatic failure. This might include enhancement or suppression of immune responsiveness by manipulation of endogenous cytokine synthesis or by cytokine administration and, at the same time, would need to employ strategies to increase hepatic regeneration.

We and our colleges have been interested in understanding the interaction of viral components and host factor and their contribution to the development of fulminant viral hepatitis. Our previous work has demonstrated that a novel gene fgl2/fibroleukin prothrombinase plays a pivotal role in the pathogenesis of both experimental and human severe forms of viral hepatitis. By hydrodynamic delivery, a selected mouse fgl2 (mfgl2) anti-sense plasmid significantly reduced mfgl2 expression in vivo, markedly ameliorates inflammatory infiltration, fibrin deposition and hepatocytes death, prolonged the survival time period and elevated the survival rate from 0 up to 33.3% in Balb/cJ mice with MHV-3 induced fulminant hepatitis. Efficient and specific mfgl2 gene silence targeted by the constructed mfgl2 antisense plasmid sheds light on the future investigation of gene therapeutic strategies for patients with fulminant viral hepatitis and disease such as acute rejection of xeno- or allograft transplantation and SLE, which fgl2 gene has been shown to be largely involved in the disease development.

Our recent studies have also demonstrated that HBc and HBx proteins initiated the transcription of human fgl2 gene through c-Ets-2 transcription factor, which was dependent on the activation of ERK and JNK signal pathway in corresponding to either HBc or HBx proteins. This work provides new insights in the interaction between HBV virus and host gene hfgl2 expression. The transcription factor c-Ets-2 could be a new therapeutic target for diseases intervention such as fulminant or severe AOC hepatitis B.

S-26

Impact of Steatosis on Chronic Hep-B & C

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There are several predisposing factors for the development hepatocellular carcinoma (HCC) in hepatitis B and C virus infected individuals. Among those, the alcoholic consumption age, extent of fibrosis and possibly high transaminase are contributing factors to the development cancers. However, there is no detailed study on body weight on the development cancers. In our cohort, we found the patients who are obese or at least body mass index beyond 35 had significant increase of HCC among hepatitis C virus infection. This illustrates not just obesity contribute to NASH but also the development of cancer in hepatitis C patients. This may partly explain the difference in the incidence of cancer among different countries.

S-27

Treatment of Chronic Hep – B: When to Start, When to Stop, and When to Alter Therapy

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- Chronic hepatitis B is diagnosed in patients with elevated HBV DNA levels (defined below) and elevated ALT levels or necroinflammation on liver biopsy.
- The natural history of HBV infection can be divided into 4 phases: immune tolerance, immune clearance (HBeAg-positive chronic hepatitis B), nonreplicative (inactive HBsAg carrier), and reactivation (HBeAg-negative chronic hepatitis B).
- Treatment is currently recommended for patients in the immune clearance and reactivation phases, i.e., HBeAg-positive or

HBeAg-negative chronic hepatitis B.

- ALT criteria used for determining the indications for therapy should be the revised upper limits of normal, i.e., 19 U/L in women and 30 U/L in men.
- The primary goal of therapy for chronic hepatitis B is long-term suppression of serum HBV DNA, which will likely reduce progression to cirrhosis and HCC.
- The FDA-approved therapies for chronic hepatitis B in the U.S. include interferon alfa-2b (1991), lamivudine (1998), adefovir (2002), entecavir (2005), peginterferon alfa-2a (2005), and telbivudine (2006), which have certain advantages and disadvantages.
- The currently preferred treatments include adefovir, entecavir, peginterferon alfa-2a, and telbivudine (if HBV DNA undetectable 24 weeks after beginning treatment); standard interferon alfa-2b has been replaced by peginterferon alfa-2a, and lamivudine is not a preferred first-line drug due to high rates of resistance.
- HBeAg-positive chronic hepatitis B patients should receive treatment when HBV DNA levels are ≥ 20,000 IU/mL and ALT levels are elevated, particularly ≥2-fold.
- HBeAg-negative chronic hepatitis B patients should receive treatment when HBV DNA levels are ≥ 2,000 IU/mL and ALT levels are elevated.
- Patients considering peginterferon alfa-2a therapy should be tested for HBV genotype; genotype A responds much better than genotype D (both common in Caucasians), and genotype B responds somewhat better than genotype C (both common in Asians).
- Patients with chronic hepatitis B and cirrhosis with HBV DNA levels ≥ 2,000 IU/mL (or possibly any detectable HBV DNA) should be treated. There is increasing evidence for combination nucleoside/nucleotide therapy in these patients, and therapy should probably be long-term for both HBeAg-positive and HBeAg-negative patients.
- The rates of resistance with long-term therapy are high with lamivudine (65-70% at 4-5 years), intermediate with telbivudine (21.6% in HBeAg-positive and 8.6% in HBeAg-negative patients at 2 years), lower with adefovir (29% at 5 years), and very low with entecavir in the absence of prior lamivudine resistance (~ 1% after 4 years). Patients with lamivudine resistance have a 39.5% rate of novel mutations after 4 years of entecavir therapy. Resistance does not occur with interferon or peginterferon therapy.
- Serum HBV DNA should be measured at week 12 to confirm initial response to treatment (>1 log10 IU/mL decrease from baseline) and at week 24 to ensure adequate suppression of virus (<2,000 IU/mL), and then every 3-6 months to confirm suppression or detect virologic breakthrough (>1 log10 IU/mL from nadir on treatment).
- On-treatment monitoring strategies to define early virologic responses that are predictive of better outcomes and a reduced risk of viral resistance have been recently proposed (roadmap concept). Virologic responses at week 24 are categorized as complete, partial, or inadequate. Complete virologic response is defined as negative HBV DNA (<60 IU/mL). Partial virologic response at week 24 is defined as HBV DNA levels <2,000 IU/mL, and inadequate virologic response is defined as HBV DNA levels ≥2,000 IU/mL.
- Potential future therapies for chronic hepatitis B include peginterferon alfa-2b and other nucleos(t)ide analogues, such as tenofovir that is in late-stage study and will likely be licensed in 2008. Clevudine and pradefovir are in earlier phases of study.

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Table 1: Advantages and Disadvantages of Current Therapies for Chronic Hepatitis B

Agent	Advantages	Disadvantages
Interferon	HBsAg loss Short treatment duration No drug resistance	Parenteral administration Frequent side effects
Lamivudine	Oral administration Excellent tolerance Use in ESLD Use in adefovir failures	Drug resistance: common (~20%/year, and up to 70% with 4-5 years of therapy)
Adefovir	Oral administration Excellent tolerance Use in ESLD Use in lamivudine failures	Less potent, with suboptimal responses not uncommon Drug resistance: delayed and less common (0% at year 1, 2% at year 2, 7% at year 3, 15% at year 4, and 29% at year 5 of therapy)
Entecavir	Oral administration Excellent tolerance High potency in lowering HBV DNA levels Use in adefovir failures	Drug resistance: rare in nucleoside naïve patients (0.1% at year 1, 0.4% at year 2 and 1.1% at year 3), but common in patients with lamivudine resistance (6% at year 1, 14% at year 2, and 32% at year 3)
Peg-IFN	HBsAg loss Fixed duration of treatment No drug resistance	Parenteral administration Frequent side effects but less than interferon
Telbivudine	Oral administration Excellent tolerance High potency in lowering HBV DNA levels	Drug resistance: intermediate rates (5% at year 1, and 21.6% at year 2 in HBeAg-positive patients, and 8.6% in HBeAg-negative patients)

ESLD, end-stage liver disease.

Table 2: Recommendations for Treatment: HBeAg-Positive Patients

HBV DNA[a]	ALT[b]	Treatment Strategy
<20,000	Normal	•No treatment •Monitor every 6-12 months[c] •Consider therapy in patients with known significant histological disease even if low-level replication
≥20,000	Normal	•Low rate of HBeAg seroconversion for all treatments •Younger patients often immune tolerant •Consider biopsy; particularly if older than age 35-40 years; treat if disease. In the absence of biopsy, observe for rise in ALT levels. If treated, adefovir, entecavir, peginterferon alfa-2a, or possibly telbivudine preferred[d,e]
≥20,000	Elevated	• Adefovir, entecavir, peginterferon alfa-2[a], or possibly telbivudine are preferred[d,e] • If "high" HBV DNA; adefovir, entecavir or telbivudine preferred over peginterferon alfa-2a

a. IU/mL (1 IU/mL is equivalent to approximately 5.6 copies/mL)
b The upper limit of normal for serum ALT concentrations for men and women are 30 IU/L and 19 IU/L, respectively.
c. Upon initial diagnosis, every 3 months for 1 year to ensure stability.
d. Genotyping may be useful to help decide between treating with peginterferon alfa-2a rather than with adefovir or entecavir i.e. peginterferon has been shown to be more effective in patients with genotype A versus D.
e. Peginterferon alfa-2a, entecavir and telbivudine are preferred over lamivudine as they have been shown to be superior in randomized clinical trials, and lamivudine is limited by high rates of resistance. However, telbivudine has a moderate rate of resistance, which can be minimized if an undetectable HBV DNA is achieved after 24 weeks of therapy.

Table 3: Recommendations for Treatment: HBeAg-Negative Patients

HBV DNA[a]	ALT[b]	Treatment Strategy
<2,000	Normal	• No treatment; majority inactive HBsAg carriers • Monitor every 6-12 months[c] • Consider therapy in patients with known significant histological disease even if low-level replication
≥2,000	Normal	• Consider biopsy; treat if disease present. In the absence of biopsy, observe for rise in serum ALT levels. • If treated, adefovir, entecavir, peginterferon alfa-2a, or possibly are telbivudine preferred[d]
≥2,000	Elevated	• Adefovir, entecavir, peginterferon alfa-2[a], or possibly telbivudine are preferred[d] • Long-term treatment required for oral agents

a. IU/mL (1 IU/mL is equivalent to approximately 5.6 copies/mL)
b. The upper limit of normal for serum ALT concentrations for men and women are 30 IU/L and 19 IU/L, respectively
c. Upon initial diagnosis, every 3 months for 1 year to ensure stability
d. Lamivudine is not considered a reasonable treatment option due to the high risk of resistance with long-term therapy, and proven inferiority to peginterferon alfa-2a and entecavir in randomized clinical trials. Telbivudine has a moderate rate of resistance, which can be minimized if an undetectable HBV DNA is achieved after 24 weeks of therapy.

Updated from Keeffe EB, et al. Clin Gastroenterol Hepatol. 2006; 4:936-962.

Table4: Recommendations for Treatment: Cirrhotic Patients (HBeAg Positive or Negative)

HBV DNA[a]	Cirrhosis	Treatment Strategy
<2,000	Compensated	• May choose to treat or observe • Adefovir or entecavir preferred[b]
≥2,000	Compensated	• Adefovir or entecavir are first-line options • Long-term treatment required, and combination therapy may be preferred[c]
<200 or ≥200	Decompensated	• Combination with lamivudine, or possibly entecavir, plus adefovir preferred[c,d] • Long-term treatment required, and combination therapy may be preferred[c] • Wait list for liver transplantation

a. IU/mL (1 IU/mL is equivalent to approximately 5.6 copies/mL)
b. Although there are no data available for peginterferon alfa-2a, it may be an option in patients with early well compensated cirrhosis; no data are available for telbivudine
c. Combination therapy with lamivudine, or possibly entecavir, plus adefovir has a theoretical advantage of a lower likelihood of the development of resistance
d. Limited data available for entecavir, and no data available for telbivudine; peginterferon alfa-2a contraindicated

Updated from Keeffe EB, et al. Clin Gastroenterol Hepatol. 2006; 4:936-962.

Table 5: Potential Management of Hepatitis B Antiviral Drug Resistance

Lamivudine resistance	Continue lamivudine and add adefovir (preferred over switch to adefovir) or tenofovir Switch to emtricitabine/tenofovir[1]
Adefovir resistance	Continue adefovir and add lamivudine (preferred over switch to lamivudine) Switch to or add entecavir (if no prior lamivudine resistance) Switch to emtricitabine/tenofovir[1]
Entecavir resistance	Switch to or add adefovir or tenofovir[1]
Telbivudine resistance	Continue telbivudine and add adefovir or tenofovir[1] Switch to emtricitabine/tenofovir[1]

Updated from Keeffe EB, et al. Clin Gastroenterol Hepatol 2006; 4:936-962, and Lok ASF and McMahon. Hepatology 2007; 45:507-539.
[1]Not approved by FDA

S-28

Cipto Mangunkusumo Surgical Experience in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is one of the commonest malignancies in the world, and south East Asia being one of the regions with the highest incidence. In 1995, hospital based study

in Indonesia showed HCC was at the first rank for gastrointestinal malignancy followed by colorectal, gastric and pancreatic cancer. As the knowledge in biological behaviour and natural history of this malignancy became widely known, in recent years, there are more options evolving as the treatment of this disease. Surgery, percutaneous ethanol injection therapy (PEIT), radio frequency ablation (RFA), transarterial embolization (TAE), transarterial chemotherapy, transarterial chemo-embolization (TACE) and systemic therapy such as immunochemotherapy are among these options. In Cipto Mangunkusumo hospital, there were 350 cases of hepatocellular carcinoma hospitalized during 2004-2006. The mean age of the patients was 51 years old, with gender distribution of male to female ratio of 2:1. About 90 % of the cases was treated nonoperatively in the hepatology division. Only a small percentage (7.5%) was treated in the surgery department. Hepatitis B and C as the primary disease for this malignancy were detected in about 38 % and 34 % of the cases respectively. In our institution there are several options for local treatment of HCC. Ethanol injection, radiofrequency ablation transarterial embolization, transarterial chemotherapy and transarterial chemoembolization were done besides surgery. At the digestive surgery division, there were 14 cases which received surgical treatment in these last 3 years. Among these, in 5 cases (1.7% of the hospitalized patient) the tumor was resected, 2 of which were located in the right lobe, whereas the rest were located in the left lobe. The other nine cases underwent laparoscopic biopsy, drainage, or exploration due to lack of resectability. The number of surgical therapy was apparently quite low, compared to cases with non operative treatment. During a study during June 1998 – June 1999, there were 77 new cases of HCC treated in hepatology division. 15.6 % of which (12 cases) received TAE/ Trans Arterial infusion, 3 % (3 cases) undergo PEIT, 2.6 % (2 cases) received immunochemotherapy, whereas the majority of 77.9 % received only symptomatic care. Observing these conditions, it's understandable that there were still no consistent guideline in our institution and the resection rate at our department was still low, only 1.4% of all HCC hospitalized cases. Surgery for hepatic resection as the main treatment with satisfying results should be done more often. Therefore early detection and consistency with the available guidelines needed to be enforced to achieve these goals.

