

'Prevention of Viral Hepatitis in Greece: Lessons learnt and the way forward'

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This pre-meeting document is a list of selected abstracts from a Pubmed MEDLINE search on 'Greece and {viral hepatitis or HAV or HBV or HCV or HDV or HEV}' and a Web of Science search on 'Greece and viral hepatitis'.

The abstracts are ranged per year of publication from recent to 'historical' and for each year in reversed alphabetical order of the first author's name.

G. Zacharakis, J. Koskinas, S. Kotsiou, E. Pouliou, M. Papoutselis, F. Tzara, N. Vafeiadis, E. Maltezos, A. Archimandritis and K. Papoutselis. Natural history of chronic hepatitis B virus infection in children of different ethnic origins: a cohort study with up to 12 years' follow-up in northern Greece. *J Pediatr Gastroenterol Nutr*, 2007; 44: 1: 84-91

AIM: To investigate the mode of transmission and the natural history of chronic hepatitis B virus (HBV) infection in children of different ethnicities in Greece. This study was part of the Interreg I-II EC project. PATIENTS AND METHODS: One hundred seventy-three hepatitis B surface antigen (HBsAg)(+) carriers, median age 6.9 (5-12) y, were prospectively followed-up for a mean period of 5.3 (1-12) y for serological markers of HBV infection, serum alanine aminotransferase (ALT), HBV-DNA, alpha-fetoprotein levels and ultrasonography. RESULTS: Vertical transmission predominates (61.8%) in Moslem children and horizontal (44%) in those born in Russia. At entry, 73 of 173 (42%) HBsAg(+) genotype D children were hepatitis B e antigen (HBeAg)(+), ranging from 27% to 67% among ethnic groups; 55 of 173 (32%) had ALT > 2 x upper normal limit (UNL), ranging from 21% to 39%. Of 100 anti-HBe(+) children, 85 (85%) were inactive carriers. During the follow-up period, seroconversion to anti-HBe was observed in 40 of 73 (55%) children with an annual rate of 11%; 35 of 40 (87.5%) had biochemical remission, and 28 of 35 (80%) lost HBV-DNA. In the anti-HBe(+) group, 27 of 100 (27%) lost HBV-DNA and 9 of 100 (9%) lost HBsAg. The annual seroconversion rate for HBeAg was significantly lower: in children with vertical transmission compared with horizontal (7.7% vs 14.8%, respectively, $P < 0.001$) and in Muslim children compared with both Christian children and those born in Russia (8.6% vs 12%, respectively, $P < 0.001$). No differences were found among the ethnic groups after adjusting for the mode of infection. Two of 173 children had progression of liver disease. CONCLUSIONS: The differences in HBeAg(+) status and seroconversion rate among the ethnic groups are related to the time/mode of HBV infection. The majority of children who developed anti-HBe immunity had biochemical remission, and a substantial number of the inactive carriers lost viremia during the observation period of up to 12 y.

G. V. Papatheodoridis, J. Goulis, D. Christodoulou, S. Manolakopoulos, M. Raptopoulou, E. Andrioti, N. Alexandropoulos, S. Savvidou, A. Papachristou, E. Zervou, K. Seferiadis, P. Kousidou, E. Vogiatzakis and E. Tsianos. High prevalence of elevated liver enzymes in blood donors: associations with male gender and central adiposity. *Eur J Gastroenterol Hepatol*, 2007; 19: 4: 281-7

OBJECTIVE: Nonalcoholic fatty liver disease is an increasingly recognized condition, but its exact prevalence is unknown. In this prospective, multicenter study, we evaluated the prevalence of elevated alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl-transpeptidase levels as indirect markers of nonalcoholic fatty liver disease in volunteer blood donors as well as their associations with epidemiological and anthropometrical characteristics. METHODS: Alanine aminotransferase, aspartate aminotransferase and gamma-glutamyl-transpeptidase levels were determined in blood donors from four transfusion centers during the morning sessions of a 3-month period. Cases with positive hepatitis B surface antigen, anti-hepatitis C virus, anti-HIV or elevated

liver enzymes and alcohol abuse were excluded. RESULTS: Abnormal liver enzymes were found in 17.6% of 3063 participants (alanine aminotransferase: 14.5%, aspartate aminotransferase: 4.6%, gamma-glutamyl-transpeptidase: 4.7%). Individuals with abnormal compared with those with normal liver enzymes or alanine aminotransferase values were more frequently men and had higher weight, body mass index, waist, hip and neck circumference ($P < 0.001$ for all comparisons). The prevalence of abnormal liver enzymes was also associated with the transfusion center ranging between 8.8 and 22.1% ($P < 0.001$) and alcohol consumption ($P = 0.001$). In multivariate analysis, presence of elevated enzymes was independently associated with male sex, higher weight or body mass index, higher waist circumference and transfusion center. CONCLUSIONS: More than 15% of Greek blood donors exhibit elevated liver enzymes, most likely as a result of unrecognized nonalcoholic fatty liver disease. The prevalence of nonalcoholic fatty liver disease is mainly associated with male sex, obesity and waist circumference, but it may range significantly among different population groups.

G. Imvrios, V. Papanikolaou, D. Vrochides, N. Ouzounidis, A. Papagiannis, I. Fouzas, D. Giakoustidis, N. Antoniadis, S. Iosifidou, K. Patsiaoura, E. Zafiriadou and D. Takoudas. Liver transplantation outcomes in patients with cirrhosis and hepatocellular carcinoma: Experience of a single center in a viral hepatitis endemic area. *Transplantation Proceedings*, 2007; 39: 5: 1508-10

Our center has performed 205 orthotopic liver transplantations (OLT) in 201 patients. Hepatocellular carcinoma (HCC) was discovered in 32 (15%) patients, 5 of whom were diagnosed incidentally in recipient explants. The main underlying diagnosis was viral hepatitis ($n = 28$; 87.5%). Most patients (17; 53.1%) were diagnosed as having Child class B cirrhosis. Single tumors measuring < 3 cm were diagnosed in 29 (90.6%) patients. Downstaging chemoembolization was performed in 7 (21.8%) patients. Preoperative alpha FP levels were normal in 20 (62.5%) patients. In the rest ($n = 12$; 37.5%), aFP levels normalized immediately after the OLT. In the latter group, 2 patients had a delayed (2 years) postoperative increase in aFP levels; both patients had tumor recurrence in the graft. All patients with hepatitis B received antiviral treatment with HBIG and lamivudine. There were 9 deaths (28.1%) in the immediate postoperative period (< 30 days). One-year survival rate was 62.5% ($n = 20$). Actuarial 5-year survival rate was 55%, and actuarial 10-year survival rate was 40%. In conclusion, OLT has become the standard treatment for patients diagnosed with HCC in a population that shows cirrhosis most of the time to be secondary to viral hepatitis, provided that recipients are selected according to the size of the neoplasm and that they receive adequate antiviral prophylaxis.

E. Gigi, T. Lalla, E. Orphanou, E. Sinakos, E. Vrettou and M. Raptopoulou-Gigi. Long term follow-up of a large cohort of inactive HBsAg (+)/HBeAg (-)/anti-HBe (+) carriers in Greece. *J Gastrointest Liver Dis*, 2007; 16: 1: 19-22

AIM: To investigate the long-term outcome and the risk of progression to chronic hepatitis B in inactive hepatitis B surface antigen carriers. MATERIAL AND METHODS: A total of 307 HBsAg (+)/HBeAg (-)/antiHBe (+) subjects with initially normal alanine aminotransferase (ALT) levels and undetectable/ low serum HBVDNA with hybridization assay and later with PCR (10(5) copies/ml), were followed-up every 6 months for a period of 3 to 21 years (7.45 +/- 3.75 years). RESULTS: 234 out of the 307 HBsAg (+) patients (76.2%) had persistently normal ALT and undetectable / low (10(5) copies/ml) HBVDNA during follow-up. In 73 patients (23.8%), a reactivation of the disease with elevated ALT and positive HBVDNA ($> 10(5)$ copies/ml) was recorded during the follow up. Thirty-five out of 73 patients

underwent liver biopsy, while 22 of them received treatment. Twenty-four patients (7.8%) lost HBsAg after a mean of 7.4 +/- 3.6 years. Regarding the complications of chronic hepatitis B, only one patient developed compensated cirrhosis and no one developed HCC. CONCLUSIONS: Our results show that in almost 24% of inactive chronic hepatitis B carriers reactivation of the disease may occur even after many years. However the risk of liver-related complications is very low in these subjects.

N. K. Gatselis, E. Rigopoulou, A. Stefanos, M. Kardasi and G. N. Dalekos. Risk factors associated with HCV infection in semi-rural areas of central Greece. *Eur J Intern Med*, 2007; 18: 1: 48-55

BACKGROUND: Hepatitis C virus (HCV) appears to be endemic in most parts of the world, but there is considerable geographic variation. In order to assess the geographic distribution of HCV in Thessaly, in central Greece, we conducted a retrospective study in HCV-infected patients attending the Academic Liver Unit of Thessaly University from 1999 to 2003. We also investigated whether variation among regions could be attributed to differences in risk factors. METHODS: We evaluated the records of 309 HCV patients whose origin and/or residence was in Thessaly. To identify risk factors that were independently associated with the place of birth and/or residence, adjusted odds ratios (OR) were calculated by logistic regression analysis. We also studied the medical records of 150 HCV-negative patients from the same areas in order to evaluate whether there are differences in risk factors reported by HCV-positive and HCV-negative patients. RESULTS: We found three municipalities with a high HCV frequency. The use of non-disposable, multiple-use glass syringes for medical purposes in the past was the only potential risk factor more frequently identified in these areas than in other places (OR=2.3; $p < 0.05$). This risk factor was significantly ($p < 0.001$) associated with older age of the infected patients. CONCLUSIONS: This study shows that the spread of HCV in the three regions may have occurred several years ago as a result of the use of multiple-use glass syringes. Differences in prevalence rates among different age groups, as well as among different areas, indicate the need for extensive studies to determine HCV epidemiology and to develop appropriate prevention programs.

M. E. Falagas, I. Karydis and I. Kostogiannou. Percutaneous exposure incidents of the health care personnel in a newly founded tertiary hospital: a prospective study. *PLoS ONE*, 2007; 2: 2: 194

BACKGROUND: Percutaneous exposure incidents (PEIs) and blood splashes on the skin of health care workers are a major concern, since they expose susceptible employees to the risk of infectious diseases. We undertook this study in order to estimate the overall incidence of such injuries in a newly founded tertiary hospital, and to evaluate possible changes in their incidence over time. METHODOLOGY/PRINCIPAL FINDINGS: We prospectively studied the PEIs and blood splashes on the skin of employees in a newly founded (October 2000) tertiary hospital in Athens, Greece, while a vaccination program against hepatitis B virus, as well as educational activities for avoidance of injuries, were taking place. The study period ranged from October 1, 2002 to February 28, 2005. Serologic studies for hepatitis B (HBV) and C virus (HCV) as well as human immunodeficiency virus (HIV) were performed in all injured employees and the source patients, when known. High-titer immunoglobulin (250 IU anti-HBs intramuscularly) and HBV vaccination were given to non-vaccinated or previously vaccinated but serologically non-responders after exposure. Statistical analysis of the data was performed using Mc Nemar's and Fisher's tests. 60 needlestick, 11 sharp injuries, and two splashes leading to exposure of the skin or mucosa to blood were reported during the study period in 71 nurses and two members of the

cleaning staff. The overall incidence (percutaneous injuries and splashes) per 100 full-time employment-years (100 FTEYs) for high-risk personnel (nursing, medical, and cleaning staff) was 3.48, whereas the incidence of percutaneous injuries (needlestick and sharp injuries) alone per 100 FTEYs was 3.38. A higher incidence of injuries was noted during the first than in the second half of the study period (4.67 versus 2.29 per 100 FTEYs, $p = 0.005$). No source patient was found positive for HCV or HIV. The use of high-titer immunoglobulin after adjustment for the incidence of injuries was higher in the first than in the second half of the study period, although the difference was not statistically significant [9/49 (18.37%) vs 1/24 (4.17%), $p = 0.15$]. CONCLUSIONS/SIGNIFICANCE: Our data show that nurses are the healthcare worker group that reports most of PEIs. Doctors did not report such injuries during the study period in our setting. However, the possibility of even relatively frequent PEIs in doctors cannot be excluded. This is due to underreporting of such events that has been previously described for physicians and surgeons. A decrease of the incidence of PEIs occurred during the operation of this newly founded hospital.

L. S. Elefsiniotis, I. Glynou, H. Brokalaki, L. Magaziotou, K. D. Pantazis, A. Fotiou, G. Liosis, H. Kada and G. Saroglou. Serological and virological profile of chronic HBV infected women at reproductive age in Greece - A two-year single center study. *European Journal of Obstetrics Gynecology and Reproductive Biology*, 2007; 132: 2: 200-3

Objective: Seroprevalence of HBsAg in 26,746 women at reproductive age in Greece and evaluation of HBeAg/anti-HBe serological status as well as serum HBV-DNA levels in a subgroup of HBsAg(+) women at labor.

Study design: Serological markers were detected using enzyme immunoassays. Serum HBV-DNA was calculated using a sensitive quantitative PCR assay, with a lower limit of quantification of 200 copies/ml.

Results: Overall, 1.53% of women were HBsAg(+) and the majority of them (64.96%) were Albanian. Among Albanian women the mean prevalence of HBsAg was 4.9%, 5.57% among Asian women, and 1.29% among women from Eastern European countries. The prevalence of HBsAg among African (0.29%) and Greek women (0.57%) was very low and significantly lower in comparison with the mean value of the studied population. Only 2.67% of HBsAg(+) women were HBeAg(+). Of a subgroup of women in labor with available serum samples 28.6% had undetectable levels of viremia (<200 copies/ml) and 15.9% had extremely low levels of viral replication (<400 copies/ml). Only 12.7% of pregnant women evaluated at labor exhibited extremely high serum HBV-DNA levels (>10,000,000 copies/ml) whereas 42.8% of them exhibited HBV-DNA levels between 1500 and 40,000 copies/ml.

Conclusions: The overall prevalence of HBsAg is relatively low among women at reproductive age in Greece but is higher among specific ethnic populations (Asian, Albanian). The HBeAg(-)/antiHBe(+) serological status is a finding observed in the vast majority of HBsAg(+) women of our study population, and a significant percentage of them (approximately 44.5%) exhibit extremely low or even undetectable levels of viral replication at labor, suggesting possibly that only a proportion of HBsAg(+) women in Greece exhibit an extremely high risk of vertical transmission of the infection. (C) 2006 Elsevier Ireland Ltd. All rights reserved.

V. Papaevangelou, C. Hadjichristodoulou, D. Cassimos and M. Theodoridou. Adherence to the screening program for HBV infection in pregnant women delivering in Greece. *BMC Infect Dis*, 2006; 6: 84

BACKGROUND: Hepatitis B infection (HBV) is a major Public Health Problem. Perinatal transmission can be prevented with the identification of HBsAg(+) women and administration of immunoprophylaxis to their newborns. A national prevention programme for HBV with universal screening of pregnant women and vaccination of infants is in effect since 1998 in Greece. **METHODS:** To evaluate adherence to the national guidelines, all women delivering in Greece between 17-30/03/03 were included in the study. Trained health professionals completed a questionnaire on demographic data, prenatal or perinatal screening for HBsAg and the implementation of appropriate immunoprophylaxis. **RESULTS:** During the study period 3,760 women delivered. Prenatal screening for HBsAg was documented in 91.3%. Greek women were more likely to have had prenatal testing. HBsAg prevalence was 2.89% (95%CI 2.3-3.4%). Higher prevalence of HBV-infection was noted in immigrant women, especially those born in Albania (9.8%). Other risk factors associated with maternal HBsAg (+) included young maternal age and absence of prenatal testing. No prenatal or perinatal HBsAg testing was performed in 3.2% women. Delivering in public hospital and illiteracy were identifiable risk factors for never being tested. All newborns of identified HBsAg (+) mothers received appropriate immunoprophylaxis. **CONCLUSION:** The prevalence of HBsAg in Greek pregnant women is low and comparable to other European countries. However, immigrant women composing almost 20% of our childbearing population, have significant higher prevalence rates. There are still women who never get tested. Universal vaccination against HBV at birth and reinforcement of perinatal testing of all women not prenatally tested should be discussed with Public Health Authorities.

A. Mariolis, C. Mihos, I. Magaziotou, A. Alevizos, V. Gizlis, M. Papathanasiou, I. Lentzas, E. Konstantinou and I. Elefsiniotis. Seroepidemiological study of viral hepatitis among workers of the Cleaning Department of the Municipality of Vyronas: Preliminary results of a single centre study. *Public Health*, 2006; 120: 11: 1088-9

A. Katsoulidou, V. Sypsa, N. C. Tassopoulos, J. Boletis, A. Karafoulidou, I. Ketikoglou, D. Tsantoulas, I. Vafiadi, G. Hatzis, A. Skoutelis, E. Akriviadis, T. Vasiliadis, G. Kitis, G. Magiorkinis and A. Hatzakis. Molecular epidemiology of hepatitis C virus (HCV) in Greece: temporal trends in HCV genotype-specific incidence and molecular characterization of genotype 4 isolates. *J Viral Hepat*, 2006; 13: 1: 19-27

This study aimed to estimate the overall HCV genotype distribution and to reconstruct the HCV genotype-specific incidence in Greece during the recent decades. It also focused at the identification of genotype 4 subtype variability in Greek isolates. A total of 1686 chronically infected HCV patients with detectable serum HCV RNA by RT-PCR, belonging to different risk groups were studied. Amplified products from the 5'-noncoding region were typed using a commercially available assay based on the reverse hybridization principle. The HCV genotype-specific incidence was estimated using a previously described back calculation method. HCV genotype 1 was the most prevalent (46.9%) followed by genotype 3 (28.1%), 4 (13.2%), 2 (6.9%) and 5 (0.4%). A high prevalence of genotype 1 (66.3%) in haemophilia patients was recorded whereas HCV genotype 3 was found mainly among patients infected by I.V. drug use (58.2%). Data on the temporal patterns of HCV genotype-specific incidence in Greece revealed a moderate increase (1.3-1.6 times) for genotypes 1 and 4, and a decrease (1.5 times) for genotype 2 from 1970 to 1990, whereas there was a sharp (13-fold) increase for genotype 3. The molecular characterization of 41 genotype 4

HCV isolates belonging to various risk groups revealed that, subtype 4a was the most frequently detected (78%). Phylogenetic comparison of the Greek 4a isolates with all HCV-4a isolates reported worldwide so far revealed a topology which does not discriminate Greek isolates from the others. HCV-4 does not represent a recent introduction in Greece.

V. German, G. Giannakos, P. Kopterides, K. Liaskonis and M. E. Falagas. Serologic indices of hepatitis B virus infection in military recruits in Greece (2004-2005). *BMC Infect Dis*, 2006; 6: 163

BACKGROUND: The prevalence of hepatitis B virus infection in Greece has been decreasing over the last decades. However, recent epidemiological data are lacking. **METHODS:** We studied 1,840 Army recruits from 05/2004 until 10/2005, and performed serological testing for HBsAg, anti-HBsAg, and anti-HBcAg. We also examined their association with several factors, including age, residential area, socioeconomic class, and educational level. **RESULTS:** Mean age (+/- SD) of the recruits was 20.5 (+/- 2.1) years. Antibodies to HBV core antigen [anti-HBcAg (+)] were found in 31 (1.68%) of 1,840 participants. Only 6 (0.32%) were HBsAg (+)/anti-HBsAg (-)/anti-HBcAg (+), while 21 (1.14%) were HBsAg (-)/anti-HBsAg (+)/anti-HBcAg (+), and 4 (0.22%) were HBsAg (-)/anti-HBsAg (-)/anti-HBcAg (+). Overall, 1,144 recruits (62.17%) had antibodies against HBsAg [HBsAg (-)/anti-HBsAg (+)/anti-HBcAg (-)]; 665 recruits (36.14%) had undetectable anti-HBsAg levels. Multivariable analysis showed that younger age (OR: 0.87; 95% CI: 0.82-0.92) and advanced educational level (OR: 1.59; 95% CI: 1.32-1.93) were independently associated with serologic evidence suggestive of previous HBV vaccination. **CONCLUSION:** We document a further decline of the prevalence of chronic HBV infection among Greek military recruits, a fact that may support the effectiveness of the ongoing immunization programme.

