92 patients from 17 to 88 with chronic persistent hepatitis (CPH), chronic active hepatitis (CAH), cirrhosis (C), and "reactive" hepatitis (RH) were studied. Levels of PGE, its synthesis in the microsomal fractions and the liver homogenates, along with PGE2 degradation rate in the hepatic tissue were tested. PGE levels in the liver specimen from patients with CAH, CPH and RH did not differ significantly. The patients with active C had significantly lower PGE levels than those having benign chronic hepatitis (CH). The microsomal synthesis of PGE in the patients with CPH, CAH, and C was considerably higher than in the RH cases, while the tissue homogenates from the patients with HC synthesized decreased amounts of PGE. In vitro hepatic degradation level of PGE2 did not differ in the CH patients, and was sharply increased in the RH patients (in comparison to CPH and RH). PGE levels and its synthesis by the microsomal fractions and the tissue homogenates were the lowest in the patients with B-virus CH, while PGE2 in vitro degradation rate in those patients was the highest (in the presence of viral replication, confirmed by HBsAg and DNA-polymerase).

Relative to baseline, PGE formation in the tissue homogenates of patients with C, along with the increase in its microsomal synthesis, characterizes the enhanced PGs incorporation in membrane phospholipids. Low levels of PGE in the hepatic tissue of active C patients are probably due to high rates of its degradation. The factors, which accompany B-virus hepatitis reproduction in liver tissue, can notably impact PGE metabolism, resulting in its lower levels and altering cytoprotection.

1028 Effects of the Japanese Herbal Medicine "Inchinko-To" (TJ-135) on In Vitro IFN-γ Production of Peripheral Blood Mononuclear Cells

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Primary biliary cirrhosis (PBC) is an intractable autoimmune disease. There are no effective remedies for a gradually increasing jaundice in the advanced stage. The Japanese herbal medicine "Inchinko-to" (TJ-135, Tsumura, Tokyo) is often administered to PBC patients and its diminishing effect on jaundice has been reported. However, the immunological mode of action of this drug has not been investigated. We examined the effects of TJ-135 on in vitro production of interferon (IFN)-γ which is considered to be an important factor in the etiology of autoimmune diseases.

To PBMC collected from 12 volunteers, either one of the stimulants or a stimulant together with TJ-135 (final concentration: 6.3, 12.5, 50.0 or 200 μg/ml) or a control drug was added and cultured for 4 days. IFN-γ levels in the supernatant were measured by ELISA. The control drugs were dexamethasone, OK-432, or another herbal medicine "Sho-saiko-to" (TJ-9) which possesses immune regulatory effects. The ratio of production level "when TJ-135, or a control drug, was added to the culture" to "when only a stimulant was added" was obtained as the production index (PI) and expressed in terms of percent.

Average production level of IFN-γ induced by PWM was 1,600 IU/ml. With TJ-135, its PI decreased to 86 ~ 33% as the drug concentration increased (p < 0.01). PIs in the control culture were 63% with the steroid, 175 with OK-432, and 64 with TJ-9. The average level with rL-2 was 450 IU/ml. With TJ-135, PIs decreased to 80 ~ 42%. PIs were 66% with the steroid, 498 with OK-432, and 97 with TJ-9. The cultures using PHA-L showed similar results.

The results showed that TJ-135 possesses similar suppressive effects on in vitro IFN-γ production of PBMC as a steroid. We reported in 1992 that PBMC patients are in a condition of IFN-γ overproduction. TJ-135 could favorably reduce the abnormalities.

1029 Interferon Therapy in Patients with Chronic Hepatitis C

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Background: The clinical course of chronic hepatitis C in patients with primary hypogammaglobulinemia seems to be severe. The effect of interferon treatment in these patients is unknown.

Patients and methods: In 10 C HCV-positive patients with primary hypogammaglobulinemia interferon therapy was given due to sustained increase in liver transaminases and histological changes compatible with chronic liver disease. HCV RNA was assayed with PCR at 0, 9, 12 and 15 months. Genotyping was performed according to a modified Okamoto method. The dose of recombinant alpha interferon 2b (Intron-a, Schering Plough) was 3 MIU 3/7 days for 12 months. Most patients have been followed for >12 months after cessation of therapy.

Results: Four patients had a complete biochemical response, five had a partial response (at least 50% while there was one non-responders. Only one patient had a sustained biochemical response, all other responders relapsed within 3 months after cessation of therapy.

Improved histological findings were seen in 4/5 patients where liver biopsies prior to and following IFN therapy were available. In two patients with improved liver function during IFN therapy liver biopsies have 2~3 years later demonstrated severe progression.

Patients with only one detectable HCV genotype (genotype V, n = 4) all had a complete biochemical response while in those with double or triple infections (genotypes V, I and III) only partial or no response was seen. None of the patients became HCV RNA negative at any time-point of the study.

Conclusion: IFN therapy in patients with primary hypogammaglobulinemia seems to be associated with a relatively high biochemical response rate. Both biochemical and histological improvement, is, however, only short-lasting. None of the patients cleared their HCV RNA during treatment, in spite of normalization of liver enzymes.

1029 Long-term Response After Interferon Withdrawal in Patients with Chronic Hepatitis C

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The aim of this study was to establish the rate of sustained response to alpha-interferon therapy in patients with chronic hepatitis C and the possible presence of predictive factors of response. 81 patients, 48 males, mean age 47 ± 11, with chronic hepatitis C from 6 ± 1 years diagnosed by serological, clinical and histological data, responders to previous interferon therapy, were included in the study and followed up for at least 12 months after interferon withdrawal during which no therapy was accomplished. We considered as responders the patients who showed a complete normalization of liver enzymes after interferon therapy at a dosage of 3 MU t.i.w. for (6-120 patients) or 12 (41 cases) months. Patients were controlled every 3 months and a statistical analysis was made at the end of the study.

Patients with persistent normalization of liver enzymes (long-term responders) were 30/81 (37%) while the remaining 51/81 (63%) showed a relapse. We did not find any predictive factor of response since no significant difference was noted as to age, sex, duration of the disease, duration of the therapy and pre-treatment liver enzymes between long-term responders and relapsers. Moreover from our data we showed that 4% of relapses arise within 6 months from interferon withdrawal, 11.7% between 6 and 12 months and 9.8% after 12 months from interferon stopping.

In conclusion we can say that the rate of sustained response after at least 12 months from interferon withdrawal is satisfactory (37% of responders) but it is necessary to follow up long-term responders for a longer period as relapses can arise also 1 year or more after the end of interferon treatment.
1030 Long-Term Follow Up of Sustained Responders to Alpha Interferon in C-Virus Chronic Hepatitis


The late outcome of C-virus chronic active hepatitis (HCV-CAH) in sustained responders to interferon treatment is not completely known.

184 patients with HCV-CAH (88 with Child A cirrhosis) were treated with alpha interferon 3 or 6 MU iiw for at least 6 months between 1989-1992. A complete response (normalization of ALT during treatment) was obtained in 57% of the subjects. In this group 32 patients were identified as sustained responders (normal ALT at 6 months after treatment withdrawal) corresponding to 17.4% of the total subjects (11.3% of the cirrhotic group and 23% of the CAH group). Monthly laboratory tests showed normal ALT levels without relapses in all the sustained responders during the successive follow up of 15-60 months. No patient showed appearance of autoimmune antibodies. The liver biopsy repeated in two subjects 4 years after treatment, showed inactive cirrhosis in one whose initial diagnosis was severe CAH and normalization of the liver histology in the other one with an initial diagnosis of mild CAH. The preliminary data from the RibA III test and PCR determination of HCV-RNA show that the anti HCV test remains positive in all cases, while viral replication persists in some cases even when liver histology appears normal.