S-29

CURRENT IMAGING FOR CHOLANGIOCARCINOMA

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Tumors of the biliary tracts are uncommon but serious problems. Most patients with such lesions present with jaundice due to obstruction of the biliary tree by the tumor. The tumors generally are small and difficult to visualize with the standard imaging studies such as ultrasonography and computed tomography scanning, but these techniques may provide a clue to the level of the obstruction

Cholangiocarcinoma is the most important primary tumor of the bile ducts and may involve either the intrahepatic or the extrahepatic bilibary ducts. These tumor variety is the second most common primary hepatic malignancy after hepatocellular carcinoma.

The primary cancer of the bile duct arising from the malignant transformation of the epithelial cells. The highest prevalence of intrahepatic cholangiocarcinoma is in Southeast and Esatern Asia. The risk factors include the chronic biliary inflammation and cholestasis, liver fluke infections, the Primary Sclerosing Cholangitis, Caroli disease, Choledocal cyst and chronic intraductal stones.

Depend on the pathologic classifications there are the Intra hepatic type (divided in the peripheral and hilar tumor 8-13%) and Extra hepatic type (87-92 %)

The liver cancer study group of Japan classified the cholangiocarcinoma as Mass-forming Intrahepatic Cholangiocarcinoma, Intraductal and Periductal infiltrating intrahepatic cholangio carcinoma. Hilar cholangocarcinoma is under the heading of intrahepatic cholangiocarcinoma, but their clinical and radiologic features as well a surgical management are more similar to those of extrahepatic cholangiocarcinoma. The Extrahepatic cholangio carcinoma is divided in infiltrating extra hepatic Cholangio carcinoma and polypoid extra hepatic Cholangiocarcinoma.

There are several imaging modalities (ultrasonography, MSCT, MRI), and their diagnostics values for detection will be discussed. Ultrasonography has been widely accepted as an initial screening procedure for bile duct dilatation in patients with jaundice.

MRI, MRCP, Contrast Enhanced Computed Tomography with optimal acquisition timing, permits improved lesion detection and will improve the characterizations of lesions.

The overall high accuracy of MSCT and MRI are similar. MRCP evaluation could be used as a complimentary examination.

Oral Presentation

OP-1

Prevalence of fatty liver and its risk factors in population of Southern China

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Aims: to investigate the prevalence of fatty liver disease (FLD) and its risk factors in the general population in southern China.
Methods: A cross-sectional survey with multiple-stage stratified cluster and random sampling was performed. All residents aged over 7 from three communities in city and three villages were selected for the survey. Questionnaire, physical examination, serum lipid-profile, and ultrasonographic examination of liver were undertaken.
Results: Response rate was 89.6%. Of total 3543 participants, 609 (17.2%) were diagnosed as FLD (male 18.0%, female 16.7%). The prevalence increased with age. Before 50 years old, the prevalence in males was significantly higher than that in females, but opposite result was observed after 50 years ($P<0.01$). The overall prevalence of alcoholic fatty liver (AFL) and nonalcoholic fatty liver (NAFLD) was 2.2% and 15.0%. In children the rate of NAFLD was 5/379 (1.3%); in adults ALD and NAFLD, 2.5% and 16.6%. FLD prevalence in rural area (12.9%) was significantly lower than that (23.0%) in urban ($P<0.01$). After adjusted for age, sex and residence area, the overall standardized prevalence of FLD, ALD and NAFLD was 11.3%, 2.2% and 9.1% respectively (in adults 14.5%, 2.9% and 11.7%). Logistic regression analysis demonstrated that female, educational levels and rural area were inversely associated with FLD. While alcohol drinking, heavy tastes, BMI, waist circumference, waist hip ratio, triglyceride, fasting serum glucose levels and hypertension were directly correlated to fatty liver.
Conclusions: FLD is common in southern China with NAFLD being the major type. Metabolic disorders are closely associated with FLD.

OP-2

PD-1 upregulation is associated with HBV-specific T cell dysfunction in chronic Hepatitis B patients

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Objective: To measure the PD-1 expression on HBV-specific CD8 T cells and investigate the role of PD-1/PD-L1 pathway in T-cell responses of patients with different HBV infection statuses.
Methods: 11 convalescent acute hepatitis B patients (AHB), 71 chronic hepatitis B (CHB) patients and 20 healthy controls (Table 1) were enrolled. PD-1 expression on total CD8 and HBV-specific CD8 T cells were tested in vitro, and PD-1 Ligands expression on PBMC were also tested by flow cytometry. Under the stimulation of recombinant HBV-Ag, the cellular proliferation and IFN-gamma production of PBMC with or without PD-1 blockade were analyzed by MTT assay and ELISA, respectively.
Results: Compared to the convalescent AHB patients, PD-1 was significantly upregulated on CD8 T cells, especially on the HBV pentamer-positive CD8 T cells from CHB patients (Fig. 2). And one of its ligands, PD-L1, but not PD-L2, was significantly upregulated on PBMC from CHB patients (Fig. 1). In CHB patients, HBV-specific T cells and cellular proliferation could be observed under the recombinant HBV-Ag stimulation (Fig. 2 and Fig. 4), and blockade of PD-1/PD-L1 pathway significantly enhanced the IFN-gamma production and cellular proliferation of PBMC (Fig. 4). Furthermore, PD-1 expression on pentamer-positive CD8 T cells was positively associated with plasma viral load in CHB patients (Fig. 3 and Fig. 5).
Conclusion: PD-1 upregulation on HBV-specific CD8 T cells is engaged in the dysfunction of T cells and high viraemia in CHB patients, and the antiviral T-cell responses could be improved by the blockade of this inhibitory PD-1/PD-L1 pathway.
Keywords: chronic hepatitis B, PD-L1, pentamer, serum viral load, blockade

OP-3

THE MANNOSE BINDING LECTIN GENE POLYMORPHISMS IN CHRONIC HEPATITIS B PATIENTS

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Background: Mannose binding lectin (MBL) is a calcium-dependent C type lectin with a structural analogy to complement component C1q and plays an important role in host immune defense because of its ability to activate the complement system and phagocytosis. The MBL gene encodes MBL, is located on chromosome 10 and consists of four exons. Single nucleotide polymorphism (SNPs) in this gene diminished level of MBL serum and the functional of MBL. Thus, its leads to an opsonic defect that impairs phagocytosis. No data about genetic factor especially MBL gene in chronic B Hepatitis patients in Indonesia. We investigate the association of SNPs codon 52 and 54 MBL gene with hepatitis B virus persistence and progression disease in chonic hepatitis B patients.
Methods: We enrolled 55 chronic hepatitis B patients and 15 healthy (anti HBs positive) patients in Mohammad Hoesin General Hospital, Palembang South Sumatera Indonesia. MBL gene mutation at codon 52 and 54 was detected by polymerase chain reaction – restricted fragment length polymorphisms (PCR-RFLP).
Results: There were a significantly difference frequency of homozygote mutant allele codon 52 in healthy and chronic hepatitis B patient; 13,3% vs 70,9% (p=0,000). The frequency of homozygote mutant allele codon 54 in healthy patiens was 26,7% and 40% in chronic hepatitis B patients (p=0,000). The frequency of homozygote mutant allele codon 52 in patient with hepatocelluler carcinoma or hepatic cirrhosis related hepatitis B was 49,1% and 21,8% in chronic hepatitis B without complication (p=0,000; OR=2,42; 95% CI).
Conclusion: This study suggested that polymorphism at codon 52 of MBL gene is associated with persistence and disease progression of hepatitis B. The polymorphism at codon 54 is associated with persistence but not associated with disease

progression.
Keyword: Mannose Binding Letin; Hepatitis B; Single Nucleotide Polymorphism

OP-4
CBD stone is the most cause of obstructive jaundice patient: evaluation from ERCP
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Background: Obstructive jaundice may caused by extrahepatic cholestatic (CBD stones, pancreas and ampula cancer, CBD stricture, cholangiocarcinoma) and intrahepatic cholestatic
Aim: To know what's the cause of obstructive jaundice based on ERCP evaluation
Methods: We did the retrospective study based on data of ERCP in Cipto Mangunkusumo Hospital in October 2004 until Mei 2007
Results: We evaluated 95 patients which has done ERCP examination, complete data in 76 patients. Male was more frequent than female (61.8% vs 38.2%), with age range was 20-80 years old (age mean was 48.47 years old). We found CBD stones in 33 (43.4%) patients, papila vateri tumour in 10 (13.2%) patients, caput pancreas cancer in 8 (10.5%) patients, CBD stricture in 3 (3.9%) patients, cholangiocarcinoma in 1 (1.3%) patient, Klatskin tumour in 1 (1.3%) patient and unknown etiology obstructive in 4 (5.3%) patients. Obstructive icterus was the most indication in ERCP examination, in 47 (61.8%) patients, followed by cholelithiasis in 22 (28.9%) patients. Sphincterotomy and stones extraction has done in 17 (22.4%) patients, ductal cleansing in 3 (3.9%) patients, CBD stenting was performed in 17 (22.4%) pasien. Surgery consult in 13 (17.1%) patients. ERCP failed reported in 15 (19.7%) patients, most in caput pancreas cancer patients-6 (40%) patients and papila vateri tumour in 4 (26.7%) patients.
Conclusion: We found CBD stones was the most cause of obstructive jaundice, based on ERCP evaluation. ERCP has done successfully in 80.3% patients and therapeutics has done in 48.7% patients.
Keywords: obstructive jaundice, ERCP, CBD stones

OP-5
DISTRIBUTION OF HBV SEROTYPE AND GENOTYPE IN WEST SUMATERA :
REVISITING ADR-ZONE IN WEST INDONESIA
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Introduction: Indonesia has a specific pattern of geographical distribution and genetic diversity of hepatitis B virus (HBV). Four major HBsAg serotypes (adw. adr, ayw, and ayr) and three HBV genotypes (B, C and D) circulate in Indonesia. An exceptional finding was the adr predominance in Padang of West Sumatra albeit located in the adw zone. Here, we evaluate the HBsAg prevalence and HBV genetic characteristics in population and patients with chronic liver disease (CLD) in West Sumatra including Padang .
Method: A total of 611 sera from healthy population were screened for HBsAg, and 49 from HBsAg positive CLD patients (chronic hepatitis B, liver cirrhosis, hepatocellular carcinoma) were collected. HBV DNA was extracted and studied for the genetic characteristics within the S and PreS2 regions (by sequencing and phylogenetic analysis). HBV serotype was determined from the deduced amino acids encoded by S gene.
Result: Among 611 populations, HBsAg was detected in 33 (5.4%). HBV DNA was positive in 28 (84.8%) of HBsAg positive population and 37 (75.5%) of CLD patients. The distribution of HBV genotypes indicated 23 (82.1%) HBV/C and 5 (17.9%) HBV/B in population, and 24 (64.9%) HBV/C and 13 (35.1%) HBV/B in patients. The HBsAg serotype distribution showed 21 (75%) adrq+, 6 (21.4%) adw and 1 (3.6%) ayr in populations; 25 (67.6%) adrq+, 9 (24.3%) adw, 1 (2.7%) ayr, and 2 (5.4%) ayw1 among patients. Isolates from population showed intact gene, while 9 (24.3%) from patients had deletion in the Pre-S2 region.
Discussion: The HBsAg prevalence in West Sumatera decreased from 19% to 5.4%, meaning an effective Hepatitis B public health intervention. This study confirms that genotype C/adrq+ is the predominant genotype and serotype in west Sumatra. This interesting finding can be a start to trace the people migration and to associate the disease pathogenesis and manifestations in people originating from Padang living in other parts of Indonesia or abroad. HBV isolates with deletion in the preS2 region found in patients is in agreement with the reports from other endemic countries and could be the result of host-agent interaction of HBV replicating in chronically active hepatitis.
Keywords: HBsAg, HBV DNA, Genotype, Serotype.

OP-6
The SVR of combination PEG-IFN Alfa-2a (40 KD) and Ribavirin In Chronic Hepatitis C Patients In Indonesia
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Background and Aims: In two previous randomized, multicenter phase III studies, overall sustained virological response (SVR) for patients treated with was 56-63%. Fifty two percents of patients with genotype 1 reached SVR and genotype 2-3 was 84%. This study was intended to evaluate the efficacy and safety profile of PEG-IFN alfa-2a (40KD) and ribavirin combination in the treatment of CHC patients in Indonesia (Jakarta).
Methods: A total of fifty seven CHC patients were treated with PEG-IFN alfa-2a 180 mcg SC once weekly plus Ribavirin 800-1200 mg/day, 48 weeks for genotype 1, and 24 weeks for other genotypes (2, 3, 10 and undetermined). All the patients were assessed for SVR 24 weeks after the end of treatment.
Results: EVR was achieved by 90.9% (20/22) genotype 1, and 100% (8/8) genotype non-1. The EOT and SVR in genotype 1 was 94.3% (33/35) and 71.4% (25/35), respectively and genotype non-1 was 100% (22/22) and 86.4% (19/22). The most frequent

adverse events observed in 57 patients in this study was flu-like symptoms (91.1%). Laboratory abnormalities (anemia, neutropenia and thrombocytopenia) were found in 33.3%, 17.8%, and 4.4%, respectively.
Conclusion: In patients with chronic hepatitis C in Indonesia (Jakarta) treated with PEG-IFN alfa-2a (40 KD) plus ribavirin seemed to show a better efficacy profile compare to other study.