S. Elefsiniotis, V. Paparizos, C. Botsi, K. D. Pantazis and A. Katsambas. Serological profile and virological evaluation of hepatitis B and hepatitis C virus infection among HIV infected patients in Greece. *Cent Eur J Public Health*, 2006; 14: 1: 22-4

In this study we evaluate the prevalence of HBV and HCV infections and the HBV and/or HCV viral load as well as HCV genotype among 737 HIV-infected patients. 89/737 (12.1%) were HBsAg(+) and the majority of them (60.7%) were HBeAg(+), in contrast to general Greek population; anti-HBc seropositivity was detected in 48.1% of the study population. Serum HBV-DNA levels were 5.75 +/- 1.66 (-log₁₀ copies/ml) and HBeAg(+) coinfecting patients had significantly higher levels than HBeAg(-) ones (7.40 +/- 0.64 vs 4.59 +/- 1.01, respectively, p < 0.001). 8.2% of HIV-infected patients were anti-HCV(+) and the majority of them (85.7%) had HCV-RNA levels more than 700.000 IU/l. The most common HCV-genotype was genotype-1 (12/28, 42.9%), representing a difficult-to-treat special population.

I. S. Elefsiniotis, K. D. Pantazis, I. D. Ketikoglou, S. I. Koutsounas and E. V. Tsianos. Changing serological status and low vaccination-induced protection rates against hepatitis B characterize chronic hepatitis C virus-infected injecting drug users in Greece: need for immunization policy. *European Journal of Gastroenterology & Hepatology*, 2006; 18: 11: 1227-31

Objective To evaluate the serological status of hepatitis B virus infection among Greek injecting drug users with chronic hepatitis C virus infection; to correlate hepatitis B virus

infection status with the possible time of infection and the principal genotype of hepatitis C virus infection.

Methods: Two hundred and thirty consecutive injecting drug users with chronic hepatitis C virus infection were evaluated for serological markers of hepatitis B virus infection. One hundred and three of them (44.8%) reported intravenous drug use beginning before 1992 (group A) and 127/230 (55.2%) after 1992 (group B). Statistical analysis of data was based on Student's t-test and chi(2) analyses.

Results: Eighty-five of 103 patients from group A (82.5%) and 28/127 (22%) from group B had serological markers of previous hepatitis B virus infection ($P < 0.001$). Eleven patients from group A (10.6%) and 78 (61.4%) from group B were seronegative for all hepatitis B virus markers ($P < 0.001$). Only 3.8% (4/103) of group A patients and 16.5% (21/127) of group B had vaccination-induced protective antibody levels (anti-HBs) against hepatitis B ($P=0.02$). The majority of patients were infected with hepatitis C virus genotype-3 (64.7% from group A vs 56.7% from group B, $P=0.42$). The percentages of patients infected with genotype-1 were also comparable in both groups (15.5% from group A vs 30.8% from group B, $P=0.09$). A significantly higher percentage of group A patients were infected with genotype-4 (19.7%) than those in group B (4.9%, $P=0.02$).

Conclusion: The serological profile of hepatitis B virus infection among Greek hepatitis C virus-infected injecting drug users is changing. The proportion of successfully vaccinated hepatitis B virus injecting drug users, although significantly higher than the previous decades, is still relatively low. Vaccination policy in this high-risk group for viral hepatitis is urgently needed.

G. Dounias and G. Rachiotis. Prevalence of hepatitis A virus infection among municipal solid-waste workers. *Int J Clin Pract*, 2006; 60: 11: 1432-6

A study was conducted among 151 municipal workers (72 solid-waste workers, and 79 workers not exposed to waste). Total antibodies against Hepatitis A virus (HAV) were measured, and socio-demographic information was collected using a self-administered questionnaire. Univariate analysis has shown that occupational exposure to waste, age, duration of employment and educational status were significantly associated with the prevalence of anti-HAV(+). Municipal Solid Waste Workers had a higher prevalence of anti-HAV(+) in comparison with municipal workers not exposed to waste. Duration of employment was significantly associated anti-HAV(+). Multivariate analysis revealed an independent association of anti-HAV(+) with occupational exposure to waste and ageing. Our results suggest a potential causal role of occupational exposure to waste, in the development of HAV infection.

G. Baltayiannis, K. Katsanos, P. Karayiannis and E. V. Tsianos. Interferon-alpha therapy in HBeAg-negative chronic hepatitis B: a long-term prospective study from north-western Greece. *Alimentary Pharmacology & Therapeutics*, 2006; 24: 3: 525-33

To determine the long-term response to interferon-alpha therapy in patients with hepatitis B e antigen-negative chronic hepatitis B, and the factors independently associated with response and survival.

Sixty-three patients with documented hepatitis B e antigen-negative chronic hepatitis B treated with interferon-alpha for a year were followed-up for a period of 6 years.

Sustained biochemical and virological response was seen in 34.91% and 33.33% of patients at 6 and 12 months of follow-up, respectively, and histological improvement in 54.5% of sustained responders compared with non-responders (7.1%, $P = 0.004$, chi-squared test), at 6 months of follow-up. Multivariate analysis showed that patients with hepatitis B virus-

DNA levels at 6 months of treatment < 10 000 copies/mL had a low probability of relapse, compared with those with levels > 10 000 copies/mL (P = 0.032). Age (> 65 years) and hepatitis B virus-DNA level at 6 months of treatment (> 10 000 copies/mL) were the independent factors for disease progression and survival (P = 0.041 and P = 0.044 respectively). At 6 years, a sustained response was still present in 19.04% of patients and 4.8% of them had developed anti-HBs.

Hepatitis B virus-DNA monitoring by quantitative polymerase chain reaction at 6 months of treatment may allow for early prediction of response to interferon-alpha, and may serve as an indicator of disease progression in the future.

E. K. Zervou, N. K. Gatselis, E. Xanthi, K. Ziciadis, S. P. Georgiadou and G. N. Dalekos. Intrafamilial spread of hepatitis B virus infection in Greece. *Eur J Gastroenterol Hepatol*, 2005; 17: 9: 911-5

OBJECTIVE: No study has investigated the intrafamilial spread of hepatitis B virus (HBV) in Greece. We conducted a 9-year prospective study to determine the rate of HBV spread in family members when a member is identified as an HBV carrier, the possible routes and risk factors for transmission of HBV and the family members with the highest risk of infection according to kinship degrees. **METHODS:** A total of 387 family members of 166 hepatitis B surface antigen (HBsAg) carriers were investigated for the detection of HBV infection markers using standard enzyme immunoassays; 6.696 blood donors from the same area were used as controls. **RESULTS:** Serological markers of past or current HBV infection were detected significantly more frequently among family members of HBsAg carriers (23.2 and 15.8%, respectively) compared with blood donors (14.1 and 0.85%, respectively). The prevalence of the above markers was higher among siblings, husbands and parents of the carriers. Offspring of the female index cases had higher rates of current or past infection. HBV infection markers were significantly increased in family members who reported common use of syringes (P<0.001), birth in rural areas (P<0.001) and a low level of education (P<0.001). **CONCLUSIONS:** We demonstrated a high risk of HBV transmission among family members of HBsAg carriers, which was associated with special risk factors for contracting HBV. Our findings indicate the need for strict adherence to the universal guidelines of vaccination against HBV and also the need for an immediate investigation of other potentially infected relatives among family members of HBsAg carriers.

G. H. Zacharakis, J. Koskinas, S. Kotsiou, M. Papoutselis, F. Tzara, N. Vafeiadis, A. J. Archimandritis and K. Papoutselis. Natural history of chronic HBV infection: A cohort study with up to 12 years follow-up in North Greece (part of the Interreg I-II/EC-project). *Journal of Medical Virology*, 2005; 77: 2: 173-9

The aim of the study was to assess the long-term outcome of chronic hepatitis B surface antigen (HBsAg) carriers in the general population in North Greece (Thrace), an area with an intermediate endemicity. This was a part of the Interreg I-II EC project. Two hundred sixty three chronic HBsAg(+) carriers, median age 34 years (20-65), were evaluated prospectively for a median follow-up of 5 years (2-12). Hepatitis B virus (HBV) markers and ALT were examined every 6 months and serum HBV-DNA every 12 months. Liver biopsy was undertaken at presentation and every 2-4 years. Fourteen of 263 (5.3%) subjects were HBeAg(+) and 249/263 (94.7%) HBeAg(-)/ anti-HBe(+) of whom 48 (19.3%) had elevated ALT, and HBV-DNA levels ranging from 1.4 x 10⁵-4 x 10⁷ copies/ml. Inactive carriers (98/195 (50.3%)) had detectable HBV-DNA (median 2.6 x 10³ range 0.042 x 10⁴-1.9 X 10⁴ copies/ml); 4/195 (2%) exhibited HBV reactivation during the observation period (all had HBV-DNA > 10⁴ copies/ml at presentation). Patients (7/14 (50%) HBeAg(+))

developed anti-HBe(+), annual rate 10%. Subjects (16/195 (8%)) lost HBsAg, all were inactive carriers; 10 developed anti-HBs (annual rate 1%). Liver biopsy was normal or with minimal changes in 92/95 (97%) inactive carriers and remained so at 4 years follow-up. In contrast, 4/48 (8.3%) HBeAg(-)/anti-HBe(+) patients with active disease had deterioration of liver histology. In this cohort study: (a) the annual seroconversion rate was 1% for the HBsAg and 10% for the HBeAg, (b) 23.6% of the HBsAg(+) carriers had active liver disease and 39% moderate fibrosis at presentation of whom a small proportion deteriorated over the observation period, (c) HbsAg carriers with HBV-DNA level <10(4) copies/ml had persistently normal ALT and unchanged liver histology over the follow-up period of up to 12 years.

V. Sypsa, G. Touloumi, G. V. Papatheodoridis, N. C. Tassopoulos, I. Ketikoglou, I. Vafiadis, G. Hatzis, D. Tsantoulas, E. Akriviadis, S. Koutsounas and A. Hatzakis. Future trends of HCV-related cirrhosis and hepatocellular carcinoma under the currently available treatments. *J Viral Hepat*, 2005; 12: 5: 543-50

SUMMARY: The epidemic of hepatitis C virus (HCV) infection is a major public health issue. We conducted a comprehensive analysis to estimate future HCV-related morbidity and mortality, using a model which is the first to take into account currently available treatments. We reconstructed the incident infections per year in the past that progressed to chronic hepatitis C (CHC) in Greece. Then, the natural history of the disease was simulated in subcohorts of newly infected subjects in the presence or absence of treatment using yearly estimates of the number of treated patients obtained from national databases. Annual estimates of the incidence and prevalence of CHC by fibrosis stage, hepatocellular carcinoma (HCC) and mortality were obtained up to 2030. The current proportion of naive CHC patients receiving treatment in Greece is 1.2% per year. Treatment of 1.2-10% of naive CHC patients per year would reduce the cumulative number of incident cirrhosis and HCC cases from 2002 to 2030 by 10.8-39.4% and 12.8-39.8%, respectively and decrease the number of prevalent cirrhosis and HCC cases in 2030 by approximately 17-48% compared with the number estimated under the assumption of no treatment. Approximately 17 cirrhosis cases or six HCC cases or 10 premature deaths would be prevented for every 100 treated patients. However, the prevalent cirrhotic/HCC cases because of HCV and HCV-related deaths would not plateau until 2030. Despite the introduction of effective treatment, HCV-related morbidity and mortality will likely increase during the next 20-30 years in Greece. Intensive primary prevention efforts coupled with increased access to the currently available treatments are necessary to control the chronic consequences of HCV epidemic.

V. Sypsa, M. Psychogiou, A. Katsoulidou, G. Skoutelis, S. Moutafis, V. Hadjiconstantinou, J. Kakavas, V. Kalapothaki, J. Boletis and A. Hatzakis. Incidence and patterns of hepatitis C virus seroconversion in a cohort of hemodialysis patients. *Am J Kidney Dis*, 2005; 45: 2: 334-43

BACKGROUND: The aim of this multicenter hemodialysis (HD) cohort study is to prospectively investigate the incidence of hepatitis C virus (HCV) infection in Greece from 1993 to 1995 and delineate early virological and serological events associated with HCV seroconversion in the HD setting. **METHODS:** Sequential serum samples collected weekly from 562 patients were tested biochemically and serologically by means of a second- (EIA-2) and third-generation enzyme immunoassay (EIA-3). All patients with positive antibody to HCV test results (anti-HCV +) and sequential samples from seroconverting patients were tested for HCV RNA. **RESULTS:** Anti-HCV prevalence at study entry was 29% (163 of 562 patients), and viremia was detectable in 110 of 163 anti-HCV + patients (67.5%). HCV

incidence was 6.2 cases/100 person-years. Seroconversions could not be attributed to transfusions after study entry (only 1 patient had been administered transfusion), and HD unit was associated with increased hazard for seroconversion ($P = 0.002$), even after adjusting for potential differences among their patients. According to Kaplan-Meier estimation, the median interval by which the HCV RNA assay detected HCV infection earlier than anti-HCV testing was 246 and 154 days for EIA-2 and EIA-3, respectively. Detectable HCV RNA and at least 2 consecutive abnormal alanine aminotransferase levels in the preseroconversion period were observed in 29 of 30 (97%) and 14 of 32 patients (44%), respectively. Reductions in HCV RNA levels immediately after seroconversion were transient or did not occur. **CONCLUSION:** On the grounds of apparent nosocomial transmission, the wide window period of HCV infection in HD patients emphasizes the need for strict adherence to specific infection-control measures in this setting.

S. P. Savvas, J. Koskinas, C. Sinani, A. Hadziyannis, F. Spanou and S. J. Hadziyannis. Changes in epidemiological patterns of HCV infection and their impact on liver disease over the last 20 years in Greece. *J Viral Hepat*, 2005; 12: 5: 551-7

SUMMARY: The aim of this study was to investigate the relative frequency of hepatitis C virus (HCV) genotypes in Greek patients with chronic infection as well as possible secular changes in their distribution in relation to modes of transmission, age and time at acquisition of the infection and other variables. We evaluated 434 unselected patients, 241 males and 193 females with a median age of 46.2 years (18-75), with chronic HCV infection presenting during the period 1996-2000. HCV infection was confirmed by the detection of HCV-RNA by polymerase chain reaction (PCR), while HCV genotyping was performed by the Inno-LiPA assay. Liver biopsies were evaluated according to Ishak's scoring system. Of 434 patients, 167 had a history of blood transfusion [post-transfusion hepatitis (PTH)], 80 were i.v. drug users and in 187 the route of infection remained unknown. The overall distribution of HCV genotypes 1, 2, 3 and 4 was 47, 8.3, 27 and 15.2%, respectively. Genotype 3 was common in younger adults and i.v. drug users, whereas genotype 1 predominated in older people and PTH patients ($P < 0.001$ for both). Infection acquired before 1981 (group A) was related to transfusion and genotype 1, while after 1981 (group B) with i.v. drug use and genotype 3 ($P < 0.01$). Biopsy was available in 369 (85%) patients, of whom 22.5% had cirrhosis; 29.8% in group A and 9.9% in group B. In a multivariate analysis, cirrhosis was strongly associated with the duration of infection ($P = 0.013$). Our study revealed a change of HCV genotype distribution in the last 20 years among Greek patients with chronic HCV infection as a result of epidemiological changes in HCV transmission. The presence of cirrhosis was associated only with the duration of infection. These observations have impact both on prevention and treatment.

E. I. Rigopoulou, I. Stefanidis, C. Liaskos, E. K. Zervou, C. Rizos, P. Mina, K. Zachou, C. Syrganis, E. Patsidis, G. Kyriakopoulos, L. Sdrakas, N. Tsianas and G. N. Dalekos. HCV-RNA qualitative assay based on transcription mediated amplification improves the detection of hepatitis C virus infection in patients on hemodialysis: Results from five hemodialysis units in central Greece. *Journal of Clinical Virology*, 2005; 34: 1: 81-5

Background: End-stage renal disease patients (ESRD) on maintenance hemodialysis (HD) are at increased risk of acquiring hepatitis C virus (HCV) infection. An early and accurate diagnosis of HCV infection is important for the prevention of viral transmission and the management of ESRD patients on HD but conventional ELISA and PCR have often failed to reveal active HCV infection. **Objectives:** This study evaluated the prevalence of HCV infection

in ESRD patients from all HD units in central Greece using a sensitive HCV-RNA transcription mediated amplification (TMA) assay and compared its sensitivity with that of anti-HCV ELISA. Stud); design: Anti-HCV antibody (third generation ELISA), HCV-RNA (TMA) and HCV genotypes (HCV TMA-LiPA) were determined in 366 ESRD Greek patients.

Results: In total, 132 (36%) ESRD patients were HCV positive by ELISA or TMA; 44 by TMA alone, 16 by ELISA alone and 72 positive by both assays. More than half of the viraemic patients had genotype 3a.

Conclusions: HCV-RNA (TMA) assay appears to increase the accuracy in the diagnosis of HCV infection in HD patients compared to the anti-HCV ELISA and could serve as an additional screening tool in these patients. (c) 2005 Elsevier B.V. All rights reserved.

G. Rachiotis, C. Goritsas, V. Alikakou, A. Ferti and A. Roumeliotou. Vaccination against hepatitis B virus in workers of a general hospital in Athens. *Med Lav*, 2005; 96: 1: 80-6

BACKGROUND: Protection against hepatitis B virus infection by vaccination is considered to be an important preventive measure for health care workers. OBJECTIVES: Investigation of vaccination coverage against hepatitis B virus in health care workers of a regional general hospital in Athens and assessment of predictive factors possibly associated with the likelihood of vaccination. METHODS: In a cross-sectional study, a questionnaire survey was carried out on 175 health care workers of a regional general hospital in Athens. The questionnaire included questions concerning socio-demographic factors, HBV vaccination status and reasons for non-vaccination, as well as questions about knowledge of routes of transmission and the complications of HBV infection. Compliance with preventive practices against HBV infection was also assessed. RESULTS: Overall vaccination coverage was 57.1%. Logistic regression analysis revealed that occupation and use of gloves were independently associated with the likelihood of vaccination against HBV. Doctors recorded an odds ratio (OR) for vaccination of 4.45 in comparison with nurses/paramedics. Health care workers who wore gloves always/most times demonstrated an odds ratio of 2.79 for vaccination against HBV in comparison with those who never/rarely used them. CONCLUSIONS: Our study illustrates the characteristics of health care workers with lower prevalence of vaccination against HBV in a representative sample of these workers in a regional general hospital in Athens: nurses/paramedics, those with low level of compliance with use of gloves, and those in non surgical departments. Educational interventions as part of a vaccination programme and continuing education on universal precautions could help increase HBV vaccination coverage among health care workers of the hospital under study.

