1325 **SOMATOSENSORY EVOKED POTENTIALS (SSEPs) IN PATIENTS (PTS) WITH ACUTE HEPATIC FAILURE (AHF) : A REAPPRAISAL.**

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Recording of the median nerve SSEPs is a non invasive method for monitoring brain function. In one study of pts with AHF, the absence of the N70 wave, a delayed cortical potential, was found to correlate with death or emergency liver transplantation (ELT). The aims of the present study were to assess the prognostic values of the N20 and N70 waves latencies of the median nerve SSEPs in pts with AHF.

Eighty bilateral median nerve SSEPs were recorded in 39 pts (20 men; 16-74 yrs) when all of them had prothrombin ratio < 50% and all of them, but 5, clinical encephalopathy. No sedative drug was given. The cause of AHF was viral hepatitis (21 pts), drug-induced hepatitis (9), autoimmune hepatitis (4), Reye's syndrome (2) and miscellaneous (3). According to their outcome, the patients were alloted in 3 groups: I (spontaneous recovery, 12 pts), II (ELT, 13 pts) and III (death without ELT, 14 pts). Among these 3 groups, SSEPs waves were evaluated on the initial record (39 pts; subgroups Ia, IIa and IIIa), on the first record when the Glasgow coma score (GCS) was < 12 (27 pts; subgroups Ib, IIb and IIIb) and on the 2nd record obtained within 24 to 60 hours after the initial one (15 pts; subgroups Ic and [IIc+IIIc]). In each subgroup, the mean (±SD) latency (ms) of the N20 and N70 waves was calculated. Values obtained in normal subjects were used as controls.

With regard to the N20 wave latency, mean values (normal in subgroups Ia, IIa, Ib, Ic) were protracted ($p<0.0001$) in subgroups IIb, IIIa, IIIb and [IIc+IIIc], but overlap of individual values between the subgroups was frequent. The N70 wave mean latency was protracted ($p<0.0001$) in the 8 subgroups, but did not differ significantly between subgroups Ia, IIa and IIIa, between subgroups Ib, IIb and IIIb, and between subgroups Ic and [IIc+IIIc]. Finally, the N70 wave was lacking on at least one SSEPs record in 5 pts with the GCS < 12 : among them, 3 died and 2 were transplanted.

We conclude that, in pts with AHF and GCS < 12, (a) protracted N20 wave latency is often associated with the absence of survival without ELT, but has a limited individual prognostic value; (b) protracted N70 wave latency has no prognostic value, but the absence of this wave is associated with a poor outcome. Thus, median nerve SSEPs afford few additional information to improve early prognostic evaluation in pts with AHF.

1326 Levels of Effector and Immunoregulatory Cytokines in Acute Liver Failure

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We have recently reported that levels of proinflammatory cytokines, interleukin 6 (IL-6) and tumour necrosis factor-α (TNF-α) are significantly higher in patients with acute liver failure (ALF) who died or required orthotopic liver transplantation (OLT) than in subjects who survived without OLT (*J Hepatol 1998:28;53)*. The aim of the present study was to investigate the levels of the cytopathic cytokine interferon-γ (IFN-γ) and of the immunoregulatory cytokines IL-4, IL-10 and transforming growth factor-β1 (TGF-β1) in ALF. We measured cytokine serum levels in 55 children (34 male, median age 2 years, range 1 day-15 years) with ALF of various etiologies using sensitive enzyme linked immunoabsorbent assays (ELISAs). Fourteen children survived and 41 died or required liver transplantation. Duration of symptoms before referral varied from 2 days to 3 weeks (median of 1 week). Thirty nine healthy children (20 male, median age 2 yrs, range 2 days-13 yrs) were studied as controls. Levels of IFN-γ, TGF-β1, IL-4 and IL-10 were increased significantly in patients with ALF when compared with healthy controls ($p=0.005$ for all). Levels of IFN-γ and TGF-β1 were significantly higher in ALF patients who died or required OLT than in subjects who survived without OLT ($p=0.02$ and 0.006 respectively) while levels of IL-4 and IL-10 did not differ significantly between the two groups. The increased cytokine levels in patients as compared to healthy controls may be due to a decreased hepatic clearance. The higher levels of IFN-γ and TGF-β1 in the most severly affected patients may reflect a pathogenic role.