OP-7

Characterization of circulating CD4+CD25+ regulatory T cell in patients with chronic HBV infection

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Aims: To determine the frequency, phenotypic markers and cytokines production of circulating CD4+CD25+ Tregs in HBV infected patients with different statuses, and to investigate the immunoregulatory role of CD4+CD25+ Tregs from chronic hepatitis B (CHB) patients.
Methods: The frequency and specific markers of circulating Tregs from 79 CHB patients, 26 asymptomatic HBV carriers (ASC), 12 acute hepatitis B (AHB) patients and 20 healthy controls were analyzed by flow cytometry. The cytokines production of CD4+CD25+ Tregs under anti-CD3 or HBV-antigen stimulation were tested by ELISA. The cellular proliferation and IFN-g production of autologous peripheral blood mononuclear cells (PBMCs) co-cultured with Tregs were also measured.
Results: The CD4+CD25high frequency in AHB patients was comparable to that of healthy controls, while it was significantly increased in CHB patients. CD4+CD25+ Tregs produced interleukin (IL)-10 but little or no IFN-g under anti-CD3 stimulation. In CHB patients, the frequency of CD4+CD25+ Tregs was positively correlated with serum viral load, and Tregs were capable of suppressing proliferation and IFN-g production of PBMCs stimulated by HBV-antigen in vitro. Combined using of anit-PD-1 and anti-CTLA4 monoclonal antibody partially restored cellular proliferation whereas significantly increased IFN-g production of PBMCs co-clutured with Tregs at a ratio of 2:1.
Conclusion: The frequency of circulating CD4+CD25+ Tregs is significantly upregulated in chronic HBV infected patients, and Tregs may play an important role in viral persistence of CHB patients by modulating virus-specific T-cell immune responses.
Keywords: CD4+CD25+ Tregs; chronic hepatitis B; Foxp3; PD-1; HBV DNA load

OP-8

DECOMPENSATED HEPATIC CIRRHOSIS PATIENT WITH POSITIVE HBV-DNA, BEING NOT REACTIVE BY GIVING THE NUCLEOSIDE ANALOGUE FIRSTLY AND THAN WITH ONE INJECTION OF PEGYLATED INTERFERON

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Background: Decompensated liver cirrhosis is contra indicated for interferon treatment
Aim: Decompensated liver cirrhosis with positive/reactive HBV-DNA can be treated with peggylated interferon after progression of the patient's health
Method: A Decompensated Hepatic cirrhosis patient which 2 times pre comatous, healthier after treated with nucleotide analog for 3 months than an ampoule of pegylated interferon being injected subcutaneously, and the HBV-DNA to be not reactive
Result: With an injection of pegylated interferon to decompensated liver cirrhosis with positive HBV-DNA patient (after treated with nuccleotide analog), the HBV-DNA to be not detectcted
Conclusion: Progression of the decompensated hepatic cirrhosis patients health, to whom the policy about interferon treatment may be wisely to be revised, may be they can get pegylated interferon treatment in order to optimalize the treatment policy.

OP-9

Hepatitis B Virus Proteins Induce Activation of Hfgl2 Transcription through C-Ets-2 Transcription Factor

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Fibrinogen-like protein 2 (fgl2) /fibroleukin also known as fgl2 prothrombinase was identified to belong to the fibrinogen protein superfamily. Fgl2 was expressed mainly in activated macrophages and endothelial cells. Fgl2 gene encodes for two different types of proteins which are membrane bound fgl2 and soluble fgl2. Fgl2 prothrombinase has been shown to have the attributes of a serine protease capable of directly cleaving prothrombin to thrombin leading to fibrin deposition and act as blood coagulation factor X. Previous work has demonstrated that fgl2 participated in the pathogenesis of fulminant hepatitis or human severe acute on chronic (AOC) hepatitis B, fetal loss, xenotransplant rejection and so on. Previous work also found mouse fgl2 (mfgl2) expressed strongly in susceptible mouse post murine hepatitis virus-3 (MHV-3) infection. The nucleocapsid protein of MHV-3 induced transcription of mfgl2 and invoked the hepatic nuclear factor 4α as a key transcription factor participating in the regulation of mfgl2 gene expression.
In Asia, hepatitis B virus (HBV) is still one of the most frequent causes of liver failure. Fgl2/fibroleukin gene plays a pivotal role in the pathogenesis of both experimental and human severe form of viral hepatitis. However the viral and host factors involved in the transcription of hfgl2 gene have not been defined. The aim of this study was to define the viral and host factors involved in the

transcription of human fgl2 (hfgl2). HBc, HBs or HBx expression plasmids were cotransfected with a hfgl2 luciferase report construct into Chinese Hamster Ovary (CHO) cells and HepG2 cells respectively. Luciferase assay showed that HBc or HBx protein, but not HBs protein significantly enhanced hfgl2 transcription activity in both CHO cells and HepG2 cells. Expression of these plasmids in eukaryotic cells was detected by immunohistochemistry and Western blottingting. The transcriptional activity which HBV proteins induced hfgl2 gene was determined by the activity of luciferase and β-galactosidase served as internal control. The results showed that CHO cells transfected with eukaryotic expressing plasmids of HBV proteins could express HBV encoding proteins transiently. Relative luciferase activity in CHO cells transfected with pcDNA-HBc or pcDNA-HBx was at an average of 5.4-fold and 6-fold elevation when compared with the control group, and 8.7-fold and 11-fold respectively in HepG2 cells. These results indicate that HBc and HBx protein but not HBs activate the transcription of hfgl2 gene.
A strong regulatory region from -712 to -568 (relative to the transcriptional starting site) was shown to be responsible for hfgl2 gene transcription in response to HBc or HBx proteins expressed by respective expressional plasmids. By site-directed mutagenesis, the overlapping cis-elements LEF/c-Ets in the region of -712/-568 was demonstrated to play an important role in hfgl2 gene transcription in response to HBc protein, while two cis-elements LEF/c-Ets and HSTF in the same domain were found to account for hfgl2 transcription in response to HBx protein. EMSA assays using nuclear extracts from THP-1 cells showed that an Ets family member c-Ets-2 bound to the cognate cis-element in hfgl2 promoter which was shown to be responsible for hfgl2 gene transcription in response to viral proteins. ChiP assay using c-Ets-2 antibody found that the DNA fragment, which bound to transcription factor c-Ets-2, was within the sequence of hfgl2 promoter. It was evidenced c-Ets-2 partially translocated into the nucleus of THP-1cells in response to both HBc and HBx by confocal immunofluorescence study and Western blotting. shRNA interference of c-Ets-2 expression was able to decrease the relative luciferase activity of hfgl2 promoter by 64.8%.
In human, c-Ets-2 protein was highly expressed in PBMC isolated from patients with severe AOC hepatitis B when compared with health controls. Increased activation of P-ERK, P-JNK and P-p38 MAPK were found in PBMC isolated from patients with severe AOC hepatitis B when compared with health controls. Treatment with ERK inhibitor PD098059 but not P-p38 MAPK inhibitor SB203580 or JNK inhibitor SP600125 abolished the upregulated expression of c-Ets-2 in response to HBc protein, while JNK inhibitor SP600125 but not ERK inhibitor PD098059 or P-p38 MAPK inhibitor SB203580 abolished the upregulated expression of c-Ets-2 in response to HBx protein, suggesting ERK and JNK MAPK signal pathways were involved in the expression of c-Ets-2 in response to HBc and HBx proteins respectively.
In conclusion, these studies have demonstrated that HBc and HBx initiated the transcription of hfgl2 gene through c-Ets-2 transcription factor, which was dependent on the activation of ERK and JNK signal pathway in corresponding to either HBc or HBx proteins. This work provides new insights in the interaction between HBV virus and host gene hfgl2 expression. The transcription factor c-Ets-2 could be a new therapeutic target for diseases intervention such as fulminant or severe AOC hepatitis B.
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OP-10

Histological Diagnosis in NASH

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NAFDL has a broad spectrum, characterized by hepatic steatosis, in absence, of history of significant alcohol use or other known liver disease.
NASH is a progressive form NAFDL, which could lead to cirrhosis and liver failure.
Lesmana et al, based on study of 30 cases of NASH, concluded, that most of the metabolic syndrome features were found in patients with NASH.
The diagnosis of NASH is a clinico-pathological correlation, because the parenchymal injury and fibrosis cannot be detected by imaging studies or laboratory test.
The histological study was based on 17 cases, using Histological Scoring System, included steatosis, hepatocyte balloning, lobular inflammation and fibrosis.

OP-11

Hepatitis C virus and Tuberculosis co-infection in HIV / AIDS : a preliminary report

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Co-infection of Hepatitis C virus and Tuberculosis in patients with HIV-AIDS will potentially result in a worsening of disease, even with ARV management. We reported a preliminary study n clinical manifestation, immunologic and virologic response to ARV treatment in the triple infection patients as well as in HIV infected patients, without hepatitis C and TB co infection.
Materials and methods: Cross-sectional descriptive study was done in the outpatient clinic of Kramat 128, a small private hospital in Jakarta, throughout June and July 2007. Status of HCV infection was confirmed by total HCV ELISA antibody test and tuberculosis by chest X-ray or sputum acid fast smear. Viral load was determined by Polymerase Chain Reaction (PCR) method and CD4 count done by flow cytometry. Cerebral toxoplasma infection was confirmed by cerebral CT-scan examination. The data were then analyzed using SPSS 14th and nonparametric tests.
Results: One hundred and thirty patients were admitted, and divided in to four groups, 52.3%(68/130) were HIV and TBC co infected, 21.5%(28/130) were HIV and HCV co infected, 16.2%(21/130) were triple infected with HIV, HCV and TBC and 26.2 %(34/130) were without HCV and TB co infection.
Male and intravenous drug user was the main characteristics of all groups. The triple infected patients came with a more severe clinical manifestations, fever, cough, weight loss and shortness of breath (38.1% vs.16.5%, 0.15-0.61 vs. 0.9-0.24 95% CI, p=0.024) and higher hospitalization rate (38.1% vs. 7.3%, 0.15-0.61 vs. 0.2-0.7 95% CI, p=<0.001) compared with the other groups all together.
Patients with triple infections also had more toxoplasma encephalitis (38% vs.5.9%, 0.15-0.61 vs. -0.2-0.14 95% CI, p=0.003), lower CD4 concentration at presentation (132 vs. 232 cells/μl, 53-212 vs. 152-312 95% CI, p=0.035), and slower CD4 rise in 6 month (80.6 vs. 185.2 cells/μl, 5.4-155.8 vs. 111.6-258.8 95% CI, p=0.06) compared to the single HIV infected group.

Furthermore, at presentation, triple infected patients also showed higher percentage of low CD4 count (less than 200 cells/μl) compared to those without HCV and TB (80% vs. 53.3% or 16/20 vs. 16/30, p=0.099).
Virologic response after 6 months of antiretroviral therapy revealed less virologic response in the triple infection groups, only 45.5% of them had undetectable viral load, compared to the group without hepatitis C and TB (88.9%, p=0.013).
Conclusion: In this study, triple infections with HIV, HCV and TBC were associated with a more severe clinical manifestation and higher hospitalization rate. Patients with triple infection showed a lower CD4 status at presentation and a less immunologic response at 6 months after ARV treatment, compared to those without. The virologic response (viral load undetected) of patients without triple infection is significantly higher than the triple infected groups.
Keywords: Triple infections, Human Immunodeficiency Virus infection, Hepatitis C infection, Tuberculosis infection, CD4, viral load, toxoplasma encephalitis.

OP-12
Grade 3-4 Liver Enzyme Elevation during HAART in HIV and Hepatitis C Co-infected Adults
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The use of highly active antiretroviral treatment (HAART) has prolonged the survival of HIV infected patients. But, all classes of antiretroviral drugs have been reported to cause liver toxicity. Previous studies demonstrated the association of liver toxicity with hepatitis C co-infection. However, incidence and risk factor data for liver enzyme elevations in large cohorts of HCV/HIV co-infected patients are lacking.
The objective of this study was to evaluate the incidence of grade 3-4 liver enzyme elevation (LEE) in HIV/HCV co-infected patients after the introduction of HAART, the clinical significance to the patients and to determine if there were any factors that could predict its development.
A retrospective cohort study of HIV/HCV co-infected adults in Pokdisus AIDS Clinic Ciptomangunkusumo Hospital was conducted. All patients were antiretroviral naïve and never had interferon therapy before. Patients who started taking fist line combination therapy in Indonesia (NNRTI based regimen) between January 2004 to August 2006 and who were followed for at least 6 months after were included in this study. Hepatitis B coinfection, and age less than 17 years were excluded.
A total of 59 grade 3-4 LEE (any increase by > 5 times upper normal limit of ALT or any increase of 100 U/L from baseline ALT) developed in 284 patients during the follow up (20.8%). The median time to the onset of grade 3-4 LEE was 20 weeks (min-max 2-80 weeks). Only 27.1% accompanied with symptoms, i.e.: nausea and jaundice. Two patients developed decompensated liver diseases, one of them ended with death. In 5 patients, grade 3-4 LEE coincided with nevirapine or efavirenz-related rashes. Fifty-two patients (88.1%) continued their antiretroviral regimen throughout the entire episode of hepatic flare. The median peak level of ALT was 2311 IU/L (IQR, 174–327). Lower baseline ALT was the only factor significantly correlated with grade 3-4 LEE in this study.
Keywords: liver enzyme elevation, highly active antiretroviral therapy, HIV/HC

Moderated Poster

MP-1
ULTRASOUND in GI-TRACT PROBLEMS

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Background: To establish the diagnosis of GI-tract problems is not as easy as it sounds. For years, many tools with high technology of high resolution are coming to help the clinicians to establish a correct diagnosis. One of them is Ultrasound (US). What can US do?
Material and Methods: Since the year 1980, many cases with dyspepsia are sent to our Unit and from 2005 up to 2007, 942 patients were put into a retrospective study: M 415 and F 527, 20-68 yrs. The equipment used were Medison Accuvix XQ and Toshiba Power Vision 8000. All patients were put on fasting 5 hours prior examination. The endoscopy were done before or after the US study in most cases and in some cases followed by CT-scan.
Result: Our findings were HCC, cholecystitis, Gallstones, CBD-stones, Bile duct cyst, pancreatitis, pancreatic tumor, pancreatic cyst, ascaris in the gallbladder/CBD, gastric cancer, colon cancer, lymphomas, appendicitis, colitis, gynecological cyst, ovarian cancer and no US abnormalities. Dealing with GI-tract problems is advisable not to put endoscopy as the only tool to establish its etiology.
Conclusions: Ultrasound proves to be very useful, practical and economical as a first step procedure to reveal the etiology of GI-tract problems, especially in cases where endoscopy got difficulties and CT-scan or other modalities are to expensive

MP-2
RhoA RNAi inhibits the invasion and metastasis of hepatocellular carcinoma in vitro

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RhoA, a member of the small GTPases superfamily, was found to be increased in some human cancers and played an important role in tumor morphology especially in the invasion and metastasis of the tumor. Our study found that elevated RhoA expression is highly associated with hepatocellular carcinoma (HCC). At nucleic acid level and protein level˝it was revealed that RhoA was predominantly expressed in thirty samples of HCC tissues and hepatoma cell lines (HepG2,SMMC7721,HepG2.2.15 and Hep3B), while with weak expression or absence in matched adjacent nontumorous tissues and non-hepatoma cell lines(LO2) examined. In the HCC tissues samples, statistical data of the clinical pathology (including the size and the malignant degree of tumor, the numbers of transferred lymph nodes and organs) also showed that the mRNA and protein expression level of RhoA correlated positively with the degree of invasion and metastasis of HCC. Furthermore, RNAi was employed to specifically knockdown endogenous RhoA expression in the four hepatoma cells and LO2 cell. Then, Cell migration activity which was examined using a Boyden chamber assay decreased in the four hepatoma cells, in which flow cytometry analysis after cell was stained with Carboxyl Fluorescein Acetoacetoxy Esters (CFSE) also showed that cell proliferation activity decreased, but both of these were not indicated in LO2 cell. These data suggest that RhoA plays an important role in the invasion and metastasis of HCC. So RhoA may represent a new targeted gene that could be useful for the evaluation of tumor prognosis and therapy in HCC.