O. Katsarou, G. Touloumi, A. Antoniou, A. Kouramba, A. Hatzakis and A. Karafoulidou. Progression of HIV infection in the post-HAART era among a cohort of HIV+ Greek haemophilia patients. *Haemophilia*, 2005; 11: 4: 360-5

AIM: The study aims to describe the course of HIV-1 infection in the pre- and post-HAART period in a cohort of HIV+ haemophilia patients followed up for up to 21 years. METHODS: The cohort includes 158 haemophilic men with known seroconversion dates followed up prospectively for a median time of 12 and 5.7 years in the pre- (1980-96) and post-HAART period (1997-2003), respectively. RESULTS: The risk of developing AIDS was lowered by 56% in the post- as compared to the pre-HAART period. Of the 158 patients 69 developed AIDS in the pre-HAART period while of the 59 subjects still alive and AIDS free on 1/1/1997 six developed AIDS. The rate of PCP (12.0 cases per 1000 person-years) and NHL (5.4 cases per 1000 person-years), the most common causes of AIDS diagnosis in the pre-HAART era, were remarkably reduced in the post-HAART era (both rates: 2.8 cases per

1000 person-years). On the contrary, the corresponding risk for non-AIDS deaths was fourfold increased in the post-HAART period. Of the 38 non-AIDS related deaths in both periods, 13 occurred post-HAART. The predominant cause of non-AIDS mortality in both periods was end-stage liver disease (ESLD) (7 pre- and 4 post-HAART). The rate of non-AIDS related cancers was also increased during the post-HAART period. CONCLUSION: In this haemophilia cohort the risk of AIDS has substantially reduced in the post-HAART period, but the rate of non-AIDS mortality tended to increase. Among haemophilia subjects, due to the high rates of HCV/HIV coinfection, ESLD, the predominant cause of non-AIDS mortality, will become an increasingly important clinical problem.

T. Kafkia, M. Kourakos, B. Lagkazali, M. Eleftheroudi, P. Tsougia, M. Doula, A. Laskari, G. Thanassa, J. Y. De Vos and M. Elseviers. European practice database: results from Greece. *Edtna Erca J*, 2005; 31: 1: 43-8

The survey (EPD) took place during December 2002-January 2003 and presents renal care in Greece. A questionnaire, structured at European level and translated into Greek, was sent to all dialysis centres (114) by post. The questionnaire was returned from 74 centres (64.9%). Some important results were: low use of peritoneal dialysis (13.3%), half of PD patients over 65 years old, one ninth of patients on transplantation waiting list, isolation for HBV positive patients (less for HCV and HIV), high use of AV fistulae (71.2%), maintenance and repair of dialysis machines by company technicians, absence of renal dieticians and social workers (but availability from hospital employees) one nurse every 5.54 patients (3.72 if nurse assistants are included), disinfection between shifts carried out chemically (hot or cold) and puncturing of vascular access performed mainly by nurses and nurse assistants. Data can be used to pressurise government for more scientists in the multidisciplinary team to be hired in hospitals, develop further research topics and to develop continuous education programmes.

I. S. Elefsiniotis, B. Hero, A. Mariolis, K. D. Pantazis, N. V. Fotos, I. Ketikoglou and G. Saroglou. Serological profile of HBV infection and liver histopathology among injecting drug users with chronic HCV infection in Greece. *Eur J Intern Med*, 2005; 16: 7: 496-500

BACKGROUND: The aim of this study was to evaluate the serological status of HBV infection and liver histology in chronic HCV-infected injecting drug users (IDUs) and to correlate them with the possible time of infection and the principal HCV genotype. METHODS: Some 130 prior IDUs with chronic HCV infection were consecutively evaluated for the serological status of HBV infection. Fifty-eight (44.62%) reported intravenous drug use beginning before 1992 (group A) and 72 (55.38%) after 1992 (group B). HCV genotyping was available in 86 patients (PCR). Liver biopsy was performed in 48 patients (Ishak scoring system). There was no available data about alcohol consumption in the study population. Statistical analysis was based on the t-test and the chi(2) test ($p < 0.05$). RESULTS: Some 82.8% of group A patients had previous HBV infection, whereas only 22.2% of group B patients did ($p < 0.001$). Among group A patients, 10.3% were HBV-seronegative whereas 61.1% of group B patients were ($p < 0.001$). Only 3.4% of group A patients were HBV-vaccinated compared to 16.7% in group B ($p = 0.016$). HCV genotype was not associated with HBV serological status. No significant differences were detected in age, sex, possible time of infection, HBV serological status, or HCV genotype among those with higher vs. lower total grading scores. Seventy-five percent of patients had mild or no detectable fibrosis unrelated to the possible period of infection, the HBV serological status, and the HCV genotype. CONCLUSIONS: The serological profile of HBV infection is changing among Greek chronic HCV-infected IDUs, while the percentages of successfully HBV-vaccinated IDUs are relatively

low. Severe liver disease is an uncommon finding in these patients, irrespective of the possible time of infection, the HBV serological status, and the HCV genotype.

I. S. Elefsiniotis, I. Glynou, I. Magaziotou, K. D. Pantazis, N. V. Fotos, H. Brokalaki, H. Kada and G. Saroglou. HBeAg negative serological status and low viral replication levels characterize chronic hepatitis B virus-infected women at reproductive age in Greece: a one-year prospective single center study. *World J Gastroenterol*, 2005; 11: 31: 4879-82

AIM: To evaluate the seroprevalence of hepatitis B surface antigen (HBsAg) in 13 581 women at reproductive age and the hepatitis B e antigen (HBeAg)/anti-HBe status as well as serum hepatitis B virus (HBV)-DNA levels in a subgroup of HBsAg(+) pregnant women at labor in Greece. METHODS: Serological markers were detected using enzyme immunoassays. Serum HBV-DNA was determined by a sensitive quantitative PCR assay. Statistical analysis of data was based on parametric methodology. RESULTS: Overall, 1.156% of women were HBsAg(+) and the majority of them (71.3%) were Albanian. The prevalence of HBsAg was 5.1% in Albanian women, 4.2% in Asian women and 1.14% in women from Eastern European countries. The prevalence of HBsAg in African (0.36%) and Greek women (0.29%) was very low. Only 4.45% of HBsAg(+) women were also HBeAg(+) whereas the vast majority of them were HBeAg(-)/anti-HBe(+). Undetectable levels of viremia (<200 copies/mL) were observed in 32.26% of pregnant women at labor and 29.03% exhibited extremely low levels of viral replication (<400 copies/mL). Only two pregnant women exhibited extremely high serum HBV-DNA levels (>10 000 000 copies/mL), whereas 32.26% exhibited HBV-DNA levels between 1 500 and 40 000 copies/mL. CONCLUSION: The overall prevalence of HBsAg is relatively low among women at reproductive age in Greece but is higher enough among specific populations. The HBeAg(-)/anti-HBe(+) serological status and the extremely low or even undetectable viral replicative status in the majority of HBsAg(+) women of our study population, suggest that only a small proportion of HBsAg(+) women in Greece exhibit a high risk for vertical transmission of the infection.

G. Dounias, E. Kypraiou, G. Rachiotis, E. Tsovili and S. Kostopoulos. Prevalence of hepatitis B virus markers in municipal solid waste workers in Keratsini (Greece). *Occup Med (Lond)*, 2005; 55: 1: 60-3

AIM: To evaluate the prevalence of hepatitis B virus (HBV) markers among municipal solid waste workers (MSWWs) in Keratsini (Greece). METHODS: We assessed in a cross-sectional study the prevalence of biological markers of HBV infection (HbsAg, anti-Hbc, anti-Hbs) and their association with exposure to waste and other socio-demographic factors in 166 municipal employees in Keratsini (Greece). RESULTS: The prevalence of anti-Hbc (+) did differ significantly between exposed and non-exposed employees to waste. Older employees had a significantly higher prevalence of anti-Hbc (+). MSWWs who were anti-Hbc (+) were less educated than non-exposed employees. Logistic regression analysis has shown that the exposure to waste and age were independently associated with the anti-Hbc positivity. CONCLUSION: Occupational exposure to waste is possibly associated with the acquisition of HBV infection. Immunization of MSWWs should be considered to reduce the risk of HBV infection.

V. Sypsa, G. Touloumi, N. C. Tassopoulos, I. Ketikoglou, I. Vafiadis, G. Hatzis, D. Tsantoulas, E. Akriviadis, J. Delladetsima, M. Demonakou and A. Hatzakis. Reconstructing and predicting the hepatitis C virus epidemic in Greece: increasing trends of cirrhosis and hepatocellular carcinoma despite the decline in incidence of HCV infection. *J Viral Hepat*, 2004; 11: 4: 366-74

In this study, a comprehensive methodology for modelling the hepatitis C virus (HCV) epidemic is proposed to predict the future disease burden and assess whether the recent decline in the incidence of HCV may affect the future occurrence of cirrhosis and hepatocellular carcinoma (HCC) cases. Using the prevalence of HCV, the distribution of chronic hepatitis C (CHC) patients within the various transmission groups and their infection-onset times, it was possible to reconstruct the incident infections per year in the past that progressed to CHC in Greece. The natural history of the disease was simulated in subcohorts of newly infected subjects using transition probabilities derived either empirically between fibrosis stages 0-4 or from literature review. Annual estimates of the incidence and prevalence of CHC by fibrosis stage, HCC and mortality in Greece were obtained up to 2030. HCV incidence peaked in the late 1980s at five new infections/10,000 person-years. Under the assumption of 20-100% decline in HCV incidence after 1990, the cumulative number of incident cirrhosis and HCC cases from 2002-2030 was projected to be lower by 9.6-48.2% and 5.9-29.5%, respectively, than that estimated under the assumption of no decline. However, the prevalent cirrhotic/HCC cases and HCV-related deaths are predicted to decline in the next 30 years only under the assumption of complete elimination of new HCV infections after 1990. Despite the progress in the reduction of HCV transmission, primary prevention does not seem adequate to reverse the rise in the incidence of cirrhosis and HCC.

I. Stefanidis, E. K. Zervou, C. Rizos, C. Syrganis, E. Patsidis, G. Kyriakopoulos, L. Sdrakas, N. Tsianas, E. I. Rigopoulou, V. Liakopoulos and G. N. Dalekos. Hepatitis E virus antibodies in hemodialysis patients: an epidemiological survey in central Greece. *Int J Artif Organs*, 2004; 27: 10: 842-7

Hepatitis E virus (HEV) is the causative agent for enteric non-A, non-B hepatitis. Transmission is mainly via the fecal-oral route but the possibility of an additional parenteric transmission has been raised. Patients undergoing chronic hemodialysis (HD) have an increased risk of exposure to blood transmitted agents. Previous studies concerning prevalence of antibodies to HEV (anti-HEV) among HD patients gave conflicting results. The aim of the study presented here was to determine the prevalence of anti-HEV among HD patients of a well-defined semi-rural region in central Greece (Thessalia region). All patients (n=351, 234 males, mean age 60+/-14 years) who were being treated in the HD units of central Greece (n=5) during 2001 were tested for anti-HEV antibody. Two commercially available specific solid-phase enzyme-linked immunoassays were applied for anti-HEV detection. Hepatitis B virus markers, antibodies to HCV, HIV and HTLV were also screened in all patients by commercially available assays. Serum aminotransferase (AST, ALT) levels were measured by spectrophotometry. 17 anti-HEV-positive patients were found and prevalence was 4.8%, varying from 1.8 - 9.8% in the various HD units. Prevalence of HBsAg and anti-HCV was 5.7% (2.9 - 15%) and 23.6% (11.5 - 36.2%) respectively. The anti-HEV prevalence was increased compared to healthy blood donors in Greece (0.26%, p < 0.01). The highest prevalence of anti-HEV was seen at the HD unit of the General Hospital of Karditsa (9.8%). Risk factors for anti-HEV antibody were not identified: no association was found between anti-HEV positivity and age or sex, duration of HD, hepatitis B or C virus infection markers, previously elevated aminotransferase levels or history of transfusion. Our investigation of HEV infection in the cohort of HD patients in central Greece showed that the

prevalence of anti-HEV was greater than in healthy blood donors. There was no association to blood borne infections (HBV, HCV). The high prevalence of anti-HEV we found in one HD unit was probably related to a local infection in the past. However, long-term prospective studies are needed in an attempt to identify whether intra-unit factors are also responsible for the increased prevalence of serologic markers of HEV infection among HD patients.

D. Siagris, M. Christofidou, A. Tsamandas, A. Lekkou, K. Thomopoulos and C. Labropoulou-Karatza. Cryoglobulinemia and progression of fibrosis in chronic HCV infection: cause or effect? *J Infect*, 2004; 49: 3: 236-41

OBJECTIVES: Mixed cryoglobulinemia (MC) is the most common extrahepatic manifestation of HCV infection. The aim of this study is to determine the prevalence of MC in HCV infected Greek patients and to identify if it is associated with liver histology or the mode of HCV transmission. **METHODS:** One hundred and twenty-six patients with chronic HCV infection were evaluated for the presence of serum cryoglobulins, autoantibodies and viral markers. One hundred and eighteen of them underwent liver biopsy and each specimen was evaluated according to the grading and staging system described by Ishak et al. **RESULTS:** Cryoglobulins were detected in 37/126 (29.4%) HCV patients and cryocrit values ranged between 0.5 and 6.5%. Only two patients presented clear clinical manifestations of MC. In patients with MC, a higher grading (6.40+/-2.06 vs. 5.27+/-2.55, p=0.013) and staging score (3.71+/-1.45 vs. 2.83+/-1.84, p=0.007) was noted in liver biopsy compared to those without MC. Logistic regression analysis identified staging score (OR, 1.33; CI, 1.06-1.66, p=0.015) as the only independent variable associated with cryoglobulinemia. Correlation between the presence of cryoglobulins and the mode of HCV transmission was not found. **CONCLUSIONS:** Greek patients with chronic HCV infection have high prevalence of cryoglobulinemia. A clear association between the presence of serum cryoglobulins and staging score of chronic hepatitis was found, with no difference in patients' age or the duration of infection. It is possible that cryoglobulinemia results in more rapid hepatic fibrosis in HCV infected patients.

P. Panagopoulos, A. Economou, A. Kasimi, P. Spyropoulou, N. Kanellopoulos, L. Dadiotis and E. Salamalekis. Prevalence of hepatitis B and C in the maternity department of a Greek district hospital. *J Matern Fetal Neonatal Med*, 2004; 16: 2: 106-10

OBJECTIVE: To define the prevalence of infection with hepatitis B virus (HBV) and hepatitis C virus (HCV), and the modifications observed during the last 8 years, amongst parturients who gave birth in our department. **DESIGN:** This was a retrospective study. **PATIENTS:** The 5497 parturients who gave birth in our department between October 1994 and September 2002. **RESULTS:** On average, 3.87% (213) of the pregnant women tested positive for hepatitis B surface antigen; 2.90% amongst pregnant Greek women and 4.67% amongst pregnant immigrant women. Among all pregnant women, 0.80% (44) tested positive for antibodies against HCV; 0.16% amongst Greek women and 1.33% amongst immigrant women. **CONCLUSIONS:** HBV prevalence in pregnant women did not seem to be affected by the increase of immigrants in our obstetric population over the course of time. HCV prevalence in the pregnant women, however, did seem to follow the increase of immigrants in our obstetric population. Economic and security issues unfortunately deprive some neonates, born to mothers with HBV infection, from the use of hepatitis B immunoglobulin.

E. Giannoulis, T. Economopoulos, K. Mandraveli, K. Giannoulis, C. Nikolaides, E. Zervou, E. Papageorgiou, D. Zoulas, A. Tourkantonis, G. Giannopoulos and G. Fountzilias. The prevalence of hepatitis C and hepatitis G virus infection in patients with B cell non-Hodgkin lymphomas in Greece: a Hellenic Cooperative Oncology Group Study. *Acta Haematol*, 2004; 112: 4: 189-93

Our aim was to investigate the association between chronic hepatitis C virus (HCV) infection and B cell non-Hodgkin lymphoma (NHL) in the Greek population. We studied 120 patients (70 men and 50 women, mean age 59 years) diagnosed with NHL. One hundred and eight had B cell NHL (90%) and 12 had T cell NHL (10%). The presence of anti-HCV antibodies in patients and controls was investigated using the monoclonal enzymatic immunoassay (MEIA) method. The detection of HCV RNA and hepatitis G virus (HGV) RNA in patients with B cell NHL and anti-HCV-positive controls was performed using an RT-PCR technique. Anti-HCV antibodies were present in only 2 of the 108 patients with B cell NHL (1.9%), while the prevalence of HCV infection in the healthy population was 0.6%, and in patients with various solid tumors treated with chemotherapy, it was 0.99%. Ten of the 108 B cell NHL patients (9.26%) were diagnosed as HGV RNA positive, while the prevalence of HGV infection in 285 Greek blood donors was 0.7%. Our findings do not confirm a strong association between HCV infection and B cell NHL for Greek patients. The increased prevalence of HGV infection detected in patients with NHL could imply the potential participation of HGV in the pathogenesis of NHL.

S. P. Georgiadou, K. Zachou, E. Rigopoulou, C. Liaskos, P. Mina, F. Gerovasilis, E. Makri and G. N. Dalekos. Occult hepatitis B virus infection in Greek patients with chronic hepatitis C and in patients with diverse nonviral hepatic diseases. *J Viral Hepat*, 2004; 11: 4: 358-65

Occult hepatitis B virus (HBV) infection has been reported in patients with chronic hepatitis C who are negative for HBV surface antigen (HBsAg). However, the significance of 'silent' HBV in hepatitis C virus (HCV) infection is unknown. We investigated 540 subjects for the presence of occult HBV in Greek HCV patients, patients with nonviral liver diseases and healthy donors in an attempt to determine the frequency and importance of this phenomenon. One hundred and eighty-seven anti-HCV(+)/HBsAg(-) patients' sera were investigated for the presence of HBV-DNA by polymerase chain reaction. Two hundred and eighty-two selected blood donors (positive for antibodies to HBV core antigen) and 71 patients with various nonviral hepatic diseases consisted the control groups [both controls were anti-HCV(-)/HBsAg(-)]. HBV-DNA was detected in 26.2% of HCV-infected patients vs 8.5% of patients with nonviral diseases ($P = 0.003$) and 0/282 of donors ($P = 0.0000$). HBV-DNA was neither associated with HBV markers, nor with the clinical status of HCV and nonHCV patients. Neither epidemiological, histologic and virologic data nor the response to therapy were associated with the HBV-DNA detection. Hence one quarter of HCV-infected patients had occult HBV infection. Similar findings were not found in both control groups. Occult HBV infection in Greek patients with chronic hepatitis C does not seem to modify the progression of chronic liver disease. Further studies of longer duration are needed in order to clarify the role of 'silent' HBV infection in HCV-infected patients.

I. S. Elefsiniotis, C. Mpotsi, V. Paparizos and K. D. Pantazis. Long-term follow-up of HIV/HBV coinfecting patients from a Greek center. *J Clin Virol*, 2004; 30: 3: 280-1

M. Arvanitidou, P. Mamassi and A. Vayona. Epidemiological evidence for vaccinating wastewater treatment plant workers against hepatitis A and hepatitis B virus. *European Journal of Epidemiology*, 2004; 19: 3: 259-2

Exposed to sewage workers of a wastewater treatment plant and a control group in Thessaloniki, Greece, were examined for antibodies against hepatitis A (anti-HAV) and hepatitis B virus (HBV) infection markers. The main objective of this study was to investigate for epidemiological evidence so as to recommend vaccination of the occupationally exposed workers against these viral infections. Antibodies against hepatitis A virus were detected in 65.7% of the wastewater treatment plant workers and in 32.6% of the control group. The prevalence of anti-HAV was significantly higher in less educated persons and was increasing with age ($p < 0.001$), whereas in logistic regression analysis the adjusted seroprevalence of wastewater treatment plant workers was 3.5 times higher ($p < 0.01$) than the control population. Serologic evidence of past HBV infection was observed in 32.4% of the exposed to sewage population and in 5.8% of the controls. Multivariate analysis showed that variables significantly and independently related to previous HBV infection was occupational exposure to sewage (OR: 5.81; 95% CI: 2.07-16.29) and age over 40 years old (OR: 4.49; 95% CI: 1.51-13.33). These results support the vaccination policy of young and sensitive to hepatitis A and B virus wastewater treatment plant workers in our region.

