Annals of Hepatology

# Panamerican Congress of Gastroenterology

## Abstracts Liver Section

**1. Hepatic expression of ghrelin, adiponectin and its receptors in patients with nonalcoholic fatty liver disease**

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**Background and aim:** Nonalcoholic fatty liver (NAFLD) is a chronic disease of growing importance around the world because of its relation with obesity and insulin resistance. Adiponectin and ghrelin are hormones that participate in hepatic lipid metabolism, and their expression in liver tissue could have important effects in NAFLD. The aim of this study was to evaluate hepatic ghrelin, adiponectin and AdipoR expression in patients with NAFLD, comparing them with normal subjects. **Material and methods:** A cross-sectional clinical study was performed at the Liver Unit of the Medica Sur Clinic and Foundation in patients with clinical-pathological diagnosis of NAFLD and controls. Patients were classified according to their clinical-pathological diagnosis in three groups: normal liver, nonalcoholic hepatic steatosis and nonalcoholic steatohepatitis (NASH). Adiponectin, AdipoR1, AdipoR2 and ghrelin mRNA levels were assessed by PCR-RT in all biopsies. Statistical analysis was made with central tendency measures and the Mann-Whitney U-test due to the characteristics of the sample. We considered significant differences with a $p$-value <0.05. **Results:** We studied 21 subjects, 3 had a normal liver biopsy, 14 with nonalcoholic steatosis and 4 with NASH. Patients with NAFLD exhibited greater levels of HOMA-IR and triglycerides ($p<0.05$). We observed a nonsignificant trend towards higher ghrelin expression in patients with NASH > nonalcoholic steatosis > normal. Patients with NASH had significantly higher mRNA adiponectin levels than normal subjects ($p<0.05$). No difference was observed between the groups according to AdipoR expression. **Conclusions:** Adiponectin overexpression was observed in patients with NASH, suggesting a compensatory hepatocellular response to insulin resistance in an inflammatory environment. Although nonstatistically significant, higher ghrelin expression was detected in patients with NASH, thus, despite hypoghrelinemia, *in situ* production might participate in hepatic fatty acid deposition.

**2. Assessment of the effect of medical treatment on nutritional status and body composition of hepatitis C-infected patients**

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**Background:** Since the beginning of this century, there was growing concern for study dietary effect on liver diseases and its nutrimental supply for energy intake. Unfortunately, the potential benefits offered by harsh nutrimental diet are still a matter of controversy in clinical hepatology. **Objective:** To assess the nutritional status and body composition among chronically Hepatitis C Virus (HCV)-infected patients, who received combination therapy with pegylated interferon (peginterferon) alpha 2a plus Ribavirin. **Material and methods:** Twenty eight HCV-infected patients were evaluated in a longitudinal and prospective study, conducted between January and April 2006. All individuals were enrolled at the time they start combination therapy with peginterferon alpha 2a plus ribavirin. Patients were subjected to clinical, dietary and nutritional evaluations, which include measurements of anthropometrical, hematological and biochemical markers, as well as advising in feeding plans according to their nutrimental requirements. **Results:** Seventeen out of the 28 patients (60.7%) were females and 11 (39.3%) were males; mean age was of 46.5 ± 9.3 years. Clinical evaluation showed no alteration in 29% of cases; whereas mild, moderate and severe alterations account for 25% (7), 42% (12) and 4% (1) of cases, respectively. By dietary evaluation, nutritional risk was identified in 17 patients (60.7%), but absent in the remaining 11 patients (30.3%). Nutritional status appraisal revealed 2 cases (7%) of malnutrition, 18 cases (54%) of obesity and 9 patients (29%) within normal status throughout the study. Body composition by mid-arm muscle area (MMA) measurements at the start of study was normal in 3 patients (11%), depleted in 13 (46%) and increased in 12 (43%); in contrast at the end of the study, body composition was normal for only two patients (7%), depleted in 10 (36%) and increased in 16 (57%). Similarly, initial percentages of fat mass were normal in 4 patients (14%), lessened in 6 (21%) and augmented in 18 (64%); percentage of individuals with normal fat mass fell to 2% at the end of study, as lessened fat mass reach up 32% and augmented fat mass practically remained constant (61%). Normal waist-to-hip ratio (WHR) was present in 13 individuals (46%) and abnormally high in 15 (54%), but remained unaffected during the therapy course. At begin of study, hematological analysis revealed 8 cases of anemia (29%), 12 cases of leukopenia (43%), 13 cases of lymphopenia (46%) and 3 cases of thrombocytopenia (11%); by the end of study, anemia cases (12) increased to 43%, leucopenia, lymphopenia and thrombocytopenia reached up reached up levels of 57% (16 cases), 64% (18 cases) and 18% (5 cases), respectively. Biochemical analysis showed normal ALT values for 50% of patients (14) at begin of study, and this was slighly increased to 54% (15) by the end of study; initial hypertriglyceridemia and hyperuricacidemia were present in 18% (5) and 36% (10) of cases, but final percentages were diminished 14% (4) and 29% (8) of cases, respectively. Hypercholesteremia was present in 2 patients (7%) and remained unaltered throughout evaluation trial. **Conclusions:** Preliminary results of this study show the biochemical and nutritional alterations in patients provoked by medical treatment. The MMA showing a trend to increase, suggesting interstitial fluid retention, and gradual depletion of fat mass were the most relevant alterations. During therapy, patients were very likely to present any of the following signs: anemia, leukopenia, lymphopenia and thrombocytopenia. Taking into account these features will allowed clinicians to take a better nutritional approach of this kind of patients, in order to establish interventions at nutritional level, which in turn must lead to normalization of the aforementioned parameters and to diminishing the adverse effects of medical therapy. Finally, an improved quality of life must be addressed for these patients.

**3. Atopy as a predictor for beneficial response to interferon alpha therapy in Slovak patients with hepatitis B**

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**Background:** Similarly to atopy, HBeAg-positive chronic hepatitis B (CHB) is also characterized by a skewing of the immune system towards a Th2 phenotype. Thus, we aimed to determine whether the presence of atopy might influence HBeAg/antiHBe status and outcome of antiviral therapy. **Methods:** We studied 73 treatment-naive patients with CHB, 39 men and 34 women aged 16-60 years (mean 32 years) with a positive HBV-DNA assay (Digene). Serological markers HBeAg and anti-HBe were tested by ELISA (MONOLISA, Sanofi Pasteur. The atopic status was determined on the basis of 2 or more positive skin prick tests from a panel consisting of 7 aeroallergens. After baseline

evaluation, all patients were treated with interferon-alpha (IFN) 10 MIU thrice weekly for 24 and 48 wks respectively, depending on HBeAg status. **Results:** The prevalence of atopy in the entire cohort was 34 %. In the subgroup of HBeAg-positive patients the prevalence of atopy was significantly higher than in the HBeAg-negative patients (61.5% *vs* 2.9%, p< 0.0001, Chi-square test). One year after completion of the treatment, HBV-DNA was undetectable in 32.8 % of all patients. The proportion of responders was significantly higher among atopic patients than in non-atopic patients (52% *vs* 22.9%, p=0.012, Chi-square test). **Conclusions:** Consistently with the Th1/Th2 paradigm, our results demonstrated an inverse association between anti-HBe positivity and atopy. This finding and higher response rate to IFN in atopic patients lead us to conclude that both strong Th1 and synchronous costimulatory Th2 activities may be required for a successful HBV elimination.

**4. Triple therapy with interferon alfa 2ª, ribavirin and amantadine in chronic hepatitis C in nonresponders and relapse patients**

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**Introduction:** The standard therapy for the treatment of hepatitis C are ineffective in almost 50% of patients . Amantadine, one antiviral agent that is has shown in some studies activity for hepatitis C virus join with interferon and ribavirin is useful in nonresponders and relapse patients with sustained virological response around from 13% to 29%. o date the optimal therapy in patients with chronic hepatitis C, not responders or undergoes relapse to the therapy with interferon and ribavirin it continues being a problem without solving. **Objective:** To determine the security and effectiveness of the triple therapy with interferon, ribavirin and amantadine in patients with chronic hepatitis C nonresponders and relapse. **Materials and methods:** The study included 30 patients , with an mean age of 41 years (18 - 64 years) , 17 women (55.5%) and 13 men (44.4%). 26 patient with genotype 1 (85%), 3 patient with genotype 2 (11%), and 1 patient with genotype 3 (3.7%).

The study population include two groups of patients : Nonresponders: 23 patients (76%) and patients with relapse when suspending the treatment: 7 patients (23.3%) The administered therapy was pegilated interferon alfa 2a 180 mcg/week , ribavirin VO 1,000 mg/day (weight <75 kg) or 1,200 mg/day (weight >75 kg) and amantadine VO 200 mg/day (100 mg twice day) during 48 weeks. All the patients had detectable HCV RNA by PCR (+), the patients were followed and PCR determination´s being made at week 12 to determine early viral response (EVR), defined like HCV RNA undetectable or less than two logarithms with respect to the basal value, determinations at 48 week of treatment , defined like end of treatment response (ETR) and another 6 months after treatment: sustained virological response (SVR) was defined as undetectable serum HCV- RNA by PCR. **Results:** 30 patients were included, 1 patient stopped treatment for plaquetopenia, and another patient died by cause nonrelated to the hepatic disease. The preliminary data show in the group of nonresponders an EVR of 60%, and in the relapse group of 85%, with ETR in nonresponders of 17%, and 42% in relapse group. The results of SVR is in nonresponders 4% and in relapse group 28%. The presented adverse effects were: significant anemia (<10 gr/dL in 37% (10/27), and severe anemia (<8.5 gr/dL ) in 0%, leucopenia in 51% (14/27) of patients, plaquetopenia in 14% (4/27), ith ALT normalized in 25.9% (7/27) to the 12 weeks of treatment. **Conclusions:** The preliminary results show an early viral response and end of treatment response equal to the previous published studies, but the sustained virological response is lower than de other studies. The adverse effects are the same to those of the conventional therapy with interferon and ribavirin alone. Although controlled studies are required it could be another therapeutic alternative in not responders and relapse patients.

**5. Long-term follow-up of patients receiving an orthotopic liver transplant for hepatitis C cirrhosis treated with anti-IL2-R antibodies during immunosuppressive induction.**

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**Background:** Hepatitis C is the main indication for liver transplantation worldwide and the intensity/type of immunosuppression (IS) has been associated with early and aggressive recurrence in the post-liver transplant (LT) period. The use of anti-Interleukin-2 receptor antibodies (anti-IL2-R), in the induction phase of IS has been debated in these settings; conflicting results regarding rejection and recurrence have been reported. **Aim:** 1) To evaluate the long-term outcome of patients receiving a LT for hepatitis C, treated during the induction phase of IS with either Daclizumab or Basiliximab. 2) To analyze the disease recurrence and acute rejection during follow-up. **Methods:** 14 patients were included, mean age 45.5 years (range 33-58), 5 women. Four patients received Basiliximab (20 mg on day 0 and 5 post-LT) and 10 Daclizumab (1 mg/kg on day 0 and 5 post-LT) in addition to standard IS (tacrolimus 0.075 mg/K/d and metil-predinosolone). For the purpose of the study rejection was defined as the persistent elevation of GGT, alkaline phosphatase and AST/ALT, corroborated by liver biopsy after ruling out biliary abnormalities. This study analyzed the time elapsed between LT and rejection, grade, long term survival, therapy for acute rejection, recurrence of hepatitis C and timing between LT and its documentation. **Results:** Four patients (28.5%) presented with hepatocellular carcinoma; 2 diagnosed incidentally in the explanted liver and two received pre-LT treatment: 1 radiofrequency ablation, 1 surgical resection. Six patients (42.8%) presented hepatitis C recurrence with a mean time of 17.5 months (range 4-30). All recurrences were diagnosed biochemically (including HCV-RNA) and histologically. No episodes of rejection presented during follow-up (1-52 months). Two cases of cholestatic fibrosing hepatitis were documented. One of them presented early recurrence of hepatitis C (4 months), the other one had late recurrence (12 months). Long term survival is similar to that of patients transplanted for non-hepatitis C liver disease. **Discussion and Conclusion:** This study suggests that the use of anti-IL2-R in the induction of IS after LT is not a major factor favoring recurrence of hepatitis C. Neither is an important issue when time for recurrence is analyzed. Recurrence rate is similar to that reported elsewhere (50-90%). Timing for recurrence seems delayed in our study although this might be secondary to the small number of patients. Our data add support to the knowledge that variables other than the aggressiveness during induction therapy might be responsible of hepatitis C recurrence. Larger randomized trials are needed to confirm our results.