In conclusion these data show that patients with normal ALT levels 6 months after treatment withdrawal may be considered clinically cured, but the persistence of virus replication in some of these requires continuous follow up.

1031 Household Transmission of Hepatitis C Virus (HCV)

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Introduction At present about 500 million people are thought to be, or have been infected with HCV and most of them have never been exposed to blood products and are not drug addicts. In these cases an apparent parental transmission of the virus should probably be considered as shown by retroviral cases where the rate of HCV seropositivity seems to be higher in household contacts (particularly in sexual partners) of HCV carriers than in general population (i.e. 1.51% among blood donors in Southern Italy). However a recent study provides no evidence for sexual transmission of HCV.

Aim To evaluate the intrafamilial diffusion of HCV in close contacts of patients with histologically proven chronic hepatitis C (anti-HCV pos.ve index cases).

Methods 75 contacts of 23 anti-HCV pos.ve index cases and, as a control group, 71 contacts of 21 anti-HCV neg.ve index cases without liver disease were studied. As a whole 44 were spouses, 99 were siblings, 2 were parents and 1 was a cohabitant. Each family consisted of 4-6 members. All subjects were screened once for anti-HCV by two ELISA II assays and, in case of a positive result, by RIBA II (ORTHO), for HBSAg (ELISA) and for HDAg.

Results Anti-HCV antibodies were present in 4/75 (5.3%) contacts of anti-HCV pos.ve index cases: 2 were spouses, 1 was a parent and 1 was a sibling. All of them had ALT increased values. HBSAg positivity was detected in 2 siblings. 2/71 (2.8%) contacts of anti-HCV neg.ve index cases resulted anti-HCV pos.ve (a parent and a sibling) and showed slightly high levels of ALT.

No HBSAg was found in this group.

The Odds Ratio for contacts of anti-HCV pos.ve index cases was 1.93 (95% C.I. = 0.34-10.96).

Conclusions (1) As the Odds Ratio results no significant (power of 21%), the importance of intrafamilial spreading of HCV should be ascertained in a large case-control study: so also the role of HCV sexual transmission will be evident if a high degree of viral homology among HCV genotypes is found in HCV infected couples; (2) HBSAg was detected only in 2/146 subjects (1.4%) to underline both the improved social and hygienic conditions and, to a smaller extent, the efficacy of the vaccination programmes.

1032 Does HDV Infection Always Require HBV? A Multicentric Study Performed on Liver Biopsies from HBV Negative Patients

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Introduction Contrary to the belief that HDV can be spread only under circum-
stances that transmit also HBV, the model of liver transplantation has shown that the "defective virus" can be transmitted independently from HBV. This "autonomous" HDV infection mainly affects family members of HBV carriers. At present it is not clear if the HDV infection is an "independent" event usually associated with a normal or minimally changed liver histology. Upon reactivation of HBV, HDV becomes pathogenic. Aim To investigate if autonomous HDV infection can naturally occur in non-transplanted subjects in a geographical area (Puglia) where HDV is highly endemic. Methods 510 normal liver biopsies, obtained from patients surgically treated for non-liver-related diseases (mean age 47 ± 9 years, male/female male/female 92/34) showing only minimal histological changes were tested for HDAg. The reactions were visualized using 3-amo-n-ethyl carbazole as a substrate. HDAg positive samples were tested for the presence of HDV-RNA by in situ hybridization using a digoxigenin labelled synthetic oligonucleotide specific for HDV-RNA. Results HDAg was not detected in any of the 125 liver samples showing minimal histological changes, but it tested positive in 25/10 (0.4%) normal liver biopsies showing a nuclear homogenous staining detectable in 2-5% of the hepatocytes. This result was not confirmed by in situ hybridization and when 3-amo-n-ethyl carbazole was changed with diaminobenzene/Chromogenit A50. Conclusion Autonomous HDV infection or HDV transmission from HBV carriers could have been already superinfected by HBV. Different approaches are therefore needed to assess potential autonomous HDV replication.

1033 Analysis of Etiologic Factors of Chronic Liver Disease in Southern Italy

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In our area, it has been shown that viruses play a relevant role in the gene-
sis of chronic liver disease while alcohol is less frequently involved as eti-
ologic agent. Objective To assess the impact of different etiologies in patients with liver disease living in Southern Italy. Methods Between September 1991 and September 1992, 400 consecutive patients were referred to our Hospi-
tal for assessment of presumed chronic liver disease. 242 pts. (136 M, 106 F, mean age 64.6 yrs., range 19-82) underwent echo-assisted percutaneous liver biopsy. All pts. were questioned about alcohol consumption and assessed for liver function tests. Serological markers of hepatitis B and D virus infection were determined by ELISA; anti-HCV antibodies were detected using ELISA II (Clone Systems IFCI). HCV-Ab positive pts. were tested with a second genera-
tion RIBA (Ortho Diagnostic Systems) only if suitable for Interferon treatment. Results Of 242 pts. who had a liver biopsy, in 25 (10.3%) histological diagno-
sis was inconclusive. In the other 217 pts., histology showed chronic persis-
tent hepatitis (CPH) in 13 (6%), chronic active hepatitis (CAH) in 68 (31.3%), cirrhosis in 136 (62.7%). Among histopathologically evaluated subjects, any etiologic factor was found in 21 out of 217 (9.5%). The prevalence of an-
tibodies to HCV alone was 56% (122 out of 217 pts.). Anti-HCV joined with other etiologic factors in further 16% of pts. HBSAg positive subjects were 16.5% (including etiologic associations). When HBSAg was detected as a single agent (23 out of 217 pts. 10.6%), 19/23 (82.6%) of these resulted HBAg positive, and showed generally histological features of CAH or cirrhosis. Only one pt. resulted HDV +, in 39/217 cases (18%) a double and triple etiologic asso-
ciation was documented, particularly between alcohol and HCV (26 pts, 19 of them with cirrhosis). In 8/39 cases (20.5%) HCV and HCV coexisted. Alco-
hol alone was found in 9/217 cases (4%), but, if associated to viruses, were identified in 18%. Conclusions Our results reveal: (1) high prevalence of HCV as etiologic factor in chronic liver disease (alone or together with other fac-
tors). (2) Hepatic histology showed advanced chronic liver disease in most of our patients. (3) Liver biopsy performed in anti-HCV positive pts. showed cirrhosis (with or without CAH) in 34/217 pts. (15.8%), of which 60% showed HBD in 234/217 pts. (10.8%), confirming the possible existence of severe liver damage in asymptomatic patients. (4) Low rate of chronic hepatitis B and D, probably related to de-
creasing incidence of both infections due to vaccination programme, or to advanced liver disease that contra indicates liver biopsy. (5) Alcoholism is a secondary etiologic factor in our population of patients with chronic liver disease.

1034 Thymus Factor (TFX) in the Treatment of Chronic Hepatitis B in Children

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Chronic hepatitis B is a severe and often progressing disease, caused by disor-
ers in immunoregulatory system. The purpose of this study was the evaluation of TFX effect on the clinical course of the disease in children. A group of 17 children (8 girls and 9 boys, mean age 16.5 years, ranges 7.8–13.7 years) was subjected to TFX treatment. All the patients had shown histological
and biochemical signs of active liver disease at least 6 months before the treatment. The decrease of CD4/CD8 factor to less than 1.3 was an indication for the treatment. HBSAg was found in all children; HBeAg in 12/17; anti-HBe in 5/17. In the latter group the process of active hepatitis maintained despite seroconversion. After 6-month treatment with TFX, CD3 and CD4 lymphocytes increased, CD8 decreased and normalisation of both, CD4/CD8 factor and biochemical investigations was observed. Low CD4/CD8 values and lack of clinical and biochemical improvement were still present in 2 children. Seroconversion in “s” and “e” systems occurred 3–6 months after immunological and biochemical investigations came back to normal values. 4/17 (23.5%) eliminated HBs and anti-HBs appeared; 9/12 (75%) eliminated HBs. No side effects were observed. Clinical, biochemical and immunological improvement maintained within the next 12 months of observation. No reversion in “e” system was observed, whilst one more child eliminated HBeAg. The obtained results indicate that TFX has a favourable effect on T lymphocytes regeneration and function and on clinical improvement, biochemical investigations normalisation and liver histological changes withdrawal.