MP-3
Success rate of ERCP for identification and stenting in Obstructive Jaundice

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Background: Obstructive jaundice can be caused by malignancy or benign. The treatment of these situations is drainage by biliary stenting, PTBD, or surgical procedures. In advanced malignant jaundice, the stent placement is often difficult.
Aim: To evaluate the success rate of malignant obstructive jaundice evaluation of ERCP and the success rate of stent placement
Methods: We did the retrospective study based on data of ERCP in Cipto Mangunkusumo Hospital in October 2004 until July 2007
Results: We evaluated 100 patients which has done ERCP examination, 92 (92.0 %) of them have clinical diagnosis of obstructive jaundice (direct bilirubin > indirect bilirubin). Of obstructive jaundice patients: male patients were 55 (59.8 %) and female were 37 (40.2 %), with age range 20 – 84 (median age was 51).
Those with obstructive jaundice was found to have no malignancy in 47 (51.1 %) patients, malignancy in 28 (30.4 %)patients, and 17 (18.5 %) of them need further diagnostic evaluation. From 75 patients, only 36 (48.0 %) patient were attempted to have stent placement, 32 (42.7 %) patients don't have stent placement, and 7 (9.3 %) patients have no data.
We done descriptive study on 36 patients who attempted to have stent placement, 19 (52.8 %) patients succed in stent placement, whereas 17 (47.2 %) have failed. Further evaluation showed that age and sex were not affecting stent successfulness, and malignancy was showed to be a factor of stent failure (malignancy: 16 fail and 6 success (27.3 %) vs non malignancy: 1 fail and 13 success (92.85 %)).
Conclusion: ERCP can identify the cause of obstructive jaundice in 81.5 % patients. This procedur success rate of stent placement was 52.8 %. The success rate of biliary stenting in malignant obstructive jaundice was 27.3 %, and the success rate of biliary stenting in non-malignant obstructive jaundice was 92.85 %.
Keywords: obstructive jaundice, malignancy, ERCP, stent placement.

MP-4

Radiofrequency ablation of problematically located hepatocellular carcinoma: tailored approach

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Background: The challenge for radiofrequency ablation (RFA) of hepatocellular carcinomas (HCC) in problematic locations is that outcome is limited due to insufficient ablation or injury of nearby structures. This study aimed to evaluate effective strategy and treatment results of RFA in these cases.
Methods: Ultrasound guided percutaneous RFA was performed in 326 HCC patients. Among them, 249 tumors in 215 patients located at liver periphery, including 54 adjacent to GI tract, 110 close to the diaphragm, 49 close to the gallbladder, and 36 tumors close to liver surface. The sizes of the tumors ranged 1.2 – 7.0 cm (average 3.7 +/-1.3 cm). Individualized treatment strategy was established for tumors in various locations, including "artificial ascites", "lift-expand" electrode placement, "draw-expand" electrode placement, "Supplementary ablation", and "accumulative multiple ablations" techniques. Treatment outcome was compared with another 64 central-located tumors (control group) in the same patients. One-month post-RFA contrast CT was used to evaluate early necrosis rate of the treated tumors.
Results: Early tumor necrosis were obtained in 91.6% (228/249) of the problematically located HCC, including 90.7% (49/54) of the tumors adjacent to GI tract, 90.9% (100/110) near the diaphragm, 91.8% (45/49) by the gallbladder, and 94.4% (34/36) close to liver surface. The necrosis rate of control group was 98.4% (63/64), which was higher than the tumors close to diaphragm (P=0.049). Local tumor recurrence was 8.4% (21/249), comparing with 3.1% (2/64) of the control group (P>0.05). The 1-, 2- and 3-year survival rate of this group were 81.6%, 63.8%, and 53.6%, respectively. Major complications occurred in 3.2% (11/343) of the treatment sessions, including haemorrhage in 2, nearby structure injury in 5, and needle tract seeding in 4 patients. Conclusions: Individualized treatment strategy for problematically located HCC is helpful in improving RFA outcome and expending indications for the therapy.
Keywords: radiofrequency ablation, hepatocellular carcinoma, survival rate, complications, ultrasound

MP-5

Efficacy of molecular adsorbent recirculating system in the treatments of the liver failure patients with hyperbilirubinemia

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Objective: To evaluate the efficacy of molecular adsorbent recirculating system （MARS） in the treatments of the liver failure patients with hyperbilirubinemia and investigate the influencing factors of reducing serum bilirubin（SBil）.
Methods: 17 patients with liver failure were performed MARS therapy for 6 hours per time in addition to standard medical treatment. Serum samples were detected at the different time of MARS treatment.
Results: The SBil were reduced significantly 28% after the treatment with MARS($p<0.05$). The main reduction of SBil occurred at first 3-hours (22.2%), the next 3-hours reduced only 5.8%. 4 cases with hepatic encephalopathy（SBil <350umol/L） did not decreased obviously after MARS therapy. However, the consciousness of the patients was improved gradually as therapeutic time going on. After 5-hour treatment with MARS, instead of a new anion exchange resin for another 3-hour treatment the SBil only decreased 5.1%.
Conclusion: The clearance of the SBil in the patients with the liver failure occurred mostly in pre-3-hour treatment of MARS. As the SBil being less than 350 umol/L, the clearing ability of SBil by MARS is limited. The size of anion exchange resin is not the cause of affecting SBil clearance. It indicates the decrease of SBil in the MARS treatment was affected by the period of exchanging course.
Keywords: MARS, Liver failure, Bilirubin

MP-6

ENDOSCOPY PROFILE IN LIVER CIRRHOTIC PATIENT AT DR. SAIFUL ANWAR HOSPITAL MALANG

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Background: Nowadays endoscopy is the gold standard to visualizing esophagus, gaster, and duodenum. Upper GI bleeding in the liver cirrhotic patient not only occurred by rupture of esophagus varices,but also because of erosive or ulcer in the stomach and duodenum.
Objective: To describe upper GI tract endoscopy in liver cirrhotic patient at Dr. Saiful Anwar Hospital
Methods: Descriptive analytic from our liver cirrhotic patient at endoscopic unit, Dr. Saiful Anwar Hospital in 6 months (October 2006 -April 2007).
Result: Liver cirrhotic patient who performed endoscopy were 55 persons, consist of 37 men, and 18 women with the mean aged was 48,84 + 12,987. The most frequent symptoms were abdominal bloating 19%, followed by vomiting 18%, and nausea 17%. The indication to perform endoscopy because of dyspepsia was 13 patients and upper GI bleeding was 42 persons. Endoscopy profile were esophagus variceal grade I (46%), Grade II (35%), grade III (19%). The normal gastric mucosa was 11 %, and we found congestive gastropathy with erosion and ulcer on 89% of the patients. The most common source of upper GI bleeding were mucosal erosion (48%), rupture of esophagus variceal (33%), and ulceration (19%), There was no correlation between gender and grade of variceal esophagus (p=0,764).
Conclusion: The most common endoscopy features in liver cirrhotic patient on our hospital were esophagus variceal grade I-II with congestive gastropathy. And the most frequent source of upper GI bleeding was not the rupture of Oesophageal varices but due to mucosal erosion bleeding.

MP-7

The Use of Urine Specimen for Detection of Anti-Hepatitis A Virus (Anti-HAV) Antibodies in Healthy Children

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Objective: To evaluate the use of urine as an alternative specimen for detection of anti-hepatitis A virus (anti-HAV) antibodies in

healthy children.
Material and Method: The study was observational cross-sectional diagnostic test comparing urine and serum sample for anti-HAV detection in healthy children between 5 – 12 years old at Rusun Sombo Simokerto Surabaya. Using consecutive sampling, urine and serum specimens collected from 84 children during September and October 2005, 11 samples were excluded because of lytic serum. Enzyme-linked immunosorbent assays technique was performed for anti-HAV examination using AxSYM ® HAVAB ® 2.0 (Abbot, Wiesbaden, Germany).
Result: From 74 samples, 43 boys (58.1%) and 31 girls (41.9%), seropositives were 38 (51.4%) and only 3 (4%) of them were uropositives. Using seroreactivity as a "gold standard," the sensitivity and specificity for anti-HAV were 7.9% and 100%. Mc Nemar test resulted only weak correlated between urine and serum specimen in anti HAV detection. Difference between the proportions of serum and urine positivity for anti-HAV was noted ($P > 0.05$)
Conclusion: Urine appears not to be comparable to serum for detecting anti-hepatitis A virus (anti-HAV) antibodies in children. Therefore, urine specimen could not be use for detection of anti-hepatitis A virus (anti-HAV) antibodies in healthy children.

MP-8
Short and Long Term Efficacy of High Intensity Focused Ultrasound Therapy for Advanced Hepatocellular Carcinoma
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Aims: To investigate the short and long-term efficacy of high intensity focused ultrasound therapy (HIFU) in patients with advanced hepatocellular carcinoma (HCC).
Methods: Patients with unresectable HCC received either HIFU plus supportive (HIFU group, n=151), or supportive treatment only (control group, n=30), according to their willingness. Short-term efficacy including the improvement in tumour imaging parameters, decrease in the serum AFP levels, symptom relief (Karnofsky Performance Status, numerical rating scales) and response rates, and long-term efficacy including the increase of the survival rates and improvement of quality of life (QOL) was monitored.
Results: The tumour imaging parameters, serum AFP levels and symptom scores were improved significantly in HIFU group compared with control (all $p<0.05$). In HIFU group, a complete and a partial response were achieved in 28.5% (n=43) and 60.3% (n=91) cases, while the rates were 0% and 16.7% (n=5) in control group. The overall response rate (88.8%) was significantly greater in HIFU group than that (16.7%) in controls ($p<0.01$). In addition, the one- and two-year survival rates were 50.0% and 30.9% in the HIFU group, which were significantly greater than those (3.4% and 0%) in controls (both $p<0.01$). The QOL score was 83.1±8.0 in 3 months after HIFU, which was significantly greater than the pre-HIFU score (67.7±5.9) and the score in 3 months after treatment (69.0±8.5) in control group (both $p<0.05$). No severe complications occurred during and after HIFU.
Conclusion: HIFU is an effective and safe ablation therapy with satisfactory short and long-term efficacy for patients with HCC.

MP-9
NAFLD patients with T2DM are older and more severe than those without T2DM
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Background: T2DM is characterized by insulin resistance and the insulin resistance is closely correlated to NAFLD. As we know, T2DM is one of risk factors of NAFLD, whereas the result in one study, show that the elevations of aspartate (AST) and alanine aminotransferase (ALT) independently predict T2DM. The presence of T2DM significantly increases the severity of NAFLD.
Objective: To know correlation the clinical features of NAFLD in patients with and without T2DM
Method: Cross sectional study of 42 NAFLD patients (by ultrasonography) in Dr. Saiful Anwar Hospital. All these patients, we examined the anthropometry and blood chemistry.
Results: The mean age of the patients was 52,8 ± 11,7 years. T2DM was diagnosed in 22 patients (52%). The mean age of diabetic patients and non-diabetic patients were 57,4 ± 9,8 years and 48,8 ± 11,2 years (p=0,013), respectively. Both of group have component of metabolic syndrome, but there were no significantly difference, except serum triglyceride levels in diabetic patient was significantly higher 341,1 ±156,9 mg/dl (p=0,006) than non-diabetic patients. Based on clinical features, there was significantly correlation in severity of NAFLD in diabetic patients (r = 0,378; p =0,033).
Conclusions: In NAFLD patients with T2DM, the mean age patients are older and the clinical feature is more severe than in patient without T2DM, suggested the NAFLD is previous occurred in natural history than T2DM. A longitudinal study is needed to know whether the T2DM is risk factor of NAFLD or just related pathologies.
Keyword: fatty liver, type-2 diabetes mellitus, clinical features.
Glossary: NAFLD: Non-alcoholic fatty liver diseases; T2DM: Type-2 diabetes mellitus

MP-10
Tumor necrosis factor-α genetic polymorphisms in nonalcoholic fatty liver disease
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Background/Aims: To study the prevalence of genetic polymorphisms (G to A) in TNF-α promoter area 308 and 238 sites in Chinese people and their relationship to nonalcoholic fatty liver disease (NAFLD).
Methods: 117 patients with confirmed NAFLD and 120 healthy volunteers were included. Clinical and laboratory data were collected. Genotypes of TNF-α308 and 238 were determined by PCR-RFLP.
Results: The G/A genotypes distribution of TNF-α308 was not significantly higher in NAFLD group than that in controls (9.4% vs. 6.7%, $P>0.05$). Allele frequency of A was 4.7% in NAFLD patients compared to 3.3% in controls ($P> 0.05$). However the G/A polymorphism of the TNF-α 238 was significantly higher in

NAFLD group than in controls (29.9% vs. 15.8%, P<0.05). Allele frequency of A in NAFLD group (15.0%) also differed significantly from that (7.9%) in controls (P<0.05). Plasma levels of TNF-α (14.4±2.3 ng/L), fasting insulin (FINS) (9.9±2.1 uIU/ml) and Homa insulin resistance index (HOMA-IR) (3.2 ±1.0) were significantly higher in 238 G/A group than these in 308 G/A group (10.1±2.0, 8.0 ±3.4, 2.2 ± 0.6) and in 238 G/G group (10.1±2.0, 8.0±1.8 and 2.2±0.6) (P<0.01). Multiple logistic regression analysis showed that plasma levels of TNF-α, FINS and HOMA-IR were risk factors of **NAFLD.Conclusion:** 1. There existed 308 and 238 G to A genetic polymorphisms of TNF-αpromoter area in Chinese people. 2. TNF-αpromoter 238, but not 308, G to A polymorphism was associated with NAFLD pathogenesis.