**6. Long-term follow-up of liver transplant (LT) patients receiving anti-IL2-R antibodies during the induction phase of immunosuppression. Clinical characteristics, rejection episodes and survival analysis.**

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**Background:** Acute rejection is a common complication after liver transplantation (LT) presenting in 17-70%. Furthermore steroid-resistant rejection is a cause of lower graft survival. The use of anti-Interleukin 2-Receptor antibodies (anti-IL2-R) in the induction phase of immunosuppression (IS) has been described to decrease rejection episodes after LT. Long-term follow-up reports of patients induced with these agents are scarce and anecdotal. **Aim:** 1) To evaluate the long-term outcome of patients receiving either Basiliximab or Daclizumab as part of the induction phase of IS after LT. 2) To analyze the factors associated with acute rejection. 3) To analyze the survival and recurrent disease in this population. **Methods:** 33 LT patients received standard IS with tacrolimus 0.075 mg/K/d and metil-predinosolone plus either Basiliximab (20 mg on day 0 and 5 post-LT) or Daclizumab (1 mg/Kg on day 0 and 5 post-LT). Etiology of liver disease, number and grade of acute rejection episodes, primary disease recurrence and survival (Kaplan-Meier) were analyzed. **Results:** 14 patients (42%) transplanted for hepatitis C cirrhosis, 9 (27%) for primary biliary cirrhosis, 2 (6%) for Wilson's disease, 2 (6%) for primary sclerosing cholangitis, 2 (6%) for hemochromatosis and 1 (3%) for each of the following: al-

coholic, autoimmune and Caroli's disease. Mean age was 42 years (range 17-63), 18 women. Median follow-up: 52 months (range 1-77). 11 patients received basiliximab and 21 daclizumab, one patient refused to receive anti-IL2-R. Four patients presented acute rejection; one presented an early (day 26 after LT) episode while 3 other patients presented with late (more than 3 months after LT) rejection (one episode each), all were associated with non-compliance with IS. Six patients with hepatitis C recurred during follow-up (42.8%). No other etiology presented recurrence. Long-term survival showed no statistically significant differences when all etiologies were compared. Among the patients receiving anti-IL2-R no graft was lost to rejection. **Discussion and Conclusion:** Anti-IL2-R are safe to use during the induction phase of IS after LT regardless of the etiology of the liver disease. The only episode of early rejection occurred during an episode of sepsis and can be explained by de novo synthesis of interleukins induced by the systemic inflammatory status of the patient. Non-compliance with IS was the main factor for late rejection presentation. Patients transplanted for hepatitis C have a recurrence rate similar to that reported elsewhere and cannot be attributed to the use of anti-IL2-R alone. Larger randomized trials are needed to confirm our results.

**7. Detection of collateral vein flow of the esophagus by endoscopic ultrasound in patients with esophageal varices eradicated by banding**

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**Introduction:** he endoscopic treatment of esophageal varices (EV) with banding was introduced in 1986, demonstrating until the moment security and effectiveness, with the inconvenience of the reported recurrence from the 15 to 65%; influencing in this the presence of collateral esophageal veins. **Objective:** To detect by endoscopic ultrasound (EUS) collateral veins of the esophagus in patients with previously esophageal varices eradicated by banding. **Study design:** Transverse, descriptive and analytic, with measures of central tendency. **Methods:** During the understood period of May of 2005 to May of 2006, all the patients that previously their esophageal varices were eradicated by endoscopic banding, were included, an endoscopic ultrasound was done( EUS), taking into account gender, age, etiology of the hepatic cirrhosis, grade of hepatic (Child) inadequacy, number of banding sessions necessary for the eradication of EV, as well as the number of months after the last banding session. By EUS was evaluated the presence of periesophagic collateral veins (small adjacent glasses to the muscularis characteristic of the esophagus) of light (> 2 mm of diameter), severe (• 2 mm of diameter) type; collateral esophageal veins (big veins separated from the muscularis characteristic of the esophagus) of light (< 5 mm of diameter), severe (• 5 mm of diameter) type, perforating (those that have penetrated the wall of the esophagus and they are connected with peri and paraesophageal veins, veins of the union esophaogastric junction (EGJ), diameter of the azygos vein, as well as endoscopic findings. **Results:** 30 patients were included, 17 of those an radial EUS was carried out and in 14 a linear EUS was done, 21 were men, with a medium age of 63, (range: 3 -78), most of them with ethylic etiology and in functional class Child B; they were light periesophagic veins in 13 and severe in 4, paraesophagic light veins in 15 and severe in 3, perforating veins in 14 patients, with diameters in these of 3.83 ± 1.8 mm, diameter of veins of the EGJ of 3.12 ± 1.7 mm, with diameter in the azygos vein of 6.78 ± 1.94 mm. **Conclusions:** According to other reported studies, a more narrower endoscopic follow-up has to be taken to the 4 patients with severe periesophagic veins and in the 14 patients with perforating veins, due to more risk of esophageal varices recurrence, for what could be advisable to carry out EUS in patients after eradication of EV via endoscopic banding, so a posterior to banding follow-up plan can be determine.

**8. Hepatitis B, hepatitis C and HIV in substance abuse patients in Mexico**

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Prevalence of viral hepatitis and HIV infections in the general substance abuse population in Mexico seems to be low. Prevalence of hepatitis C virus in the general population in Mexico is 1.2% whereas HIV prevalence is 0.3%. In a previous study we found a prevalence of viral hepatitis of 0.9% and HIV of 12% in a sample of 322 drug addicts where 2.5% of the patients were injection drug users (IDU). No other similar study has been reported in the last 5 years. **Methodology:** We sampled all patients attending actively a rehabilitation program at Youth Integration Centers (Centros de Integración Juvenil) from 10 treatment centers in West Central Mexico who voluntary accepted participating in the study. A structured history was used to investigate the pattern of drug use and presence of risk factors. Blood sampling started in December 2005. **Results:** We studied 159 patients (127 male, 32 female), with a mean age of 27.7 years; 62% of the patients had used some kind of substance for over 5 years of time, 13.6% from 3-5 years, and 12.1 had been active users for 2-3 years. There were 6 (3.8%) injection drug users (IDU).Latest drug use was: cocaine (27.7%), alcohol (19.5%), methamphetamine (16%), cannabis (14.5%). There was family history of substance abuse in 72% of the patients. There were 20 (12.6%) patients positive for some infection: 19 (12%) for HCV, 4 (2.5%) for HIV and one patient positive to HBV. Those positive for HCV, HBV and HIV tended to have multiple risk factors including tattoos (70%), piercing (35%), promiscuity (25%), STD (15%), surgical procedures (10%), unsafe sex (10%). Only one antibody positive patient was IDU. In a sub-group of 30 subjects in prison prevalence of HCV was 40%, HBV 3.3 % and HIV 6.6%. **Conclusions:** Prevalence of hepatitis C and HIV antibodies among substance and drug users attending CIJ clinics in West central Mexico is high. HCV positive cases have increased in the past 5 years. So far intravenous drug use is not very common in this population and thus does not seem to be as frequent a risk factor as other factors such as tattooing, piercing and risky sexual practices.

**9. Putting the fibrotest into practice**

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**Aim:** To explore the clinical utility of the Fibro-Actitest to become an integral part of the assessment of chronic hepatitis C patients (CHC). **Methods:** We included 333 consecutive outpatients with CHC referred to a Gastroenterology Clinic with Fibro-Actitest performed at their first evaluation. **Results:** Forty seven patients (14%) had minimal or absent fibrosis (F0-F1), 107 (32%) moderate fibrosis (F2) and 179 (54%) advanced fibrosis (F3-F4). Most patients (66%) had an Actitiest • 2. Cross tabulation revealed that 62% of patients with advanced fibrosis had abnormal aminotransferases (ALT), whilst 71% of patients with minimal fibrosis had normal ALT ($p<0.001$). A direct Spearman correlation occurred between the increased fibrosis score and the levels of a2-macroglobulin ($p<0.001$). Sensitivity and specificity of ALT for fibrosis were 62% (IC 95% 56-67) and 70% (IC 95% 56-81) and for a2-macroglobulin 76% (IC 95% 71-81) and 75% (IC 95% 61-85), respectively. All patients with cirrhosis scored F4. **Conclusions:** The majority of patients with CHC consulted for evaluation at an advanced stage of the disease. The use of ALT to stage and monitor patients with CHC can lead to an inaccurate estimation of fibrosis in more than a third of the patients. Determination of a2-macroglobulin enhances the predictability of fibrosis but still overlooks >20% of cases. Our analysis favors the use of the Fibro-Actitest instead of any single determination of their components.

**10. Interferon • pegylated and ribavirine modulate the production of interleukin-8 by peripheral blood mononuclear cells from patients with chronic hepatitis C**

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**Introduction:** Hepatitis C virus infection (HCV) is the most relevant cause for the development of cirrhosis and hepatocellular carcinoma. Resistance to the antiviral therapy has been associated the non- structural protein 5A (NS5A). It has been report that NS5A not only induces IL 8 production *in vitro* but also represses the antiviral action of interferon alpha (INF alpha). Protein NS4 blocks the Th1 response trough IL 10 secretion by monocytes. **Aim:** To investigate the effect of pegylated interferon (pegIFN)-alpha 2 and ribavirine on IL-8 production by peripheral blood mononuclear cells (PBMC) from patients with chronic hepatitis C (CHC). **Materials and methods:** We evaluated 28 patients with CHC. They were classified according their response to antiviral treatment in two groups: non-responders (NR=12) and responders (R=16). PBMC were obtained from peripheral blood by isolation with Ficoll-Hypaque, the cells were cultivated at 37ºC and 5% $CO_2$ and saturated humidity for 24 hr during 0, 2, days, 1, 3, 6, 12 months of treatment and 6 months following. The supernatants were collected and used to determine IL-8 by ELISA. Dates were analyzed with the Wilcoxon test. **Results:** IL-8 secretion were significant different between Responders (R) and Non Responders (NR) at 2 days of treatment: 6773 ± 4355 pg/mL vs 5172 ± 911 pg/mL (P=0.05), at 3 months 7677 ± 11733 pg/mL *vs* 3029 ± 1695 pg/mL (P=0.008), and at 6 m 5485 ± 975 pg/ml *vs* 4567 ± 914 pg/mL (p=0.023). At 6 m following, IL-8 production was more elevated in NR vs R: 4183 ± 6081 pg/mL *vs* 742 ± 720 pg/mL (P=0.05). **Conclusions:** Patients with chronic hepatitis C responders to treatment have a consistent inflammatory/chemotactic response. In non responders to treatment showed an increase in IL-8 which could participate in the inhibition of the antiviral activity treatment