**1035** Response of Anti-HCV-Positive Chronic Hepatitis with & Without HBSAg in Serum to Alpha-2 Interferon Therapy

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The aim of the present study was to compare the response to α-interferon (IFN) therapy in Egyptian patients with chronic hepatitis who had abnormal serum aminotransferase levels and were positive for anti-HCV but negative for HBeAg in serum. Group 1 included 18 patients who were positive for HBSAg and anti-HBe. While group 2 included 24 patients who were negative for both. All patients received IFN at a dose of 3 million units S.C. 3 times/week for 6 months and were followed up clinically, biochemically and hematologically during this treatment period and for 6 more months. A second liver biopsy was done for every patient after the completion of IFN therapy. Both the percentage of complete response with normalization of ALT during therapy and the overall response rate at 6 months (when patients with a partial response were also included as responders) showed no significant differences (p > 0.05) between group 1 (61.1% and 66.7% respectively) and group 2 (62.5% and 70.8% respectively). Also, there was no significant difference (p > 0.05) in the overall relapse rate in responders by 6 months after cessation of therapy, between both groups (58.3% and 58.6%). Our results suggest that HCV plays the leading role in the pathogenesis and the activity of liver disease in patients positive for anti-HCV, HBSAg and anti-HBe in serum. Also, the persistence of HBSAg (in absence of HBeAg) in serum seems not to affect the response of patients with chronic hepatitis C to therapy with IFN.

**1036** Chronic C Hepatitis Prognosis in Patients Older than 60 Years of Age

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Introduction: The development of cirrhosis and secondary complications during the course of a chronic C hepatitis appears after a prolonged follow up. Aim: To evaluate the prognosis and characteristics of chronic C hepatitis patients older than 60 years of age.

Subject and methods: We reviewed the analytic, echographic and endoscopic findings in 141 chronic C hepatitis patients (RIBA II). This prospective study lasted 13.5 ± 9 mo (range 2–36). HBS Ag positive patients were excluded. The disease prognosis was determined by the development of complications and/or portal hypertension assessed by abdominal ultrasounds and endoscopy. In addition biopsy was obtained in 27 patients.

Results: Main age was 68 ± 5.6 (range 60–84); 49 (34.8%) were males and 92 (65.2%) females. In 14.9% of the cases the probable origin of the disease was post infectious. portal hypertension was present in 14.9% of cases. The presence of portal hypertension was associated with a worse prognosis (p < 0.001). Mortality occurred in 8 pts (5.7%). Six patients developed hepatocarcinoma.

Conclusion: Chronic C hepatitis in patients older than 60 years of age has a bad prognosis.

(1) During the follow up, 13.5 mo, 14% of the patients presented complications, being ascites the most frequent.

(2) In 31.2% of the patients endoscopy showed esophageal varices.

(3) There is an important group of asymptomatic patients who have cirrhosis proven in biopsy (9 of 21 cases).

**1037** Two Year Old Hepatitis A Vaccine (Havrix) Retains Its Immunogenicity

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Aim: The purpose of this randomised double blind study was to determine the difference in the seroconversion rate between newly produced and two year old Hepatitis A virus (HAV) vaccines.

Methods: 215 (60 males, 155 females) healthy non-immune volunteers between the age of 18 and 39 were recruited. 1 ml of HAV vaccine (Havrix; SmithKline Beecham Pharmaceuticals) was administered by intramuscular injection into the deltoid at months 0, 1 and 6. Three groups of one quarter each received a different vaccine lot, each of which had been stored for 1 and 6 years, respectively. Whilst the final quarter received a recently produced vaccine as control. Anti-HAV total Ig levels were measured using an ELISA competitive assay technique (validated against Wellcozyme anti HAV total Ig k) at months 0, 1, 2, 6 and 7. Adverse reactions were recorded on diary cards which were collected at months 1, 2 and 5.

Results: There were three defaulters (1 self withdrawal, 1 pregnancy, 1 adverse drug reaction). 212 completed the study but to date serology results are only available up to month 2 in 205 (53 males, 152 females) vaccines. All (100%) of the 205 vaccines completed the trial were responders by month 2. This implies that by month 2 there is no difference in seroconversion rates between old and new Havrix vaccines. All serology results will become available when the code is broken at study conclusion in February 1994.

Conclusion: This is the first study to show that two year old HAV vaccine has an equal seroconversion rate as newly produced vaccine. This has significant implications for HAV vaccine production programmes and should reduce the cost by allowing a longer shelf life, especially important with a vaccine production lead time of 9 months. This suggests that further work can be carried out to determine the immunogenicity of vaccines stored for longer than two years.

**1038** Anti-HCV + and Immunological Disorders: Clinical and Epidemiological Findings

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Aim of work: to check the incidence of immunological disorders in patients with chronic active liver disease Anti-HCV +, before giving INF therapy.

Patients and methods: During the second half of 1993 the sera of 870 subjects (94% admitted to our division were tested for Anti-HCV using Elisa (Murex, Wellcome) and riba second generation (Pasteur). Each sera which resulted Anti-HCV+ was also tested for presence of autoantibodies ANA-H, AMA, AKA, LKM1, cryoglobulins, anti-HAV total, anti HCV total, anti HCV IgG and Immunological Disorders: Clinical and Epidemiological Findings.

Results: Anti-HCV+ was detected in 90/870 subjects (10.34%) admitted in our division. In 25/90 Anti-HCV+ patients (27.78%) associated immunological disorders were found with the following features:

- Cryoglobulinemia was found in 7 patients, but only 1 was associated with typical symptoms. Another case was associated with autoimmune hemolytic anemia and another was associated with Sjogren syndrome and ANA.

- ANA+ was found in 7 patients, 1 case was associated with anti-thyroglobulin (ATA-t), Microsomal Antibodies (ATAm) and anti-paraetial-cells antibodies (APCA).

- ATA+ and ATAm+ were found in 2 patients of which 1 case with APAC+ associated.

- High levels of circulating immunocomplexes were estimated in 6 patients of which 1 case associated with skin lesions urticaria-like, 1 case with porphyria cutanea tarda, 1 case with vasculitis and 1 case with diffuse vasculitis and membranous glomerulonephritis with severe proteinuria. The ANCA levels were not estimated.

- LMl- and SMA- associated antibodies were found in 1 patient.

- SMA- AA autoantibodies were found in 2 patients.

In the control group we found ANA+ in 18 of the 235 subjects (7.6%).

Conclusions: The prevalence of immunological disorders is significantly higher (P > 0.05) in patients Anti-HCV+ than in subjects Anti-HCV−. We also noted a concordance between high frequency of Anti-HCV positivity.
and high frequency of associated immunological disorders in our hospital population. We believe that these numbers will increase in the future if the research of these phenomena will be enhanced.

**1039** Evaluation of Asymptomatic Anti-HCV Positive Blood Donors

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*Purpose:* Assessment of asymptomatic, anti-HCV positive blood donors with reference to potential routes of transmission, biochemical and pathological characteristics.

*Method:* All routinely screened blood donors from Copenhagen University Hospital Gentofte found anti-HCV positive assayed by ELISA test and confirmed by RIBA test, were consecutively referred to medical department in a two years period. Medical history was taken, blood samples collected and liver biopsy performed.