E. K. Zervou, D. S. Boumba, C. Liaskos, S. Georgiadou, E. V. Tsianos and G. N. Dalekos. Low prevalence of HCV, HIV, and HTLV-I/II infection markers in northwestern Greece: results of a 3-year prospective donor study (1995-1997). *Eur J Intern Med*, 2003; 14: 1: 39-44

Background: The risk of infection with transfusion-transmitted viruses has been reduced remarkably. A zero-risk blood supply, however, remains a popular goal. A 3-year prospective donor study was conducted in the Epirus region of Greece to determine the prevalence of human immunodeficiency virus (HIV), human T-lymphotropic virus (HTLV), hepatitis B virus, and hepatitis C virus (HCV). Herein, we report the prevalence of HIV, HTLV, and HCV infection markers in this area. Methodology: Between January 1, 1995 and December 31, 1997, 6696 donors were investigated for the presence of anti-HIV, anti-HTLV, and anti-HCV antibodies using standard enzyme immunoassays (EIA). Every sample with anti-HCV reactivity by third-generation EIA was further investigated using a third-generation recombinant immunoblot assay (RIBA 3.0) and HCV-RNA by a combination of polymerase chain reaction (PCR) and DNA EIA. Results: None of the donors tested positive for anti-HIV or anti-HTLV antibodies. In contrast, anti-HCV was detected in 41 donors (0.61%). Using a RIBA 3.0 test, eight donors tested positive and eight had indeterminate results, while 25 tested negative. Seven of the eight donors with both EIA and RIBA 3.0 reactivity had increased levels of aminotransferases and detectable serum HCV-RNA. The remaining 34 donors had repeatedly normal aminotransferases and three times negative HCV-RNA. Liver biopsy was performed in anti-HCV/HCV-RNA-positive donors (7/41). The lesions were compatible with chronic hepatitis C in all of them. Conclusion: A zero prevalence of HIV and HTLV infection markers was found. Although the number of annual donations in this study was relatively low, the negative data for HIV and HTLV clearly indicate that rates of these infections are low in our region and that infected donors will be seen infrequently. HCV infection in blood donors remains very low in our region and is similar to the data reported in other industrialized countries. In fact, the prevalence of definite HCV infection seems to be very low (7/6696; 0.1%). However, a significant proportion of anti-HCV-reactive donors by third-generation EIA (33/41) had indeterminate or negative results by the RIBA 3.0. The latter donors were repeatedly negative for HCV-

RNA. This finding may indicate that some donors tested false-positive for anti-HCV, although the possibility of true HCV infection contracted in the distant past cannot be excluded. In our opinion, close attention to mandatory principles of transfusion medicine, along with the screening of plasma donors using nucleic acid amplification technology, are the only methods that can further ensure the safety of our blood supply.

A. Roussos, C. Goritsas, T. Pappas, M. Spanaki, P. Papadaki and A. Ferti. Prevalence of hepatitis B and C markers among refugees in Athens. *World J Gastroenterol*, 2003; 9: 5: 993-5

AIM: To assess the prevalence of hepatitis B and C serological markers in a population of refugees living in Athens. METHODS: One hundred and thirty refugees (81 males and 49 females, mean age +/-SD: 31.7+/-8 years) were included in the study. The hepatitis B virus surface antigen (HBsAg), the hepatitis B virus core antibody (anti-HBc) and the hepatitis C virus antibody (anti-HCV) were detected using a third-generation immunoassay. RESULTS: Twenty individuals (15.4 %) were HBsAg positive and 69 (53.1 %) were anti-HBc positive. The prevalence of HBsAg and anti-HBc was higher among refugees from Albania and Asia (statistical significant difference, $P < 0.008$ and $P < 0.001$ respectively). The prevalence of these markers was found irrelevant to age or sex. Anti-HCV was detected in the serum of 3 individuals (2.3 %). No differences among age, sex or ethnicity regarding anti-HCV prevalence were found. CONCLUSION: It can be concluded that refugees living in Athens are an immigrant population characterized by a high incidence of HBV infection. The prevalence of HBV markers is higher among refugees from Albania and Asia. It is therefore believed that the adherence to general precautions and the initiation of HBV vaccination programs will be necessary in the future, especially in these communities. Although the prevalence of HCV infection seems to be relatively low, extended epidemiological surveys are needed to provide valid results.

I. Raptis, J. Koskinas, T. Emmanouil and S. Hadziyannis. Changing relative roles of hepatitis B and C viruses in the aetiology of hepatocellular carcinoma in Greece. Epidemiological and clinical observations. *J Viral Hepat*, 2003; 10: 6: 450-4

Chronic infection with hepatitis B virus (HBV) has been reported in two-thirds of cases of hepatocellular carcinoma (HCC) in Greece from 1973 to 1995, while chronic hepatitis C virus (HCV) infection in 10% of them. We studied the roles of HBV and HCV in HCC in Greece between 1996 and 2000 compared with the past, and possible differences in clinical and laboratory characteristics of HBV- and HCV-related HCC. Complete clinical and laboratory data from 306 patients with HCC, diagnosed from January 1996 to December 2000, were analyzed. Chronic HBV and HCV infection were detected in 52.3 and 21.6% of the patients, respectively. The ratio of HBV- to HCV-related HCC was 2.42. Compared with the data prior to 1996, there was a 101.8% increase in the relative frequency of HCV ($P < 0.0001$) and an 11.8% decrease in that of HBV ($P = 0.033$), with a -56.3% change in the ratio of HBV- to HCV-related HCC cases. Statistically significant differences in the male/female ratio, median age and frequency of multifocal lesions were found in HBV- vs HCV-related HCC. Although HBV still represents the major aetiological factor of HCC in Greece, its role has significantly decreased in the last 5 years, while a more significant increase has occurred in HCV-related HCC. The two aetiological types of HCC differ in Greece in demographic, epidemiological and other features.

E. E. Mazokopakis, E. S. Ganotakis and C. D. Lionis. The Greek armed forces are vulnerable to HAV infection. *Mil Med*, 2003; 168: 5: V

N. P. Lekka, C. Paschalis, A. Papadourakis and S. Beratis. Characteristics of inmates receiving prescribed benzodiazepines in a high-security Greek prison. *Compr Psychiatry*, 2003; 44: 5: 409-14

The aim of the current study was to investigate the characteristics of Greek inmates that were taking regularly benzodiazepines (BZDs) at therapeutic doses, in the high-security prison of Patras, Greece. Three hundred eighty-four prisoners were included in the study. BZD users (BUs, n = 192), compared with non-BZD users (NBUs, n = 192), were significantly more often unemployed before imprisonment; were significantly more often single, divorced, or widowed; were significantly more often on remand; were taking in significantly greater proportions antidepressant and antipsychotic medications; had significantly more often a history of psychiatric hospitalization; and had significantly more often a history of illicit intravenous (IV) drug use. BUs were significantly more often positive on serum antibodies to hepatitis C (anti-HCV), and scored significantly higher on Hamilton's Rating Scale for Anxiety (HAM-A) and Zung's Self-Rating Depression Scale (SDS). Multivariable logistic regression analysis showed that the history of psychiatric hospitalization, history of illicit drug use, history of unemployment, symptoms of anxiety, and anti-HCV positivity were independently associated with BZD use in this prison. Medical and psychiatric interventions focusing on anxiety problems, depression, drug addiction, and HCV in this group of BUs are warranted.

C. A. Gogos, K. P. Fouka, G. Nikiforidis, K. Avgeridis, G. Sakellaropoulos, H. Bassaris, A. Maniatis and A. Skoutelis. Prevalence of hepatitis B and C virus infection in the general population and selected groups in South-Western Greece. *Eur J Epidemiol*, 2003; 18: 6: 551-7

Greece is a country of intermediate endemicity for hepatitis B and low endemicity for hepatitis C with a downward trend during the last years. In the present study we investigated the prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection in the region of South-Western Greece and tried to identify the most important risk factors of transmission. This is a unique epidemiological study, as it is the first community based study in the general population of Greece, with a methodological approach based on multi-staged random sampling. The prevalence of HBV infection seems to be decreasing with a 22.6% rate of HBV markers and a 2.1% rate of chronic HBV carriers. We found male sex, old age and intrafamilial exposure as the major independent risk factors of HBV transmission, while sexual contact, absence of condom prophylaxis and living in rural areas seem to have also a significant impact for HBV infection. No relation was found between HBV transmission and working in health care facilities, pre-existing hospital admissions and history of transfusion. The prevalence of anti-bodies to the HCV was found 0.5%, even lower than the rate reported in the Mediterranean region. Parenteral exposure was the main risk factor for the transmission of HCV infection.

O. Giotakos, P. Bourtsoukli, T. Paraskeyopoulou, P. Spandoni, S. Stasinou, D. Boulougouri and E. Spirakou. Prevalence and risk factors of HIV, hepatitis B and hepatitis C in a forensic population of rapists and child molesters. *Epidemiol Infect*, 2003; 130: 3: 497-500

The aim of the present study was to assess the prevalence as well as the possible risk factors of HIV, hepatitis B and hepatitis C, in 194 male prisoners who had been convicted for rape (n=105) or child molestation (n=89). HBsAg, HBeAg, anti-HBc, anti-HBs, anti-HCV and anti-HIV-1/2 were tested for. The participants also completed a standard sociodemographic questionnaire, indicating possible risk factors, the Barratt Impulsiveness Scale, and the life-time history of aggression. Anti-HIV antibodies were not found in any of the prisoners. HBsAg was found in 25 (13%), anti-HBc in 94 (49%), anti-HBs in 40 (21%) and anti-HCV in 13 (6.5%) subjects. Logistic regression analysis showed that anti-HCV positivity was associated with intravenous drug use (OR 20.7, 95% CI 1.1-4.9, P<0.001), while HBsAg positivity was associated separately with being foreign (OR 4.0, 95% CI 0.2-2.5, P<0.1), as well as with impulsiveness score (OR 1.06, 95% CI 0.01-0.11, P<0.02). The prevalence of HBV and HCV infection in this sex offender sample was highly increased in relation to the general population. Since it has been proved that sex offenders are a high-risk group for reoffending, monitoring their health is a necessary step towards prevention of sexually transmitted diseases being spread.

B. Petrunov, M. Kojouharova, P. Teoharov, I. Haidushka, P. Sotirova, M. Sredkova, I. Russev, G. Zacharakis, F. Tzara, N. Vafeiadis, J. Papathanasiou and K. Papoutselis. EU project interreg II: Seroepidemiology study on hepatitis C and B viral infections prevalence in Bulgaria and Northern Greece. *Journal of Hepatology*, 2002; 36: 138-9

E. K. Zervou, G. N. Dalekos, D. S. Boumba and E. V. Tsianos. Value of anti-HBc screening of blood donors for prevention of HBV infection: results of a 3-year prospective study in Northwestern Greece. *Transfusion*, 2001; 41: 5: 652-8

BACKGROUND: The risk of infection with transfusion-transmitted viruses has been reduced remarkably. However, a zero-risk blood supply remains a popular goal. Some authorities have introduced the screening for antibody to HBc (anti-HBc) as a surrogate test for the presence of several infectious agents. A 3-year prospective study was conducted in the Epirus region of Greece to determine the prevalence of several blood-borne viruses. One component of the study was the prevalence of HBV infection markers and the potential value of anti-HBc testing of donors in this area.

STUDY DESIGN AND METHODS: Between January 1, 1995, and December 31, 1997, some 6696 donors were investigated for the presence of HBV infection markers by standard EIAs. Every sample that tested HBsAg-negative but anti-HBc-reactive alone or in combination with either or both antibodies to HBV e antigen (anti-HBe) and low-titered antibodies to HBsAg (anti-HBs < 20 mIU/mL) was further investigated for the presence of HBV DNA by a combination of PGR and DNA EIA.

RESULTS: Of these 6696 donors, 15.8 percent tested positive for at least one serologic marker of HBV infection (HBsAg prevalence, 0.85%). Anti-HBc reactivity alone or in combination with either or both anti-HBe and low-titered anti-HBs was found in 282 donors (4.2%). None tested HBV-DNA positive. No transfusion-associated HBV infections were recorded in the recipients of the above 282 blood units.

CONCLUSION: A moderate prevalence of HBV infection markers was found. However, taking into account previous studies from this region, it appears that the HBsAg prevalence has

declined. In addition, the present study cannot recommend the introduction of anti-HBe screening as a surrogate marker of occult HBV infection. The adoption of this exclusion criterion in this region would result in unacceptably high rejection rates among otherwise healthy donors. The absence of any case of transfusion-associated HBV infection after the transfusion of all HBsAg-negative, anti-HBc-positive units appears to provide further support for the negative HBV DNA results. Before a consideration of screening donors, efforts must be focused on reducing the number of false-positive anti-HBe results.

V. Sypsa, E. Hadjipaschali and A. Hatzakis. Prevalence, risk factors and evaluation of a screening strategy for chronic hepatitis C and B virus infections in healthy company employees. *Eur J Epidemiol*, 2001; 17: 8: 721-8

A cross-sectional study was carried out in employees of 17 Greek companies with the aim of assessing the prevalence of hepatitis B (HBV) and hepatitis C (HCV) virus, identifying associated prognostic/risk factors and evaluating the effectiveness of a questionnaire as a pre-screening tool. All participants were asked to complete a questionnaire and a random sample of them was asked to provide a blood sample for hepatitis B core antibody (anti-HBc), hepatitis B surface antigen (HBsAg) and antibodies to hepatitis C (anti-HCV) testing. Individual questions or combinations of them were evaluated in terms of their ability to detect HBV or HCV(+) cases. Of 9085 eligible employees, 6074 (67%) completed the questionnaire. Of 990 samples obtained, 19.9% were anti-HBc(+), 2.6% HBsAg(+) and 0.5% anti-HCV(+). All anti-HCV(+) cases had multiple parenteral risk factors. Multiple logistic regression identified associations between anti-HBc and older age, family members with chronic hepatitis, job category and history of transfusion before 1992. HBsAg(+) was associated with older age and history of transfusion before 1992. None of the risk/prognostic factors had sufficient sensitivity and specificity for HBV but report of at least one risk factor identified all HCV(+) cases. Anti-HCV screening of those with at least two parenteral risk factors not only identified all anti-HCV(+) cases but also resulted in 86% decrease in the screening cost. Under the light of recent treatment advances, targeted questionnaire-based screening of asymptomatic people may prove to be a cost-effective way to face hepatitis C.

M. Raptopoulou-Gigi, E. Orphanou, T. H. Lalla, A. Lita and A. Garifallos. Prevalence of hepatitis C virus infection in a cohort of pregnant women in northern Greece and transmission of HCV from mother to child. *Eur J Epidemiol*, 2001; 17: 3: 263-6

The prevalence of hepatitis C virus (HCV) infection and the mother-to-child transmission of HCV were studied in 2408 pregnant women. Positive antiHCV were detected in 47 women (1.95%), 21 of whom (44.7%) were HCVRNA(+), but only seven had abnormal aminotransferases. Three/21 HCVRNA(+) women had an abortion. We lost contact with other 10 women. Thirty-four babies were tested for antiHCV, HCVRNA and levels of aminotransferases at birth and at the age of 6 and 12 months. AntiHCV were detectable in all babies at birth and these maternally acquired antibodies disappeared by the age of 12 months in all but two of who were infected with HCV. HCVRNA was detected at birth in one (6.25%) baby born out of 16 HCVRNA(+) mothers and this baby also had abnormal aminotransferases. However, HCVRNA was undetectable and aminotransferases returned to normal levels by the age of 6 months. In another baby born also from an HCVRNA(+) mother, the HCVRNA was detected for the first time at the age of 12 months. The HCV genotype from both babies was the same as their mother's. These results show that (a) the high prevalence in the group of pregnant women studied can possibly be attributed to the fact that 311/2408 (12.91%) of them came from the former eastern countries, where

disposable syringes were not used but lately or were ex-drug addicts and (b) there is a low risk of perinatal mother-to-child transmission of HCV and this risk is related to the presence of HCVRNA in the carrier mother.

M. Koulentaki, M. Ergazaki, J. Moschandrea, S. Spanoudakis, N. Tzagarakis, P. E. Drandakis, D. A. Spandidos and E. A. Kouroumalis. Prevalence of hepatitis B and C markers in high-risk hospitalised patients in Crete: a five-year observational study. *Bmc Public Health*, 2001; 1: -

Background: So far the prevalence of viral hepatitis infection in hospitalized patients has not been extensively studied. Therefore we conducted the present five-year observational study to evaluate the prevalence of HBV and HCV infection in high-risk hospitalized patients of Crete, the largest Greek island, Due to the homogeneous population, epidemiological studies can be accurately done.

Methods: The study was carried out in two out of four District General Hospitals, and in the University Hospital of the island. Markers for HBV and HCV were studied and statistically evaluated according to age, sex and geographical area, in a well-defined hospitalized population.

Results: The total prevalence of HBsAg and anti-HCV in the three prefectures during the five-year study is 2.66% and 4.75% respectively. Overall the relative risks were higher in males than females for each hepatitis marker ($p < 0.001$). Higher prevalence of HBcAb was found in the 41-60 years age group for both sexes (males 36.17%, females 27.38%). Peak HBsAg prevalence was found in the age group of 21-40 and 41-60 years for males (5.4%) and females (3.09%) respectively. Anti-HCV prevalence increases with age reaching the highest prevalence in the age group of 41-60 years for males (7.19%) and in the 61-90 years age group for females (7.16%). For both sexes significant differences between the three locations were identified. For HBsAg a higher prevalence in Heraklion (3.96%) compared to Chania (2.30%, males: $p < 0.0001$, females: $p < 0.05$) and Rethymnon (1.45%, males: $p < 0.01$, females: $p < 0.0001$) was detected. For HCV a significantly higher prevalence in Heraklion (6.54%) compared to Chania (2.39%, males: $p < 0.001$, females: $p < 0.001$) but not in Rethymnon (5.15%, NS). A lower prevalence rate of HBcAb in Heraklion compared to Chania (20.07% versus 23.05%, males: $p < 0.001$, females: $p < 0.001$) was found.

Conclusions: These results were possibly overestimated, but nevertheless reflect the situation of the general population within the island as shown by our previous publications in other study groups. Moreover they contribute to the mapping of viral hepatitis prevalence in a geographical area of Southern Europe and may be helpful in planning public health interventional strategies.

A. Katsoulidou, D. Paraskevis, C. G. Anastassopoulou, S. E. Chryssou, V. Sypsa, J. Boletis, M. Malliori, A. Karafoulidou, N. C. Tassopoulos and A. Hatzakis. Prevalence and genotypic distribution of TT virus in Athens, Greece. *J Med Virol*, 2001; 65: 2: 423-9

The prevalence of TT virus (TTV) infection in various population groups from Athens, Greece, was assessed by the polymerase chain reaction (PCR) using two primer sets from distinct regions of the genome: the conventional set derived from the open reading frame-1 (ORF-1) and the new, highly sensitive set targeting the region that includes the TATA signal localized upstream of ORF-2. Based on both primer sets, TTV DNA was detected in 42/50 (84.0%) healthy individuals, 42/50 (84.0%) chronic hepatitis C patients, 31/39 (79.5%) acute non-A-E hepatitis patients (group I), 14/16 (87.5%) renal failure patients with acute non-A-E hepatitis (group II), 47/50 (94.0%) intravenous drug users (IVDU), 36/50 (72.0%)

hemophiliacs, and 21/31 (67.7%) hemodialysis patients. The presence of TTV was not associated with any particular risk group, and no differences were observed in relation to demographic, biochemical and virological characteristics between TTV DNA-positive and -negative patients. TTV did not seem to have a profound effect on the course of chronic C or acute non-A-E hepatitis either. Phylogenetic analysis revealed that TTV strains circulating in the greater metropolitan area of Athens belong not only to the G1 and G2 genotypes that are encountered worldwide, but also to G3 and to G5 that are found mainly in Europe and Asia, respectively. Further studies will shed light on the role of this highly prevalent virus.