MP-11

Expression of pro-Hepcidin in Secondary Hemochromatosis

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Pro-hepcidin, an 25–amino acid peptide was first identified as an anti-microbial peptide produced and expressed in the liver. Pro-hepcidin was shown to play an important role in normal iron metabolism and in both iron overload and iron deficiency state. It is thought to be the long-sought iron-regulatory hormone. Pro-hepcidin regulates iron release from the absortive cells in the proximal small intestine, macrophages and hepatocytes. In normal condition pro-hepcidin expression increased in response to iron overload when iron stores are elevated conversely its expression is decreased in iron depletion, iron deficiency anaemia or hypoxia. In secondary hemochromatosis such as in thalassemia major with multiple transfusion, its represents a unique situation where there is hypoxia and anaemia, which is expected to decrease hepcidin expression. But this condition coexists with iron overload, which ought to increase its expression. Therefore, it was of interest to study which of these factors has the influence in hepcidin expression.

Aim of Study: to know the expression of pro-hepcidin in secondary hemochromatosis subjects.

Method: serum were collected from 60 children with secondary hemochromatosis age 9-16 years old with severe anemia. Hemoglobin and reticulocyte were analyzed usng Sysmex XT2000i, iron were analyzed with Dimension AR auto analyzer, pro-hepcidin hormone were analyzed in the sera using microelisa method.

Results: The hemoglobin value ranged from 4.14-10.9 g/dl (mean 6.9g/dl), reticulocyte 0.12-11.6%, ferritin 73.4-23,216 ng/L(mean 4716.4 ng/L) transferrin saturation 56.0-106.2%. Pro-hepcidin hormone ranged from 51.6-748.0 mmol/L.

MP-12

Prevalence of Hepatitis C infection among haemodialysis patients in Semarang

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Background: Dialysis patients have lower immune respone and more susceptible to infection. The estimated prevalence of Hepatitis C Virus (HCV) infection in Hemodialysis patients is approximately 15-48 % in North America and 70- 80 % in other parts of the world, especially in Middle East (Egypt) and Southeast Asia. Currently Indonesia doestn't have data on the prevalence of HCV infection on Hemodialysis patients nationally.

Objective: To determine the prevalence of Hepatitis C Virus (HCV) infection among patients from hemodialysis in Semarang.

Methods: This was a cross –sectional study. The sample consisted of 124 patients from hemodialysis unit in Semarang to estimate the prevalence of Hepatitis C Virus (HCV) infection.

Results: One hundred and twenty four patients met inclusion criteria, which consisted of 73 males (58,9%) and 51 females (41,9 %). The prevalence of hepatitis C Virus (HCV) infection among patients from Hemodialysis units in Semarang was 64,5 %. We found significant association betwen duration on Hemodialysis (p=0,000, r = 0,549) with Hepatitis C Virus infection, and number of transfusions (p= 0,003, r = 0,263) with Hepatitis C Virus infection.

Conclusion: Based on this study, we concluded that the prevalence of Hepatitis C Virus infections in haemodialysis units in Semarang was high prevalence. Futhermore the significant relationships between duration on haemodialysis and number of tranfutions with Hepatitis C Virus (HCV) infection.

Keyword: Hepatitis C Virus infection, Hemodialysis

MP-13

Non Visualized Gallstones in the Previously Suspected Gallbladder Cancer of a Young Male (A CLINICOPATHOLOGY CONFERENCE REPORT)

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Background: Gall bladder abnormalities commonly occurs in the elderly. For instances, gallbladder cancer commonly occurs in elderly females (females are three to four times more frequent comparing to males). Similar to the antecedent, gall stones usually happens in elder females as well (females are two times fold more frequent comparing to males). Both of them can be distinguished by using systematic clinical process. There is still a probability of being wrong though our endeavor to find the truth exerted sophisticated modalities. In the other hand we can conclude that every finding is not merely parallel to the fact. Simply we say the accuracy of our clinical judgment in diagnosing never reaches 100%.

Case: Here, we are going to present a case of a young male (23

years old) with recurrent abdominal colic. The physical examination was normal, and so were the laboratory results, except increament of ALP & γGT. An upper gastrointestinal endoscopy showed erosive gastroduodenitis. Abdominal ultrasound depicted a mass inside gall bladder without any accoustic shadow. Abdominal CT scan performed by the other radiologist strengthened the ultrasound finding. By adding small amount of contrast agent, there was an enhanced mass inside gall bladder. Gall baldder removal was performed to confirm the diagnosis and to relieve the symptomps. The gall bladder was entirely analyzed for histotologic and clinical pathologic examination.
Conclusion: After gall badder removal, we now surely diagnose him cholelithiasis with chronic cholecystitis. The patient recovered from the disease after undergoing surgical intervention.
Keywords: Non visualized gall stones, recurrent abdominal colic, young male

MP-14
GLOMERULAR FILTRATION RATE IN LIVER CIRRHOSIS
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Background: Liver cirrhosis (LC) is often accompanied by functional renal failure. The mortality was significantly greater in LC patients with creatinine clearance less than 50 ml/min compared with greater than 80 ml/min (36% versus 9%, respectively; $p<0.001$). The development of Hepatorenal Syndrome (HRS) is associated with mortality rates approaching 90% and the median survival time was only 12 days after diagnosis.
Indicators of moderately impaired renal function are of great clinical importance. Serum creatinine concentration, the best establish simple parameter of glomerular filtration rate (GFR), has some disadvantages: its concentration depends on sex and muscle mass and shows marked increases only at severely reduced creatinine clearance values.
Cystatin C has recently been suggested as a sensitive marker of GFR and as early indicator of impaired renal function. Cystatin C serum concentration appears to be independent of sex and muscle mass. The determination of cystatin C is not affected by billirubun or haemolysis.
Objective: To understand correlation between GFR (based on cystatin C levels) and hepatic index in patients with LC at Dr. Soetomo Hospital.
Methods: Study design: Cross-sectional
Population: Liver cirrhosis patients who had eligible inclusion and exclusion criteria.
Results: GFR (based on cystatin C levels) in patients with LC with mild hepatic failure is 60.625 ± 17.631, moderate hepatic failure is 50.231 ± 12.029, and severe hepatic failure 16.960 ± 8.438. There was a strong negative correlation between GFR (based on cystatin C levels) and hepatic index based on score levels (r -0.646; 0.0001) and based on stadium levels (r -0.636; p 0.001) in LC patients.
Conclusion: There was a strong negative correlation between GFR (based on cystatin C levels) and hepatic index.
Keyword: glomerular filtration rate, cystatin C, liver cirrhosis

MP-15
Protective Effect of Soybean on Hepatotoxicity of Tetracycline Induction
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Objective: Soybeansa containing lecithin have a protective effect. Tetracycline, widely used as a non-prescription antibiotic, causes hepatic steatosis.
Method: As many as 40 Rattus norvegicus were used. Twenty rats were given only three times tetracycline 30 mg body weight for as long as 30 days, while the 20 remaining rats were given three times 1 ml soybean extract followed by tetracycline, which was given at a dose similar to the treated group. After 30 days of observation, the two group were mechanically scarified, and the livers were processed for histopathologic examination. Microscopic findings from the two groups were compared with each other.
Result: Both groups showed hepatic steatosis-microvesicular form, which visually gave no dfifference in microscopic findings.
Conclusion: From this observation it could be concluded that soybean extract, which contains lecithin, has no function in protection against the hepatotoxic effect of tetracycline.

MP-16
The Characteristic of Esopahgeal Varices Patients at Cipto Mangunkusumo Hospital from 2003 – 2005
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Background: Esophageal varices are abnormally dilated veins of the esophagus as the result of portal hypertension. Esophagogastroduodenoscopy is the gold standard in the diagnosis of esophageal varices. There were few study about characteristic of esophageal varices patient in Indonesia.
Aim: To determine the characteristic of esophageal varices patients on esophagogastroduodenoscopy examination.
Methods: Retrospective study based on data of esophagogastroduodenoscopy reports in Cipto Mangunkusumo Hospital from January 2003 until December 2005.
Results: From 1662 patients we found esophageal varices in 198 patients (11.9%). Male was more frequent than female (69.2% vs 30.8%). According to age, there were 34.3% patients in 50-59 years old, 27.8% in 60-70 years old, 18.2% in 40-49 years old, 8.6% in < 30 years old, 6.1% in > 70 years old and 4.5% in 30-39 years old. Based on the grading of esophageal varices, we found 49% in grade III, 25.3% in grade II, 20.2% in grade I and 5.5% in grade IV. In the year of 2003, from the total of 491 patients we found esophageal varices in 12% patients. With 47.5 % in grade III, 23.7% in grade II, 16.9 % in grade I and 11.9% in grade IV. In the year of 2004, from the total of 446 patients we found esophageal varices in 11.9% patients. With 52.8 % in grade III,

32.2% in grade II, 7.5 % in grade I and 7.5 % in grade IV. In the year of 2005, from the total of 725 patients we found esophageal varices in 11.9% patients. With 47.7 % in grade III, 30.2% in grade I, 22.1 % in grade II and 0 % in grade IV.
The association between gender and grading of esophageal varices was not significant (p=0.694). And the association between age group and grading of esophageal varices was also not significant (p=0.569).
Conclusion: Esophageal varices was found in 11.9 % patients on esophagogastroduodenoscopy examination. More frequent in male, 50-59 years old and in garde III. From the year 2003 to 2005, there was an increase in the proportion of grade I esophageal varices and a decrease in the proportion of grade IV. There was no association between gender and age group with the grading of esophageal varices.
Keywords: esophageal varices, esophagogastroduodenoscopy

MP-17
Study of UDCA Having Obvious Restraining Effect for the Rat Hepatocyte Apoptosis Endoplasmic Reticulum Stress Route of Acute Hepatic Failure
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Objective: To study UDCA restraining the rat hepatocyte apoptosis endoplasmic reticulum stress of acute hepatic failure and its fore-and-aft change of every index, including the change of Caspase-12. To observe the curative effect differences of the two kinds of different area medicine. Methods Inducing the rat to form the model of acute hepatic failure by celiac injection, afterward, restraining each group by different medicament, detecting the level of blood serum transaminase and observing the pathological change of hepatocyte, evaluating evolvement course of every group hepatocyte apoptosis and putrescence; Detecting DNA apoptosis cingulum of hepatocyte by immunoelectrophoresis; Detecting Caspase-12mRNA expression level of liver organization by RT-PCR˜Observing the two kinds of pharmic effect. **Results:** The model of the rat acute hepatic failure was established by D-Gal successfully, every group of the rats did not die in 24h,the most in 24h-48,every group did not die if time was over 96h.For model group, the number of apoptosis cell in liver organization became more after 24h,the number got an eyeful of it after 48h.Whereafter, putrescence was dominant, and after 7d the case straightened up, along with liver function ALT reached flood tide numerical value after 48h, synchronously, TBIL was not obvious and ALB did not change. Caspase-12mRNA also reached flood tide numerical value after 48h, along with the number of its representation reduced inchmeal. The number of apoptosis cell in liver organization was a few for Ursodeoxy group, its distributing was dispersive after 48h and its character showed change like air balloon, regeneration after trauma began to appear through 72h. The effect of electron microscope and pathology accord with each other ,at the same time ,the differences of liver function ALT were more obvious than model group($P<0.01$). Caspase-12mRNA expression quantity was more obvious than model group ($P<0.01$). Besides the difference of statistics above,we can observe directly that every group of slice all have obvious differences throuth the intuitionistic chart of the expression of DNA-ladder and Caspase-12mRNA .But UDCA group were between model group and Ursodeoxy group, the differences were more obvious than the two others group($P<0.01$).
Conclusions: UDCA has obvious restraining effect for the rat hepatocyte apoptosis endoplasmic reticulum stress route of acute hepatic failure, and the differences of the two kinds of medicament are very obvious, so Ursodeoxy is better than UDCA.
Keywords: UDCA; acute hepatic failure; apoptosis; endoplasmic reticulum stress; Caspase-12

MP-18
Levels of Adiponectin and Enzyme Alanine Aminotransferase in Obesity Patients With and Without Fatty Liver (A Preliminary Study)
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Background: Obesity individual have higher lipolysis that will increase the level of free fatty acid in the circulation will result in the increment of triglyceride , that might have the consequence of increasing fatty liver. On the other hand, the increase of free fatty acid can result in the insulin resistance. Insulin resistance increase reactive oxygen species which in turn disturbing the activity of liver's cells and resulting in the change of transaminase enzyme. The increase of reactive oxygen species is also due to obesity which affecting the lipid peroxidation and trigger inflammation to occur as can be seen in increase of cytokines and the reduction of adiponektin. Enzyme alanine aminotransferase actually is a glucogenic enzyme, and increased ALT has been demonstrated to be an indicator of impaired insulin signaling. Increased ALT is considered a consequence of hepatocyte damage in NAFLD. Adiponectin as an antiinflammation cytokine which is thought to make some of the feature of obesity to obesity with fatty liver.
Aim: The aim of this study is to investigate the level of adiponektin and enzyme alanine aminotransferase in obese patients with and without fatty liver
Methods: This study is an observational research with case control design. One hundred sixty subjects of this study are patients who come to private clinic and hospitals. The criteria of obesity is waist circumference for Asian > 90 cm (IDF criteria) , fatty liver feature are detected by ultrasonography. The subjects are divided into two groups, i.e. obesity with fatty liver as the case group (80 subjects), and obesity patients without fatty liver as the control group (80 subjects). Blood sample were analyzed in Prodia Clinical Laboratory for adiponektin using ELISA from Daiichi International.Co and enzyme alanine aminotransferase using colorimetric from Roche Diagnostic. Level of ALT divided in 2 categories (ALT < 41 U/L, ALT > 40 U/L) Prior to all the above procedure an informed consent was given and explained to the individual involved.
Result: Level of ALT in control subject (23 ± 6.6 U/L), in case subject (61 ± 14 U/L), level of adiponektin in control subject (3.7 ±1.1 mg/dl) in case subject (3.2± 1.1 mg/dl). Level of adiponektin in categorized ALT in control subject (ALT < 41 U/L: 4.01 ± 1.3 mg/dl, ALT > 40 U/L: 3.5 ± 0.9 mg/dl, with p = 0.364), in control subject (ALT < 41 U/L: 3.8 ± 1.2 mg/dl, ALT > 40 U/L: 2.8 ± 0.8 mg/dl, with p = 0.007)
Conclusion: Obesity subjects with fatty liver have higher enzyme alanine aminotransferase level as compare to subjects without

fatty liver. On the contrary, obesity subjects with fatty liver have lower adiponectin as compare to subjects without fatty liver.