*Results:* Among 11,500 volunteer blood donors, 21 were anti-HCV positive, but HBsAg- and anti-HIV negative. Sixteen accepted further examination, six women and ten men, the median age was 34 years (range 24-62). All were asymptomatic, without history of liver disease nor other diseases, and no one received any medication. Two had a daily alcohol intake >5 g, while nine did not have a daily consume. Nine had previous transfusy intravenous drug abuse, five combined with tattooing, while three were tattooed only. None had a history of blood transfusion. Thirteen accepted blood sampling and liver biopsy, one with an alcohol consume >5 g/day. Transaminases (ALT and AST) were elevated more than 1.5 times the upper limit of normal in five. Alkaline phosphatase was slightly elevated in one, IgG elevated in two, while IgA and IgM were normal in all samples. Chronic aggressive hepatitis (CAH) were seen in two, one had cirrhosis, three had chronic persistent hepatitis (CPH) combined with elevated transaminases, five had changes in accordance with CPH but with normal transaminases, only two had a normal biopsy. No alcoholic hepatitis were seen.

*Conclusion:* Thirteen asymptomatic blood donors with antibodies to hepatitis C virus underwent liver biopsy. Morphological changes compatible with chronic liver disease were seen in 11. Thus, all patients with antibodies to HCV should be offered evaluation, including liver biopsy.

**1040** Unusual Side Effects of α Interferon in the Treatment of Chronic Viral Hepatitis


*Goal:* To describe some rare effects induced by α interferon observed during the treatment of patients with chronic viral hepatitis.

*Methods:* There were 105 (155 HCV positive and 40 HbsAg positive) patients, enrolled on treatment schedules with a 2b interferon; every patient has a weekly consultation in the first month of therapy, followed by a monthly consultation.

*Results:* The unexpected observed side effects (13%) during treatment were: A. Neurological (n = 10); B. Dermatological (n = 10); C. Endocrine (n = 1); D. Psychiatric (n = 5).

Clinical events in group A consisted in pain ocular movements, during the first 2 months of therapy. In group B, seborreic eczema of face and scalp were observed in 3 men and 1 woman before the 6th month; papulose dermatitis, generalized in 1 man at 1st month and on the forearm in another, at 4th month; vasculitis in the legs of 1 male patient, and frontal cutaneous atrophy in 2 men, before the 6th month; at the 7th month after treatment, one patient presented with the same lesion.

In group C, hypothyroidism developed in 1 woman at 6th month. In group D, depression was diagnosed in 2 women and 1 man at 6th month; psychotic syndromes occurred in 1 woman at 5th month and obsessive-neurosis in 1 man at 4th month.

Only the frontal cutaneous atrophy lesion did not subside after interferon withdrawal, which has been the curative attitude in all other. No relation was found between the development of side effects and type of hepatitis, schedule of treatment, age or sex of patients.

*Conclusion:* (1) A careful clinical follow-up of interferon treated patients is mandatory, so that unexpected findings may be detected and described. (2) These rare side effects subsided after interferon withdrawal, excepted for the frontal cutaneous atrophy.

**1041** Should We Perform Liver Biopsies in HCV Positive Individuals with Normal Liver Function Tests?


*Introduction and Aim:* It is questionable whether a positive Riba 2 test is invariably associated with some degree of liver lesion (Esteban et al. 1991). We tried to assess the need of performing liver biopsies in this individuals, to define whether or not there was liver lesion.

*Methods:* From a cohort of referred patients to our liver unit outpatient clinics (including blood donors, iv. drug users and routinely screened families with HCV positive members), a total of 30 individuals consented to perform liver biopsy: they had at least two blood tests, 6 month apart availing amino transferases, ggt, alkaline phosphatase, HBV markers and HCV antibody (Riba 2 test, Ortho); these were submitted to a thorough inquiry assessing demographic characteristics, possible risk factors for exposure to hepatitis viruses, physical examination and abdominal ultrasound (US).

*Results:* No treatment with Interferon was performed before.

*Results:* The time of infection with HCV was predominantly between 5-10 years; only two had jaundice, and most common risk factors were use of nondisposable needles in 26/30 previous use of iv drugs in 16/32, sojourn in Africa in 6/30 and surgery in 6/30. US showed no signs of nodularity.

Histology was abnormal in 28/30, showing minimal lesions in 3/30, chronic persistent hepatitis in 19/30, chronic active hepatitis in 4/30 and cirrhosis in 2/30.

*Conclusions:* (1) A thorough clinical interview determined at least one identifiable risk factor in 100% individuals. (2) Only 7% did not have any evidence of liver damage. (3) Liver biopsy is in fact the only way to assess liver lesion in hcv positive individuals.

**1042** Can UDCA Increase Interferon Response in Chronic Hepatitis

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*Interferon (IFN) induces ALT normalization in about 50% of patients with hepatitis C. Ursodeoxycholic acid (UDCA) on the other hand, is a well known anticholestatic agent. This effect is probably correlated to the substitution of toxic hydrophobic bile acids with UDCA. The end-point of this study was the stable normalization of ALT levels, during UDCA administration (600 mg/day) in patients who after 6 months of IFN (3 MU/thrice weekly) were still non-responders and thus were given additional medication with UDCA. IFN was continued to complete a year of treatment and then suspended while UDCA was maintained during the 6 month follow-up period.

57 non-responders (mean age 50 yrs, 38 M/19 F) at 6th month of IFN treatment were divided into 2 groups: the first group (42) was assigned to additional therapy with UDCA, while the second group (15) continued IFN alone and thus acted as controls. All patients had histologically proven chronic active hepatitis anti-HCV positive (ELISA II generation test).

In the control group 2 patients responded to treatment but thereafter relapsed during the initial follow-up period. In the UDCA-IFN group there were 13 non-responders: 7 remained such throughout the 6 month follow-up period, during which IFN was suspended and UDCA was continued alone, while 6 suffered relapse. When responders were divided according to pretreatment yGT levels 3/16 (19%) and 4/26 (15%), normal and high levels respectively, had sustained response. An additional finding in this study was that elevated yGT levels were strongly correlated to male sex (Odds ratio 4.2 χ2 test p < 0.04).

These data support the growing evidence that UDCA can be used to help induce ALT normalization in patients not responding to IFN treatment.

**1043** Interferon Therapy to Chronic Hepatitis C

A. Miyazaki, S. Watanabe, Y. Yokoi, T. Komada, N. Kitami, N. Sato. Dept of Gastroenterology, Juntendo University, Tokyo, Japan

We have studied the effect of α-interferon (IFN) on amino transferases (ALT) and HCV-RNA levels in 48 patients with chronic hepatitis C. Methods: Histologically, 48 patients were 5 CPH, 29 CAH2A and 14 CAH2B. The type of α-IFN used was natural in 18 patients, recombinant α-2a in 19 patients, recombinant α-2b in 11 patients. 6 MU or 10 MU IFN was given daily for the first 2 weeks and then three times per week for the 24 weeks. ALT was evaluated during 6 months after treatment, and serum HCV-RNA by PCR was examined before, and 6 months after the end of treatment. The genotype was investigated with 39 patients (type II 64%, III 18%, IV 13%, III + II 5%).

*Results:* Twenty nine (60%) of 48 patients showed normalization of ALT at day of treatment. Normalization of ALT at the 6 months after the end of treatment was recognized twenty one patients (44%). Twenty eight (65%) of 43 patients showed HCV-RNA negative at the end of treatment, but at the 6 months after the end of treatment HCV-RNA negative was recognized thirteen (37%) of 35 patients. There are no significant difference between each histological groups, and also between each type of α-IFN used in normalization of ALT and disappearance of HCV-RNA. And further, there was no significant difference between each genotype in normalization of ALT and disappearance of HCV-RNA. The serum HCV-RNA tiers at pretreatment were measured in 26 patients. Nine (56%) of 16 patients in low levels of HCV-RNA...
were titrated against a World Health Organisation anti-HAV immunoglobulin.