**11. Predictors of advanced liver fibrosis and cirrhosis in chronic hepatitis C Patients: Influence of metabolic disturbances**

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**Background:** The rate of liver fibrosis (LF) progression in chronic hepatitis C patients (CHC) is variable, this variability has lead to search the risk factors for accelerated fibrosis. Diabetes, obesity and elevated serum triglycerides are associated with non-alcoholic fatty liver disease, in CHC this metabolic disturbances could add to HCV liver-induced damage. **Aim:** To identify predictors of advanced fibrosis and cirrhosis in CHC patients. **Method:** Consecutive CHC patients with HCV-RNA detectable in serum and a liver biopsy performed before treatment were included. LF and inflammatory activity were scored by means of METAVIR staging system. The association between advanced fibrosis (F • 2) and cirrhosis (F4) with the following variables were investigated: gender, age at infection (in patients with known duration of infection acquired by blood transfusion), ALT elevated or persistently normal (ALT normal in at least three separated serum samples during a 6 month period), diabetes, glucose intolerance, hypertriglyceridemia, metabolic syndrome (obesity, diabetes/glucose intolerance, hypertriglyceridemia), overweight (body mass index • 25 < 30 kg/m$^2$) and obesity (body mass index • 30 kg/m$^2$). For statistical analysis logistic regression were used. **Results:** One hundred and fifty nine patients were studied with a mean age of 49.34 ± 12.37 years-old, 95 (60%) were female. One hundred seventy (74%) patients had elevated ALT and 42 (26 %) had persistently normal ALT. Mean HCV-RNA was 518000 UI/mL (8000 – 11100000), 80% of patients were infected with HCV genotype 1, 15% genotype 2, 4% genotype 3 and 1% genotype 5. Mean serum glucose, total cholesterol, HDL and LDL cholesterol were 94 mg/dL (67 – 347), 159 mg/dL (39 – 254), 39 mg/dL (12 – 83) and 92 mg/dL (20 – 172), respectively. Twenty percent of patients were diabetics (n=32), 6% (n=9) had glucose intolerance, 15 % (n=24) had hypertriglyceridemia and 16 % (n=26) had hypercholesterolemia. Median of body mass index was 27 kg/m$^2$ (17.5 – 40.8), 47% (n=75) of cases had overweight and 25 % (n=40) were obese. Twenty one percent (n=34) of patients had metabolic syndrome. Stages of LF were as follows: F0 19% (n=30), F1 30% (n=48), F2 14% (n=23), F3 13% (n=21) and F4 23% (n=37), 81 (51%) patients had advanced fibrosis. Diabetes is a predictor of advanced fibrosis (RM=3.47, IC 95%; 1.39 – 8.67, P=0.008) and of cirrhosis (RM=2.9, IC 95 %; 1.13 – 7.42, P=0.03). Elevated ALT is a predictor of cirrhosis (RM=3.82, IC 95 %; 1.26 – 11.56, P=0.01) and the presence of moderate-severe inflammatory activity in liver biopsy was associated with advanced LF (RM=2.5, IC 95%; 1.26 – 5, P= 0.009). **Conclusions:** Elevated ALT is a predictor of cirrhosis in CHC patients. The prevalence of diabetes, overweight, obesity, metabolic syndrome and dyslipidemia in our group of patients was high. Diabetes is a predictor of advanced liver fibrosis and cirrhosis in CHC patients. In the Mexican population with high prevalence of diabetes this association must be taken into account in the approach of CHC patients.

**12. Inflammatory response of peripheral blood mononuclear cells from patients with chronic hepatitis C (CHC)**

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**Introduction:** Hepatitis C constitutes a serious world health problem. Hepatitis C pathogenesis includes an immunological component which plays a central role in the host responses to viral infections. The origin of bacterial endotoxemia in CHC patients can be a multifactorial process where lipopolysaccharide (LPS) could arrive from an exogenous or endogenous source. **Aim:** To identify the production of pro- and anti-inflammatory cytokines production by peripheral blood mononuclear cell (PBMC) from CHC patients and their response to LPS. **Materials and methods:** We included 34 CHC patients anti-HCV(+) and ARN-HCV(+) naïve to antiviral treatment. PBMC were isolated with Ficoll-Hypaque and were cultivated at 37ºC and 5% $CO_2$ and saturated humidity for 24 hr with and without LPS (1µg/mL) in RPMI 1640. Supernatants were collected and used to determine the secretion for IL 1b, TNF-a, INF g, IL 8, IL 6, IL 4, IL 10 and TGF-b by ELISA. Statistical analysis of data was made using the Wilcoxon test. **Results:** No differences were observed on the PBMC secretion of IFN-g and IL 4 with or without LPS stimulus after 24 h of treatment. No significant differences were observed between the control and LPS treatment after 24 h on IL 1b, TNF-a, IL 10 and TGF-b secretion while IL 6 and IL 8 secretion were increased 4 folds approximately, 1840 ± 2143.1 pg/mL *vs* 5635.5 ± 5197 pg/mL (p=0.001) and 8333.1 ± 7222.8 pg/mL *vs* 404333.3 ± 26491.5 pg/mL (p=0.01) respectively. **Conclusion:** Our results confirm that endotoxines activate the pro inflammatory cytokines secretion and could enhance the inflammatory process induced by the HCV.

**13. Cryoglobulinemia in subjects with chronic hepatitis C virus infection**

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**Background:** The spectrum of extrahepatic manifestations of chronic hepatitis C virus (HCV) infection is wide, mainly due to mixed cryoglobulinemia (MC). More than 40% of HCV-infected patients have a high level of circulating cryoglobulins, but only a few percentage have symptoms due to this condition, mainly skin, joint, renal and neurologic affection. This variability had been related to viral and host fac-

tors. In Mexico the frequency of MC and its clinical presentation is unknown. **Objective:** To evaluate the prevalence of cryoglobulinemia and its clinic impact in a group of mexican patients with chronic HCV infection. **Methods:** Were included ninety patients with chronic HCV infection, confirmed with positive serum HCV RNA levels, 59% female, with a median age of 69 ± 13 years, suitable to receipt combined antiviral therapy. Levels of cryoglobulins were measured in all patients. The mainly manifestations of MC was investigated in all the cases. Demographic, biochemical and viral factors associated with the presence of CM was analyzed. Results were expressed in mean ± SD and frequencies. Groups with and without cryoglobulins were compared using the Mann-Whitney U test or the Fisher exact test. **Results.** Thirteen patients (14.5%) had high levels of serum cryoglobulins, but only four of these showed symptoms (membranoproliferative glomerulonephritis, arthritis, purpura and polyneuropathy in one; mononeuritis multiplex y arthritis in other one; focal and segmental glomerulosclerosis with proliferative component in other; and sicca syndrome in the last one). Significant differences were observed in age, with oldest patients in cryoglobulins group (56 ± 7 *vs* 47 ± 13 years, p=0.001), patients older than 59 years have 28% more risk to develop MC (OR 1.28, IC 95% 1.030-1.589). In patients with cryoglobulinemia, the prevalence of non-1 HVC genotipe was 31% *vs* 17% (p=0.23), and smooth-muscle antibody was present in 30.7% *vs* 13% (p=0.09). **Conclusion:** Prevalence of cryoglobulinemia in mexican patients in a third level hospital is, lesser than the others reports in literature, and only 4% had symptoms, mainly with renal, joint and neurologic involvement. These data are different from the other series, where skin lesions are the most common. Age and tendency to have SMA were the unique factors with significant difference associated with presence of cryoglobulinemia. It is necessary perform trials with more number of patients in order to found differences in other variables. In addition, other question for answer is if there will be improvement in manifestations of cryoglobulinemia and decrease in their levels with antiviral therapy.

**14. Black bean extract inhibits liver fibrosis after $CCl_4$ induced injury**

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**Introduction:** Cirrhosis is a distortion of the liver normal architecture caused by oxidative-stress processes originated by the Kuppffer cell's free radicals and release of inflammatory cytokines. This inflammatory response is accompanied by an extreme fibrosis produced through the paracrine action of fibrogenic factors generated by main hepatic cells. The increasing fibrosis generates qualitative and quantitative changes in the extracellular matrix, as a result of and increases of type I and IV collagens. The regulation of these proteins is crucial to the pathogenesis of the diseases. Over the last years, the effects of antioxidative compounds like flavonoids, flavones and phenolic derivates has been studied as hepatoprotective and antifibrotic activators. **Methodology:** Wistar rats (90-100g) were divided into five different groups and received different doses of intraperitoneal $CCl_4$ shots over eight weeks; in addition, in three of the five groups, 7 mg/kg of bean skin extract, 70 mg/kg of bean skin extract and 70 mg/kg of quercitine was given. At the end of the experimental stage, fibrosis was assessed through histological and morphometric analysis. The fibrogenic gene expression was measured trough real time QRT-PCR. **Results:** Intraperitoneal $CCl_4$ caused severe changes in the liver architecture, showing interstitial fibrosis, inflammatory infiltrate and collagen deposits. The qualitative and quantitative histological analysis demonstrated that the high been skin dosage receiving rats (70 mg/kg) decrease the liver collagen deposit, reducing significantly the fibrosis by 20% in comparison with the control group. By molecular analysis, clearly it is observed that the low presence of interstitial collagen is inherent to a low gene expression, because the relative collagen I and IV fibrogenic gene expression were 8.93 and 1.3 (damaged groups) and 20.15 and 4.7 respectively in the control group. The 70 mg/kg of quercitine treated animals showed the same tendency to the one exhibited by the animals treated with high bean extract dosage but with less notorious results. In the case of 7 mg/kg bean extract, far from being beneficial, it caused toxicity (demonstrated by the high fibrosis levels) and increasing mortality. **Conclusions:** The bean extract, under an adequate dosage, can be a good therapeutic alternative to the cirrhosis treatment, since it reduces significantly the histological and genetic progress of the disease. It is clear that the extract diminishes mortality in treated animals. The use of antioxidants derived form our black bean extract, given in low dosages after damage induction, may lead to the production of pro-oxidant compounds, as a result of a poor metabolism, thus associating to an increased liver damage.