E. Mazokopakis, J. Vlachonikolis, A. Philalithis and C. Lionis. Seroprevalence of hepatitis A, B and C markers in Greek warship personnel. *European Journal of Epidemiology*, 2000; 16: 11: 1069-72

A seroepidemiological study was conducted to assess the seroprevalence of hepatitis A, B and C markers in 285 males (mean age: 24.4 +/- 4.4 years) aboard a Greek warship. Two hundred and sixty three serum samples were tested. None was found to be positive for HAV antibodies, three persons (1.1%) were positive for HBsAg, four persons (1.5%) were positive for anti-HBc and one person (0.4%) was positive for anti-HCV. Forty-five persons (17.1%) had developed titres anti-HBs > 10 IU/L. The establishment of a vaccination policy against hepatitis A among warship personnel is strongly recommended.

C. Lionis, I. G. Vlachonikolis, S. Skliros, A. Symeonidis, B. P. Merkouris and E. Kouroumalis. Do undefined sources of hepatitis C transmission exist? The Greek study in General Practice. *J Viral Hepat*, 2000; 7: 3: 218-24

A seroepidemiological study was carried out in 15 primary health care (PHC) centres in rural Greece to determine the prevalence of hepatitis C virus (HCV) in the surgeries of Greek General Practitioners (GPs) and to further clarify the transmission of hepatitis C in Greece. Serum samples were obtained from 1961 subjects (1259 females) aged ≥ 15 years, who visited GP surgeries between July 1996 and February 1997 in 15 PHC centres located in three large Greek regions (Macedonia, Attika and Crete). Subjects who participated in the study fulfilled the following criteria: history of blood transfusion; hospital admission of > 7 days' duration without surgical or other intervention; use of intravenous drugs (current or previous); or women with a history of medical or paramedical abortion. Nearly 65% (1263 subjects) of the participants in this study reported hospital admission with a length of stay > 7 days. Antibodies to HCV (anti-HCV) were found in 67 participants (3.5%), 41 of whom were females and 44 of whom were aged ≥ 61 years. The highest prevalence (4.8%) of anti-HCV was found in Crete, and differences among the Greek regions were statistically significant ($P < 0.05$). Multivariate statistical analysis showed that in addition to regional differences, the following variables had a statistically significant effect on the prevalence of anti-HCV: history of dental surgery; use of intravenous drugs; hospital admission for > 7 days; and the high consumption of alcoholic drinks. Hence there is a significant variability in the prevalence of hepatitis C in well-defined PHC areas of Greece. Several risk factors for acquiring HCV infection have been identified. Screening for HCV risk factors may enable Greek GPs to identify HCV-infected patients.

H. E. Kuper, A. Tzonou, E. Kaklamani, S. Hadziyannis, N. Tasopoulos, P. Lagiou, D. Trichopoulos and S. Stuver. Hepatitis B and C viruses in the etiology of hepatocellular carcinoma; a study in Greece using third-generation assays. *Cancer Causes Control*, 2000; 11: 2: 171-5

OBJECTIVES: The purpose of this study was to describe the role of hepatitis B virus (HBV) and hepatitis C virus (HCV) in the etiology of hepatocellular carcinoma (HCC). **METHODS:** During a 4-year period from January 1995 to December 1998, blood samples and questionnaire data were obtained from 333 incident cases of HCC from Athens, Greece, as well as from patients in two control groups, also from Athens. Controls were 272 metastatic liver cancer (MLC) patients and 360 patients hospitalized for injuries or eye, ear, nose or throat conditions. Coded sera were tested for hepatitis B surface antigen (HBsAg) and antibodies to hepatitis C virus (anti-HCV) by third-generation enzyme immunoassays. **RESULTS:** The odds ratios (with 95% confidence intervals) in logistic regression modeling comparing the HCC cases to the combined control series were 48.8 (30.5-78.3) for the presence of HBsAg and 23.2 (11.4-47.3) for the presence of anti-HCV. The odds ratio for concurrent infection with HBV and HCV was 46.2 (9.9-216.6) compared to infection with neither virus. **CONCLUSIONS:** Although HBV and HCV are both important causes of HCC in this study population the data do not suggest, neither do they conclusively refute, a super-additive interaction between the two infections in the development of this malignancy. In this population, 58% of HCC cases can be attributed to HBV, 12% to HCV, and 3% to dual infection with these viruses.

H. Kuper, C. Hsieh, S. O. Stuver, L. A. Mucci, A. Tzonou, X. Zavitsanos, P. Lagiou and D. Trichopoulos. Birth order, as a proxy for age at infection, in the etiology of hepatocellular carcinoma. *Epidemiology*, 2000; 11: 6: 680-3

First-born and second-born children are exposed to common infections after enrollment at school, whereas later-born children are exposed to these infections earlier through their older siblings. We have evaluated whether birth order is a risk factor for hepatitis B virus (HBV)-related, hepatitis C virus (HCV)-related, and apparently virus-unrelated hepatocellular carcinoma (HCC) in a large case-control study that included 333 HCC cases and 632 controls. In comparison with controls who were carriers of hepatitis B surface antigen (HBsAg), HBsAg-positive HCC cases were more likely to have been later-born children (odds ratio per increase in birth order = 2.0; 95% confidence interval = 1.2-3.6). There was no such evidence for anti-HCV-positive cases compared with anti-HCV-positive controls or for virus-negative HCC cases compared with virus-negative controls. We conclude that early infection with HBV increases the risk of HBV carriers to develop HCC, over and beyond its role in facilitating the establishment of a carrier state.

C. Goritsas, I. Plerou, S. Agaliotis, R. Spinthaki, K. Mimidis, D. Velissaris, N. Lazarou and C. Labropoulou-Karatza. HCV infection in the general population of a Greek island: prevalence and risk factors. *Hepatogastroenterology*, 2000; 47: 33: 782-5

BACKGROUND/AIMS: Although HCV seroprevalence in blood donors in Greece is low (0.2-0.4%) epidemiologic characteristics of HCV infection in the general population have not been studied enough. The objective of this study was to examine the seroprevalence of HCV infection and associated risk factors in the general population of Zakynthos, a Greek island with a well-defined mixed (urban and rural) population. **METHODOLOGY:** A household health survey was carried out in a randomly selected sample of 718 adults. A questionnaire was completed and a blood sample was obtained from all participants. Serum samples were

tested for anti-HCV antibodies by third generation enzyme-linked immunosorbent assay and supplemental test. The influence of sociodemographic characteristics and possible associated risk factors on the HCV seroprevalence was investigated by logistic regression analysis. RESULTS: The overall anti-HCV prevalence was 1.25%. A well-defined rural area with a significant higher prevalence (6.8% vs. 0.62%; $P < 0.001$) was identified. There was a trend of increasing prevalence with age, with a significant difference ($P < 0.027$) between the age groups 15-44 (0%) and over 45 (2.15%). The logistic regression analysis confirmed a significant association between anti-HCV positivity and: increasing age ($P < 0.001$), history of blood transfusion (0.0001), intramuscular injections ($P < 0.04$). CONCLUSIONS: The results of this field-survey in a well-defined general population, indicates that HCV seroprevalence (1.25%) is much higher than that of blood donors in the same area. The increasing prevalence with age and the association with parenteral exposure indicates that HCV infection can mainly be attributed to parenteral techniques in the past. The identification of a concrete rural area with particularly high seroprevalence needs further study of the whole population of the area.

A. Dimitrakopoulos, A. Takou, A. Haida, S. Molangeli, A. Gialeraki and T. Kordossis. The prevalence of hepatitis B and C in HIV-positive Greek patients: relationship to survival of deceased AIDS patients. *J Infect*, 2000; 40: 2: 127-31

OBJECTIVES: To determine the prevalence of hepatitis viruses B (HBV) and C (HCV) co-infections in HIV-infected patients and the overall impact of these co-infections on deceased AIDS patients survival. METHODS: One hundred and eighty-one patients (159 males, 22 females) infected with HIV, attending an academic AIDS unit in Athens, Greece, constituted the study population. The study population consisted of 124 homo/bisexual men, 34 heterosexuals, 12 intravenous drug users (IDU) and 11 blood transfusion recipients. Virological markers tested for HBV infection included HBsAg, anti-HBs and total anti-HBc by enzyme-linked immunoassays. Detection of HCV antibodies was carried out by third generation enzyme-linked immunoassay, and repeatedly positive samples were further tested by a supplemental enzyme-linked immunoassay; only sera reactive by both methods were considered to be HCV-positive. RESULTS: The prevalence of HBV markers was 67.4%: 71.8% in homo/bisexuals, 35.3% in heterosexuals, 91.7% in IDUs and 90.9% in blood transfusion recipients ($P = 0.00004$). The prevalence of HCV antibodies was 13.8%: 8.1% in homo/bisexuals, 8.8% in heterosexuals, 58.3% in IDU and 45.5% in blood transfusion recipients ($P < 0.000001$). The prevalence of HCV antibodies was not significantly higher in homo/bisexuals than in heterosexuals ($P = 0.8$). Coinfection with HBV or HCV, or both, did not influence the survival of deceased AIDS patients ($n = 73$). CONCLUSIONS: HBV infection was equally prevalent among homo/bisexuals and IDU with HIV infection, whereas HCV infection was more prevalent in IDU than in homo/bisexuals with HIV infection. The prevalence of HCV infection was equal among heterosexuals and homo/bisexuals, indicating that if sexual transmission of HCV occurs, homo/bisexuals are not at greater risk than heterosexuals. Finally, the survival of deceased AIDS patients was not affected by the presence of HBV and HCV co-infections.

G. N. Dalekos, K. G. Kistis, D. S. Boumba, P. Voulgari, E. K. Zervou, A. A. Drosos and E. V. Tsianos. Increased incidence of anti-cardiolipin antibodies in patients with hepatitis C is not associated with aetiopathogenetic link to anti-phospholipid syndrome. *Eur J Gastroenterol Hepatol*, 2000; 12: 1: 67-74

OBJECTIVE: Chronic infection with hepatitis C virus (HCV) has been found to be associated with various diseases known as extra-hepatic manifestations of HCV. Recently, HCV has been implicated as a cause of the antiphospholipid syndrome (APLS). We conducted a study in a well-characterized area for epidemiological and prospective studies in the north-western part of Greece in order to address whether an aetiopathogenesis exists between HCV and APLS. **DESIGN:** Seventy-five patients with chronic hepatitis C were investigated for the presence of anti-cardiolipin antibodies (anti-CL) and for a past medical history supportive to the diagnosis of APLS. In addition, 24 patients with well-defined APLS (primary or secondary) and 12 patients with systemic lupus erythematosus (SLE) were tested for the presence of markers of HCV infection (anti-HCV and HCV RNA). The SLE patients were anti-CL-positive but none of them had developed any of the known clinical features of APLS. In addition, 267 healthy subjects were investigated for the presence of anti-CL. **METHODS:** IgG and IgM anti-CL were determined by a quantitative isotype-specific solid phase enzyme-linked immunosorbent assay set up in our laboratory. Anti-HCV was determined using a third-generation enzyme immunoassay and a confirmatory third-generation recombinant immunoblot assay. Active virus replication was defined by the detection of HCV RNA using a combination assay based on a reverse transcriptase polymerase chain reaction and a DNA enzyme immunoassay. **RESULTS:** Of the HCV patients, 37.3% had IgG and/or IgM anti-CL ($P < 0.00005$ compared to healthy controls (2.25%)). However, the mean titres of each specific isotype were significantly lower in HCV patients compared with those found in the APLS patients ($P < 0.05$ for IgM and $P < 0.001$ for IgG isotypes). The mean titres of IgG anti-CL were also significantly lower in HCV patients compared with those found in the SLE patients ($P < 0.01$). All patients with APLS or SLE ($n = 36$) tested negative for HCV infection markers. In addition, neither thrombotic events nor thrombocytopenia were associated with a positive anti-CL test in HCV patients. **CONCLUSIONS:** A significant proportion of HCV patients (37.3%) had detectable anti-CL of low titre. However, this finding was not associated with the development of APLS. On the other hand, none of the APLS patients was positive for HCV. Taken together, our data rather failed to reveal an aetiopathogenetic link between HCV and APLS. For this reason, testing for HCV in patients with APLS or follow-up for the possibility of the development of APLS in HCV patients cannot be suggested, at least in Greek patients. More prospective studies of longer duration are required in order to address whether HCV is involved or not in the aetiopathogenesis of APLS.

G. N. Dalekos, E. Galanakis, E. Zervou, M. Tzoufi, P. D. Lapatsanis and E. V. Tsianos. Interferon-alpha treatment of children with chronic hepatitis D virus infection: The Greek experience. *Hepato-Gastroenterology*, 2000; 47: 34: 1072-6

Background/Aims: The therapeutic experience of interferon-alpha therapy against hepatitis D virus infection in affected children is rather limited. For this reason, we conducted a retrospective study (duration: 1991-1995) in order to evaluate the efficacy and the safety of interferon-a in children suffering from chronic hepatitis D in Northwestern Greece. **Methodology:** Seven children who were found to be infected with HDV in a total of 324 children seropositive for hepatitis B virus infection during the 5-year period of the study were treated with interferon-alpha, 3×10^6 U/m² body surface area, intramuscularly or subcutaneously, 3 times weekly for 1 year (after an informed consent obtained from their parents). Patients were assessed monthly by hematological serological and biochemical tests. Clinical progress, levels of serum alanine aminotransferase, hepatitis D ribonucleic

acid (HDV-RNA) and hepatitis B deoxyribonucleic acid (HBV-DNA), seroconversion of hepatitis B surface antigen (HBsAg) and Hepatitis Be Antigen (HBeAg) and liver histology were used as response criteria.

Results: Posttreatment alanine transferase levels were significantly reduced ($P < 0.05$) but Immunoglobulin M and total anti-hepatitis D virus (anti-HDV) antibodies remained positive in all, while hepatitis D ribonucleic acid persisted positive in 4 cases. In addition, no seroconversion of HBsAg or HBeAg was noted and the liver histology progress was disappointing. Side effects including mild fever, arthralgias and malaise and reversible neutropenia and thrombocytopenia were common, but not particularly disturbing. Nevertheless, the children remained fully active on treatment, felt well and attended school. Initially 4 children had been below the 10th percentile for weight and height. All thrived during treatment and two crossed above the 10th percentile indicating height velocity and body mass index increase.

Conclusions: The administration of regular interferon-alpha doses for treating children with chronic hepatitis D was safe as attested by the mild side effects and the objective clinical criteria regarding their growth, but relatively ineffective. Although the prevalence of hepatitis D virus infection is now generally decreased, this study indirectly indicates that more effective agents and new approaches at the molecular level of the hepatitis D virus genome are urgently warranted for its control in individuals already infected with the virus. Finally, the poor therapeutic results in the present study further enhance the necessity of the expanded vaccination against Hepatitis B virus according to the World Health Organization's recommendations.

M. Stamouli, V. Gizaris, G. Totos and G. Papaevangelou. Decline of hepatitis B infection in Greece. *Eur J Epidemiol*, 1999; 15: 5: 447-9

Hepatitis B has long been a serious public health problem in Greece. In recent years, a decline in hepatitis B infection is observed ascribable to many factors such as demographic and socioeconomic changes, medical precautions, use of disposable medical equipments, screening of blood donors and vaccination. We studied the prevalence of HBV infection in a sample of 1050 Greek male Navy recruits. 343 subjects (32.6%) had previously been vaccinated and were anti-HBs positive. We observed that during the last decade, the prevalence of immunes declined to 1.33% and the prevalence of any HBV marker declined to 2.28%. The HBsAg carrier rate declined from 3.9% in 1973 to 0.9% in 1986. Since then, it is stable at 0.95% because perinatal and vertical transmissions are still responsible for the majority of HBV chronic infections. Universal prenatal screening and infant immunization will contribute to a further decline of HBV infection.

A. Sotiropoulos, T. A. Peppas, E. Skliros, O. Apostolou, V. Kotsini and S. I. Pappas. Low prevalence of hepatitis C virus infection in Greek diabetic patients. *Diabetic Medicine*, 1999; 16: 3: 250-2

Aim To assess the prevalence of hepatitis C virus (HCV) among Greek patients with Type 1 and 2 diabetes mellitus (DM), in view of the previous reports of high prevalence, particularly in patients with elevated aminotransferase.

Methods We checked 423 diabetic patients (183 male, 240 female, mean age: 63 years) attending our unit, recording epidemiology data, diabetes history, treatment and classification. Patients were stratified by aminotransferase values (normal or elevated). HCV screening was performed using standard techniques. Statistical analysis was done by using the Student's t-test for continuous variables and chi-square (χ^2) for categorical data.

Results Antibodies against HCV (anti-HCV) were detected in seven out of 423 diabetic patients (prevalence 1.65%). There was no correlation between HCV titre and diabetes type, duration, treatment, obesity (body mass index, BMI) or glycaemic control (HbA(1c)). The only correlation was elevated aminotransferase values ($P < 0.01$) Among the established risk factors for HCV transmission, only history of previous transfusion was significant ($P < 0.001$).

Conclusions It remains a strong hypothesis that diabetic patients are at increased HCV infection risk, yet our findings in Greek diabetic patients were rather low. Further studies, possibly multicentre, are needed to estimate prevalence and address the question of whether a direct effect of HCV in diabetes development does actually exist.

V. Papaevangelou, E. Spanou, C. Kattamis and S. Hadziyannis. Hepatitis G virus or hepatitis GB virus type C infection in thalassaemic patients. *Transfusion*, 1999; 39: 3: 336-7

M. Koulentaki, S. Spanoudakis, E. Kantidaki, P. Drandakis, N. Tzagarakis, E. Biziagos, J. Moschandreia and E. A. Kouroumalis. Prevalence of hepatitis B and C markers in volunteer blood donors in Crete. A 5-year study. *Journal of Viral Hepatitis*, 1999; 6: 3: 243-8

Greece is a country with an intermediate prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection. Crete, the third-largest island of the Mediterranean sea, has a different prevalence of viral hepatitis, One-eighth of the total island population, of 550 000, was included in a 5-year study of blood donors from three out of four blood banks, serving three out of four prefectures of the island. Markers for HBV and HCV were studied and evaluated according to geographical area, gender and age of donor. A total of 65 219 blood donors were studied. A greater number of males than females were hepatitis B surface antigen (HBsAg) positive (0.41% vs 0.28%, respectively) with a peak at a younger age for males and older age for females. Males are more frequently exposed to HBV and become carriers more often than females. For HCV, an opposite gender trend was found, females being infected more frequently (0.49%) than males (0.37%). Statistical differences were found among geographical areas of the island, Hence, Crete is an area of low endemicity for HBsAg in blood donors. The HCV infectivity is more similar to Northern Europe than to other neighbouring countries. Differences in geographical distribution within the island and during different years indicate the need for extended epidemiological surveys for valid results.

A. Katsoulidou, D. Paraskevis, V. Kalapothaki, D. Arvanitis, P. Karayiannis, V. Hadjiconstantiou and A. Hatzakis. Molecular epidemiology of a hepatitis C virus outbreak in a haemodialysis unit. Multicentre Haemodialysis Cohort Study on Viral Hepatitis. *Nephrol Dial Transplant*, 1999; 14: 5: 1188-94

BACKGROUND: Haemodialysis patients are at high risk of infection by hepatitis C virus. The aim of this study was to investigate a hepatitis C virus outbreak which occurred in a haemodialysis unit, using epidemiological and molecular methods. METHODS: Five seroconversions to hepatitis C virus antibody (anti-HCV) were observed over a 6 month period and these were added to the four previously recorded anti-HCV-positive patients. All nine patients involved in the outbreak were tested for HCV RNA by reverse transcription-polymerase chain reaction and hepatitis C genotype determination was accomplished by a reverse hybridization assay. Furthermore, part of the NS5 region of hepatitis C genome (nucleotide positions 7904-8304) was amplified and sequenced in all HCV RNA-positive patients. Then, phylogenetic analysis of the nucleotide sequences obtained was carried out

in order to investigate any possible epidemiological linkage among patients. Detailed epidemiological records were also available for all haemodialysis patients. RESULTS: Samples from all five incident cases and three out of four prevalent HCV infections were found positive for HCV RNA. HCV genotyping studies revealed that all incident cases were classified as 4c/d, whereas one and two prevalent cases were 1a and 4c/d respectively. Sequence comparisons and phylogenetic tree analysis revealed that six of the patients harboured very similar strains and clustered together, including all incident and one prevalent case, which was implicated as index case. Further epidemiological analysis was consistent with patient to patient transmission. CONCLUSIONS: Molecular and epidemiological analysis suggested that horizontal nosocomial patient to patient transmission was the most likely explanation for the virus spread within the haemodialysis unit under study.