Conclusions: The measurement of serum HCV-RNA titers before starting the IFN therapy is important for the anticipation of the IFN therapy. Levels of HCV-RNA determined by RT-PCR, rather than the HCV genotype, were an important determinant for effectiveness of the IFN therapy.

1044 High Prevalence of Hepatitis C Virus Markers in Chronically Haemodialysed Patients From Transylvania, Romania

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Objective: to study the seroprevalence of hepatitis B (HBV), C (HCV) and D (HDV) virus markers in chronically haemodialysed patients (pts) from Cluj, Transylvania.

Patients and methods: The sera of 68 adults with terminal chronic renal failure (CRF), on maintenance haemodialysis (HD) (duration on HD: 1–7 years) have been tested for HBsAg, HBeAg, antiHBs, total antiHBc, antiHBs, anti-HBe, total antiHDV, antiHCV (ELISA, Sanofi Diagnostics Pasteur).

Results: Before the HD treatment, HBsAg has been detected in 5 out of the 68 investigated pts (7.5%). During the HD treatment, 2 subjects cleared the HBsAg, but 7 others became positive, raising the number of HBsAg positive pts to 10/68. In 50 pts (73.5%) HBV infection markers have been demonstrated. HCV infection markers have been observed in 55/68 pts (80.9%). Surprisingly, the HCV seroprevalence was very low (3/63 pts vs. 4.76%), in contradiction with the previous available data. AntiHBs have been detected in 13 out of 50 pts (28%) who displayed HBV infection markers, revealing the weak capacity of HBV clearance under the immunosuppression circumstances determined by CRF. Clinical and biochemical criteria of chronic hepatitis have been noticed in 11 pts (16.2%). HCV markers have been detected in the sera of all these subjects; only 1 pt was HBsAg positive; in 4 pts antiHBs have been demonstrated.

Conclusions: 1. In chronically HD pts from Cluj, the seroprevalence of HCV and HBV markers is very high. 2. HDV infection markers showed a much lower prevalence than those of previous studies. 3. Chronic hepatitis was demonstrated in 16.2% of pts, all of them displaying HCV infection.

1045 A Difference in Salivary Anti-hepatitis A Immunglobulin Responses Between Naturally Infected and Vaccinated Individuals

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The purpose of this study was to determine whether the saliva of individuals vaccinated with the HAVRIX vaccine (SmithKline Beecham Biologicals) could be used as a sample in monitoring their immunological response to the vaccine.

Following the manufacturer's recommended procedure, 205 non-immune individuals were vaccinated at months 0, 1 and 6. Serum and saliva samples were taken at months 0, 1, 2, 6 and 7 and assayed for anti-HAV total immunoglobulin using a competitive Enzyme Linked Immunosorbent Assay 9 (ELISA).

By month 2, 201 of 205 individuals had become seropositive. 50 of these were titrated against a World Health Organisation anti-HAV immunoglobulin standard, demonstrating titres in the range 960 mlU/ml to 1780 mlU/ml (20 mlU/ml is regarded as the minimum protective level in serum). All 205 salivas were negative in the assay. At month 7, of the 126 paired samples tested to date, all have seroconverted, while only 12 (9.8%) have "salivacoverted" demonstrating titres ranging from 20–40 mlU/ml. In a previous blind study, this same saliva-based ELISA detected anti-HAV immunoglobulin in the saliva of 68 of 72 naturally infected individuals (94.4%), who demonstrated salivary titres in the range 20–500 mlU/ml.

It would appear that the saliva of vaccinees contains a far lower concentration of anti-HAV specific immunoglobulin than that of naturally infected individuals. As a result, unless an increase in assay sensitivity can be achieved, saliva is not a useful sample for following the response of vaccinees to the HAVRIX vaccine. It may, however, be useful as a means of distinguishing between natural and vaccine-induced immunity in outbreaks.

1046 The Effect on HCV Culture of Interferon α2a

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We succeeded in serial cultivation of HCV using a cultured cell. We studied the effect on HCV of interferon (IFN) using the HCV culture this time.

Materials and method: Liver biopsy specimens from patients with chronic active hepatitis (II) were homogenized. The supernatant of homogenate was added to Chang cell suspension in Eagle MEM solution and the suspension was incubated at 37°C for 30 min. After centrifugation, the precipitated cells were suspended in the same medium and incubated in LAB-TECK chamber slide at 37°C, 5% CO2 and 95% air for 2 weeks. After culture finished, the cell suspension in new medium exchanged was left to freezing and thawing. Then the supernatant (sup) was added to new Chang cell suspension and serial cultivation was done till the 10th generation by same procedures.

Experiment 1 The sup from the 10th generation (containing HCV) was mixed with IFNα2a and incubated at 37°C for 6 hours. Subsequently, IFNα2a (monoclonal antibody) was added to the mixture. After centrifugation, the sup was added to new Chang cell suspension and the suspension was incubated at 37°C for 30 min. The precipitated cells were suspended and incubated for 2 weeks using LAB-TECK chamber slide as described above. After cultivation finished, the cells were fixed and stained by indirect immunoperoxidase method (using monoclonal HCV core antibody). Reverse transcriptase and polymerase chain reaction (RT-PCR) (plus and minus strand in 5'-noncoding region) as for HCV of the cell and sup was done.

Experiment 2 New Chang cells were suspended in the same medium containing IFNα2a and incubated at 37°C for 5% CO2 and 95% air for 6 hours. After washing and centrifugation, the cells were suspended in the same medium, all of them displaying HCV infection markers, were added to 10th generation to new Chang cell suspension and the suspension was incubated at 37°C for 30 min. After centrifugation, the precipitated cells were suspended in the same medium and incubated for 2 weeks by the same method using LAB-TECK chamber slide as described above. Subsequently, IFNα2a was added to new Chang cell suspension and incubated for 6 hours. After finishing staining and RT-PCR were done. In four experiments, 2, 5’ oligo A synthetase and protein Kinase in the fraction of supernatant and precipitate of cell culture were measured.

Results Experiment 1 showed that infection rate of cells with HCV directly treated with IFNα2a slightly decreased, Experiment 2 revealed that infection rate of cells treated with IFNα2a remarkably decreased (to 18%). Experiment 3 showed that infection rate of infected cells treated with IFNα2a moderately decreased (to 60%). Furthermore in Experiment 2, already iodinating HCV decreased and RT-PCR in minus strand became negative. PK and 25AS were elevated in Experiment 2 only.

Conclusion. Chang cells treated with IFNα2a have strong protection from HCV infection. The protection on infected cells of IFNα2a was weak. IFNα2a itself has weak direct anti-virus action. However IFNα2a has the most important action which raise antiviral state in non-infected cell as for HCV also.

1047 Etiology of Viral Chronic Liver Diseases (CLD)

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The recent introduction and diffusion of sensitive methods of determination of anti-HCV antibodies makes it possible to collect reliable data on the etiology of viral CLD.

The aim of this study is to bring out the frequency by which HBV and HCV infection is associated with CLD in subjects with hypertransaminasemia underwent to liver biopsy in the period 1990–1993. HBV has been considered etiologically relevant when HBsAg was positive. The positivity of markers of past HBV infection (anti-HBc and/or anti-HBs) was not taken into account for etiologic classification. The frequency of association with alcohol abuse has been also examined.