**15. Early virologic response is independent of baseline alt levels in patients with chronic hepatitis C treated with combination therapy**

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**Background:** Approximately 30% of patients with chronic hepatitis C (CHC) have persistently normal aminotransferases levels. Natural history of liver fibrosis in patients with normal alanine aminotransferase (ALT) is uncertain. This group of patients usually has been excluded from the clinical trials and data related to the effectiveness of the combined antiviral therapy are limited. **Aim:** To compare the early virologic response (EVR) rate during antiviral combination therapy between patients with normal and elevated ALT levels. **Patients and methods:** This is a prospective, open label study. Adult patients with positive antibodies for hepatitis C virus (HCV), detectable HCV RNA by PCR in serum and liver biopsy compatible with CHC were included. Normal ALT levels were considered when two o more determinations were in the normal range over at least six months. All liver biopsies were evaluated according to METAVIR score. A • 2 score in activity and/or fibrosis were considered as significant. Patients were treated with PEG-IFN alpha-2b (PegIntron®; Schering-Plough 1.5 µg/kg/week) and ribavirin (Cotronak® • 10.6 mg/kg/day). EVR was defined as serum HCV RNA below lower level quantification (LLQ < 5 IU/mL) at week 12 on-therapy. Significant adverse event was considered when dose reduction/discontinuation were required. Patients who withdrawal treatment were considered as non responders. Categorical variables were compared using •$^2$ and continuous variables with student's t test. The results are expressed in mean ± standard deviation. A p value < 0.5 was considered as statistically significant. **Results:** 90 patients were included, 46 had normal ALT and 44 had elevated ALT. Baseline characteristics were similar between patients with normal and elevated ALT: female sex (60 *vs* 52%), age (48.9 ± 13.4 *vs* 49.2 ± 13.2 years), body mass index (27.3 ± 4.8 *vs* 27.3 ± 5.2), viral load (1.6 ± 2.1 x $10^6$ *vs* 1.2 ± 1.9 x $10^6$ IU/mL) and genotype 1 (73 *vs* 84%). EVR was achieved in 75% of the patients without statistical differences between patients with normal and elevated ALT. The incidence of significant adverse events was similar in both groups, including severe neutropenia in 9 (10%) patients, anemia in 4 (4%), bicitopenia in 3 (3%), trombocitopenia in 2 (2%), and other events in 9 (10%). Almost third part of patients with normal ALT had advanced fibrosis in liver biopsy. Factors associated with failure of EVR were fibrosis score • 2 (p=.002) and genotype 1 (p=0.002). **Conclusions:** In the studied population, ALT level was not a predictive factor to achieve EVR. The elevated frequency of significant fibrosis observed in patients with normal ALT and an EVR rate similar to those with elevated ALT, suggest that the antiviral treatment in these patients could be indicated independently of the ALT levels. The decision to allocate treatment with peginterferon alfa and ribavirin should be based on multiple factors rather than on ALT levels alone. This work has been sponsored by Schering-Plough.

**16. Wilson's disease: Analysis of the first described cohort of native mexican patients.**

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**Background:** Wilson's disease (WD) is an autosomal recessive disorder of copper metabolism characterized by liver and neurologic involvement with a prevalence about 1:30,000. It is said to be commonest in Eastern European Jews, Sicilians, southern Italians, Arabs, Japanese, Chinese and Indians. Reports of WD in natives of central and south America are scarce and anecdotal. **Aim:** to investigate the presence of WD in native Mexican patients (at least 3 generations born in Mexico). **Methods:** In a retrospective protocol we studied patients labeled with cryptogenic liver disease from 1980 to 2002. Demographics, clinical presentation, biochemical profile, image studies and therapy were determined. **Results:** We identified 11 patients with WD; in 7 of them the disease was familial (family A=3, family B=2, family C=2) and sporadic in other 4. The clinical ad laboratory findings varied but were not different from those reported elsewhere. Nine patients started D-penicillamine and improved clinically and biochemically, 2 patients are on dietary management and 2 underwent liver transplantation. Brain MRI on 4 patients showed alterations in basal ganglia. In the transplanted patients, these brain lesions reversed in a follow-up MRI 6 months after transplant. **Conclusions:** This is the first cohort of native Mexican patients reported with WD. Further epidemiologic studies are needed to determine the prevalence of the disease in the Mexican general population.

### 17. A frequent haplotype of the gene encoding the nuclear bile salt receptor FXR is associated with gallstone susceptibility in a Mexican but not in a German population

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Cholesterol gallstone susceptibility is determined by the combination of predisposing alleles of lithogenic (*LITH*) genes and environmental factors. From quantitative trait locus mapping in inbred mice, we identified the gene encoding the nuclear bile salt receptor FXR as a candidate gene for a *Lith* locus on chromosome 10. In the current study we aimed to explore an association of genetic variation of *FXR* and gallstone prevalence in humans. To detect single nucleotide polymorphisms (SNPs), we employed systematic sequencing of *FXR* in 24 subjects. Gallstone carriers and age- and sex-matched control subjects from a Mexican and a German population were genotyped employing the TaqMan method. Haplotypes were reconstructed using the PHASE software. Significance levels were determined by logistic regression. Sequencing of *FXR* in the screening population revealed seven SNPs that were genotyped in all subjects from the Mexican (n = 156) and the German (n = 368) populations. All SNPs complied with the Hardy-Weinberg equilibrium. We identified three common haplotypes that accounted for >95% of all haplotypes observed. In the Mexican population, the most common haplotype *FXR-1* was associated with gallstone prevalence (gallstone carriers 88%, controls 78%; P = 0.02, relative risk 2.1, 95% confidence interval 1.1 – 3.9). In contrast, *FXR-1* displayed no association with gallstone prevalence in the German population (gallstone carriers 95%, controls 96%). In conclusion, our study supports an association of *FXR* alleles and cholelithiasis in selected populations. Therefore, the bile salt receptor is a potential target for prevention and non-surgical management of cholelithiasis in genetically predisposed patients.

### 18. Pylephlebitis: 1 Case report

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**Background:** Pylephlebitis (PF) or septic thrombosis of the portal vein (PV) is the blockage of the hepatic portal flow by a septic thrombi. Usually caused by suppuration or inflammation of the structures that drain through the PV and adjacents sites. Many morbid conditions leads to PV thrombosis and can be divided on 3 categories: 1) Conditions that cause PV damage and posterior thrombosis (ie intraabdominal sepsis), 2) PV intrinsic anomalies (ie. stenosis or athresia), 3) Hereditary or acquired hypercoagulability states (leading cause among adults); 8-15% of the cases are idiopathic. Clinical presentation of PF varies from asymptomatic patient (because of the hepatic artery buffer to the low PV flow) to portal hypertension sings and symptoms (variceal bleeding as the most frequent presentation). **Materials and methods:** Twenty five years old male, butcher, family history of diabetes. Tobacco, illicit drugs, tattoos, piercing, surgeries, sexual exposition, blood transfusion or trauma was denied. Alcohol consumption for 9 years (70gr/week). Past history, one month with colicky abdominal pain, intermittent fresh blood passage and mucus through the stools. Patient was referred from another institution to be studied for jaundice and fever for the past 4 weeks of unknown etiology. At admission; BP 100/50 mmHg, HR 110x´, T 38°C, RR 25x´. Physical examination, generalized jaundice, mental status preserved, right pleural effusion, torax and abdominal wall with spider webs, collateral red venous in abdomen, painless liver enlargement (5 cm below the right costal border), splenomegaly and ascites. Digestive bleeding was not found. He developed cardio-respiratory deterioration due to sepsis and bacteremia, requiring vasoactive drugs, broad-spectrum antibiotics and mechanical ventilation support at ICU. Results: WBC 15,740 (5200-12000), Granulocytes 91%, Lymphocytes 5.6%, Hb 11.9 gr/dL (12-18), MCV 88.8Ft, HMC 30.9 Pg, Platelet count 206,000, Bands 17%, toxic granulations present, and granulocytes vacuolation +. LFT´s: Total Bilirrubin 6.77mg/dL (0.01-1.0), Direct Bilirrubin 3.7 mg/dL (0.01-0.30) Albumin 2.82 mg/d (3.5-5), Amilase 65 U/L (28-100), Cholesterol 140 mg/dL (140-200), BUN 10.7mg/dL (8-18) Creat 0.82 mg/dL (0.8-1.4), Alkaline phosphatase 492 U/L (95-117), GGT 753 U/l (7-32), AST 45 U/l (5-37,) ALT 98 U/L (5-50), INR 1.39. Viral agents HIV, HCV and AgsHVB were negative. Blood culture: *E. Coli* (multi-resistance, sensitive to Imipenem). Ascitic fluid: 345 cells, 45% Granulocytes, Glucose 103 mg/dL, total proteins 420 mg/dL, SAAG >1.1. Doppler Color US: hepatomegaly, heterogeneous liver pattern, PV diameter 15 mm, hyperechogenic image on the PV lumen involving the right and left branches with multiple collateral veins. Spleen volume 988 cc. Ascitic fluid detected. Abdominal CT revelead hepato-splenomegaly, and PV luminal thrombi. Endoscopy: small esophageal varices and severe congestive gastropathy . Colonoscopy was performed because of fresh blood passage on stools, yielded only a small polyp on descending colon (diameter 3 mm). Polyp histopathology: Inflammatory polyp. Discussion: Among the multiple etiologies of PV thrombosis, sepsis-associated are extremely rare. The diagnosis has to be highly suspected in patients with abnormal liver function tests in an appropriate clinical setting. The main causes of sepsis in this selective patients group are related to complicated colonic diverticular disease, appendicitis and abscesses close to the PV. The present case had a positive *E. Coli* hemoculture , and broad spectrum antimicrobial agents were used, Imipenen treatment was selected to resolve the sepsis. Substantial improvement was seen 10 days after antibiotics and anticoagulation with acenocumarine was initiated. At present, the clinical utility of anticoagulant therapy represents a controversial issue. Nevertheless, it has been reported that some patients have partial or total PV thrombosis recanalization with anticoagulation. Actually the patient is alive and stable conditions under portal hypertension treatment at the outpatient clinic.

### 19. The effect of artificial bezoar (Gallstone powder) on proliferation of human pancreatic cancer – an *in vivo* study on nude mice

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**Introduction:** Bile pigments, including bilirubin and biliverdin, contribute importantly to the defense against oxidative stress. Moreover, recent clinical studies suggest that mildly elevated serum bilirubin levels might protect from certain forms of cancer. Artificial bezoar (powdered bovine gallstones, also known as Nui Huang) is used in traditional Chinese medicine for centuries for its antipyretic and anti-inflammatory properties. In the present study, we investigated the effect of

artificial bezoar on proliferation of pancreatic cancer. **Methods:** The study was performed on nude mice (strain CD-1, n=5 in each group) subcutaneously xenotransplanted with human pancreatic adenocarcinoma cell line PaTu. After successful attachment and growth initiation of cancer cells, the mice were treated with daily oral administration of water suspension of powdered bovine gallstones (Artificial bezoar, Biopharma, Australia) (50 mg/kg b.wt.) containing more than 50% of Ca bilirubinate. The control group did not receive any treatment. The primary endpoint was the survival time (assessed by Kaplan-Meier survival analysis). Simultaneously, tumor size progression during the first 24 days (measured every 3 days) was analyzed (by repeated measures ANOVA with Holm-Sidak post-hoc testing). **Results:** As compared to controls, mice treated with artificial bezoar survived significantly longer (39.3 ± 8.2 *vs* 45.8 ± 0.9, p=0.009). Both groups differed significantly in tumor size already since 3rd day after initiation of artificial bezoar therapy. The most pronounced difference in tumor size was detected at 24th day of therapy (0.88 ± 0.36 *vs* 3.29 ± 2.20 $cm^3$, p=0.029 in artificial bezoar *vs* control group, respectively). **Conclusions:** In our experimental model of human pancreatic cancer, substantial antiproliferative effect of orally administered artificial bezoar was demonstrated. These results suggest that bile pigments might contribute to the protection from pancreatic cancer. This work was supported by a grant No. 209071 given by the Czech Ministry of Education.

**20. Biphasic pattern of psoriatic arthritis during treatment with interferon and ribavirin for chronic hepatitis C (166)**

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**Background:** Only a few case reports have been reported describing association of psoriasis with chronic hepatitis C (CHC). It is not clear, however, if it was causal association or coincidence. A more striking association of psoriasis in the setting of HCV infection has emerged during interferon-(IFN) treatment. We describe biphasic pattern of clinical course of psoriatic arthritis(PsA) in a patient with HCV associated mixed cryoglobulinemia and its relationship to treatment with interferon-(IFN) and clearance of the of the virus. Case report: A 44-year-old Caucasian man with a long history of CHC developed dramatic worsening of his PsA in association with the two courses of IFN and ribavirine treatment. The failure of the antipsoriatic treatment and persisting viremia necessated discontinuation of the first course of IFN treatment with subsequent improvement of PsA. During the second course of treatment, the same initial deterioration was observed. However, after two months the PsA started to improve despite of continuation of IFN treatment. On review 36 months after termination of the treatment the patient continues in virological remission and his PsA remains in remission too, without any treatment. **Conclusions:** This case adds further evidence that IFN can provoke PsA, especially when additional precipitating factors such as infection are involved. The close temporal relationship between improvement of PsA and elimination of HCV infection indicates the possibility of a direct pathogenetic link between the HCV and PsA. Hence, HCV infection should be considered in all individuals with psoriasis or PsA who have risk factors for HCV infection.