1327 CEREBRAL EDEMA INDUCED BY FULMINANT HEPATIC FAILURE: GENE EXPRESSION ANALYSIS.

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Brain edema, leading to intracranial hypertension and brain herniation, is a leading cause of death in fulminant hepatic failure (FHF), however, the mechanism of brain edema remains poorly understood. The aim of this study was to identify genes which are involved in the development of brain edema using a differential display of gene expression technique. Methods. FHF was induced in male Sprague-Dawley rats (200-250 g) by removal of the anterior liver lobes and ligation of the common pedicle to the right liver lobes. The omental lobes were left intact. Rats were euthanized at 2, 6 and 12 hr post-FHF induction and at Stage IV hepatic encephalopathy (HE) (30-36 hr post-FHF induction) ($n = 6$ per group). The percentage of brain water was calculated by a gravimetric technique, and changes in gene expression in the cortex between control, sham-operated, and FHF-induced edema groups were analyzed by differential display reverse transcription PCR (DDRT-PCR) and confirmed by Northern blot analysis. Results. Cerebral edema was confirmed in rats in Stage IV HE. The percentage of brain water in the cortex from rats in this group was $81.5 \pm 0.41\%$ relative to $79.5 \pm 0.1\%$ ($p<0.01$) in control cortex. Cerebral edema was not detected in the brains of rats measured at the earlier time points post-FHF induction. Using the DDRT-PCR technique, we identified approximately 100 cDNAs which are differentially expressed in the cortex of rats with FHF-induced edema. Expression of the astrocyte-specific glutamate transporter (GLT-1), the GluR2 subunit of the AMPA/glutamate receptor gene, the carbonic anhydrase II gene, and the transcription factor, NFkB, gene were down-regulated between 6 and 12 hours after FHF induction. The expression of these genes remained down-regulated through Stage IV HE. Expression of the genes for Kid-1, a zinc finger protein and alpha II spectrin was also altered in this model of FHF-induced edema. Conclusion. The decrease in mRNA levels of GLT-1, GluR2 and NFkB found in this study support the concept that glutamate plays a role in the development of FHF-induced edema and/or associated HE. Identification and characterization of the novel genes differentially expressed in FHF may provide additional insight to the basic mechanism of brain edema. This work was supported by a Cedars-Sinai Research Institute Award.

1328 **ACUTE LIVER FAILURE: MORPHOLOGICAL PATTERNS AND ETIOLOGICAL ASPECTS IN AMAZON BASIN :**

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Aim: To delineate the characteristic histopathological patterns and etiology of liver necrosis in Fulminant Hepatitis, (FH), a retrospective study was done in Amazon Basin (Brazil). **Patients and Methods**: From 1977 to 1997, fulminant hepatitis was diagnosed in 116 inpatients, at the Instituto de Medicina Tropical do Amazonas (Brazil), and categorized into type A, B, C, D, non-ABC, and Yellow Fever hepatites according to the serologic markers or the results of polymerase chain reaction assay . All cases were confirmed by histopathological examination. **Results**: Histopathological post-mortem examination of 116 patients, 84 (72,41%) males, prevalent age between 11 - 25 years , 34 (27,59) females. Serum samples from 61 patients and the histopatological aspects was diagnosed in 6 cases HAV, 9 cases of HBV, 5 cases of coinfeccion HBV+ HDV, 2 cases of HAV+HBV, 1 case of HCV, 1 case of HBV+HCV, 22 cases of Yellow fever. In 4 cases no specific agent could be identified, although histopathological feature seemed to be toxic hepatites. All the others cases were superinfection HDV. The morphological patterns found showed in 39 (33,6%) cases massive necrosis, 22 (19%) cases with midzonal necrosis, 52 cases (44,8%) with confluent and lytic necrosis, 03 (2,3%) cases with multifocal necrosis. A specific picture of microvesicular steatosis (morula-like cells), with different intensity, was presented in 85% of the cases, independent of the etiological factor. **Conclusions**: This results demonstrated that among 116 cases of FH, the Yellow fever virus was the most frequent etiological agent, followed by the Delta virus. A peculiar histopatological pattern found in this region, in 41% of FH known as Labrea Hepatites, is a form of confluent and lytic necrosis with microvacuolar steatosis which is common to differents hepatotropic virus.