Results: 525 subjects have been studied: M = 369; age: 43.8 ± 13.2; range: 8–78 yrs; F = 156; age: 49 ± 12.2; range: 13–69 yrs; M/F = 2.4
A. M. Polifemo, Alcohol

<table>
<thead>
<tr>
<th>Type of chronic liver diseases</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>CPH</td>
<td>CLH</td>
</tr>
<tr>
<td>HBV 6(1.9)</td>
<td>23(32.8)</td>
</tr>
<tr>
<td>HCV 31(9.9)</td>
<td>92(29.4)</td>
</tr>
<tr>
<td>HBV+HCV 2(18.2)</td>
<td>21(18.2)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>1(1.1)</td>
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Conclusions: (1) The HCV is the most frequent etiological factor associated with CLD in our population (59.6%); (2) The prevalence of CLD is higher in males, which are also younger than females. (3) HbsAg is rarely associated with HCV. (4) The prevalence of cirrhosis is comparable in HBV and HCV subjects (7.1% and 11.5%) and is higher than in alcohol dependent patients.

### 1048 Potential Role of Hepatitis C Virus in Anti-HCV Negative Patients with Chronic, Fluctuating Hypertensinaminia

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The pathogenetic role of HCV in anti-HCV negative patients with chronic, fluctuating hypertensinaminia is unknown.

The aim of the present study was to evaluate the possible role of HCV, by measuring HCV-RNA using nested PCR of UTR 5' region in 15 repeat-edly anti-HCV negative patients (ELISA, 2 generation test) with chronic [1–13 years] mild-severe fluctuant hypertensinaminia. None of the patients had received blood products or transfusions in the past.

All patients concurrently underwent liver function tests, anti-HCV, liver biopsy and measurement of HCV-RNA.

Results are given as median (range). Thirteen of the 15 patients (87%) were HCV-RNA positive. The liver function tests were: ALT 51 u/l (14-1023), AST 37 mU/l (24-461), alkaline phosphates 227 mU/l (129-869), γ GT 38 mU/l (11-452), total bilirubin 0.45 mg/dl (0.38-1.8).

As far as liver histology was concerned, 8 patients had normal portal and periportal tract with mild-severe parenchymal steatosis, 6 patients had CAH and 2 of them liver cirrhosis. The length of disease duration was correlated with the greater severity of liver disease at histology.

These data confirm the pathogenetic role of HCV in patients with anti-HCV negativity and chronic hypertensinaminia.

### 1049 Low SOD-Like Activity of Peripheral Leukocytes as a Marker of Virus Replication in Chronic B Hepatitis Infection

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Hepatitis B virus replication has recently been shown to persist not only in liver cells but also in peripheral leukocytes. Since activated leukocytes release oxygen free radicals which is followed by a concomitant decrease of SOD-like activity in these cells, we measured the SOD-like activity of plasma, peripheral blood polymorphonuclear (PMN) and mononuclear cells (MNC) in 31 patients with chronic hepatitis B infection by employing the specific electron spin resonance/spin trapping method. SOD-like activity of both PMN and MNC was lower in all patients with chronic hepatitis B infection when compared with that in 25 healthy controls. SOD-like activity of PMN and MNC further decreased in all subgroups as the severity of the liver disease progressed, except of that in patients with hepatocellular carcinoma, where a significant increase was observed. SOD-like activity of both cell-types was significantly lower in HBAg positive patients when compared with HBAg negative ones. SOD-like activity of both cell-fractions was lower in patients with elevated B virus associated DNA polymerase activity than in those with normal one. Based on the strong correlation found with the progression and activity of hepatitis B infection, the measurement of SOD-like activity in peripheral leukocytes may provide a helpful additional parameter in the assessment of the severity of chronic B virus-associated liver disease.

### 1050 Durable Response to Alpha-Interferon Treatment in Patients with Chronic Hepatitis C

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The aim of our study is to evaluate the long-term response (6–12 months) in patients with chronic hepatitis C after six-months alpha-interferon treatment.

68 patients with chronic hepatitis C were included between 1990 and 1993 in alpha-interferon treatment study using 3 MU three times a week for 6 months. We observed normalization of serum alanine-aminotransferase (ALT) in 47 patients, 26 males and 21 females, mean age 46.5 ± 7.2 years. All patients responders were evaluated in order to assess the long-term efficacy of therapy. We have considered a durable response the ALT persistent normalization within 6–12 months after treatment. We have also searched, in some patients, for HCV-RNA using PCR method six and twelve months after the end of therapy.

Stability in efficacy of the treatment has been found in 18/47 patients (= 38%) after six months and in 13/47 patients (= 27%) after twelve. The re-scence of HCV-RNA has proved negative in 8/12 tested patients six months after therapy withdrawal and in 7/10 patients at twelve.

In conclusion, of 47 patients with chronic hepatitis C responders to six-months alpha-interferon therapy we have observed a durable response in 38% of cases after six months and in 27% of cases after twelve months. The HCV-RNA was negative in most tested patients.

### 1051 Hepatitis C Virus Antibodies in Chronic Alcoholic Liver Diseases in Lithuania

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The aim of this study was to investigate the prevalence of hepatitis C virus antibody (anti-HCV) in patients with chronic alcoholic liver diseases (CALD).

Serum samples from 77 patients (71 males and 6 females) with CALD were analysed for the presence of anti-HCV by an Abbott’s and Ortho’s second generation HCV EIA method. The specific laboratory diagnostic of viral hepatitis C was introduced in Lithuania in 1991 in the Clinic of Infectious Diseases.

Anti-HCV was found in 15 (19.5%) patients with CALD: 8 (53.3%) of them had alcoholic liver cirrhosis, 4 (26.6%) – chronic alcoholic hepatitis (CAH) with mild activity and 3 (20.0%) – CAH with severe activity.

In 8 (60.0%) anti-HCV positive patients VHB markers were also detected: in 7 cases (46.6%) – anti-HBc, in 4 (26.6%) – anti-HBc and antiHBe, in 1 – HBSAg. Most of anti-HCV positive patients (80%) had various risk factors for HCV infection: multiple courses of parenteral treatment, operations or other surgical procedures (10 patients), two patients had been paid plasma donors (they were infected because of violations of technology and anti-epidemic conditions in the Lithuanian blood centre), 1 – was an intravenous drug abuser.

The results showed the high frequency of anti-HCV in CALD in Lithuania and the significant association with HB viral markers. These data confirm the possibility of existence of etiologically mixed forms (alcoholic and viral) of liver injury with certain peculiarities of diagnosis and clinical course.

### 1052 Hepatitis B and C Infections in Hemodialysis (HD) and CAPD Patients: Comparative Results

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To assess the frequency of and risk factors for HBV and HCV, we evaluated the serial results of HBsAg and Anti-HCV (2nd generation) obtained by ELISA method in HD and CAPD patients.

The mean age of 44 HD patients (15 female, 29 male) was 35 ± 3 (13-72), while it was 45 ± 2 (18-79) in 51 CAPD patients (23 female, 25 male). The 2942 healthy blood donors who applied to the blood bank served as the control group. In the control group, the prevalences of HBsAg positivity and Anti-HCV positivity were 7.89% and 0.75% respectively. Serological markers in patient groups are as follows. In comparative study, HD patients are compared with control group.

Serology

<table>
<thead>
<tr>
<th>HD (n: 44)</th>
<th>CAPD (n: 48)</th>
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<tbody>
<tr>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>HbsAg</td>
<td>13/21</td>
</tr>
<tr>
<td>Anti-HCVAb</td>
<td>17/27</td>
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It is remarkable that the prevalence of HBsAg positivity and Anti-HCV positivity in HD and CAPD patient groups are significantly higher than the control group (p < 0.0001). Although the HbsAg positivity was significantly higher in HD group compared with CAPD group, the increased number of Anti-HCV AB positivity was not statistically significant. When it is taken into account...
that 6 of the 9 Anti-HCV positive patients in the CAPD group were transferred from HD, a significant difference arises between the two groups. On the other hand, duration of dialysis on HD was much shorter than that of CAPD patients which were 23 ± 3 (13–72) months and 11 ± 1 (1–28) months respectively (p < 0.001). Number of blood transfusions in the HD group on the average was 5 units and no transfusions were made in the CAPD group (p < 0.0002). There was no difference in between two groups in terms of HB vaccination and liver disease.