**21. Withdrawn**

**22. Withdrawn**

**23. Withdrawn**

**24. Withdrawn**

**25. Withdrawn**

**26. Withdrawn**

**27. Insulin sensitizers in the treatment of non-alcoholic fatty liver disease: A systematic review.**

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**Background:** Nonalcoholic fatty liver disease (NAFLD) is an increasingly recognized condition that may progress to end-stage liver disease, ranging from simple steatosis to steatohepatitis, advanced fibrosis, and cirrhosis. Currently there is no consensus regarding effective therapy for NAFLD; attempts are being made to direct treatment toward avoiding or correcting risk factors, including insulin resistance and decreasing hyperinsulinemia hepatoprotective effects. **Aim:** We performed a comprehensive systematic review to establish the evidence available about the clinical effectiveness of insulin sensitizers in NAFLD. **Search strategy***:* Electronical databases Medline (1966-March 2006), EMBASE (1988-March 2006), Cinahl (1982-March 2003), Educational Resource Information Center (ERIC) (1966-March 2006), Information Science & Technology Abstract (LISTA) (March-1967 2006), Cochrane Database of Systematic Reviews (CDSR), Cochrane Controlled Trials Register (CCTR), Database of Abstracts of Reviews of Effects (DARE) (1994 2006), Dissertions in Proquest and First Search databases and Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS). The authors also searched reference list and abstract from main gastrointestinal meetings. **Study selection criteria:** The selection criteria were: (1) studies of clinical trials using anyone or combination of insulin sensitizers in subjects with NAFLD; (2) sample of adult patients; (4) published in full manuscript form or abstract; and (5) English, Spanish, German and French language only. **Results:** Twelve studies were candidates to be evaluated. Two studies compare the utility of metformin *versus* diet, biochemical improve was observed, but not in histology. Five trials evaluate the use of metfomin in single arm studies, biochemical and insulin resistance were improved. The use of thiazolidinediones were evaluated in five studies, all of them show significative improvement in liver function tests, insulin resistance and image scores of liver steatosis. **Conclusions:** Current information do not support the use of insulin sensitizers in treatment of NAFLD, evidence from lack-methodological studies indicate that metformin could be useful, and until more high quality studies using thiazolidinediones show beneficial effects this therapy has can not be recommended.

**28. Abnormal liver function tests (LFTs) of unknown origin. Usefullness of liver biopsy**

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**Introduction:** In most patients with elevated liver function tests (LFTs) with unknown cause, a defined diagnosis is rarely reached with a subsequent specific therapy. **Aim of the study:** To valorate if the histologic information given and the liver biopsy modified the prior therapeutical attitude in this group of patients. **Material and methods:** Retrospective cohort-study including patients with abnormal LFTs of unknown origin referred for liver biopsy from January-2002 to January-2005. Knodell histologic score was used to assess the liver damage: slight histologic damage (F0-F1) and moderate to severe damage( F2-F4) . Statistical analysis with SPSS 12.0 package. **Results:** Thirty-eight patients were enrolled, medium age 40-yr-old, male 55.3%. A slight histologic damage (F0-F1) was found in 76.3% of patients in spite of 23.7% with a moderate to severe damage( F2-F4). In 5 out of 38 patients (13.2%) liver biopsy gave an ethiologic diagnosis, as follows: drug-induced hepatitis, M. tuberculosis granulomatous hepatitis, alcohol-induced hepatitis, primary biliar cirrhosis (PBC) and an adulthood ductopenia respectively. Four out of 38 biopsied patients (10.5%) received specific medical treatment: therapeutical flebotomies in 2 patients with severe steatosis and haemosiderosis, anti-tuberculous specific therapy for M. tuberculosis granulomatous hepatitis in 1

patient and ursodeoxicholic acid (UDCA) in 1 patient with PBC. Medium AT, ALT, AF, bilirrubin and GGT levels were 61.4 U/L, 89.9 U/L, 166.2 U/L, 1.4 mg/dl and 143 U/L respectively. Percutaneous ultrasound-guided liver biopsy was followed by no complications in our series. No clear relationship was found between blood tests profile and a specific etiology of the abnormality in LFTs. **Conclusions:** In our experience liver biopsy helps in clarifying the etiology of LFTs abnormalities in 13.2% of the patients with otherwise unknown cause, similar to other published series. The information given by the liver biopsy carries a 10.5% change in the therapeutic attitude.

**29. Ethanol up-regulates HCV replication and gene expression trough a mechanism that involves COX-2**

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**Background:** Despite strong epidemiological evidence the mechanisms by which alcohol accelerates liver damage in patients with hepatitis C remains unknown. The availability of the HCV replicon system containing hepatic cells has provided a unique opportunity to investigate the interaction between alcohol and HCV replicon expression. One plausible mechanism through which alcohol consumption may favor the progression and exacerbation of HCV infection is oxidative stress. Recently, the activation of cyclooxygenase-2 (COX-2) has been implicated in the HCV-associated hepatocellular carcinoma. **Aims:** We evaluated the effect of ethanol on HCV expression and the role of cyclooxygenase-2 (COX-2) expression and activity on ethanol-treated HCV replicon expressing cells.

**Methods:** We used the Huh7 HCV replicon cells and parental cells. Cells were incubated with or without ethanol (100, 150 and 200mM) for 24, 48 and 72 hours. At the end of this time, HCV RNA quantification and protein expression were measured by Real-time RT-PCR (TaqMan probes) and Western blot (using anti-HCV NPTII, anti-HCV NS5A, anti-actin and anti-COX-2 antibodies). Cell viability also was quantified by alamarblue reduction. After ethanol treatment, the levels of prostaglandin $E_2$ ($PGE_2$), the product of COX-2 activity were quantified. **Results:** Our results showed that ethanol (150mM) treatment stimulated HCV replicon expression at both HCV-RNA (up to 4.36 times) and protein levels (up to 4.0 times) and this effect was time dependent. There was no cytotoxic effect of ethanol at the concentration of 150mM on the cells. To investigate the possible mechanism (s) responsible for alcohol-mediated up-regulation of HCV RNA and protein expression in Huh7 HCV replicon cells, we examined COX-2 expression and activity in presence or absence of ethanol. We observed that COX-2 protein and $PGE_2$ levels were induced in Huh7 HCV replicon cells while they were almost undetectable in parental cells. Interestingly, we found that ethanol up-regulated COX-2 protein and $PGE_2$ levels in Huh7 replicon cells whereas the addition of ethanol to parental cells had no significant impact on COX-2 protein and $PGE_2$ levels. Furthermore, ethanol treatment showed an additive effect in COX-2 protein expression and activity induced by HCV viral proteins and in turn increased HCV viral expression. Our results suggest that COX-2 expression is involved in ethanol-induced HCV RNA and protein expression. **Conclusions:** We suggest that ethanol increases HCV replication at least in part by up-regulating a key cellular regulator of oxidative stress pathway known as COX-2 or its products. This work was supported by «*PAICYT SA1010-04* and *PROMEP/103.5/04/2590*».

**30. Replication and genic expression of the hepatitis C virus regulated by the participation of cyclooxygenase 2 (COX-2)**

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**Background:** The Hepatitis C infection represents one of the main causes of chronic hepatitis, cirrhosis and hepatocellular carcinoma (HCC) in the world. Cyclooxygenase 2 (COX-2) is an enzyme involved in the inflammatory process. The principal activity is the biosynthesis of prostaglandins; this enzyme has angiogenics properties related to the survival and the development of diverse types of cancer including the HCC. This last property has waked up great importance in the investigation due to the potential inhibitor use of COX2 like therapy against the cancer, process that also appears in the patients with hepatitis C. One has seted out, an association between the anti-inflammatory process and the regulation of the expression of proteins of the HCV, nevertheless the findings are contradictory. The elucidation of this interaction is important to understand the molecular mechanisms by means of which the HCV is able to maintain an infection persistent in infected patients. **Aims:** Evaluate the roll of the cyclooxygenase 2 enzyme in the replication and expression genic of the Hepatitis C Virus, in the replicon subgenomic system. **Methods:** The Huh-7 cells are hepatoma human cells, we used Huh-7 replicon cells express HCV replicon and parental Huh-7 cells (without replicon), were exposed a concentration of 4mM of aspirin (AAS), (inhibiting of COX-2), and incubated during 24, 48 and 72 hours with the purpose of evaluating the effect of this agent in the levels of the RNA and proteins of the HCV. Later, the expression of the VHC at transcripcional level was analyzed quantifying the viral RNA by means of RT-PCR in Real time. At post-traduccional level was identified the expression of viral proteins (NPTII, NS5A) and cellular proteins (Actina, COX2) by Western blot. In addition, to evaluate the enzymatic activity of protein COX-2, the quantification of the intracellular levels of $E_2$ prostaglandin was made ($PGE_2$). **Results:** We were observed that in the Huh-7 cells that lack the expression of viral proteins, the COX-2 expression was almost imperceptible, in opposition to the findings found in the cells of hepatoma that express proteins of the VHC, where was observed an increase in the expression of enzyme COX-2 dependent of the time (0-72h). This increase in the expression of COX2, found single in the cells that express replicon, correlates directly with an increase in the levels of the viral RNA and the effect is proportional according to the time (0 - 72h). When we treated the HCV replicon cells with 4mM of AAS by a period of 0 to 72h, was observed that the inhibitor of cyclooxygenase diminished the levels of viral RNA and viral proteins according to the time of exposition, its greater effect obtaining to 72h. In the same way, was evident that the activity of enzyme COX-2, diminished as the time of exhibition with AAS. **Conclusions:** In our system we suggest, that the COX-2 on-expression is by cause of the time and correlates with an increase in the viral protein expression. Our results suggest it inhibition of COX-2, half-full by aspirin, diminishes the expression of the RNA and proteins of the HCV; the effect on the enzymatic activity of protein COX-2 is even decreasing approval the time of exhibition with the AINEs. Therefore, we propose that enzyme COX-2 is involved in the positive regulation of the transcripcional and post-traduccional expression of the HCV. This work was supported by "PAICYT SA1010-04 and PROMEP/103.5/04/2590".

**31. Liver steatosis in overweight/obese children**

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**Objectives:** 1) The prevalence of liver steatosis in overweight/obese children 2) Correlations liver steatosis with risk factors of cardiovascular, biochemical parameters and life´s styles. **Material and methods:** We performed a transversal study of 116 patients with overweight or obesity (IBM>P90) (64 males and 52 females) between 6-14 years old (mean 10,47). Anamnesis, questionnaire over life´s styles and physical exploration including arterial blood pressure were recorded. Transaminase, TSH, uric acid and lipidic levels were tested in all patients. Oral glucose tolerance test, insulinemic resistence (HOMA) and insulinemic sensitivity (QUICKY) were tested in group of obesity patients. All children underwent an ultrasonographic study of the liver. **Results:** The

prevalence of liver steatosis was 37,9%. Values of transaminase above the elevated levels (ALT, AST and/or GGT) were present in 13,3% of the group with US liver steatosis, and this group was showed bigger grade of US liver steatosis(Grade II:44,4%; Grade III:22,2%). The correlations the biochemical parameters in the subjects, grouped according to the presence or not of liver steatosis are illustrated in table I and II. Triglycerides, LDL, total cholesterol, GPT, hyperinsulinemic, HOMA and metabolic syndrome were significantly higher among patients US fatty liver. In rest parameters, including exercise and diet, the differences were not statiscally significant. Logistic regression selected metabolic syndrome and hyperinsulinemic as factors independently associated with fatty liver (OR:182% and OR:4,3% respectively).