MP-19

Empirical study of ganyanling injection influences on histopathology of liver and HBsAg in HBV transgenic mice

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Objective: Observe the influence of ganyanling injection on pathologic changes and expression of HBsAg in liver of HBV˜adr3.2˜ transgenic mice.
Methods: HBV transgenic mice (22 cases, 8-12 weeks) in clean grade were selected for the study. They were divided randomly 3 groups˜8 cases in ganyanling injection group˜8 cases in lamivudine group and 6 cases in physiologic saline group˜.They were respectively administrated at dosage of 14.43mg/kg and 20.59mg/kg for 28d.The liver of each mouse were taken for gross pathologic, histopathologic and immunochemistry examinations under light microscope. HBsAg in liver was detected by ELISA.
Results: The swelling hepatocyte, kytoplasm balloon change, punctiform and focus necrosis and lymphocyte infiltration were found in hepatic tissue in C57BL/6JHBV transgenic mice. Pathologic changes of hepatic tissue in mices in ganyanling injection group were relieved more than in lamivudine group. Immunochemistry exam in hepatic tissue indicated that HBsAg was expressed in livers in each mouse. HBsAg was distributed lamellarly or sporadicly in kytoplasm. Expression of HBsAg weakened more in ganyanling injection group than lamivudine group. OD value of HBsAg by ELISA indicated that it in ganyanling group striking decreased ($P<0.01$). There were not significant difference of OD value between lamivudine group and physiologic saline group ($P>0.05$).
Conclusion: Ganyanling injection may protect hepatic cell and also has some effect of anti-viral.

MP-20

Percutaneous catheter drainage in critical patient with large pancreatic pseudocyst caused by blunt trauma of the pancreas: a case report

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Introduction: Imaging-guided percutaneous catheter drainage has evolved to become a first-line method to treat pancreatic pseudocysts. The indications for draining pseudocysts include presence of symptoms or complications and progressive enlargement. We report of 27 years old man with traumatic pseudocyst of pancreas who successful managed by ultrasound (US)-guided percutaneous catheter drainage.
Case report: The patient admitted with chief complaint abdominal enlargement since two months ago, gradually onset, and feel stabbing-like pain continuously. He also suffered from nausea and vomiting. He was alcoholism and history of traffic accident, his abdomen was hit by steer three months ago. On physical examination, the patient looked dyspneu, restlessness and abdominal enlargement. The result of US was suspected large pancreatic pseudocyst with more than 27 cm in diameter. We decided to perform percutaneous catheter drainage with US-guided. The pseudocyst was containing more than 3 liter of hemorrhagic fluid. After underwent drainage, we performed CT-scan with the result was insertion the drain until the tail of the pancreatic duct. The condition of patient became gradually better in the monitoring.
Discussions: The large of pancreatic pseudocyst is a very rare case. The patient falls in critical condition, because the pseudocyst had progressive enlargement. The management of this patient was still challenges. US-guided percutaneous drainage was the first priority managed the patient to reduced compression of the abdomen.
Conclusion: Percutaneous catheter drainage in critical patient with large pancreatic pseudocyst should be performed, minimally to reduced compression of the abdomen.

MP-21

Pepsinogen II in Chronic Gastritis

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Pepsinogen II is an enzyme precursor of pepsin in the stomach. It is produced by chief cells of the gastric mucosa, pyloric glands in the gastric antrum and Brunners glands in the proximal duodenum. Plasma pepsinogen II levels correlates with the condition of the gastric mucosa.
Aim of study: to know the levels of Pepsinogen II in chronic gastritis patients in relation to the endoscopic and pathologic results.
Method: Endoscopic examination, pathologic biopsy samples and blood were taken from 10 patients (2 males and 8 females, age 36-48 years old) with dyspeptic symptoms in the Ridwan Meuraksa Hospital for evaluation. Pepsinogen II was measured using microelisa method (Biohit)
Results: Blood pepsinogen II values ranged from 8.38 to 29.31 (mean 14.50 ug/L). One patient (1/10, 10%) has a low PG II levels compared to the reference values and 2 patients (2/10, 20%) has a higher level. All pathologic results were reported as chronic gastritis.

MP-22

Pepsinogen II levels in normal subjects and secondary hemochromatosis (Preliminary report)

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Many reports showed that there are organ damage in hemochromatosis due to abnormal iron deposit in parenchymal cells including in the gastrointestinal tract. Most reports were on the abnormalities in liver and pancreas. There is no reports on the

function of the stomach. Pepsinogen II is an enzyme precursor of pepsin in the stomach. It is produced by the gastric mucosa and Brunners glands in the proximal duodenum. Plasma pepsinogen II levels correlates with the function of the gastric mucosa. Thalassemia children with multiple transfusion showed symptoms of secondary hemochromatosis, with high iron levels in plasma and patenchymal cells. In this study the pepsinogen II levels were anayzed in those secondary iron overload patients as a tool to know the function of the gastric mucosa. Sixty normal subjects were also studied for the refernce value levels.

Aim of Study: to know the levels of pepsinogen II in secondary iron overload subjects.

Method: serum were collected from 6 children with secondary hemochromatosis age 9-16 years old with severe anemia. For the reference values samples were taken from 60 healthy male and female blood donors subjects. Pepsinogen II levels were assayed using microelisa method (Biohit).

Results: The reference values of Pepsinogen II in normal subjects were 11.2 - 16.68 ug/L (mean 13.94 ug/L). The levels of Pepsinogen II in iron overload subjects were 7.47 – 14.73 ug/L (mean 10.35 ug/L) significantly lower compared to the normal subjects ($p < 0.05$).

MP-23

Antiretroviral regimen selection in patients with HIV-AIDS and Hepatitis C virus co-infection

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The first line antiretroviral (ARV) regimens available for free in Indonesia are Zidovudine (AZT), Stavudine (d4T), Lamivudine (3TC), Nevirapine (NVP) and Efavirenz (EFV). Most of the patients received combination of AZT+3TC+NVP as their initial ARV. In patients with anemia during therapy the AZT will be replaced with d4T. Patients with severe chronic active hepatitis C infection will receive EFV. On the other hand, asymptomatic hepatitis C infection will still receive NVP as part of their initial ARV therapy. In this study we reported the selection of ARV regimen in patients with HIV and HCV co infection.

Materials and methods: Cross-sectional descriptive study was done in the outpatient clinic of Kramat 128, a small private hospital in Jakarta, throughout June and July 2007. Status of HCV infection was confirmed by HCV ELISA antibody test. Viral load was determined by PCR and CD4 count by flow-cytometry. Cerebral toxoplasma infection confirmed by head CT-scan. The data were then analyzed using SPSS 14th and non-parametric tests.

Results: One hundred and thirty patients were admitted, 21.5%(28/130) of them were co infected with HIV and HCV. The main characteristics of the coinfected were male and intravenous drug user (95.2% or 27/28). ARV regimens were considerably similar between the HIV and HCV co-infected group compared to the HIV single infection group. The main ARV regimen were 3TC+AZT+NVP 57.1% (16/28) vs. 60% (57/95); 3TC+d4T+NVP 14.3% (4/28) vs. 10.5% (10/95); 3TC+AZT+EFV 10.7% (14/95) vs. 14.7% (3/28); and 3TC+d4T+EFV 14.3% (4/28) vs. 11.6% (11/95) all with p=0.809.

Virologic response showed a higher failure rates in the co-infected patients (41% vs. 27%, 0.15-0.67 vs. 0.16-0.39 95% CI, p=0.278). Immunologic status showed a higher prevalence of cerebral toxoplasmosis (29% vs. 13%, 0.6-0.19 vs. 0.11-0.46 95% CI, p=0.045) and a slower CD4 improvement over 6 months of initial ARV therapy (54.05 vs. 156.43, -31.35-139.45 vs. 124.94-187.92 95% CI, p=0.026).

The majority of patients had an abnormality in liver function test, with or without co infection (73.7% vs. 58.3%). The elevations were similar between the two groups, SGOT/AST levels (102.7 vs. 57.25, 54.18-150.77 vs. 36.51-77.99 95% CI, p=0.118) and SGPT/ALT levels (67.26 vs. 70.67, 53.23-81.30 vs. 30.44-102.89 95% CI, p=0.700). There is also no difference in AZT related anemia incidence between the two groups (39.3% vs. 42.1%, 0.20-0.59 vs. 0.32-0.52 95% CI, p=0.791).

Conclusion: The combination of three antiretroviral drugs, were the same within HIV/AIDS patients with or without HCV co-infections. Patients with co-infection were at risk for higher treatment failure rates, slower immunologic response and lower immunologic function. There is no difference on liver function impairment and anemia incidence with AZT in the two groups, indicating that the same ARV regimen could be given safely in HIV/AIDS patients with or without HCV co-infection.

Keywords: Antiretroviral, HIV-AIDS, Hepatitis C, toxoplasma, immunologic response, treatment failure.

MP-24

THE PROFILES OF HEPATOCELLULAR CARCINOMA PATIENTS IN Dr. SAIFUL ANWAR HOSPITAL, MALANG

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Background: Hepatocellular carcinoma (HCC) is a one of the most common malignancies worldwide and the third most frequent cause of cancer mortality. Prognosis of patient with HCC is poor, with a mean survival of 6 month. The annual incidence in region of Asia and sub-Saharan Africa was up to 500 cases per 100.000 populations. HCC is up to 4 times more common in men than in women. The incidens 1 to 2 decades earlier in regions with a high prevalence of liver carcinoma, and the frequency of chronic HBV and HCV infection were high.

Objective: To describe the profiles of HCC patients in Dr. Saiful Anwar Hospital Malang in 2006.

Methods: A descriptive study on patients with HCC in Dr.Saiful Anwar Hospital in 2006.

Result: There was 42 of HCC with predominantly men,(3 : 1) ,we found 31 men patients (73,8%),and woman 11 patients (26,2%) and the aged of patients between 23 until 90 years. The mean age of patients was 52 ± 16,6 years old. . The mean of AST was 257 U/l and mean of ALT was 105,5 U/l. The frequency of chronic HBV infection, HCV, combination HBV and HCV, and negative were 30 (71.4%), 3 (7.1%), 7 (16,6%) 2 (0,47%), respectively. The mean of AFP level in our SHCC patient is 10376,65 ± 19.266,74 ng/ml

Conclusion: The most common cause of HCC in Dr Saiful Anwar Hospital Malang was chronic HBV infection, with men predominantly, with the mean age 52 + 16,6 years old.

MP-25

ULTRASOUND IN ACUTE HEPATOBILIARY DISEASES

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Background: Even though ultrasound (US) may be limited in the acute situation, there are still many causes of an acute hepatobiliary problems which may be studied with it.

Up until now the US procedure in studying acute hepatobiliary problems is the most practical, simple and economical as well to be put in the first place to reveal its causes, in acute abdomen as well as in other part of the body.

Methods: The indications are : sudden onset of epigastric pain, jaundice, fever, back pain, chest pain. All patients were examined in acute and difficult state, that no preparation prior US study could be done. The equipments used were Medison Accuvix-XQ and Toshiba Power Vision 8000.

Result: Trauma: free fluid, visceral laceration, subcapsular and extracapsular haematomas, rupture. Inflammatory and infective causes: liver abscesses, cholecystitis, gallstones, bile duct stone, bile duct cyst, ascaris in the gallbladder/bile duct, pancreatitis, ureter stone, appendicitis Unsuspected findings in revealing the cause of cases that we thought suffering from hepatobiliary problems, are: mechanical catastrophes: intussusception, malrotation, ileus, hernia, ovarian torsion or rupture and extra uterine pregnancy.

Conclusion: Ultrasound has much to offer in cases of acute hepatobiliary problems as well as in acute abdomen, but a good and well experienced operator is needed, particularly in cases where ultrasound is the only one procedure to establish a final diagnosis or before surgery.

MP-26

Hepatitis B and C Coinfection among HIV Patients in Saiful Anwar General Hospital Malang

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Background: Epidemiological data showed that many HIV-infected patients were coinfected by hepatitis virus, either hepatitis B (HBV) or hepatitis C virus (HCV). HIV, hepatitis B virus and hepatitis C virus share similar routes of transmission, with sexual, parenteral and perinatal transmission being the most frequent modes of acquiring these infections.

Objective: To describe event rate of hepatitis B and hepatitic C coinfection among HIV patients

Research design and methods: We colected HIV patients who were treated in internal medicine department of Saiful Anwar General Hospital Malang and sought event rate of hepatitis B and hepatitic C coinfection by cross sectional study from 1st January 2006 to 31st may 2007. Characteristic data of all patients were showed in the form of mean and standard deviation.

Results: We noted 176 patients were diagnosed as HIV positive in a several clinical staging treated during period of 1st January 2006 to 31st may 2007. The Mean age of patients was 29±5,65 y.o. Risk factors of those patients were 137 patients IDU,13 patients freesex, 27 patients got HIV because the partner was infected by HIV. We obtained hepatitis viral marker examination for 26 patiens, 23 patients from 26 (88,46%) got Hepatitis C infection with 20 patients (86,9%) of them were IDU, 2 patients (8,69%) infected Hepatitis C from sexual intercourse. There were no correlation between hepatitis C virus infection and IDU ($p>0.05$). Five patients (19,23%) got Hepatitis B infection, all of them were IDU. Two patients (7,69%) were infected by both Hepatitis C and B viral.

Conclusions: From our study, although event rate of Hepatitis C coinfection among HIV patients had significant value, there were no correlation between hepatitis C virus infection and IDU

Keyword: HIV infection, Hepatitis B infection, Hepatitis C infection, IDU, Freesex

MP-27

CONTRIBUTION OF ADVANCED OXIDATION PROTEIN PRODUCTS (AOPP) TO LIVER DYSFUNCTION IN SEVERE PREECLAMPSIA

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Background: Severe preeclampsia and HELLP (haemolysis, elevated liver enzymes, low platelet) syndrome belong to the most serious complications of pregnancy and contribute substantially to maternal and perinatal morbidity and mortality. Advanced Oxidation Protein Product (AOPP) is an inflamatory and oxidative marker that higher in severe preeclampsia than normal pregnancy. Beside that, serum transaminase was higher in severe preeclampsia than normal pregnancy. But no study correlates this parameter.

Aim: To evaluate the correlation between aspartate transaminase (AST), alanin transaminase (ALT) with Advanced Oxidation Protein Products (AOPP) and platelet count in severe preeclampsia.

Settings: Fetomaternal unit, Ulin General Hospital Banjarmasin, start from September 2006 until March 2007.

Methods: Observational, cross sectional study was conducted in severe preeclampsia patients. All subjects were measured of AST, ALT, and AOPP level. AST and ALT activity was measured by colorimetric method. AOPP level was measured by Witko-Sarsat modification method.