In dialysis patient population, the prevalence of HBV and HCV infections is higher than the general population. Number of blood transfusions and the duration of dialysis should be considered for the high infection rate among these patients.

1053 Monoethylglycinexilidide (MEGX) Formation During Interferon Therapy in Chronic Hepatitis C

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Interferon (IFN) can depress hepatic Cyt-P450 system and suggest that this effect could be inseparable from their antiviral property. We evaluate MEGX formation, depending on Cyt-P450 activity, and ALT levels, before and during 6 months of IFN therapy, in 20 patients with CAH. Plasma samples (at 5, 30 and 180 minutes after injection) were drawn at 3, 6 and 12 months of IFN therapy. MEGX was determined by TDX fluorescent immunoassay and MEGX AUC values (ng/h/ml, mean ± SD) were statistically analyzed by means of Wilcoxon two tailed test. Before therapy MEGX AUC value was 3184 ± 1148; after first, third and sixth month therapy MEGX AUC values were respectively: 3047 ± 1456, 3107 ± 1224 and 2795 ± 1256. The differences were not statistically significant, although 8 cases out of 1, 7 cases at three and 8 cases at six months showed a reduction in MEGX AUC almost of 10%. In three patients MEGX AUC resultled decreased during all time therapy. At sixth month 8 patients responded to IFN therapy (ALT lower than 50 U/ml) whereas 12 patients not responded. Between the two subgroups the differences in MEGX AUC before and after therapy (responders from 3426 ± 1446 to 2892 ± 1459 and non responders from 2900 ± 956 to 2928 ± 1341) were not significant. These preliminary results allow some suggestions: (1) IFN therapy not reduced significantly MEGX formation at every considered time; (2) although IFN delayed MEGX formation in part of the patients (in 38% of the global evaluations); (3) the MEGX formation was not related to interferon response as showed by ALT fall during therapy.

1054 Frequency of Thyroid Dysfunction After Recombinant Alpha Interferon Therapy in Greek Patients with Chronic Active Hepatitis

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We determined the frequency of autoimmune diseases, as well as the frequency of the presence and/or the development of different organ and non organ specific autoantibodies during therapy with INF-α 2b (8 x 10^6 U subcut) for at least six months, in patients with well defined chronic viral hepatitis (CVH). There were thirty-two patients (18 male, 14 female; age range from 24 to 68 years) with clinical, biochemical, serological and histological proven chronic active hepatitis (18 due to HBV, 9 due to HCV, 4 due to HDV and 1 due to both HBV and HCV).

Anti-mitochondrial, smooth muscle and antithyroid antibodies were not detected either before, or after the end of therapy. Antinuclear antibodies (ANA) were detected in 15 patients (46.9%, 95% CI: 29.1%–65.3%) before therapy (6 of them increased their titer after therapy) and in another 6 - ANA negative patients after the end of INF-α therapy (56.4%, 95% CI 40.6%–76.3%). Two patients (6.25%, 95% CI: 0.77%–20.8%) developed thyroid dysfunction (hyperthyroidism) and returned to euthyroid status after two months of the suspending of INF-α (one without antithyroid drugs). The response to therapy was not related with the presence and/or induction of ANA.

At least for our area, the presence of ANA or their slight induction following therapy with INF-α is not a contraindication to the use of INF-α in patients with CVH. Thyroid dysfunction was observed in lower frequency than those of North European Countries, whilst autoimmune diseases others than thyroid dysfunction, were not observed. Aetiological relationship, however, of the thyroid dysfunction with INF-α therapy in the context of an autoimmune response is not revealed from this study as none of the patients developed antithyroid antibodies.

1055 Therapy of Viral Hepatitis with Interferon in Eastern Bohemia

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Interferon-alpha therapy remains the only one relevant in the management of chronic hepatitis B. The economic aspect of this treatment is not negligible. From 1992 to 1993, 17 patients with chronic active hepatitis B HBeAg positive were treated with interferon-alpha.

Prior to interferon-alpha therapy, we administered corticosteroids for a period of 21 days. After an interval of three weeks, patients received interferon-alpha 3 MU every day for 21 days. From day 11 to 21 we also administered acyclovir. This scheme was used without any local improvement. With this scheme we observed a seroconversion in 29.4%/5 patients. Five patients in whom the initial schema was unsuccessful, received interferon-alpha at a dose of 3-6 MU three times a week for a period of three months. Seroconversion was observed in 3 patients.

Totally we successfully treated 8 patients, 47%. All patients developed a flu-like syndrome. Four patients had a transitory leukopenia which was not a reason to stop the treatment. Only in one patient we stopped the therapy due to a development of a severe icterus.

Interferon-alpha is active in the treatment of chronic active hepatitis B HBeAg positive. The combination with corticosteroids and acyclovir is justified. The treatment schema we used is economically more advantageous and its costs represent one third of the costs of other schema recommended in the available literature.

1056 Interferon Alone vs Prednisone + Interferon Treatment of Chronic Hepatitis B in Children


The spontaneous HBeAg/antiHBe seroconversion in Polish children with chronic hepatitis B is estimated to be about 20%.

The aim of the study was to evaluate the effect of interferon alone vs prednisone + interferon therapy of chronic hepatitis B.

76 children with biopsy proven chronic hepatitis B (M=53, F=23) aged 8 mo–14.5 yrs (mean 5.25 yrs) were analyzed. Group I – 28 pts was treated with interferon alfa 3 MU 3 TIW for 20 weeks. Group II – 48 pts was treated with 6 weeks prednison course (2 mg/kg/dose was decreased every 2 weeks) followed by interferon alfa 3 MU 3 TIW for 20 weeks. All children were observed for 6 mo after interferon had been discontinued.

At the end of therapy 34% pts from group I and 53% from group II did not lose HBeAg. 46% pts from group I and 35% from group II had HBeAg/antiHBe seroconversion. HBeAg/antiHBe seroconversion was observed in 15% pts from group I and 5% from group II. The differences were not significant. In group I ALT activity decreased from 302 U/l before treatment to 69 U/l after interferon. In group II respectively from 141 U/l to 65 U/l.

6 mo after therapy HBeAg/antiHBe seroconversion was observed in 46% pts in group I and in 45% in group II. HBeAg elimination was noted in 12% pts from group I and 5% from group II. The differences were not significant. In group I ALT activity decreased from 302 U/l before treatment to 69 U/l after interferon. In group II respectively from 141 U/l to 65 U/l.

Control liver biopsy performed 1 year after treatment in 40 children showed improvement in 71% pts from group I and in 64% pts from group II. Conclusion: Interferon induces HBeAg/antiHBe seroconversion in about 55–58% of pts. and HBV-DNA elimination in about 35–39% of pts. Prednisone pretreatment does not improve the response rate.

1057 Significance of Anti-HCV Antibodies Rather Than HCV-RNA for Screening of HCV Infection

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Many different serological assays for anti-HCV antibodies, which have been developed recently, make it difficult to understand the state of HCV infection in patients, because of the discrepant results among assays. To clarify the features of assays, we studied the serological results in comparison to the presence of serum HCV-RNA and HCV antibodies. The subjects included 208 patients (146 males and 59 females aged 25 to 67 years (mean 50.8). About 45% of the subjects had received blood transfusions. Patients were tested for anti-HCV antibodies by anti-C100-3 and anti-HCV second generation (anti-HCV II). The presence of HCV-RNA was detected by RT-PCR using Primers for the 5' non-coding region and the genotype of HCV was detected by PCR using primers from the core region.