**Table I.** Biochemical parameters.

| Parameter | No steatosis(Mean) | Yes esteatosis(Mean) | p value T-Student. |
|---|---|---|---|
| Triglycerides | 90.53 | 113.67 | 0.056 |
| HDL | 54.19 | 51.41 | 0.268 |
| LDL | 97.48 | 82.49 | 0.004 |
| Total cholesterol | 169.28 | 155.81 | 0.029 |
| GOT | 24.62 | 26.07 | 0.252 |
| GPT | 21.32 | 28.65 | 0.026 |
| GGT | 16.37 | 16.93 | 0.680 |
| Uric acid | 5.30 | 5.49 | 0.424 |
| TSH | 2.83 | 3.00 | 0.461 |

**Table II.** Group of patients with oral glucosa tolerante test.

| Parameter | No steatosis(Mean) | Yes esteatosis(Mean) | p value T-Student. |
|---|---|---|---|
| Basal glucose | 89.39 | 91.56 | 0.224 |
| Insulin | 16.50 | 23.66 | 0.033 |
| HOMA | 3.92 | 5.73 | 0.010 |
| QUICKI | 0.321654 | 0.31037 | 0.092 |

**Conclusion:** The prevalence of fatty liver is 37,9%. The metabolic syndrome and hyperinsulinemic are risk factors associated with fatty liver in children.

### 32. Profitability of liver biopsy in patients with chronic hepatitis C virus infection

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**Objectives:** 1) In all patients, clinical basal data were recorded. 2) Describe the indications for biopsy in our patients and the reasons for nontreatment after biopsy were identified the indications 3) Analyzed whether the decision to start treatment was influenced by the histological grade of the lesion 4) We also analyzed whether there is any association between histological grade and transaminase levels. **Material and methods:** We performed a descriptive retrospective study of liver biopsies performed in patients with chronic hepatitis C virus (HCV) infection from January 2002 to January 2005. **Results:** A total of 215 patients were included with chronic hepatitis C. Mean age was 42,05 years (72,6% males, 27,4% females). The indications for biopsy were transaminase levels elevated in 83,3% and transaminase levels normal in 16,2%. The percentage of patients who received nontreatment after liver biopsy was 25,1% and the causes of nontreatment were: histological minimal lesions(50%), want the patient to know the histological lesion (9,25%), the patient don't want to start the treatment (9,25%), descendents (9,25%), missing (9,25%), alcoholism (5,55%), depression (3,70%), thyroid pathology (1,85%) and treatment with phlebotomies (1,85%). The histological results were as follows: G0 (1,9%), G1 (27,6%), G2 (48,1%), G3 (21,4%) and G4 (1%); F0 (8,6%), F1 (28,1%), F2 (41%), F3 (18,1%) and F4 (4,3%). There was differences significant between transaminase levels and fibrosis stage (• 2 *vs* <2), there been fibrosis advanced (F• 2) in 41,66% of the patients with transaminase levels normal (p<0,02). **Conclusion:** The 83,3% of liver biopsies performed in patients were transaminase levels elevated Until in 25,1% of the patients nontreatment after liver biopsy; been to prevent these decision with indepent histological grade in 38,5%. The 41,66% of the patients with transaminase levels normal showed fibrosis stage ≥2.

### 33. Withdrawn

### 34. Tuberculosis post-liver transplantation associated to syndrome of inappropriate antidiuretic hormone secretion (SIADH): difficult management disease, case report.

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**Introduction:** Tuberculosis (TB) is a serious opportunistic infection in transplant patients; the incidence rate in underdeveloped countries is 0.35% to 15%. The mortality can be as high as 40%. We report a female patient with miliary tuberculosis and hyponatremia. **Case presentation:** Female patient, 45 years old, resident from Veracruz, 8 months post- OLT because Primary Biliary Cirrhosis. She was on three-drug immunosupression (Tacrolimus, Prednisone and Mycophenolate Mofetil). She presented low grade fever, dyspnea, unknown weight loss and general weakness. She was checked by a local general practitioner who prescribed one week amoxicillin. No improvement was noticed and diarrhea was added to the symptoms as well as abdominal pain. She was referred to specialized care and hospitalized. Infectious testing results came back negative, including hemoculture and acid-fast smears, as well as CMV, EBV and herpes serology. A decrease in plasma sodium level was noticed from 130 mEq/l to 117 mEq/L four days later. She was medicated with a quinolone and improved symptoms, fever resolved and she was sent home. Six weeks later the patient returned with fever, sweating, productive cough and no gastrointestinal symptoms. Plasma sodium level was 116 mEq/L and urinary sodium 117 mEq/L. Plasma sodium decreased to 106 mEq/L and she developed headache, nausea, restlessness, irritability, muscle cramps, hyporeflexia and confusion. Hyponatremia, euvolemic and hyposmolar was diagnosed (plasma osmolality 234 mmol/L, urinary osmolality 210 mmol/L). Acid-fast smears were repeated and results were positive, chest radiograph and contrast enhanced computer tomography showed pulmonary infiltration. TB treatment started with four-drug regimen (isoniazid + rifampin+ pyrazinamide + ethambutol) but hyponatremia persisted. Contrast enhanced suprarenal computer tomography was normal, plasma ADH, aldosterone and cortisol levels and urinary density were performed and SIADH was diagnosed. Mineralocorticoid treatment was started and improved all neurological symptoms. The patient is asymptomatic and monthly acid-fast smears negative while on TB treatment. **Conclusions:** TB incidence shows an increase in immunosupressed patients. TB rates in solid organ transplantation are considered 0.8%. It is known that TB can spread fast by hematological seeding through the body. Suprarenal involvement was suspected but not supported by all testing done. SIADH diagnosis was concluded based on symptoms, urinary sodium measurement and urine osmolality. We performed a fully literature search and no case study similar to this was found. We consider this the first report where post-OLT presents with military TB and SIADH. It is important to empathize that early clinical suspicion leads to an opportune diagnosis and to a successful and safe treatment with careful immunosupression monitoring.

### 35. Inhibition of HCV replication and gene expression by RNA interference

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**Background:** Hepatitis C virus (HCV) is a significant cause of morbidity and mortality, infecting over 170 million people worldwide. The best therapy available at present uses a combination of interferon-• (INF-• ) and ribavirin, but only half of the patients treated (50-55%) show a sufficient antiviral response. Small interfering RNAs (siRNA) are an efficient tool to specifically inhibit gene expression by RNA interference. RNA-directed antiviral strategies are likely to successfully block the HCV replication cycle. **Aims:** we inhibited of HCV RNA and viral proteins levels in HCV replicon expressing cells using RNA interference. **Methods:** We used the human hepatoma cell line (Huh-7) that expresses a subgenomic replicon of HCV. Cells were transfected with different concentrations of RNA interference (RNAi) (100 and 200 nM). The RNAi was directed against the NS5B region of the viral genome, because this protein is responsible of viral replication. After 2, 4 and 6 days post-transfection HCV RNA quantification and protein expression were measured by semiquantitative RT-PCR and Western blot (using anti-HCV NS5B and anti-actin antibodies). Cell viability also was quantified by Tetrazolium Salt Reduction (MTT) assay. **Results:** In transient transfection experiments using RNAi against NS5B region, we observed that the concentration of 100nM did not affected the HCV RNA levels, however, the concentration of 200nM inhibited HCV RNA levels and this effect was observed two and four days after transfection. We also monitored HCV protein expression and we observed that RNAi of 100nM and 200nM suppressed NS5B protein expression more strongly six days after transfection. **Conclusions:** Synthetic siRNA against NS5B inhibited replication and viral proteins and thereby become a powerful strategy against HCV.

### 36. Hepatitis B and C prevalence in blood donors in Veracruz, Mexico

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**Background:** Cirrhosis and other chronic liver diseases are important causes of death in Mexico. The main etiological agent related to them is Hepatitis C virus (HCV), whose prevalence has been associated with socioeconomic status and geographic situation. Most of the epidemiological studies that had been conducted in Mexico refer the prevalence in the north and center of the country, with a few evidence of the south region. The aim of the study was determinate the prevalence of Hepatitis C virus and B virus in blood donors in Veracruz, Mexico. **Methods:** A retrospective study was made in the Veracruz City's Blood transfusion state center. Serologic tests detecting Hepatitis B surface antigen (AgSHB) and HCV virus were performed. We enrolled all blood donors that presented in the period from January 1st to December 31st 2005. We obtain the follow demographic variables: sex, age, marital status, schooling and previous screening for HCV and B virus. More than three sexual partners, tattoos, IV drugs use or high risk sexual practice were considered as risk factors. A descriptive analysis was made with the SPSS/PC program 10.0 version (SPSS Inc., Chicago, IL). **Results:** A total of 8650 blood donors were tested for HCV and B virus in the Veracruz City's Blood transfusion state center. Of them, 93% were man and 7% women, with a mean age of 32.6 (9.9 DE). None of the individuals had a risk factor. We found 101 positive cases to hepatotropic viruses; the prevalence of AgSHB was 0.57%, corresponding to 5 men at 19 – 40 years. The prevalence of HCV was 1.1% (88 men and 8 women), corresponding to 96 donors at 19 – 62 years. Among the individuals with a positive test for HCV, 76% had only elementary school. From all the individuals with a positive test, only 2.97% had a previous screening for HCV and B virus. **Conclusion:** Our study was conducted among a low risk population. We found a similar prevalence to that reported in other regions of Mexico; the poor education was the only factor associated to seropositivity. It will be important to implement a prevention and health education refer to opportune diagnose, because of the low rate screening detection of HCV and B virus.

### 37. Clinical significance of elevated alanine aminotransferase in Mexico. Preliminary report

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**Background/Aim:** In the clinical setting serum aminotransferase activity is frequently used as an indicator of liver disease. In this study we analyze the prevalence and etiology of elevated alanine aminotransferase (ALT) in a Gastroenterology Clinic. Methods: We include the first ALT determination processed in 10,991 individuals, 5613 (51%) females, utilizing Vitros 250 chemistry system (Ortho-Clinical Diagnostics). Values of ALT >72 IU/L for males and > 52 IU/L for females were considered elevated. Results: ALT elevation was found in 1351 cases (12.3%), mean age 45 (range: 21-84) years, being more common in males (710, 53%, p=0.004). The etiology of ALT elevations was Viral Hepatitis in 291/1351 (21.2%) (HVA: 16%, HVB: 3% and HCV: 81%), Metabolic Syndrome and/or Obesity in 271/1351 (20%), Alcoholic Liver Disease 11/1351 (0.8%) Autoimmune and other Liver Diseases in 281/1351 (21%). Unexplained 497/1351 (37%). According to gender, a female predominance was found among VHC patients (65%, p=0.001), and a male predominance among the Metabolic Syndrome ones (70% p=0.001). **Conclusions:** Significant gender frequencies in ALT elevations related to virus (females) or metabolic syndrome (males) are recognizable. Unexplained ALT elevations are found in a high proportion of patients that can not be attributed to viral or non alcoholic fatty liver disease. This group requieres follow up and further studies to elucidate the etiology.