Result: Twenty severe preeclampsia patients were involved in this study. Correlation between systolic pressure with AOPP level is r=0,229 and diastolic pressure with AOPP level is r=0,369 ($p<0,05$). Its mean that increase of blood pressure followed by increase of AOPP level. Correlation between AST with AOPP level is r=0,309 and AOPP with ALT is r=0,026 ($p>0,05$). Its mean that no correlation between ALT and AST with AOPP level.

Conclusion: AOPP doesn't affect liver function in severe preeclampsia.

MP-28

Comparison of Effectivity Liver Diet Plus Tempe-Tahu, and BCAA Formula for the Improvement of Intelectual Function in the Subclinic Encephalopathy Hepatic Patients

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Background: Cirrhotic hepatic patients are commonly in the subclinic hepatic Encephalopathy (SHE).In this condition, the encephalopatic manifestation is not clear yet, but the patient can be found decrease intellectual function. Adequat nutrition of planting protein is needed in this condition.
Objective: To analyse the comparison of intelectual function improvement on the liver diet III plus tempe-tahu with the BCAA formula in the SHE patient.
Method: This is clinical trial open labelled randomized study, This study was performed from September to December 2006 at Gatro-hepatology Policlinic of Moh.Husein Hospital Palembang, which consist of 2 groups and each group consist of 15 sample.The 1st group got liver diet III plus tempe-tahu and the 2nd group got BCAA formula.We used number connection test (NCT) to perform intelectual function improvement.
Result: From the 1st group we found that NCT1 average was 53,41 + 10,73 and NCT2 was 38,23 ± 6,49.From the 2nd group we found that NCT1 average was 46,75 + 13,22 and NCT2 was 36,81 + 6.05. There was decrease of NCT value in each groups but not significant statistically. There was statistical differences in decreasing of NCT value between the 2 groups. The 1st group (tahu tempe) was better than the 2nd group (BCAA formula) statistically significant. ($p < 0,05$).
Conclusion: The group who got liver diet III plus tempe-tahu had better improvement in intelectual function compare to the group who got the BCAA formula.
Keywords: Subclinic Hepatic Encephalophaty, Tempe-tahu, BCAA formula, Number Connection Test.

MP-29

DOUBLE PRIMER CARCINOMA: CYSTIC DUCT HEPATOID AND DENOCARCINOMA OF THE GALLBLADDER: Case Report

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A 48-years old female admitted to the hospital because of obstructive jaundice. Her bilirubin level was very high. (2,3 mg/dL). Radiology examination suggested there was a mass in the head of the pancreas. Shunting procedure was done to decrease bilirubin level. Biopsy from gall bladder, cystic duct and liver were performed. The biopsy from gall bladder result was primary adenocarcinoma of gall bladder and emboly of hepatoid carcinoma at the serous layer. From cystic duct was hepatoid carcinoma with extensive lymphovascular embolies. The result from the liver showed biliary cirrhosis with hepatoid emboly in the portal area. The patient died soon after the operation.
Beside the case report, we also review hepatoid carcinoma.
Keywords: hepatoid carcinoma, jaundice, doule primer carcinoma

MP-30

PRE-OPERATIVE RADIOTHERAPY FOR ICTERIC TYPE HEPATOCELLULAR CARCINOMA: A CASE REPORT

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Hepatocellular Carcinoma (HCC) is still a leading health problem worldwide, due to its correlation with HBV and HCV infection and its management which is strongly dependent to patient's condition and tumor extension. Surgery, with liver resection or liver transplantation offer a good survival rate as a primary management of such cancer. But since liver resection must consider some aspect of liver function and tumor size, and liver transplantation was not a choice in Indonesia, many treatment modality has been developed which can be used to overcome this problem, such as tumor ablation, transarterial chemo embolization (TACE), chemotherapy and radiotherapy. With the development of conformal radiotherapy, the hepatitis induced radiation therapy could be minimized. This paper present a case of conformal radiation therapy utilization in icteric type HCC in RSCM. Hepatic resection was planned for this patient.
Keywords: Hepatocellular Carcinoma, icteric type, radiation therapy, conformal radiotherapy

MP-31

NECROINFLAMATION ACTIVITY AND FIBROSIS STATUS IN CHRONIC HEPATITIS B PATIENTS WITH NORMAL OR SLIGHTLY INCREASED ALT (A PRELIMINARY STUDY)

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The most important transmission route of HBV infection in Indonesia is vertical infection and early childhood horizontal transmission. As the consequence many chronic hepatitis patients existed in immunotolerant phase. The common management guidelines for such patient are monitoring without antiviral treatment. In this preliminary study we have selected patients with HBsAg positive for more than 6 months with chronic hepatitis feature in ultrasonography and agreed liver biopsy. Nineteen patient meet the criteria and 18 patients were HBeAg positive and 1 patient was HBeAg negative. From those 19 patients 14 showed normal or slighty increased ALT (< 2x upper normal limit) and 5 with ALT >2x upper normal limit. From those 14 patients histological examination using METAVIR classification showed active necroinflamation and fibrosis (more than grade 2 and stage 2) in 6 patient (42.85%), and 8 patients showed necroinflamation less than grade 2. Using conventional management guidelines at least 40% chronic Hepatitis B patients will loss the opportunity of antiviral treatment, despite the fact that those patients with significant necroinflamation will progress to hepatic cirrhosis. Thus histological assesment is invaluable for determining HBV antiviral treatment in patients with persistenly normal transaminase.

MP-32

DETECTION OF CODON 249 MUTATION OF P 53 GENE IN NON CANCER LIVER TISSUE (A PRELIMINARY REPORT)

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Introduction: The role of p53 as one of many tumour supressor genes in the development of primary liver cancer is very important because it controls the cellular growth and apoptosis. Both Hepatitis B and Hepatitis C virus inhibit the role of p53 and the infection due both virus caused mutation of gene p53 at its 249 codon. The mutation is thought as the important trigger of hepatoma development. The p53 mutation is often detected in malignant liver tissue. Using SSCP (Single-stranded conformational polymorphism) p53 mutation can not be detected in liver tissue before it become malignant. But ASPCR (Allele-specific polymerase chain reaction) can detect mutation in earlier stage before the development of malignancy. It can be used as an early molecular diagnosis of primary liver cancer. Necessary preventive intervention can be performed earlier such as antiviral intervention to decrease the viral load.
Objective: To detect gen p53 mutation in noncancer liver tissue using ASPCR.
Material and method: The material of study is 18 tissue biopsy sample from 11 chronic Hepatitis B patients, 2 patients with chronic Hepatitis C, 1 patient with Chronic Hepatitis B and C, 1 patient with active cirrhosis type B, 1 patient with Fatty Liver, and 1 patient with extrahepatic obstructive jaundice. Biopsy was performed with aspiration method using Hepafix needle. The liver tissue was fixed with formalin 10%. Histologic diagnosis was performed with H&E staining. The ASPCR is done using fresh liver tissue in 9 patients. From the other 9 patients ASPCR was done from paraffin block.
Result: The mutation in codon 249 p53 was detected in 5 patient (27.78%) consisted of 3 patients with chronic Hepatitis B, 1 patient with chronic Hepatitis C, 1 patient with combined chronic Hepatitis B and C.
Conclusion: The p53 gene mutation can be detected in liver tissue of chronic Hepatitis B or C patients before the development of primary liver cancer. This method open a possibility of an early molecular diagnosis of primary liver cancer and giving the opportunity to perform intervention to prevent primary liver cancer, for example using antiviral agent to decrease the viral load.
Keyword: gene p53 mutation, noncancer liver tissue

MP-33

42 YEARS OLD WOMEN WITH CHOLEDOCHAL CYST

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Choledocal cysts ares congenital anomalies of the billiary tract that manifest as cystic dilatation of the extrahepatic and intrahepatic bile ducts. The incidence rate of choledochal cysts I s1 in 13,000 to 15,000 in Western countries and as high as in 1000 in Japan. These cysts are not familias; females are more commonly affected than males. The classification proposed by Todani and colleagues are: type I, II, III and IV.
A 27 year old women has an upper abdominal pain as a chief complain for several days, nausea but not vomiting. She had given some medicine by a doctor, but had not cured yet and gone to the hospital. There was no fever, has a normal defecate and darker the color of urine. Physical examination: vital sign (Tens, pulse and respiratory rates, and temperature) was in a normal range, has an icteric conjunctiva, JVP was normal, no superficial lymphonodus enlargement, has a normal lung and heart. She had liver enlargement, 1 cm below arcus costae, Murphy's sign negative, epigastric pain (+), spleen was in normal size, ascites (-). Laboratories finding were: Hb: 12.8 g/dl, Leucocyte 6.700/mm3, SGOT: 46 U/L, SGPT: 107 U/L Bil Total 3.37 mg/dl. Direct Bil: 1.95 mg/dl. Ureum: 11 mg/dl, Creatinin0,64 mg/dl, B glucose 92 mg/dl. Alb: 4.1 g/dl. USG Abdomen: common bile duct very large from proximal until pars pancreaticus, sizes 58.3 X 56.0X101.8 mm; with a normal gall bladder and intrahepatic bille ducts . The pts was diagnosed as Choledochal cyst type I.. Open surgery was performed by making cysto-yeyuno shunt. Fluid from the cyst was cultured and staphylococcus sp was found and sensitive by cefotaxim. The drug was given and added with others supportive drugs. Patient was being better and discharged from hospital.

MP-34

LIVER FUNCTION TEST FOR DIABETIC NEPHROPATHY PATIENT THROUGH ADVANCED OXIDATION PROTEIN PRODUCTS (AOPP) AND PLASMA PEROXIDE LEVEL FORMATION

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Background: Diabetic nephropathy is characterised by glomerular, tubular and tubulointerstitial injury, which is mediated by a combination of haemodynamic and metabolic factors. Hyperglycaemia increases oxidative stress, activates the polyol pathway and promotes the formation of various kinds of advanced glycation end-product (AGE). AGEs are generated by the non-enzymatic reaction of ketone or aldehyde groups of sugars with free amino groups of proteins, lipids or nucleic acids. AGEs can be formed via oxidative pathways and via non-oxidative pathways. These entire products were very toxic and eliminate by liver metabolism.
Aim: To examine the correlation between Advanced Oxidation Protein Products (AOPP), peroxide level with liver function test in diabetic nephropathy.
Setting: Department of Internal Medicine Ulin General, Banjarmasin at January-December 2006.
Methods: Observational study, cross sectional and conclusive sampling. All subjects were measured of AST, ALT, netrophyl, monocyte, AOPP level, and peroxide level. AST and ALT activity was measured by colorimetric method. AOPP level was measured by Cakatay method. Plasma peroxide level was measured by FOX modification method.
Result: One hundred Chronic Renal Failure patients were admitted to haemodialysis unit. Nine of them were diabetic

nephropathy patients then involved in this study. Correlation between AOPP with liver function test (AST and ALT) is r=-0,233 and r=0,150 (p>0,05). Correlation between peroxide level with liver function test (AST and ALT) is r=0,033 and r=-0,100 (p>0,05).
Conclusion: No significant correlation between AOPP and peroxide level with liver function test in diabetic nephropathy.

MP-35
Surgical Management of severe hemorrhage as complication of sphincterotomy after ERCP
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Background: Severe hemorrhage is a rare complication of sphincterotomy after endoscopic Retrograde Cholangio - pancreaticography (ERCP). Surgical intervention is required if endoscopic means failed.
Materials and Methods: One patient suffered massive melena the day after performing sphinterotomy and stenting intended to remove multiple Common Bile Duct
(CBD) stones. Patient falled to hypovolemic state and haemoglobin level decreased to 4 gr/dl. Repeated endoscopy and epinephrine injection had been performed to control bleeding, but failed. Surgical intervention was unevitably mandatory. During exploratory laparotomy most of the bowel was fulfilled with blood, began from duodenum part 2. Duodenotomy was performed and source of bleeding was recognized from ampulla Vateri. Bleeding control was achieved by suturing the cycle of ampula vateri. Exploration at CBD founded seven small to medium caliber stones and T-tube was inserted.
Results: Melena was successfully ceased two days after surgery. Cholangiography per T-tube was created and revealed 'clear' bile tract. Patient leaved the hospital in good condition on the day 10 post operation.
Conclusion: Surgical intervention is sometimes required and effective in managing ERCP-induced hemorrhage that failed treated endoscopically.
Keywords: severe hemorrhage, sphincterotomy, Endoscopic Retrograde Cholangio-Pancreaticograph , duodenotomy.

MP-36
ANALYSIS OF PORTAL VEIN IN NORMAL POPULATION WITH COLOR DOPPLER SONOGRAPHY (PRE & POSTPRANDIAL)
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The velocity and diameter are needed to assess portal vein. The normal value of these had many variations; it needs more research especially for Indonesian people.
The purpose of this study was to obtain the range value of the flow velocity of portal vein in normal population related to age, gender, and prandial state.
There were a hundred normal patients examined using color Doppler ultrasound (CDU) after being selected by physical and grey-scale ultrasound examinations, and liver function test, as well.
The value of flow velocity was evaluated before meal, immediately, 1 hour and 2 hours after taking meal, respectively. The results showed that the flow velocity decreased gradually, as the age growing up where the lowest was 14.38 cm/sec was found in the age of more than 61 years (pre-prandial) and the highest (18,03cm/sec) was in the age 21-30 years.
The flow velocity raised after meal approximately 39% (immediately), 50% (1 hour after) and 21% (2 hours after), respectively. These ranges were similar for both genders. There were no differences in diameter between female and male, and among age groups, whereas after meal the diameter became wider than before. The average diameter of the portal vein was 9.05 mm.