M. Chatziarsenis, S. Miyakis, T. Faresjo, E. Trell, J. Vlachonikolis and C. Lionis. Is there room for general practice in penitentiary institutions: screening and vaccinating high-risk groups against hepatitis. *Fam Pract*, 1999; 16: 4: 366-8

OBJECTIVE: The purpose of this study was to determine the prevalence of hepatitis markers in inmates and staff of the Penitentiary of Neapolis on Crete and discuss the role of GPs in identifying and vaccinating susceptible subjects. METHOD: Forty-five prisoners and 20 house workers were invited to participate in the study. Hepatitis B (HBV) markers (HBsAg and anti-HBc) and hepatitis C antibodies (anti-HCV) were tested. Vaccination against hepatitis B was administered to all susceptible subjects. RESULTS: Hepatitis B carriage was found in 10 people, six of whom were prisoners. Fifteen of the subjects tested were found to be positive for anti-HBc, six of whom were house workers. Anti-HCV were found to be positive in seven prisoners and one worker. A vaccination programme against hepatitis B was introduced in 27 susceptible subjects (58.7% of unexposed subjects) and was completed in 22. CONCLUSION: Prisoners and staff at Neapolis Prison constitute a high-risk group for hepatitis B and C. Compliance rate in screening was high and GPs were successful in having a desirable response rate in the administration of vaccines.

C. G. Alexopoulos, M. Vaslamatzis and G. Hatzidimitriou. Prevalence of hepatitis B virus marker positivity and evolution of hepatitis B virus profile, during chemotherapy, in patients with solid tumours. *Br J Cancer*, 1999; 81: 1: 69-74

To prospectively evaluate the prevalence of hepatitis B virus (HBV) positivity and study the evolution of HBV profile during cancer chemotherapy, serum HBV markers and liver biochemistry were determined in 1008 of 1402 (72%) cancer patients admitted in our Unit and in all 920 (91 %) who received chemotherapy. We found that 54 (5.3%) were HBsAg carriers while 443 (44%) had at least one HBV marker positive. Of the latter, 405 (91%) were HBcAb+ve, 321 (72%) HBsAb+ve and 212 (48%) HBeAb+ve. No patient was HBeAg+ve. Among 920 chemotherapy receivers, 374 (41%) were HBcAb+ve, 280 (30%) HBsAb+ve and 178 (19%) HBeAb+ve. Fifty (5.4%) were HBsAg carriers (versus 0.6% in Greek blood donors). All 50 were systematically screened for HBsAg and HBsAb status throughout chemotherapy, during follow-up or until their death, and liver biochemistry was performed before each chemotherapy course. Stable antigenaemia was observed in 43/50 (86%) while 7/50 (14%) developed clinical and/or biochemical hepatitis. Six of these seven developed serum anti-HBs antibodies with an associated decrease of serum HBsAg titres. We conclude that reactivation of HBV infection during chemotherapy is not rare (14%), while disappearance of HBs antigenaemia is neither a frequent nor usually a permanent phenomenon.

G. Papaevangelou. Hepatitis B immunization programme: lessons learnt in Greece. *Vaccine*, 1998; 16 Suppl: S45-7

Historically, Greece has had the highest burden of hepatitis B virus (HBV) infection in the European Union (EU). Heterosexual contact is the primary means of HBV transmission in Greece, accounting for approximately 30% of acute cases in adult males and 50% of acute cases in women of reproductive age [Kattamis C, Papevangelou G. Workshop Group: Greece. *Vaccine* 1995;13:S97-S98.]. In 1982, Greece implemented a hepatitis B prevention programme aimed at high-risk groups; unfortunately, this approach had little impact on disease incidence or prevalence. At the recommendation of the WHO and the World Health Assembly and after sustained lobbying by several scientific and medical associations in Greece, the Greek government decided to implement a national prevention programme for hepatitis B. The programme, in effect from early 1998, includes the screening of pregnant women, universal infant and adolescent immunization and immunization of high-risk groups.

M. Malliori, V. Sypsa, M. Psychogiou, G. Touloumi, A. Skoutelis, N. Tassopoulos, A. Hatzakis and C. Stefanis. A survey of bloodborne viruses and associated risk behaviours in Greek prisons. *Addiction*, 1998; 93: 2: 243-51

AIMS: To determine HIV and hepatitis infection prevalence and correlates with risk behaviour. DESIGN: Cross-sectional study: voluntary, anonymous HIV, hepatitis (HCV, HBV and HDV) surveillance and questionnaire on risk factors. SETTING: Korydallos Prison, Athens and Ag. Stefanos Prison, Patra, Greece. PARTICIPANTS: Of 544 drug users imprisoned for drug related offences, all completed the questionnaire and 533 blood samples were collected. MEASUREMENTS: HIV (by anti-HIV-1), HCV (by anti-HCV), HBV (by anti-HBc, HBsAg) and HDV (by anti-HDV) prevalence. Data on demography, legal status, drug use, sharing of injecting equipment. FINDINGS: Of the 544 drug users, 375 (68.9%) had injected drugs (IDUs) at some time, 35% of whom had injected whilst in that prison. Of the 533 blood samples tested, one was positive for anti-HIV-1 (0.19%), 310 for anti-HCV (58.2%), 306/531 (57.6%) for anti-HBc, 34/527 (6.5%) for HBsAg and 12/527 (2.3%) for anti-HDV. Prevalence rates for IDUs only were 0.27% for HIV-1, 80.6% for hepatitis C, 62.7% for hepatitis B and 3.3% for hepatitis D. Ninety-two per cent of IDUs injecting in prison shared needles, indicating that IDUs inject less but share more during incarceration. Multiple logistic regression revealed needle-sharing as the most important risk factor for HCV infection in IDUs. Prior knowledge of a positive hepatitis result did not appear to inhibit IDUs from practising risky behaviours in prison. CONCLUSIONS: The epidemic of hepatitis B and C among imprisoned IDUs identified by this study constitutes a major public health problem. Prevention programmes, such as counselling, HBV vaccination, community-based methadone maintenance treatment and syringe exchange schemes, are necessary in order to prevent a further spread.

G. N. Dalekos, E. Zervou, M. Elisaf, N. Germanos, E. Galanakis, K. Bourantas, K. C. Siamopoulos and E. V. Tsianos. Antibodies to hepatitis E virus among several populations in Greece: increased prevalence in an hemodialysis unit. *Transfusion*, 1998; 38: 6: 589-95

BACKGROUND: Hepatitis E virus (HEV) has been found to be the causative agent of enterically transmitted non-A, non-B hepatitis in tropical and subtropical countries. Several investigators, however, have indicated that HEV could be endemic in Europe, albeit at a low prevalence.

STUDY DESIGN AND METHODS: The purpose of this study was to estimate the prevalence

of anti-HEV in various populations in northwestern Greece (Epirus region). Healthy blood donors (2636), refugees from southern Albania (350), children (165), injecting drug users (IDUs) (65), multiply transfused patients (62), patients with chronic viral hepatitis (75), and chronic hemodialysis patients (149) were investigated for anti-HEV by enzyme immunoassay and confirmatory Western blot assay. In addition, 380 consecutive healthy blood donors and 62 hemodialysis patients from a neighboring area (Agrinion, Greece) were investigated.

RESULTS: A very low presence of anti-HEV antibody was found among healthy blood donors from Epirus (0.23%) and Agrinion (0.53%). Anti-HEV was not detected in children, IDUs, or multiply transfused patients. In contrast, a low but significant prevalence of anti-HEV was found among refugees (4.85%), patients with chronic viral hepatitis (5.3%), and hemodialysis patients from Epirus (1.34%), as compared with healthy blood donors from Epirus: $p < 0.0001$, $p < 0.00001$, and $p < 0.10$, respectively. A high prevalence (9.7%) of anti-HEV was revealed in patients at the hemodialysis unit of the General Hospital of Agrinion ($p < 0.00005$, compared to healthy blood donors from Agrinion). No significant association was found between anti-HEV positivity and the age or sex of donors, the duration of hemodialysis, positivity for hepatitis B or C virus infection markers, history of hepatitis, increased alanine aminotransferase, renal transplantation, a history of transfusion, or the number of units transfused.

CONCLUSION: This study demonstrated a high prevalence of anti-HEV in a separate hemodialysis unit, without an association with the known routes of transmission of bloodborne viruses. This observation suggests that a still-undefined intra-unit factor or other factors are associated with HEV transmission.

G. N. Dalekos, D. S. Boumba, K. Katopodis, E. Zervou, G. Sferopoulos, M. Elisaf, E. V. Tsianos and K. C. Siamopoulos. Absence of HCV viraemia in anti-HCV-negative haemodialysis patients. *Nephrol Dial Transplant*, 1998; 13: 7: 1804-6

BACKGROUND: Immunologic alterations have been reported in chronic haemodialysis (HD) patients. Some HD patients may have, therefore, an inability to produce detectable amounts of serum antibodies to hepatitis C virus (anti-HCV). Previous studies have shown the presence of HCV viraemia in anti-HCV-negative HD patients (ranging from 1 to 15%). However, the universal epidemiologic impact of these cases remains uncertain since there are conflicting results. In this context, we conducted a study in an attempt to investigate the presence of HCV viraemia among anti-HCV-negative HD patients in a well-defined geographic area of the northwestern part of Greece. **METHODS:** During a 6 month period, 81 anti-HCV-negative HD patients were tested twice for the presence of HCV RNA, using the reverse transcriptase polymerase chain reaction (RT-PCR) combined with a DNA enzyme immunoassay (DEIA). At the same time, periodic testing for anti-HCV by two commercially available third generation assays was done. In addition, 15 anti-HCV-positive HD patients and 20 non-HD patients with well established chronic HCV infection used as internal controls were tested for the presence of HCV RNA and anti-HCV. **RESULTS:** None of the anti-HCV-negative HD patients were shown to be viraemic by the combined RT-PCR and DEIA method. During the same time period, all remained anti-HCV negative by the third generation assays. By contrast, all the patients with known HCV-infection were positive by the two enzyme immunoassays, whereas 13 anti-HCV-positive HD patients (86.7%) and 18 non-HD patients (90%) were viraemic by RT-PCR. **CONCLUSIONS:** This study demonstrated

that routine HCV RNA testing in anti-HCV-negative HD patients appears not to be necessary particularly when third generation assays are used for the detection of anti-HCV.

M. Arvanitidou, T. C. Constantinidis, J. Doutsos, K. Mandraveli and V. Katsouyannopoulos. Occupational hepatitis B virus infection in sewage workers. *Med Lav*, 1998; 89: 5: 437-44

In a cross-sectional study the employees of a Sewage Company were tested for hepatitis B virus (HBV) markers--HBsAg, anti-HBs, anti-HBc--to determine the prevalence of HBV infection and assess the risk of exposed sewage workers becoming infected, so as to evaluate the necessity for appropriate vaccination. The overall prevalence of HBV markers was 43.9% and 6.6% of the employees were HBsAg carriers. In the univariate analysis the prevalence of past and current infection was significantly associated with exposure to sewage ($p < 0.001$), age ($p < 0.001$) and with educational level ($p < 0.001$). However, the logistic regression analysis confirmed that only exposure to sewage was independently associated with positivity for HBV infection ($p < 0.001$). Workers exposed to sewage should therefore be considered for vaccination against hepatitis B virus.

C. G. Anastassopoulou, D. Paraskevis, V. Sypsa, M. Psychogiou, A. Katsoulidou, N. Tassopoulos, A. Skoutelis, M. Malliori and A. Hatzakis. Prevalence patterns and genotypes of GB virus C/hepatitis G virus among imprisoned intravenous drug users. *J Med Virol*, 1998; 56: 3: 246-52

An RT-PCR assay using primers from the 5'-UTR of the GBV-C/HGV genome was used to detect viremia, and a serological assay was used to detect past exposure to GBV-C/HGV, in sera from 106 imprisoned Greek intravenous drug users. High seroprevalence rates indicative of the parenteral route of transmission of the virus were found (32.1% for GBV-C RNA and 46.2% for anti-GBV-C E2). These rates were nonetheless lower in comparison to the corresponding rates of HCV infection markers (64.2% for HCV RNA and 77.4% for anti-HCV). Statistically significant univariate associations were observed between GBV-C-RNA positivity and younger age ($P=0.006$) and HCV-RNA positivity ($P=0.024$), as well as with higher serum alanine aminotransferase levels ($P < 0.001$); this latter association was shown to be independent of coinfection with HCV and of age by a multiple logistic regression model. Apparently, GBV-C/HGV had spread readily by needle-sharing in prison, while causing acute subclinical hepatitis in infected inmates. Phylogenetic analysis of the partial 5'-UTR of the GBV-C/HGV genome from 16 seropositive individuals, which delineated their grouping within genotype 2, also revealed a close genetic relationship between two sets of sequences from 4 drug addicts, 3 of whom admitted to sharing needles while imprisoned.

A. Tsakris, K. P. Kyriakis, S. Chryssou and G. Papoutsakis. Infection by hepatitis B and C virus in female and transsexual Greek prostitutes with serological evidence of active syphilis. *Int J STD AIDS*, 1997; 8: 11: 697-9

Two hundred and thirty female and 43 male-to-female transsexual Greek prostitutes were screened for serological evidence of active syphilis as judged by positivity in both rapid plasma reagin (RPR) test and treponemal (FTA-ABS and TPHA) tests. The rate of active syphilis was 20.9% in the male-to-female transsexual prostitutes and 4.3% in the female ones ($P < 0.001$, odds ratio = 5.82). In the former group 65.1% had evidence of hepatitis B virus (HBV) infection, and 4.7% of hepatitis C virus (HCV) infection while the respective

rates among the latter group were 50.4% and 3.9%. There was no correlation of viral hepatitis marker prevalence with positive syphilis serology.

C. Lionis, M. Koulentaki, E. Biziagos and E. Kouroumalis. Current prevalence of hepatitis A, B and C in a well-defined area in rural Crete, Greece. *J Viral Hepat*, 1997; 4: 1: 55-61

A seroepidemiological study was carried out in a geographically well-defined area in rural Crete in order to determine the prevalence of A, B and C hepatitis markers in the local population. Serum samples were obtained from 257 subjects (94 males, 163 females), aged 15 years and over, who visited the primary health care services of the Spili Health Centre between July 1993 and March 1994, and from 164 subjects (83 males, 81 females) randomly selected from households in three neighbouring villages of the study area. In samples obtained from the Spili Health Centre, antibodies to hepatitis A virus (anti-HAV) were detected in 234/244 (95.9%) subjects, antibodies to hepatitis B virus core antigen (HBcAb) were detected in 63/257 (24.5%) subjects and antibodies to hepatitis C virus (anti-HCV) were detected in 28/257 (10.9%) subjects. The corresponding figures for those randomly selected from the villages were 135/154 (87.7%), 16/164 (9.8%) and 5/164 (3%) respectively. Hepatitis B surface antigen (HBsAg) was positive in three (1.2%) subjects from the first group, while none of those recruited from the villages were positive for HBsAg. Interestingly, hepatitis markers were closely associated with age. No subjects under the age of 15 years showed evidence of prior hepatitis A infection and approximately 20% of those between 15 and 44 years of age were also negative. By contrast, practically all subjects older than 44 years were anti-HAV positive. Similarly, the majority of all those who were anti-HCV positive were older subjects. Seroepidemiology of hepatitis in this well-defined population seems to be different from other parts of Greece, at least for hepatitis B and C viruses. There is a very low prevalence of HBsAg and a very high incidence of anti-HCV. Low exposure to HAV, as found in other parts of the country, was also found in the younger generation in this rural area of Crete.

C. Lionis, E. Frangoulis, M. Koulentakis, E. Biziagos and E. Kouroumalis. Prevalence of hepatitis A, B, and C markers in school children of a rural area of Crete, Greece. *Eur J Epidemiol*, 1997; 13: 4: 417-20

OBJECTIVE: To determine the prevalence of hepatitis A, B, and C markers in children who were attending junior and senior high schools in a high risk area in rural Crete, Greece. **METHODS:** Three-hundred and thirty-four children who attended the three junior schools and one senior high school in the Agios Vassilios province of Southern Crete were invited to participate in the study. Three hundred and four of them were tested for hepatitis A, B, and C markers. Hepatitis B (HBV) markers (HBsAg and anti-HBc) as well as hepatitis A (anti-HAV) and hepatitis (anti-HCV) antibodies were tested with commercial enzyme-linked immunosorbent assay kits. **RESULTS:** Six of the 304 children (1.97%) were found to be positive for anti-HAV, 1 (0.33%) to HBsAg, 7 (2.30%) to anti-HBc and none were found positive for anti-HCV. No significant differences were seen between the prevalence of anti-HAV antibodies in males (2%) and females (1.95%), and of anti-HBc antibodies in males (3.33%) and females (1.30%). **CONCLUSIONS:** The very low prevalence of anti-HAV is obviously due to the improved conditions of hygiene and it raises the question of the possible emergence of this disease at an older age and therefore appropriate preventative strategies should be considered. The low endemicity of hepatitis B in Crete in contrast to other areas of Greece also calls for a vaccination policy probably during adolescence. The absence of hepatitis C markers in the children in contrast to the observed higher prevalence

of HCV-infected people in the adult population in the same rural area raises questions regarding possible sources of transmission of hepatitis C during the preceding years.

E. A. Kouroumalis, P. G. Skordilis, J. Moschandrea, G. Alexandrakis, N. Charoulakis, M. Tzardi and O. N. Manousos. Natural history of advanced hepatocellular carcinoma in Crete. Association with hepatitis C virus. *European Journal of Gastroenterology & Hepatology*, 1997; 9: 10: 981-88

Objective: To investigate the clinical characteristics of advanced hepatocellular carcinoma (HCC) in Crete and to analyse the natural course of the untreated disease. **Participants:** Seventy-three patients (62 men) were enrolled in a prospective 4-year study. Clinical and virological parameters were recorded. Diagnosis was based on either ultrasound guided liver biopsy or a pathognomonic increase in alpha-fetoprotein plus compatible imaging.

Methods: Statistical analysis was performed using histograms, contingency tables and one-way analyses of variance to analyse the characteristics of the disease. For survival analysis Kaplan-Meier survival curves and Cox's proportional hazards models were constructed. **Results:** HCC in Crete is a mostly male disease (7:1 male:female ratio) and unlike in mainland Greece, it is mostly a hepatitis C virus (HCV)-related disease (54% HCV positive as opposed to only 13% in mainland Greece). Prognosis was associated with Okuda classification (Okuda stage III patients have a relative risk of dying that is seven to nine times higher than for Okuda stage I), the presence or absence of hepatitis B e antigen (HBeAg) and antibody to hepatitis B core antigen (anti-HBc). By contrast the presence of anti-HCV was not associated with a worse prognosis. A unit increase of albumin concentration was associated with an 11% decrease in the hazard rate.

Conclusion: In general, Crete, despite the extremely similar population to the rest of Greece, resembles more closely the situation in Spain or Italy rather than mainland Greece.