### 38. Prevalence of risk factors for chronic viral hepatitis among patients consulting general practitioners in Mexico.

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**Introduction:** The control of chronic viral hepatitis B and C became a public policy issue since the etiology and natural history of these viral infections were recognized and there deleterious effects on human health are being appreciated by policy makers, medical practitioners and public health specialists. **Objectives:** To conduct a study to determine the prevalence of risk factors known to be associated with chronic viral hepatitis that may increase the probability of getting the disease. **Material and methods:** Volunteers recruited through 100 General Practitioner's (primary care physician) participated in a face to face survey, a questionnaire that included 11 different questions regarding risk factors for chronic viral hepatitis applied to a total of 155,339 adults aged 18-65 years. **Results:** Overall, 37,466 (24.1%) individuals were found at risk, 3148 (2.0%) had a blood transfusion before 1992 and 3862 (2.5%) were transfused after 1992; 3818 (2.5%) reported to have been in contact with chronic viral hepatitis infected patients; 4,670 (3.0%) reported more than 10 different sexual partners; 3,592 (2.3%) suffered sexually transmitted diseases; 2756 (1.8%) consumed cocaine; 1516 used IV illegal drugs; 298 (0.2%) were on long-term kidney dialysis; 285 (0.2%) had solid organ transplant; 3699 (2.4%) reported a previous liver disease; 13,640 (8.8%) had a history of tattooing, body piercing or acupuncture treatment. **Conclusions:** There is a great potential for promonting education on viral hepatitis and risk reductions within the general practitioner's practices. The risk assessment survey is an effective tool to identify intervention programs. An effective public health approach should include investigation of risk factors, diagnosis and medical treatment of chronic viral hepatitis by the general physician. This study was supported by an unrestricted grant of Schering Plough, Mexico.

**39. Frequency of hepatitis C genotype and its response to treatment in the liver unit of University Hospital**

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**Introduction:** Hepatitis C virus (HCV) is one of the leading causes of end stage liver disease in México and around the world. Eighty percent of patients with acute hepatitis will develop chronic hepatitis. There are 6 genotypes and more than 100 subgenotypes. The aim of this study was to know the frequency of genotypes and their outcomes to antiviral treatment in the northeast of the country. **Material and methods:** This is a retrospective study in which we analyze 290 patients, who had HCV diagnosis, from the Liver Unit of University Hospital. There were included those patients who had have the HCV diagnosis by PCR quantification. Were excluded those patients who didn't have follow up and untreated patients. We excluded 193 patients because they didn't have genotype. Our analyzed variables were, age, gender, biopsy, genotype; viral load, AST and ALT who were analyzed according to the algorithm of the HCV consensus of NIH. The used treatments were, peginterferon alfa2a (PEG-IFN2a, 180ug/wk) plus ribavirin (RBV, 800-1200mg qd), peginterferon alfa-2b (PEG-IFN2b, 1.5ug/kg/wk) plus RBV, interferon alfa2a (IFN2alfa, 3MU/tiw) plus RBV, natural alfa interferon (MIFN, 3MU/tiw) plus RBV, MIFN plus RBV plus timosyn (Tim, 1.6 ug/biw). monotherapy PEG-IFN2a, PEG-IFN2b and IFN2alfa. Patients with Genotype 1 (G1) were treated for 48 weeks and patients with non genotype 1 (nonG1) for 24 and 48 weeks. (eleven patients participated in controlled protocols of antiviral treatment). **Results:** Ninety seven patients were included, the characteristics of the global group were, 39 (40%) men and 58 (60%) women, mean age 45 (4-69). The genotype most frequently found was G1, 70 (72%) and subtype 1a 35 (36%). Genotype 2 was found in 12 (12%), genotype 3 in 12 (12%). Out of 43 treated patients, 31 (72%) were G1 and 12 (27%) nonG1. In the treatment group 20/43 patients had cirrhosis, 75% (15/20) was G1 and 25% was nonG1. The outcome by genotype, for G1 there was achieved an end of treatment response (ETR) in 16/31 (51%), the sustained virological response (SVR) in 14/31 (45%) and non response (NR) in 14/31 (45%).Two out of sixteen patients who had ETR, presented relapse. One (3%) patient with G1 stopped treatment because of ascitis and neutropenia, although she had virological response on week 24. For nonG1 8/12 (66%) had SVR and 4/12 (33%) NR. Twenty patients out of 31 G1 were treated with PEGIFN+RBV, 3 with PEGIFN, 12/20 achieved an early virological response (EVR), 13/23 (56%) ETR, 11/23 (45%) SVR, and 1 did not finish treatment. The mayority of patients who had EVR had SVR (83%). In 3 patients who didn't have evaluated ETR, 2 had SVR. Eight patients were treated with non pegylated interferon (nonPEG-IFN), 7 with IFN+RBV and 1 with IFN+RBV+Tim. Three out of eight (37%) had SVR and 5/8 NR. In nonG1, five received PEGIFN+RBV and 2 PEGIFN. Five out of 6 had ETR and Five/7 (71%) patients had SVR. In nonG1 who received nonPEG-IFN were 5/12(41%) patients, 2 received IFN, 2 IFN+RBV and 1 MIFN+RBV. Three out of 5 (60%) patients had SVR and 2/5(40%) NR. **Conclusions:** Genotype 1 and subtypes 1b and 1a were the most frequently . The SVR on G1 were superior in patients who received pegylated interferons, but not as high as previously reported on the literature. The majority of patients who had EVR had SVR. The sample should be amplified to confirm the results.

**40. Treatment with alpha natural interferon and ribavirin in patients with chronic hepatitis C**

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**Introduction:** There is an increasing population of patients with chronic hepatitis C (CHC) who are non-responders (NR) to antiviral treatment, specially those with genotype 1 (G1). The aim of this study was to treat in a pilot study mostly previously CHC NR patients with alpha natural interferon (Multiferon) plus ribavirin (RBV). **Material and methods:** Seven patients (4 female, 3 males) with a mean age of 45.4 years (31-56) with CHC: 5 with cirrhosis 2 with chronic hepatitis received Multiferon 6 MU/day s.c. monday to friday for 4 weeks, followed by 3 MU/3xw for 44 weeks (total 48 wk). Five patients previously received Peginterferon alpha 2a or 2b (PEG-IFN). One patient received both PEG-IFN 2a and 2b for 48 weeks each being NR. Four patients did not showed early virological response (EVR) at 12 wk on PEG-IFN alpha 2a or 2b, therefore treatment was stopped. All patients were G1: 3:1a; 1:1a/Lb, 2:1b, in one patients genotype 1 could not be subclassified. **Results:** One patient was NR to Multiferon, she was previously NR to PEG-IFN alpha 2a and 2b. Three patients showed EVR to Multiferon and RBV (basal viral load-BVL- 1,590,000:33,400 and 1,002,950 IU/mL respectively; all of them <600IU/mL at wk12) one or these patients exhibited a breakthrough during treatment with PEG-IFN alpha 2a and the other 2 patients had not shown EVR to previous treatment. One female patient on liver transplant waiting list was started on low dose Multiferon (1 MU/3xw) and 800 mg RBV, due to thrombocytophenia treatment was stopped at wk 23 for 11 weeks, it was then restarted and she completed 34 wk of treatment (BVL:110,000 IU/mL at wk 12:29,000 IU/mL at wk 43: cualitative HCV-PCR:Negative). Two patients have received antiviral treatment for less than 12 weeks (1 naive; 1 previously NR at wk 24 with PEG-IFN alpha 2a). Two out of seven patients have completed 48 wk of treatment one was NR and one had EVR and viral load at wk 48 is pending. Adverse effects were very similar to previous PEG-IFN treatments. **Conclusions:** Although this is a small pilot group it is important to note that in previously NR patients 75% (3/4) exhibited an EVR at wk 12 with multiferon and RBV so we think it is worthwhile to increase experience treating with alpha natural IFN and RBV in these patients.

**41. Utility of terlipresine and albumin in a group of patients with hepatorenal syndrome**

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**Introduction:** The Hepatorenal Syndrome (HRS) is a complication of stage liver disease. There are two forms of presentation: Type 1 is characterized by the onset of renal failure with a duration of two weeks and the survival is less than 10%. Esplacnic dilation leads to kidney's vasoconstriction; the administration of the esplacnic vasoconstrictor terlipresine could improve the kidney function in these patients. **Objective:** To evaluate the effectiveness of the infusion of terlipresine and albumin to revert the HRS, the tolerability and side effects. **Materials ands methods:** Eight patients admitted with the were diagnosis of acute kidney failure and liver cirrhosis. Patients were initially managed with albumin (1-1.5 gr/kg), furosemide in infusion or 40 mg (tid) or dopamine to renal perfusion dosage and IV liquids. HRS was diagnosed when there was no improvement after 48 hours according the criteria of the International Ascites Club and treatment was started with terlipresine in increase doses of .5 to 2 mg every 4 hours IV (with an interval of 24 to 72 hours for the increase if the creatinine did not drop • 1 mg/dL). Analysis of age, gender, etiology, presence of adverse effects to terlipresine was done. Child-Pugh and MELD scales and levels of serum creatinine; were evaluate at beginning and end of treatment. Successful treatment was defined when an improvement in renal function with decrease in serum creatinine • 1.5 mg/dL or 20% decrease of basal creatinine. **Results:** Eight patients with renal failure 5 with HRS all were men, with and average age 55 (range 41-66). Alcoholic etiology in 3, 1 with NASH, hepatitis C virus in 1. At admission MELD was 34.6 ± 7.4 and Child-Pugh of 10.8± 3.8 and at the end of treatment MELD 32.6 ± 7.9, and Child-Pugh 10.8 ± 4.9 points (Table I), Days in hospital 21 (2-38). Accumulated terlipresine dosage was 41 mg ± 35.10 with 9.4 ± 7.5 days of infusion. Creatinine at admission was 4.4 mg/dL ± 0.84 with 3.1 ± 1.4 mg/dL at discharge. A decrease in Child-Pugh, MELD and serum creatinine was evident in patients who responded to treatment (Table I). In 3 patients the basal serum creatinine drop 34, 48.6 y 69.75% respectively. Side effects

were pain and abdominal distention in 2 patients, one with an accumulate doses 20 mg at 4 day of infusion and another with 26.5 mg at 10 day. (The latter had a successful treatment); tachycardia in 1 patient with and accumulate dosage of 15 mg at second day, terlipresine was stopped. Only one patient died of HRS (20%) Another patient died of sepsis and liver failure two weeks after the HRS reversed. One patient was transplanted, another one is alive and without renal dysfunction and the last one has no follow up after he was discharged from hospital. **Conclusions:** Treatment with terlipresine and albumin reversed HRS in 3 of 5 patients (60%), with side effects in 60% of cases that required stopping treatment. The death for HRS occurred in 1 of 5 patients (20%) as opposed to 90% reported in patients with HRS and conventional treatment. In one patient it was a bridge to liver transplantation. Further prospective studies are needed, with a bigger number of patients to value the efficacy and incidence of complication of terlipresine in the treatment of HRS.