MP-37
Hepaticojejunostomy Roux en Y for Billiary tree injuries after opened and laparoscopic cholecystrectomy: Are they effective?
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Introduction: Injuries to extrahepatic billiary tree may be inflicted during any upper abdominal operation, most often during cholecystectomy, or may be due to blunt or penetrating trauma. Iatrogenic bile duct injuries are important. Firstly because are preventable and secondly because they produce considerable morbidity and occasionally mortality far exceeding that recognized for the initial operation.
Aim: To know how effectively Hepaticojejunostomy Roux en Y are in treating CBD injuries patients when are performed opened and laparoscopic cholecystectomy.
Material and Methods: In the year 2006 – 2007 we performed Hepaticojejunostomy Roux en Y for 3 CBD injuries patients. Two patiens were after laparoscopic cholecystectomy and one patien was after opened cholecystectomy referred by general surgeon.
Results: Case 1: Female 44 year old with obstructive jaundice 2 weeks after laparoscopic cholecystectomy. Case 2: Male 50 year old is referred by general surgeon with obstructive jaundice 2 weeks after convensional cholecystectomy .
Case 3: Male 47 year old, iatrogenic injury of CBD in laparoscopic cholecystectomy due to anatomy abnomarlity .All of that cases are performed hepaticojejunostomy Roux and Y . Duration of operation about 5 hours and can decrease the liver function test to become normally in 2 weeks.
Conclusion: Hepaticojejunostomy Roux and Y with tube splinted is effective to make liver function test become normal limit
Keywords: CBD injuries; Laparoscopic Cholecystectomy; Conventional Cholecystectomy

MP-38
Intestinal, Hepato-biliary & Pulmonal Ascariasis: A Case Report
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The Ascaris lumbricoides is common in tropical and subtropical

regions and it may afflict one third of population. The worm may grow in the small intestine, where ova are excreted and transmitted to other subjects. Larvae released in the duodenum, enter the portal system and traverse the liver to the lung from where they are able to travel up the respiratory tract and back into intestine where they mature to adulthood. Adult worm enter the bile duct through the ampulla, where they can cause cholangitis, particularly if secondary bacterial contamination occurs.

We reported a case, woman, 30 years old, who was undergone exploratory laparotomy due to Cholangitis caused by hepatobiliary ascariasis. She came with undernutrition, anemia and felt intermittently abdominal pain followed by scleral icteric and itched on her whole body skin. Intra-operatively, we found the worms in the Common bile duct, intra-hepatic duct with localized hepatic abscess and in jejunum. We evacuated the 43 worms from biliary tree and 21 worms from the jejunum, and then we performed cholecystectomy, Choledocho-duodenostomy by-pass, and drainage of the hepatic abscess and put the 24 f tri-ways catheter. After that drainage, the massive hepatic bleeding occured and difficult to stop, then we put some big and thick gauges as a hepatic tamponade, put subhepatic drain tube and closed the operation wound immediately and she brought to the ICU for intensive rescucitation and recovery. Three days later, we did re-laparotomy, and we found no any significantly bleeding, no sign of choledocho-duodenal anastomotic leakage and cholangitis was neither improved, nor local peritonitis.

On the second days after re-laparotomy, she got the respiratory distress, and on the thorax x ray, we found the sign of pleural effusion, then we inserted the chest tube and 400 cc pus came out, and connected it to the Water Sealed Drainage (WSD). Two days after chest tube insersion, the drainage stopped and when we tried to repair the tube posisition, 1 worm came out in the chest tube then we evacuated it and put a new chest tube and the drainage became clear and she said no respiratory problem and felt more comfort. Unfortunately, 2 days later, she passed away without any clinical deteriorisation before and the WSD still in function without significant addition. We predicted the larvae embolism as the possible cause of death.

Keywords: intestinal ascariasis, cholangitis ascariasis, ascariasis hepatic abscess, pleural & pulmonal ascariasis.

MP-39

Liver and Gastrointestinal disturbance complaint in hospitalized Malarial patients at Rote Island, East Nusa Tenggara

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Background: Malaria remains a health problems today in East Nusa Tenggara especially at Rote island. One of the important clinical manifestations of malaria is Gastrointestinal symptoms and disturbance of liver function,

Aim: To know the number of case with gastrointestinal and liver manifestation from hospitalized malarial patients in Baa General Hospital for 2 year

Method: We reported Hospitalized Malarial patients with Gastrointestinal and liver Manifestation in Baa General Hospital from 1 January 2004 until 31 December 2005. Data was taken from medical record.

Result: We have 186 patients hospitalized in 2 year, 108 male and 78 female. The most common gastrointestinal complaint was Nausea in 76,3% patients, followed by Epigastrial pain in 49,3 % patients, Vomiting in 46,1 % patients and Diarrhea in 17,2 % patients. 30, 1% patients came with Hepatomegali and right upper quadrant pain. Splenomegali found in 29,2 % patients. Transaminase serum increased in 18,1 % patients. The mean of increased SGOT was 98,2 u/l, SGPT 89 u/l and ALP 167 u/l. Jaundice found in 35,1% patients with 18,2 % have hemolytic type and the rest 81,8% have combination type

Conclusion: Liver and Gastrointestinal disturbance symptom still one of major complaint of malarial patients in Rote island, East Nusa Tenggara

MP-40

Analysis of differential expressions of two microRNAs in hepatocellular carcinoma and adjacent normal tissues by semi-quantitive RT-PCR

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Objective: To analysis the differential expressions of miR18 and miR224 in hepatocellular carcinoma(HCC) and adjacent normal tissues by semi-quantitative RT-PCR method. Method The RT-PCR method was established and optimized through the cDNAs which were reverse transcripted from poly(A) tailed-small RNAs(<200bp) extracted from hepatoma carcinoma cell line SMMC7721. Then, the expressions of miR18 and miR224 in 10 pairs of HCC and adjacent normal tissues were semi-quantitatively analyzed by this method.

Result: Compared to adjacent normal tissues, the expression of miR18 was up-regulated in 7 and down-regulated in 3 of the 10 HCC tissues; the expression of miR224 was up-regulated in 5 and down-regulated in 5 of the 10 HCC tissues. Both miR18 and miR224 were up-regulated in 5 HCC tissues in parallel.

Conclusion: Aberrant expression of miR18 and miR224 were found in HCC tissues; the semi-quantitative RT-PCR for screening the differently expressed microRNAs provides an simple method for the study of pathogenesis, diagnosis and therapy of HCC.

Keywords: HCC; microRNA; RT-PCR

MP-41

Distribution of sub-genotype B of hepatitis B virus among 4 cities of China

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Objective: To investigate the distribution of sub-genotype B of hepatitis B virus(HBV) among 4 cities (Beijing, Shijiazhuang, Wenzhou and Shenzhen) of China.

Methods: The sub-genotype Ba and Bj of HBV/B strains from patients with chronic HBV infection were detected by PCR-RFLP method. The genotype of the serum samples were identified by type-specific nested PCR with multiplex pairs of primers. Total 101 serum samples of patients with chronic HBV/B infection

were collected, 18 of the 101 serum samples were collected from Beijing, 22 of that from Shijiazhuang, 34 of that from Wenzhou and 27 0f that from Shenzhen. The results were confirmed by PCR product sequencing.
Results: All of the 101 serum samples were identified as sub-genotype Ba, Bj were not found.
Conclusions: Our results suggested that sub-genotype Ba was predominant strain of HBV/B in 4 cities.
Keywords: Hepatitis B virus; Sub-genotype; PCR-RFLP; Ba; Bj

MP-42
Identification of subgenotypes of hepatitis B Virus Genotype B with Semi-nested PCR
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Objective: To establish a simple and practicable method to identify the subgenotypes (HBV/Ba and HBV/Bj) of hepatitis B virus (HBV) isolates of genotype B (HBV/B). Method The entire nucleotide sequences of 41 HBV/B including 35 HBV/Ba(12 from china) and 6 HBV/Bj obtained from the international DNA database (GenBank) were compared and analysed in Precore Region plus the core gene(preC/C) with DNAStar software. According to the specific and conserved nucleotide sequences that were found respectively on the basis of conserved nature of those sequences within a subgenotype and on the basis of their poor homology with the sequences derived from the other HBV/B subgenotype, the specific primers for HBV/Ba(BA,nt2195-2171) and HBV/Bj(BJ,nt1998-1978) were designed respectively. All the same, The entire nucleotide sequences of 60 hepatitis B virus of Genotype C(HBV/C) obtained from GenBank and the above 41 HBV/B, were compared and analysed in P Region with DNAStar software. According to the specific and conserved nucleotide sequences that were found respectively based on the sequences between HBV/C and HBV/B, the specific primer for HBV/B (HB, nt1617-1636) was designed. HB as HBV/B specific primer (sense) and HBAS-4V (antisense, nt2316-2297) designed by Sugauchi et al (Gastroenterology 2003;124:925-923)as a universal outer primer(antisense) were used in the first-round PCR. In the second-round PCR, HB also as sense primer, BA and BJ as inner primers (antisense) were added into a single tube for PCR reaction, and the two subgenotypes of HBV/B were identified according to the length of the amplified DNA (HBV/Ba:578bp,HBV/Bj:381bp) through agarose gel electrophoresis. A total of 71 HBV DNA-positive serum samples selected randomly from our laboratory, including 49 HBV/B and 7 hepatitis B virus of Genotype B and Genotype C (HBV/B+C) samples identified with type-specified PCR designed by Naito et al (J Clin Microbiol 2001;39:362-364) and including 15 HBV/C samples identified by direct sequencing in PreS and S Region (preS/S) were detected with this semi-nested PCR. Then, 15 randomly selected first-round PCR products of HBV/B and HBV/B+C samples were sequenced directly and the sequences were compared phylogenetically with the above known HBV/Ba and HBV/Bj sequences using Blast and DNAStar softwares to test the reliability and veracity of semi-nested PCR. Results 49 HBV/B and 7 HBV/B+C samples were all identified as HBV/Ba by semi-nesteb PCR method. 15 randomly selected PCR products also were all sequenced as HBV/Ba. 15 HBV/C samples were all negative through agarose gel electrophoresis.
Conclusions: In this paper, we report a simpler,more rapid ,sensitivity and specificity method for identifying the two subgenotypes of HBV/B. Compared to PCR-RFLP, this semi-nested PCR method can be better to avoid the interference of HBV/C in HBV/B+C samples for its specificity of HBV/B and the interference of incomplete digestion with restriction enzyme,and simplifies the procesure by avoiding the procedure of digestion with restriction enzyme. Hence, this is an appropriated method for large-scale identification of the two subgenotype of HBV/B.

MP-43
CORELATION BETWEEN SERUM HYALURONIC ACID (HA) AND SEVERITY OF LIVER DAMAGE IN LIVER CIRRHOSIS PATIENTS
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Preface: Liver fibrosis process involving Hepatic Stellate Cells (HSC), Kupffer Cell, leucocyte, and various mediator such as cytokine, growth factors and collagen. Liver biopsy remain the gold standard for determining liver fibrosis level. However this procedure brings many complication, so that several parameters as the result of collagen and inhibitor matrix composition are suppose to predict liver fibrosis. Even though there is no definite specificity and sensitivity, fibrotic marker can be another option.
Background: Hyaluronic acid (HA) is a mucopolisacharida produced by fibroblast and synovial tissue. Disorder in HA uptake by receptor in sinusoid cells or the rise in HA production by fibroblast will increase HA serum level.
Subject: HA serum level in 40 cirrhotic patients was compare with 40 normal ones.
Aim and methods: To clarify if HA level can reflect fibrosis level associated with the degree of liver damage in cirrhosis base on Child Pugh (CP) classification. The methods was cross sectional study with analytic description approach.
Result: In CP. A group the HA level was 434,46 ± 86,36ng/ml, CP. B 1920,37 ± 1398,94 ng/ml and CP. C 3299,23 ± 2650,41 ng/ml. There was significant different between the HA serum level in CP. A and CP. B (p = 0,043), CP. B and CP. C (p= 0,044) and a more significant different between CP. A and CP. C (p= 0,001).
Conclusion: There is positive correlation between severity of liver cirrhosis base on Child Pugh classification with serum HA level, with regression analytic power 27,7%.
Keyword: Liver cirrhosis, Child Pugh Classification. Hyaluronic Acid

MP-44

THE KNOWLEDGE LEVEL OF PRIMARY HEALTH CENTER (PHC) DOCTORS IN HEPATITIS B AT PHC IN SURABAYA

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Background: One of doctor's functions of PHC is the ability to diagnose some disease especially in giving highly morbidity and mortality effect Hepatitis B virus infection is the world health problem that give high effect. This disease is mostly chronic that cause cirrhosis and hepatoma in the end. As far, there is no official data that give an illustration about the knowledge level PHC doctor to Hepatitis B in Surabaya.
Objective: The survey has a purpose to know the knowledge level of PHC doctor about Hepatitis B in Surabaya
Material and Methods: The survey is "cross sectional" observation study. The subject is taken from PHC doctor in Surabaya. The subject who complies with inclusion criteria is interview and ask to fill the questioner of measuring the knowledge level. The questioner is using a set of question with true or false answers criteria. This instrument is adapted from Turkey based on Taxonomy domain cognitive from Bloom, include of comprehension, application, and analysis. The data from this study is used to perform validity and reliability test based on single trial administration procedure. Analysis data is performed by qualitative descriptive approach to describe the knowledge level with knowledge value conversion as follows: ≥75 (excellent), 70.0 – 74.9 (very good), 65.0 – 69.0 (good), 60.0 – 64.9 (more than enough), 55.0 – 59.9 (enough), 49.5 – 54.9 (nearly enough, 40.0 – 47.4 (Less), < 40 (bad).
Results: Based on validity test obtained 14 items question with correlation coefficient 0.287 – 0.561 and alpha reliability index 0.639, so this instrument can be used to measure the knowledge level. The score average conversion result: comprehension 84.878 ±16.499 (excellent category), application 47.566 ±31.870 (nearly enough category), and analysis 14.634 ±35.562 (less category) statistically, the average of the knowledge level scale (combination of comprehension, application and analysis) obtained 49.023 ±19.085 include of nearly enough category.
Conclusion: By using valid and reliable instrument, the knowledge level of PHC doctor about Hepatitis B in Surabaya can be categorized nearly enough.

MP-45

Observation of matrine, a Chinese herbal medicine, in the treatment of chronic hepatitis B with hyperbilirubinemia

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Objective: To observe the efficacy of matrine, a Chinese herbal medicine, in the treatment of chronic hepatitis B with hyperbilirubinemia.
Methods: One hundred and ninety-four patients with chronic hepatitis B were divided into group A receiving matrine at a dose of 150 mg and potassium aspartate and magnesium aspartate injection 20 ml daily intravenously for 4 to 6 weeks till serum bilirubin levels returned towards normal and into group B treated with potassium aspartate and magnesium aspartate injection alone for the same goal obtained.
Results: The serum bilirubin levels in group A got back to normal in 28 days (range 21 to 42), much shorter than in group B (average in 37 with range of 27 to 53 days, $p<0.01$); During our observation, five (5.0%) and six (6.3%) patients in group A and in group B deteriorated to hepatic failure, respectively ($p>0.05$).
Conclusion: The matrine treatment for chronic hepatitis B with hyperbilirubinemia is effective.
Keywords: Hepatitis B Hyperbilirubinemia Matrine