A. Malamitsi-Puchner, S. Papacharitonos, D. Sotos, L. Tzala, M. Psychogiou, A. Hatzakis, A. Evangelopoulou and S. Michalas. Prevalence study of different hepatitis markers among pregnant Albanian refugees in Greece. *Eur J Epidemiol*, 1996; 12: 3: 297-301

Aim of the study was to record the prevalence of the various types of viral hepatitis, especially hepatitis B, in pregnant Albanian refugees in Greece. The study comprised 500 pregnant refugees of mean age 25.1 +/- 4.6 years. In Albania, all women had lived in overcrowded houses and had been exposed to non throw-away needles and syringes. Various indices for all hepatitis types were determined. The prevalence of HBsAg was 13.4%, of anti-HBs 53%, of total anti-HBc 70.8%, of anti-HBc IgM 0.4%, of HBeAg 1.2%, of anti-HBe 58.6%, of anti-HAV 96.2%, of anti-HAV IgM 1%, of anti-HDV 0.4%, of anti-HCV 0.6% and of anti-HEV 2%. HBeAg was found positive in 7.5% of HBsAg carriers. Prevalence of hepatitis B markers, as determined by HBsAg and/or anti-HBs and/or total anti-HBc was significantly higher in those with a history of previous hospitalization in Albania ($p = 0.01$) and those with previous history of hepatitis ($p = 0.02$). The high prevalence of hepatitis B markers in pregnant Albanian refugees proves that HBV infection is highly endemic in Albania and the possibility of perinatal transmission to the offsprings urges for HBV vaccination programmes. On the other hand improvements in the socioeconomic conditions and the sanitation system in Albania is anticipated to reduce the incidence of HAV and HBV infections.

G. N. Dalekos, E. Zervou, M. H. Merkouropoulos and E. V. Tsianos. Prevalence of hepatitis B and C viruses infection in chronic alcoholics with or without liver disease in Ioannina, Greece: low incidence of HCV infection. *Eur J Epidemiol*, 1996; 12: 1: 21-5

Intravenous heroin abusers comprise a high risk group for hepatitis B and C viruses (HBV and HCV) infection. Chronic alcoholics with liver disease (LD) also comprise a high risk group for HBV infection whereas the frequency of antibodies to HCV (anti-HCV) ranges from 27-42.6%. In this study, HBV and HCV infection markers were determined in alcoholic patients with (83 patients) or without LD (68 patients) in order to assess the prevalence of these markers (HBsAg, HBsAb, HBcAb and anti-HCV). The reason for the study was a lack of established data in this group of patients in Greece. The disease control groups consisted of 70 non-alcoholic hospitalized patients and 60 heroin addicts, whereas 1342 healthy blood donors were also investigated. Our results showed significantly increased prevalence of HBV infection markers in chronic alcoholic patients compared to healthy controls and non-alcoholic hospitalized patients. The findings were independent of the presence or absence of LD. In contrast to heroin addicts, where anti-HCV antibodies were observed in 90%, there was no difference in the prevalence of anti-HCV antibodies in chronic alcoholics (with or without LD), nonalcoholic hospitalized patients or healthy controls. In conclusion, we found that in this area of north-western Greece, chronic alcoholics, independent of the presence of LD, comprise a high risk group for HBV infection but very rarely have HCV infection. The latter finding may reflect technical or socio-economic differences regarding the lifestyle of our patients, and our population in general.

M. A. Psychogiou, N. C. Tassopoulos, G. V. Papatheodoridis, E. Tzala, R. Klarmann, H. Witteler, G. G. Schlauder, H. Troonen and A. Hatzakis. Hepatitis E virus infection in a cohort of patients with acute non-A, non-B hepatitis. *J Hepatol*, 1995; 23: 6: 668-73

BACKGROUND/AIMS: The aim of this study was to determine the frequency of hepatitis E virus infection in a cohort of patients with acute non-A, non-B hepatitis in Greece. **METHODS:** Serial serum samples of 198 patients with acute non-A, non-B hepatitis and a single serum specimen from 316 healthy subjects were tested for IgG and IgM antibodies to hepatitis E virus (anti-HEV). **RESULTS:** Anti-HEV IgG was found in 15/198 (7.6%) of acute non-A, non-B hepatitis patients and 7/316 (2.2%) of healthy controls ($p=0.007$). Anti-HEV IgM was found in 2/198 (1.0%) acute non-A, non-B hepatitis patients and in none of the healthy subjects. Neither anti-HEV IgM (+) case reported any risk factor and neither had travelled in areas endemic for hepatitis E virus infection. HEV-RNA was detected by reverse transcription polymerase chain reaction in one patient. The prevalence of anti-HEV IgG was 7/45 (15.6%), 1/46 (2.2%), 5/30 (16.7%) and 2/77 (2.6%) in acute non-A, non-B hepatitis reporting transfusion, intravenous drug use, occupational/hospitalization, and unknown transmission, respectively ($p=0.007$). Anti-HEV IgG was found in 13/122 (10.7%) and 2/76 (2.6%) of acute non-A, non-B hepatitis patients positive and negative for anti-HCV, respectively ($p=0.03$). A similar association was found with anti-HBc ($p=0.007$). The prevalence of anti-HEV IgG was significantly higher in cases reporting transfusion [OR=7.3, 95% C.I. 1.4-37.7, $p=0.017$] and occupational/hospitalization [OR=6.8, 95% C.I. 1.2-38.2, $p=0.029$], as transmission category after controlling for age. **CONCLUSIONS:** These findings

indicate that: (a) hepatitis E virus may be a cause - although not a frequent one - of sporadic or community-acquired acute non-A, non-B hepatitis in Greece; (b) hepatitis E virus may share transmission routes with hepatitis B and C viruses; and (c) the hypothesis that hepatitis E virus may be transmitted by parenteral routes deserves careful consideration.

K. Makris, V. Kouvelis, I. Drakopoulos, E. Oikonomou and A. Maniatis. Frequency and characteristics of post-transfusion hepatitis in Greece with emphasis on hepatitis C: comparing second- and third-generation assays. *Transfus Med*, 1995; 5: 3: 213-24

In order to evaluate the role of hepatitis C virus (HCV) in post-transfusion hepatitis (PTH) in Greece we prospectively followed 143 transfusion recipients, receiving 790 units of blood and/or products from 789 donors, between October 1989 and December 1991. The mean number of units transfused per patient was 5.52. PTH was observed in 18 patients (12.59%). One patient (0.70%) developed hepatitis B, in four (2.80%) hepatitis could be attributed to CMV infection, 10 (6.99%) developed hepatitis C and three (2.10%) showed only raised alanine aminotransferase (ALT) levels. The risk of PTH per 1000 units transfused was 22.8. The patient who developed hepatitis B (PTH-B) was transfused with four units, one of which was positive for anti-HBc and anti-HBe. Seven of the 10 patients (70%) who developed hepatitis C (PTH-C) were transfused with at least one unit seropositive in the anti-HCV screening with 2nd-generation tests (ELISA-2 and RIBA-2), whereas 9/10 of PTH-C cases (90%) were transfused with at least one unit positive in 3rd-generation assays. Of the three patients who showed only ALT elevation, none was transfused with anti-HCV seropositive blood, although one of them was transfused with at least one unit with elevated ALT levels. We conclude that: (1) the incidence of PTH in Greece remains high, (2) screening of all donations for anti-HCV with an ELISA-2 does not exclude transmission of HCV and (3) ELISA-3 and RIBA-3 seem to be more sensitive in blood donor screening and in detecting seroconversions than ELISA-2 and RIBA-2.

C. P. Goritsas, A. Athanasiadou, A. Arvaniti and C. Lampropoulou-Karatza. The leading role of hepatitis B and C viruses as risk factors for the development of hepatocellular carcinoma. A case control study. *J Clin Gastroenterol*, 1995; 20: 3: 220-4

A double case control study evaluated the role of hepatitis C virus (HCV) and hepatitis B virus (HBV), alcohol drinking, and tobacco smoking as potential risk factors for hepatocellular carcinoma (HCC). Fifty-one patients with HCC, 34 of whom had underlying cirrhosis, were analyzed against 51 hospital controls and 34 patients with cirrhosis, respectively. Sera from patients of all three groups were tested for HBV markers and anti-HCV antibodies. The polymerase chain reaction technique was used to detect HCV RNA in the anti-HCV-positive samples. Alcohol drinking and smoking habits were recorded for all patients. HCC risk was significantly related to the presence of hepatitis B surface antigen (HBsAg) [relative risk (RR) = 18], HCV infection (RR = 8), and alcohol abuse (RR = 4). When the presence of cirrhosis was taken into account, only HBsAg positivity was significantly associated with HCC development (RR = 6.7), indicating that HCV infection and alcohol abuse are related to HCC indirectly through the cirrhotic process. No significant interaction between HCV and HBV infection in the causation of HCC was found. Through the computation of population-attributable risk, it was found that 46% of the HCC cases in Greece could be attributed to HBsAg positivity but only 4% to HCV infection. In conclusion, HBV infection is the major risk factor in the development of HCC in Greece, either by inducing cirrhosis or by direct oncogenic effect. HCV infection is also related to HCC development, albeit indirectly through the cirrhotic process.

G. N. Dalekos, E. Zervou, F. Karabini and E. V. Tsianos. Prevalence of viral markers among refugees from southern Albania: increased incidence of infection with hepatitis A, B and D viruses. *Eur J Gastroenterol Hepatol*, 1995; 7: 6: 553-8

BACKGROUND: Since 1991, thousands of refugees from southern Albania have entered north-western Greece, an area with low-to-moderate endemicity for infection with hepatitis viruses. We examined the prevalence of several markers of viral infection in this population in order to ascertain the likely impact of its presence on the epidemiology of hepatitis infections in north-western Greece. **DESIGN:** Consecutive unselected serum samples were obtained from refugees resident in three different reception camps. **SETTING:** A university hospital. **STUDY POPULATION:** One thousand and twenty-five refugees (662 males and 363 females, age range 0-81 years) and 1984 healthy controls (1293 males and 691 females, age range 0-80 years). **INTERVENTIONS:** None. **RESULTS:** We found a significantly greater prevalence of markers of infection with hepatitis A virus (prevalence of antibodies to hepatitis A virus 98.2%), hepatitis B virus (HBV; prevalence of HBV s antigen 22.2%, prevalence of HBV c antibody 70.6%, prevalence of HBV s antibody 40.5%, prevalence of HBV e antigen 21.1%, prevalence of HBV e antibody 46.2%), hepatitis C virus (prevalence of antibodies to hepatitis C virus 1.75%) and hepatitis D virus (prevalence of antibodies to hepatitis D virus 12.7%) among refugees from southern Albania than in healthy Greek controls. These markers were found with significantly greater frequency among younger refugees (< 30 years of age) than in older members of the same population. **CONCLUSIONS:** We conclude that refugees from southern Albania are a new immigrant population characterized by a high incidence of infection with hepatitis A, B and D viruses. This finding may reflect the low socioeconomic status of the immigrant population and the poor hygienic conditions experienced by its members. The high incidence of HBV and HDV infections in the population from Albania will probably increase the prevalence of infection with these viruses in Ioannina and subsequently in the whole of the Epirus region. We therefore believe that rigorous adherence to general precautions and the initiation of hepatitis B vaccination programmes will be necessary in future, both in our area and in Albania.

N. C. Tassopoulos, K. Krawczynski, A. Hatzakis, A. Katsoulidou, I. Delladetsima, M. G. Koutelou and D. Trichopoulos. Case report: role of hepatitis E virus in the etiology of community-acquired non-A, non-B hepatitis in Greece. *J Med Virol*, 1994; 42: 2: 124-8

The aim of this study was to determine the frequency of hepatitis E virus (HEV) infection in a population of Greek adults with community-acquired (sporadic) non-A, non-B hepatitis found to be seronegative for antibodies to hepatitis C virus (anti-HCV). All patients admitted to the Liver Unit of Western Attica General Hospital and diagnosed as having acute community-acquired non-A, non-B hepatitis between February, 1986, and May, 1990, were enrolled in follow up studies (n = 66). Nineteen patients with HCV infection and 11 patients with acute non-A, non-B, non-C hepatitis that progressed to chronicity were excluded. Convalescent sera were tested for antibody to HEV (anti-HEV) by a fluorescent antibody blocking assay in 33 of 36 eligible patients. One of the 33 (3%) patients was found to be positive for anti-HEV. Anti-HEV testing of all 20 available serum specimens from this patient showed evidence of anti-HEV seroconversion at the fourth week after the onset of hepatitis. The patient had not travelled abroad or within Greece or had not had apparent contact with people from foreign countries for the previous 3 months. These data show that HEV infection is not a major cause of community-acquired non-A, non-B hepatitis in Greece. However, the reported case of HEV hepatitis suggests that HEV may retain a low endemicity

in Greece. More extensive seroprevalence studies are needed for an accurate estimation of the extent of HEV infection in the southeastern European countries.

A. Roumeliotou, A. Papachristopoulos, D. Alexiou, V. Papaevangelou, G. Stergiou and G. Papaevangelou. Intrafamilial clustering of hepatitis A. *Infection*, 1994; 22: 2: 96-8

The intrafamilial clustering of hepatitis A virus infections (HAV) in families with an index case of sporadic hepatitis A was studied. Four hundred and three family members (84.3%) of 113 children with acute hepatitis A admitted to the Paediatric Department of the West Attica Hospital were included in the study. Epidemiological data and serum samples were collected within 1 week after the patient's admittance to the hospital. Enzyme-immunoassays were used to detect recent or past HAV infections. The attack rate of HAV infections in susceptible family members was found to be similar in susceptible fathers (16.6%, 1/6), mothers (23.5%, 4/17) and siblings (18.1%, 37/204). The infected family members belonged to 22 families. The attack rate was found to be higher in families with a lower immunity level, while the social class was not found to play an important role. The administration of ISG prevented further spread of hepatitis A among those susceptible. Our data suggest that immunoglobulin for HAV prevention should be given not only to children but also to parents and other adult family members in areas with a low prevalence of anti-HAV among adults.

I. Vafiadis, J. Boletis, H. Papastathi, J. Delladetsima, C. Stathakis, A. Hatzakis, A. Kostakis and G. Vosnides. Hepatitis C virus infection among Greek renal transplant patients. *Gut*, 1993; 34: 2 Suppl: S57-8

In this study, the prevalence of hepatitis C virus (HCV) infection among renal transplant recipients was high, directly proportional to the haemodialysis time before transplant and inversely proportional to the time after this. There was evidence of previous infection with hepatitis B virus (HBV), and a high prevalence of abnormal liver function tests. Virus induced chronic hepatitis lesions were rare, probably as a result of immunosuppression.

G. Papaevangelou, G. Totos, A. Roumeliotou and A. Safary. Brief report: hepatitis A vaccination in Greek military recruits. *J Med Virol*, 1993; 40: 1: 1-4

Improved standards of sanitation have contributed to a shift in the prevalence of hepatitis A in countries such as Greece. Children are now coming into first contact with the infection at an increasingly later age, leaving more adults susceptible to the disease. In military forces where close living conditions prevail, the likelihood of infection is even more pronounced. An inactivated hepatitis A vaccine has been developed and has been administered successfully to over 24,000 healthy children and adults. This vaccine would be of considerable benefit to military personnel worldwide. The reactogenicity and immunogenicity of a hepatitis A vaccine were evaluated in 200 female military recruits, aged from 17 to 23 years, vaccinated according to a primary vaccination schedule at 0 and 1 months with a booster dose at 6 months. Symptoms reported following vaccination were generally mild and transient. Soreness at the site of injection was the most frequent local symptom and

malaise was the most common general symptom. Clinically significant increases in serum liver enzyme levels were not detected. All subjects had seroconverted after the primary vaccination course and maintained anti-HAV titres up to the time of the administration of the booster dose. The booster dose produced more than a tenfold increase in the geometric mean titre (GMT).

S. J. Hadziyannis, G. Giannoulis, E. Hadziyannis, E. Kaklamani, A. Alexopoulou, S. Dourakis and D. Trichopoulos. Hepatitis C virus infection in Greece and its role in chronic liver disease and hepatocellular carcinoma. *J Hepatol*, 1993; 17 Suppl 3: S72-7

The aim of this study was to evaluate the prevalence of hepatitis C virus infection (HCV) in Greece, to estimate its frequency in chronic liver disease and to explore the role of HCV infection in the aetiology of hepatocellular carcinoma. A series of 1034 patients with chronic liver disease of various aetiologies and 299 patients with hepatocellular carcinoma allocated to two case-control studies was tested for anti-HCV. Twelve recent reports on HCV infection in Greece were reviewed and analyzed. The results of the present study indicate the existence of a large pool of HCV infection in Greece and an impressive spread of the virus in high-risk groups. Chronic HCV infection was found to account for 83.6% of patients with chronic non-A, non-B hepatitis parenterally transmitted, 56.5% of cases of sporadic community-acquired disease and for almost 1/4 of all patients with chronic liver disease. The relative risks for development of hepatocellular carcinoma of patients with chronic HCV infection was 6.3 in the first and 13.7 in the second case-control study, increasing to 20.0 and 18.7, respectively, when hepatitis B surface antigen (HBsAg) was positive. Serum HBV-DNA was positive and/or anti-HBc IgM levels were high in 12 of 15 (80%) patients with hepatocellular carcinoma positive only for HBsAg, and in 7 of 15 (47%) positive both for HBsAg and antibodies to HCV. The present data support the view that hepatitis B and C virus have an interacting role in the origin of hepatocellular carcinoma.

N. C. Tassopoulos, A. Hatzakis, I. Delladetsima, M. G. Koutelou, A. Todoulos and V. Miriagou. Role of hepatitis C virus in acute non-A, non-B hepatitis in Greece: a 5-year prospective study. *Gastroenterology*, 1992; 102: 3: 969-72

The prevalence of hepatitis C virus (HCV) infection in 182 prospectively followed adult patients (110 males, 72 females) with acute non-A, non-B hepatitis and its correlation with progression to chronic hepatitis were studied. These patients were followed for a mean of 24.7 +/- 13.1 (range, 6-57) months. By using a specific enzyme immunoassay for the detection of antibodies against C100-3 polypeptide of HCV, 96 (52.7%) were found antibody positive. HCV was implicated in 64/89 (71.9%) of the cases with classical parenteral exposure but only in 18/64 (28.1%) of the community-acquired cases. Progression to chronic hepatitis was observed more frequently in antibody-positive than in antibody-negative cases (60/96 or 62.5% vs. 27/86 or 31.4%, $P = 0.00002$). Progression was also observed more often in males than in females (66/112 or 58.9% vs. 21/70 or 30.0% $P = 0.0001$), both in the antibody positive (48/68 or 70.6% vs. 12/28 or 42.9%, $P = 0.01$) and in the antibody negative (18/44 or 40.9% vs. 9/42 or 21.4%, $P = 0.043$) cases. These data indicate that (a) acute hepatitis due to HCV is characterized by a high rate of chronicity, especially in males, and (b) a non-A, non-B, non-C agent or a different strain of HCV may be responsible for the majority of the community-acquired cases of non-A, non-B hepatitis in Greece.

E. Kaklamani, D. Trichopoulos, A. Tzonou, X. Zavitsanos, Y. Koumantaki, A. Hatzakis, C. C. Hsieh and S. Hatziyannis. Hepatitis B and C viruses and their interaction in the origin of hepatocellular carcinoma. *Jama*, 1991; 265: 15: 1974-6

Serum taken from patients in a case-control study in Athens, Greece, was used to examine the interactive roles of hepatitis B virus (HBV) and hepatitis C virus (HCV) in the origin of hepatocellular carcinoma (HCC). An enzyme immunoassay for anti-HCV was used to test serum taken from 185 cases with HCC, 35 cases with metastatic liver cancer (MLC), and 432 hospital controls. Weakly positive anti-HCV results were more strongly related to MLC than to HCC, implying that these anti-HCV results are false positive. By contrast, strongly positive anti-HCV results were significantly related to HCC (relative risk [RR], 6.3), whereas no significant association was evident for MLC (RR, 0.6). The association of anti-HCV with HCC was substantially higher among subjects whose radioimmunoassay was positive for hepatitis B surface antigen (RR, 20.0) than among those whose radioimmunoassay was negative for this marker (RR, 4.8). These findings indicate that HCV infection has an interactive role in the origin of HCC.