Results: One hundred sixty of 198 (80.8%) patients were anti-C100-3 positive. All of the 161 (100%) patients proved anti-HCV II. One hundred seventy eight of 188 (94.7%) patients were HCV-RNA positive and 105 (5.3%) were negative. We further compared anti-C100-3, anti-HCV-II and HCV-RNA reactivities on a total of 143 patients. Thirty two (23.8%) patients, who were proven HCV-

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RNA positive, were negative by anti-C100-3, but all were positive by anti-HCV II. One hundred thirty four (93.7%) patients proven anti-HCV II positive, were all positive by HCV-RNA. But 9 (6.3%) patients who were proven HCV-RNA negative, were positive by anti-HCV II. We determined the genotype of these 9 patients and found 3 patients had type III, the patient who had type IV and the remaining 5 were again negative in this test.

Conclusions: (1) Anti-HCV II was more sensitive and specific than the anti-C100-3, and was available for screening of chronic HCV infection. Detecting HCV-RNA was not practical for the full screening of chronic infection. (2) In a small number of patients with genotype III or IV, HCV-RNA could not be detected by RT-PCR using primers for the 5' non-coding region. If chronic hepatitis C patients are HCV-RNA negative but anti-HCV II positive, we can assume that the genotype of some of them are III or IV.

1058 A Model of Computerized Problem-Oriented Gastroenterological Record-Chart in a Clinical Unit

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In order to overcome the limits of the traditional paper record-chart, we have realized a computerized problem-oriented specialist record-chart (CCC-SOP), with the following aims: (1) administrative and clinical management of patients; (2) efficient and controlled data gathering, not limited to specific pathologies or instrumental methods; (3) quick information retrieval. The CCC-SOP (realized in CA-Clipper), comes from the accurate individuation of the administrative role (admission, discharge, certification and movement), medical (problem-oriented patient management, diagnosis and therapy), and paramedical (management of patients, automatic requests to centralized services, physiologic parameters collection, scheduling of therapies and diets). An automatic recording in the chart is provided by the Endoscopy Service. The informations gathered (private data, history, physical examination, laboratory tests, reports of instrumental tests, counsellings and therapies) are processed in real time by a multiuser multitasking operative system (MOS, Software-Link) installed on a central unit (based on 80486 microprocessor) in which, in a star configuration, terminals and personal computers with associated printers are linked through an intelligent multiprot board (Specialix). The integrity and privacy of the data files are gained by encryption technique and a hierarchy of access permissions. Since January 1983 about 1900 record-charts are actually available on line with high grade of information for intelligibility, correctness and adequacy of data. Besides the didactic role (record analysis, diagnostic and therapeutic protocols evaluation) and the scientific role (clinical and epidemiological analysis) the CCC-SOP can improve the medic-patient and paramed-medic-patient relation and is an precious instrument of control of the Department of the Hospital performance and throughput in order to increase the qualitative standards of the care.

1059 In Vivo Comparison of 3D Ultrasonography and Magnetic Resonance Imaging in Volume Estimation of Abdominal Organs

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Background: A system for acquisition of 3D ultrasound images has been developed and applied for volume estimation of the left gastric antrum, the gallbladder and kidneys. This 3D ultrasound system (3D-US) has been validated in vitro both on phantoms and organs and demonstrated high accuracy and precision. Objective: The purpose of this study was to evaluate the accuracy of the 3D-US compared with MRI in volume estimation of abdominal organs in vivo. Methods: The system was very versatile and could be used in a variety of clinical situations, including oncology. Results: The 3D-US correlated well (r = 0.82, p < 0.001) with MRI in volume estimation. The overall accuracy of 3D-US was 91% ± 8% (3D-US/MRI) ± 100% ± 5 SD, and the limits of agreement were −49.0 ml; 16.7 ml. 3D-US detected a 17% mean reduction in kidney volume after vatsalva maneuver (p = 0.008).

Conclusions: The present 3D-US is accurate in volume estimation in vivo and the system holds promising potentials for dynamic studies.

1060 Laura, A User Developed Data System in a Gastroenterology Ward


Most systems developed to facilitate medical data handling and knowledge extraction fail to embrace all necessary aspects of information, and require time-consuming training and strict adhesion to preset routines. When not met, data quality and user compliance may be impaired. Our aim was to develop a system to improve task planning, daily data handling and to facilitate quick access control within the daily routine work.

Based on the nurses priority, daily administrative routines were included in an applicable, short-version data system. No formal training exceeding that obtained by daily use of the program was necessary. Ideas and suggestions from the staff were incorporated when brought forward. Each user only entered data relevant to their own requirements. Applications for free text (medical records), numeric data (lab values) and data storage were developed within commercially available programs (Word, Excel, Access) with a compiler like programming tool in a Novel net.

The program includes standardized informations on previous and present history, clinical examination and statements. Diagnosis, planned and performed investigations, time of stay and specific comments are registered, laboratory results imported on-line and medical reports automatically extracted from the initial medical history and later evaluations. Data may be extracted to different information tools.

The user-based development secured high levels of enthusiasm, facilitated learning and improved data quality and updating. Radiological results are still not available pending appropriate standardization within the hospital.

1061 A Peculiar Combination of Neuroendocrine Tumours: Hepatocellular Carcinoma with PNET Differentiation Accompanied by Insulinoma of the Pancreas

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Hepatocellular carcinoma developed in a cirrhotic liver which revealed the common, well-differentiated structure of that tumour. Some nodules of this cancer displayed such well circumscribed fields resembled the usual oat-cell structure of so-called Primitive Neuroectodermal Tumour (PNET). These cells are very similar to those of oat-cell carcinoma of the lung. It is well known that the latter tumours can have an endocrine function and structure. By the other hand, the special neoplasms of the G-tract, the APUD-omas are also neuroectodermal origin. In the presented case the autopsy couldn't detect any primary malignant change in the lung. The cells of oat-cell type of PNET component showed a very strong positive staining for NSE by immunocytochemical method. The other malformation found in the pancreas was cystic tumour macroscopically. This neoplasm revealed microscopically small uniform cells in which insulin could be demonstrated by immunocytochemical investigation.

1062 Tissue-Specific Expression of Incretin Hormones in the Gut of Nod-Mice

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Glucose-dependent insulinotropic peptide (GIP), cholecystokinin (CCK), and peptide-NKY-like peptide-1 (GLP-1) are insulinotropic gut hormones. We have evaluated their distribution of expression in the gut of NOD mice which serve as a model of insulin-dependent diabetes mellitus. We addressed the question whether this pattern is different between insulin-deficient, hyperglycaemic diabetic and non-diabetic mice. Specific cDNAs encoding rodent GIP, GLP-1 and CCK were utilized in in situ hybridization conditions with Northern blot technology. After such conditions were achieved, high-stringency RNA-slot blot-hybridization was utilized to analyze total RNA extracted from all parts of the intestine saved from non- (n = 5) and diabetic (n = 10) mice. The blots were quantified by UV-scanning densitometry. Data was expressed as mRNA/18s rRNA in % of total specific mRNA. The expression of all three hormones followed typical patterns. The GIP gene was greatly expressed in the duodenum and upper jejunum (60%) and lower jejunum and ileum (20%) with a continuous decrease from the upper to the lower part. The CCK-expression followed a similar pattern but was even more pronounced in the duodenum (70%). The expression of the proglucagon gene encoding the major incretin GLP-1 had an opposite appearance. The highest expression was found (app. 80%) in the large intestine. The ileum contained (app. 12%) of the message, virtually no expression (<10%) was seen in the upper gut.