**Table I.** Child. Pugh, MELD and serum creatinine

| Success to treatment (3) | Child-Pugh | Meld | Serum creatinine |
|---|---|---|---|
| Pre-treatment | 13.3 ± 1.24 | 38 ± 3.4 | 4.4 ± .79 mg/dL |
| Post-treatment | 9 ± 3.2 | 33.3 ± 9.07 | 2.1 ± .68 mg/dL |
| Without success to treatment (2) | | | |
| Pre-treatment | 7 ± 2.8 9 | 29.6 ± 10.6 | 4.5 ± 1.27 mg/dL |
| Post-treatment | 9 ± 5.6 | 31.5 ± 9.9 | 4.5 ± .57 mg/dL |

**42. Evaluation of the antioxidative and hepatoprotective effect of Herbs from North-Eastern of region México**

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Several studies have examined the effects of plants used traditionally by herbalist to treat diseases of the liver. The aim was to evaluate the antioxidative and hepatoprotective effects of herbs from north-eastern region of Mexico. **Materials and methods:** Ethanoholic extracts from different parts of *Centauria americana (1), Juglans mollis (2), Turnera diffusa (3), and Florencia cernua (4),* were studied for possible antioxidative and hepatoprotective effects. Antioxidative effects were measured spectrophotometrically in terms of ascorbate equivalents by the absorbance reduction of 2,2'difenyl-1-picryhydrazyl radicals (DPPH). The hepatoprotective effect was evaluated through the carbon tetrachloride ($CCl_4$) toxic effect over the Huh7 cellular line, previously treated with different doses of extract (10,100, 1000, and 5,000 • g/mL) and measured through the of alanin aminotransferase (ALT) and aspartate aminotansferase (AST) liberation in the supernatent of cellular culture. **Results:** All the extracts were compared vs. a toxicity control group which consisted of Huh7 cells treated with $CCl_4$ (20mM). All the extracts showed an antioxidative effect by the DPPH method: (1) 45.6 ± 25 ascorbate equivalents, (2) 55.4 ± 7.1 ascorbate equivalents, (3) 57.5 ± 7.1 ascorbate equivalents, (4) 57.0 ± 5.7 ascorbate equivalents. An hepatoprotective effect was shown at doses of 10 and 100 mg/mL by *Turnera diffusa, Juglans mollis* and *Florencia cernua* when the Huh7 cells were treated with $CCl_4$ (20 mM) while the same effect was observed in the four studied doses (10-5,000 • g/mL) for the plant *Centauria americana.* The alterations induced by $CCl_4$ were diminished as it was observed by ALT and AST reduction of levels in 86/78%, 84/79%, 98/92% and 90/82% for the extracts of *Centauria americana* at doses of 10, 100, 1000 and 5000 • g/mL, respectively. The levels of ALT and AST were diminished in 86/73% and 84/73% for the extracts of *Juglans mollis* at doses of 10 and 100 • g/mL. The levels of AST were only diminished in 55% and 42% for the extracts of *Turnera diffusa* at doses of 10 and 100 • g/mL. The levels of ALT and AST were diminished in 84/75% and 82/55% by the extracts of *Florencia cernua* at doses of 10 and 100 • g/mL. **Conclusions:** The hepatoprotective effect of the herbal extracts on the toxic effect by $CCl_4$ over the Huh7 cellular line can be due to the antioxidative properties that were presented by the extracts.

**43. Withdrawn**

**44. Risk factors and prevalence of hepatitis virus B and C serum markers among nurses at a tertiary-care hospital in Mexico City, Mexico: a descriptive study.**

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Background & aim: Alcohol consumption and viral infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) are the first causes of chronic hepatopathy in Mexico. Medical personnel are at high risk of developing HBV and HCV infection because both viruses are transmitted parenteraly. The aim of this study was to determine the prevalence of HCV and HBV infection as well as risk factors in nurses working at Medica Sur Clinic and Foundation. **Methods:** The complete nurse staff personal from our hospital was included; a questionnaire of risk factors for HCV and HBV infection was assessed. HBV and HCV infection (anti-HCV anti-HBc, and HBsAg) was determined to all of them. In anti-HCV positive persons HCV genotype and viral load was assessed. **Results:** Three hundred seventy six nurses where studied, Anti-HBc was positive in 1.6% of all participants, none were positive for HBsAg. 0.8% of all studied population was positive for anti-HCV. Major risk factors for HBV infection where tattooing and having more than 4 sexual partners previously, and for HCV infection transfusions before 1992 and age. Only one person was anti-HCV positive with a viral charge of 5 X $10^6$ copies, genotype 2b. **Conclusions:** HCV seropositivity in people with high risk was lower than general population. None was positive for HBV infection.

**45. Liver biopsy at Medica Sur. An 8-year experience**

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**Background and aim:** Currently, an increasing incidence of liver disease has been observed. Chronic liver disease and cirrhosis represent the fourth leading cause of death in Mexico; therefore, early diagnosis are of vital importance. Liver biopsy is a useful tool for the diagnosis and grading of cronic liver disease in both the asymptomatic patients with abnormal liver enzymes and the chronically ill. The aim of this study is to report the experience with this method in our institution. **Material and methods:** A descriptive retrospective study of the liver biopsy studied in our Pathology Department from january 1999 to june 2006 was performed. Material from all biopsias was available for review. We analyze the age and sex of the patient, type of biopsy and hystopathological diagnosis. **Results:** A total of 652 liver biopsies were analyzed, from which 331 belong to males (50.7%) and 321 to females (49.3%). Eighty-seven biopsias are performed annually in our hospital, 82.66% are performed in patients in age range of 18 to 65 years. Obtaining method was available in 96.8%; 406 were percutaneos biopsies (62.2%), 183 surgical biopsies (28%), 22 fine-needle aspiration biopsies (3.3%) and 8 transjugular biopsies (1.2%). The main diagnosis were: chronic active hepatitis in 170 cases (26%), from which 29.4% were hystologically identified as chronic viral hepatitis C; nonalcoholic fatty liver disease in 110 cases (16.8%), 71 cases with steatosis (64.5%) and 39 with steatohepatitis (35.4%); metastases in 83 cases (12.7%); liver cirrhosis in 71 cases (10.8%), from which 12 cases were due to hepatitis C virus (16.9%); and cholestasis alone in 29 cases (4.4%). **Conclusions:** The main histological diagnosis was chronic active hepatitis, with hepatitis C virus as the main etiological factor. Most

biopsies were performed in patients in the productive age range. The annual number of biopsies was constant, being the percutaneous technique the more frequent.

**46. Gallstone and cardiovascular disease: an association mechanism.**

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**Introduction:** Gallstone disease (GD) is a very frequent disease in Mexico. GD is associated to obesity, metabolic syndrome and cardiovascular disease, conditions that share insulin resistance, metabolic and hormonal alterations that have low levels of Insulin-like growth factor-1 (IGF-1). Interestingly, the thickness of the intima-media complex in the common carotid artery had been associated to an increment in the incidence of coronary heart disease (CHD). **Aim:** The objective of this study was to investigate the association between the presence of GD, the thickness of the carotid intima-media complex and the levels of IGF-1. **Materials and methods:** We carried out a cases and controls study in the Integral Diagnostic and Treatment Center at Medica Sur Clinic and Foundation. Cases were defined by subjects with GD by ultrasound (US), and controls by patients without evidence of GD by US. Anthropometric, biochemical and hormonal (IGF-1 and insulin) variables were measured. The diagnosis of metabolic syndrome was determined according to the ATP III criteria. The thickness of both right and left carotid intima-media complex was made by high-resolution B Mode ultrasonography. Odds ratio was calculated for the variables of the cases according to the levels of IGF-1 and thickness of the carotid intima-media complex, considering a difference statistically significant for values of $p < 0.05$. **Results:** 76 patients were included, 25 cases and 51 controls. Statistically significant difference was observed for BMI (28.1 ± 3.97, $p < 0.05$), waist perimeter (106.5 ± 0.11, $p < 0.05$), body fat percentage (32.7 ± 4.9, $p < 0.05$), HOMA index > 2.5 (2.5 ± 2.7, $p < 0.05$) as well as for thickness of the intima-media complex (0.58 ± 0.20 $p < 0.05$). No statistically significant difference was observed for the serum levels of IGF-1. **Conclusions:** Results from this study demonstrate an association statistically significant between GD and carotid atherosclerosis. This association could lead to an early identification of subjects with high coronary risk and for the prevention of the digestive and cardiovascular morbidity and mortality.

**47. Withdrawn**

**48. Decrease natural killer cell activity in patients with chronic hepatitis C infection**

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**Background/aim:** Natural killer cells (NK) constitute the first line of immunological defense against pathogens and play a fundamental role in the recruitment of specific T cells against virus infections because its capacity to directly attack infected cells through cytolytic mechanisms, and indirectly by the secretion of cytokines that induce an antiviral environment. Therefore, we decided to evaluate *ex vivo* NK cells activity of patients with chronic hepatitis C infection (CHC) and healthy volunteers without infection (HV) through the secretion of interferon-• (IFN-•), Th1 (TNF-• ) and Th2 (IL-4) cytokines, as well as their perforin expression. **Material and methods:** Seventeen patients with CHC without previous antiviral treatment and 17 HV were evaluated. CHC patients were HIV-and HBsAg-negatives and all were positive for anti-HCV and HCV-RNA. NK cells were isolated from mononuclear cells of peripheral blood through magnetic negative selection and the purity of NK cells by flow cytometry analysis was 89.6 ± 5.8%. NK cells were cultivated without stimulus and under different stimulation protocols with: lipopolysaccharide (LPS 1 µg/mL), interleukin-2 (IL-2 1000 U/mL), interleukin-12 (IL-2 1000 U/mL), and its combinations (LPS+IL-2 and LPS+IL-12) in RPMI-1640 medium at 37° C with 5% of $CO_2$ and saturation humidity. After 72 h, cellular suspension was collected for determination of IFN-•, TNF-• and IL-4 by ELISA and cells were marked with anti-perforin human conjugated with FITC for flow cytometry analysis. **Results:** IFN-• secretion was significantly lower CHC patient cells compared to HV cells in the following conditions: without stimulus (1.7 ± 2.7 pg/mL *vs* 19.7 ± 32.6 pg/mL, $P$=0.01), with LPS (5.6 ± 10.1 pg/mL *vs* 42.9 ± 39.6 pg/mL, $P$<0.001), LPS+IL-2 (10.6 ± 18.6 pg/ml *vs* 43.5 ± 47.6 pg/mL, $P$=0.03) and LPS+IL-12 (21.3 ± 39.1 pg/mL *vs* 55.2 ± 138.4 pg/mL, $P$=0.05). Although, secretion lower under the stimulation with IL-2 (8.1 ± 9.2 pg/mL *vs* 31.9 ± 39.6 pg/mL, $P$=0.59) and IL-12 (5.3 ± 5.7 pg/mL *vs* 40.3 ± 111.9 pg/mL, $P$=0.41) these differences did not reach statistical significance. Perforin expression of NK cells of CHC patients was significantly lower in all conditions, including without stimulus (6.3 ± 7.4% *vs* 11.3 ± 4.1%, $P$=0.02), with LPS (7.5 ± 2.2% *vs* 28.2 ± 16.3%, $P$<0.001), IL-2 (6.8 ± 4.7% *vs* 26.7 ± 16.4%, $P$<0.001), IL-12 (6.0 ± 4.2% *vs* 30.1 ± 14.6%, $P$<0.001) and combination of LPS+IL-2 (8.5 ± 6.8% *vs* 27.9 ± 17.7%, $P$<0.001) and LPS+IL-12 (5.7 ± 5.9% *vs* 29.7 ± 17.4%, $P$<0.001), compared to HV cells. We did not find any significant difference in the secretion of TNF-• and IL-4 between both groups. **Conclusions:** The *ex vivo* activity of NK cells of CHC patients is diminished in basal state and after stimulation with bacterial products and differentiation cytokines. These findings suggest that chronic HCV infection deteriorate NK cells function, which could contribute to the alteration of innate immune response and favor the chronicity of the infection.