E. J. Hatziandreu, A. Hatzakis, S. Hatziyannis, M. A. Kane and M. C. Weinstein. Cost-effectiveness of hepatitis-B vaccine in Greece. A country of intermediate HBV endemicity. *Int J Technol Assess Health Care*, 1991; 7: 3: 256-62

We evaluated the cost-effectiveness of (a) a vaccination program for the prevention of hepatitis B; and (b) the two commercially available vaccines (Merck Sharp and Dohme; Pasteur Institute) in Greece, a country of intermediate endemicity. We examined cases of hepatitis-B infection prevented and the expected medical costs among the high-risk groups of medical and nursing students, hospital personnel, and the general population. Employing a vaccination program reduces considerably the risk of infection, especially in the high-risk groups, while it increases the total cost. The vaccines are very comparable in terms of both health and economic outcomes. Sensitivity analysis indicated that vaccine cost, incidence of hepatitis B, and compliance were the key factors for the choice of (a) whether to undertake an extensive program to prevent hepatitis-B infection and its chronic sequelae; and (b) which vaccine to administer.

S. J. Hadziyannis, C. Papaioannou and A. Alexopoulou. The role of the hepatitis delta virus in acute hepatitis and in chronic liver disease in Greece. *Prog Clin Biol Res*, 1991; 364: 51-62

HDV infection has been documented in Greece for more than 3 decades. Its epidemiology appears to be changing over the years with a decrease in the general Greek population and an invasion of the delta virus in the community of drug addicts. For the time being HDV infection has a low endemicity in the general greek population, it has been detected with high endemicity in a rural community and it is spreading epidemically in the new, increasing population of Greek drug addicts. Chronic HDV infection has been detected constantly over 20 years with a higher frequency in HBsAg positive chronic liver disease (19.5-33.5%) than in asymptomatic HBsAg carriers with normal liver enzymes (5.9-9.2%). However, in the community of Archangelos, where HDV infection is highly endemic, and probably also all over Greece, the total number of chronic HDV carriers with minimal or no liver disease appears to be higher than those with severe liver damage. HDV infection plays a significant role in terms of morbidity and mortality from acute and chronic liver disease in Greece but the situation would have been much worse if chronic HDV infection was invariably associated with severe liver damage.

N. C. Tassopoulos and G. J. Papaevangelou. Correlation of hepatitis B surface antigen clearance with the route of hepatitis B virus infection. *J Gastroenterol Hepatol*, 1990; 5: 3: 252-5

We studied 563 consecutive adults with acute hepatitis B hospitalized from May 1981 to May 1983 and their habitual heterosexual partners. Radio-immunoassays for the detection of serological markers of hepatitis A virus (HAV) and hepatitis B virus (HBV) and enzyme-immunoassay for the detection of IgM antibody to hepatitis B core antigen (IgM anti-HBc) were used. Of the 563 patients, 503 (89.7%) were hepatitis B surface antigen (HBsAg) positive and 60 (10.7%) were HBsAg negative on admission. Absence of HBsAg on admission was observed significantly more frequently in patients infected possibly by the heterosexual route than in the remaining patients (23.3% versus 6.6%; P less than 0.001). This finding was independent of sex. These data show that the route of HBV infection rather than the sex appears to have a more important role in the rapid clearance of HBsAg.

D. A. Papanastasiou, I. T. Spiliopoulou, O. G. Papageorgiou and N. G. Beratis. Hepatitis B in household contacts of children with beta-thalassemia. *Acta Haematol*, 1990; 84: 4: 182-5

The hepatitis B virus (HBV) markers have been studied in 184 household contacts of 110 thalassemic patients and 184 normal individuals matched for age and socioeconomic status with the study subjects. The mean age (+/- SD) in both patients and control subjects was 31.1 +/- 13.5 years. HBV infection had occurred in 51.6% of the household contacts and in 32.1% of the control subjects. This difference is highly significant (p less than 0.001). The most frequent marker observed was the antihepatitis B core IgG followed by the antihepatitis B surface antibody. It is noteworthy that none of the thalassemic patients infected in the past was seropositive for the hepatitis B surface antigen at the time of the study, whereas its frequency in the general population was 8.1%. The findings indicate that the household contacts of thalassemic patients have a greater seroprevalence for hepatitis B infection. Furthermore, the household contacts of thalassemic patients are infected at a younger age than the control population. The high infection rate with HBV in all groups tested suggests that vaccination should be considered not only for the household contacts of thalassemic patients but possibly for the entire Greek population.

N. C. Tassopoulos, G. Theodoropoulos, M. H. Sjogren, R. Engle and R. H. Purcell. Serological markers of hepatitis B virus and hepatitis D virus infections in Greek adults with primary hepatocellular carcinoma. *Infection*, 1989; 17: 1: 17-9

Primary hepatocellular carcinoma (PHC) has been linked etiologically to chronic hepatitis B virus (HBV) infection by epidemiologic and molecular lines of evidence. Serologic evidence of HBV and hepatitis delta virus (HDV) infection was assessed in sera from 47 Greek patients with PHC. Radioimmunoassays for the detection of serological markers of HBV and HDV infections and molecular hybridization techniques for the detection of HBV DNA sequences were used. Serological evidence of HBV infection was found in 93.6% of PHC patients. Of the 47 patients, 20 (42.6%) were positive for HBsAg, 43 (91.5%) were positive for anti-HBc and 21 (44.7%) were positive for anti-HBs. Anti-HBe was detected in a high percentage (90%) of HBsAg positive PHC patients. Anti-HBc IgM was also detected in 90% of HBsAg positive PHC patients; in contrast, HBV DNA was detected only in 5% of them. None of the 47 patients had serological evidence of HDV infection. These data show that HBV appears to be the principal etiological agent of PHC in Greece.

S. Sklavounou-Tsouroutsoglou, D. Catriu-Nikolakaki, F. Athanassiadou-Piperopoulou, J. Ntoutos, J. Mavromichalis, D. Sofianou and J. Papapanayotou. Hepatitis B vaccination in children with thalassemia in northern Greece. *Biomed Pharmacother*, 1989; 43: 7: 527-30

Sera from 101 children with thalassemia, aged between 6 months to 15 years, were examined for detection of HBV infection. Of these 101 children, 18 negative for all HBV markers were vaccinated against HB with "Hevac B" vaccine from the Pasteur Institute. Our results show that 3 inoculations at one-month intervals have induced an excellent antibody (anti-HBs) response in all vaccinated children, affording full protection against HBV infection. There were no noticeable local or general reactions to "Hevac B" vaccine. Our results, in accordance with other reports, have revealed that hepatitis B vaccine is highly immunogenic for children with thalassemia and is particularly well tolerated.

N. C. Tassopoulos, M. Alikiotis, F. Limotirakis, P. Nicolakakis, H. Mela and M. Paralogou-Ioannides. Acute sporadic non-A, non-B hepatitis in Greece. *J Med Virol*, 1988; 26: 1: 71-7

The influence of non-A, non-B (NANB) agent(s) on the aetiology of acute sporadic viral hepatitis and its possible transition to chronic hepatitis were studied. Acute sporadic NANB hepatitis was diagnosed in 134 (13.5%) of the 993 Greek adults who were admitted consecutively to the Western Attica General Hospital from February 1986 to September 1987. The male to female ratio was 2.1:1, and the mean age of the patients was 39.7 +/- 17.5 years (range: 16-77 years). Serological markers of past hepatitis B virus infection were detected in 32.1% of the patients. Possible risk factors occurring within 6 months of the onset of hepatitis were parenteral drug abuse in 43 (32.1%), blood transfusions in 26 (19.4%), possibly iatrogenic in 22 (16.4%), homosexual practice in one (0.7%) and no recognized risk factors in 42 (31.4%) patients. The most common source of infection was parenteral drug abuse (65%) in patients less than 30 years old and unknown (41.9%) in patients older than 30 years old. Chronic hepatitis, defined by biochemical criteria, was observed in 55.6% of the cases irrespective of the risk factor. These data show that parenteral drug abuse made a significant contribution to the spread of NANB agent(s) but not homosexual practice and that the rate of chronicity was high.

G. J. Papaevangelou and A. Roumeliotou-Karayannis. Reduction of HBV infections and mass immunisation. *Lancet*, 1988; 1: 8575-6: 53-4

N. C. Tassopoulos, G. J. Papaevangelou, M. H. Sjogren, A. Roumeliotou-Karayannis, J. L. Gerin and R. H. Purcell. Natural history of acute hepatitis B surface antigen-positive hepatitis in Greek adults. *Gastroenterology*, 1987; 92: 6: 1844-50

We prospectively followed up 821 adults with acute viral hepatitis hospitalized at the Athens Hospital for Infectious Diseases between May 1981 and May 1983. Radioimmunoassays for the detection of serologic markers of hepatitis A virus, hepatitis B virus, and hepatitis delta virus, and molecular hybridization techniques for the detection of serum hepatitis B virus deoxyribonucleic acid and hepatitis delta virus ribonucleic acid were used. Based on the results of an enzyme immunoassay for the detection of immunoglobulin M antibody to hepatitis B core antigen (Corzyme-M), 563 cases were diagnosed as acute hepatitis B and 45 as acute hepatitis superimposed on hepatitis B surface antigen carriage. Development of

the hepatitis B surface antigen carrier state was observed in only 1 (0.2%) of the 507 cases with acute hepatitis B that were followed. In contrast, hepatitis B surface antigen persisted in all the latter cases. Acute hepatitis superimposed on hepatitis B surface antigen carriage was attributed to hepatitis A virus superinfection in 2 (4.4%), hepatitis delta virus superinfection in 22 (48.9%), reactivation of chronic type B hepatitis in 12 (26.7%), seroconversion from hepatitis B e antigen-positive to anti-hepatitis B e antibody-positive in 2 (4.4%), presumed superinfection by non-A, non-B agent(s) in 6 (13.4%), and the first clinical manifestation of chronic active hepatitis in 1 (2.2%) case. These data show that acute clinical hepatitis B in adults seems to be a self-limited disease and rarely leads to the development of the carrier state in this epidemiologic setting and hepatitis delta virus superinfection and spontaneous reactivation of chronic hepatitis B are the principal causes of acute hepatitis superimposed in hepatitis B surface antigen carriers in an area with a moderately high prevalence of hepatitis B virus infections.

A. Roumeliotou-Karayannis, N. Tassopoulos, E. Karpodini, E. Trichopoulou, M. Kotsianopoulou and G. Papaevangelou. Prevalence of HBV, HDV and HIV infections among intravenous drug addicts in Greece. *Eur J Epidemiol*, 1987; 3: 2: 143-6

The prevalence of HBV, HDV and HIV infection was studied in 288 imprisoned intravenous drug addicts (IVDA) and 329 controls. Commercially available radioimmunoassays for the detection of HBV and HDV serologic markers and enzyme-immunoassays for IgM anti-HBc and anti-HIV were used. Anti-HIV positive results were confirmed by Western Blot. The prevalence of HBV serologic markers among IVDA (77.1%) was found considerably higher than among controls (22.5%). An increased prevalence of HBsAg carriers (6.9%) and anti-HBc alone positives (9.7%) was also found. IVDA carriers were more frequently HBeAg positive (25.0%) and HDV serologic markers were detected in 35.0% (7/20) of them. Anti-HIV were detected in 6 (2.1%) IVDA but in none control. These data show the widespread HBV and HDV infections among Greek IVDA and suggest the need for continuation of the initiated hepatitis B vaccination program. Anti-HIV prevalence is yet low. However there is urgent need for an extensive campaign to limit the further spread of the HIV among this high risk group.

G. J. Papaevangelou. Benign and fulminant HDV hepatitis in Greece. *Prog Clin Biol Res*, 1987; 234: 395-402

N. C. Tassopoulos, M. H. Sjogren, J. R. Ticehurst, R. E. Engle, A. Roumeliotou-Karayannis, J. L. Gerin, R. H. Purcell and G. Papaevangelou. Significance of IgM antibody to hepatitis B core antigen in a Greek population with chronic hepatitis B virus infection. *Liver*, 1986; 6: 5: 275-80

IgM antibody to hepatitis B core antigen (IgM anti-HBc) may indicate an active immune response to persistent infection with hepatitis B virus (HBV). We studied 186 Greek HBsAg carriers for IgM anti-HBc and attempted to correlate it with other HBV and hepatitis delta virus (HDV) markers. Overall, IgM anti-HBc was detected more frequently than HBV DNA in this population (50% vs 34, p less than 0.001); this was also true for the 149 of the 186 HBsAg carriers with antibody to hepatitis B e antigen (anti-HBe) (48% vs 22%, p less than 0.001). The opposite was found in the carriers positive for hepatitis B e antigen (HBeAg): HBV DNA was observed in 93% and IgM anti-HBc in 64% of the cases (p less than 0.05). The detection of these markers was independent of sex. Serum alanine aminotransferase (ALT) levels were significantly more elevated in patients with positive tests for IgM anti-HBc

and HBV DNA than in patients positive only for HBV DNA (p less than 0.001) irrespective of their HBeAg or anti-HBe status. Moreover, the detection of elevated ALT was independent of the intensity of the HBV DNA hybridization signal. Antibodies to hepatitis delta antigen (HDAg) were only found in 4 (2.4%) of 167 patients tested.

N. C. Tassopoulos, G. J. Papaevangelou, J. R. Ticehurst and R. H. Purcell. Fecal excretion of Greek strains of hepatitis A virus in patients with hepatitis A and in experimentally infected chimpanzees. *J Infect Dis*, 1986; 154: 2: 231-7

The presence of hepatitis A virus (HAV) in stool samples was determined in 36 children (mean age, 8.9 years) and 38 adults (mean age, 19.9 years) with acute type A hepatitis. Three stool samples, taken on admission and thereafter at three-to-five-day intervals, were collected from each patient. The first day of dark urine was considered to be the onset of illness. Molecular hybridization of cloned HAV cDNA to fecal extracts was used to detect HAV RNA; radioimmunoassay was used to detect HAV antigen. In all of the samples tested, HAV RNA was detected significantly more frequently than HAV antigen (28.4% vs. 8.1%, P less than .001). HAV RNA was detected with equal frequency in both children and adults during the first week of illness. However, HAV RNA was detected more frequently in children than in adults during the second week of illness (45.7% vs. 18.9%, P less than .05). Among patients with HAV RNA, detection in multiple samples was more frequent in children than in adults (38.9% vs. 7.9%, P less than .01), especially among males.

N. C. Tassopoulos, G. J. Papaevangelou, A. Roumeliotou-Karayannis, A. Smedile, R. Engle, J. R. Ticehurst, S. M. Feinstone and R. H. Purcell. Fulminant hepatitis in asymptomatic hepatitis B surface antigen carriers in Greece. *J Med Virol*, 1986; 20: 4: 371-9

Eleven male fulminant hepatitis (FH) patients (mean age: 47.7 +/- 16 years) positive for hepatitis B surface antigen (HBsAg) but negative for IgM antibody to hepatitis B core antigen (IgM anti-HBc) were admitted consecutively to the Athens Hospital for Infectious Diseases between May 1981 and November 1983. Because of the absence of IgM anti-HBc, determined by an enzyme immunoassay, these patients were considered to be HBsAg carriers with a superimposed acute hepatitis. Three of the 11 patients received immunosuppressive chemotherapy during the six months before the onset of the acute hepatitis. None of the patients was homosexual or a drug addict. Infection with hepatitis A virus (HAV), hepatitis B virus (HBV), or hepatitis delta virus (HDV) was detected with serologic markers and/or molecular hybridization techniques. Fulminant hepatitis was attributed to spontaneous reactivation of chronic hepatitis B in four patients, chemotherapy-induced reactivation of chronic hepatitis B in three patients, HDV superinfection in one patient and possible superinfection by non-A, non-B agent(s), HDV, or HDV-like agents in three patients. Reactivation of chronic hepatitis B was an important cause of apparent acute hepatitis in heterosexual male HBsAg carriers from an area with a high prevalence of HBV infection.

D. J. Papaioannou, E. P. Kaklamani, N. G. Parissis, I. G. Koumantaki, D. T. Karalis and D. B. Trichopoulos. Hepatitis B virus (HBV) serum markers in Greek leprosy patients. *Int J Lepr Other Mycobact Dis*, 1986; 54: 2: 245-51

The prevalence of HBsAg, anti-HBs, and anti-HBc in the sera of 217 patients with the two polar types of leprosy and 382 hospital controls was studied in order to investigate the

degree of exposure of Greek leprosy patients to HBV and the ability of these patients to clear HBV from the blood. Two distinct serological patterns were analyzed: effective exposure, characterized by the presence of one or more of the three serological markers, and active infection, characterized by the presence of HBsAg. From the statistical analysis it was found that TT as well as LL cases had a higher prevalence of effective exposure in comparison to controls (p less than 10^{-5} and p less than 10^{-6}). No significant difference was found between the two polar leprosy types (p greater than 0.30) or between bacteriologically positive and negative LL cases (p greater than 0.30). As far as the prevalence of active infection is concerned among the effectively exposed subjects of all groups, no significant difference existed between TT cases and controls, LL cases and controls, the two polar leprosy cases combined and controls, the two polar leprosy groups, and LL cases positive and negative for *Mycobacterium leprae* (p for all comparisons greater than 0.30). It is concluded that leprosy cases are at a high risk of HBV infection, but the prevalence of active infection among those effectively exposed does not differ between leprosy cases and hospital controls.

B. Panis, A. Roumeliotou-Karayannis, G. Papaevangelou, S. C. Richardson and F. Mitsis. Hepatitis B virus infection in dentists and dental students in Greece. *Oral Surg Oral Med Oral Pathol*, 1986; 61: 4: 343-5

The prevalence of hepatitis B virus (HBV) markers in 416 dental students, 115 dentists, and 329 members of the general population was studied in Athens. Markers were present in 36 students (8.7%), 34 dentists (29.6%), and 74 controls (22.5%). Four students (1.0%), 3 dentists (2.6%), and 6 controls (1.8%) were carriers of hepatitis B surface antigen (HBsAg). The prevalence of HBV infections increased with age significantly faster in the dental profession than in the general population, showing an increased risk. Of 22 dentists in practice for more than 20 years, 12 (54.5%) had HBV markers and 4 (18.2%) reported a clinical hepatitis infection. These data show that members of the dental profession should also be included in the national hepatitis B vaccination program.

G. Theodoropoulos and G. Hadzis. Incidence and significance of hepatitis B and A virus serologic markers in Greek cirrhotic patients. *Gastroenterol Jpn*, 1985; 20: 5: 436-40

The incidence of serological markers of hepatitis B and A virus infection was studied by radioimmunoassay in 89 Greek cirrhotic patients. Controls consisted of 90 patients without liver disease. HBsAg was detected in 62 (69.5%) patients, anti-HBs in 35 (39.3%), anti-HBc in 60 (67.4%), HBeAg in 13 (14.6%), anti-HBe in 58 (65.1%), and the anti-HAV in 86 (96.6%). The corresponding figures for the control group were: HBsAg 4 (4.5%), anti-HBs 34 (37.7%), anti-HBc 41 (45.5%), HBeAg 3 (3.3%), anti-HBe 21 (23.3%), and anti-HAV 86 (95.5%). This high incidence of positive reactions in cirrhotic patients strongly suggests the possibility that HBV infection may be an important causative factor in the development of cirrhosis in Greece. No association could be established between hepatitis A virus infection and cirrhosis.

N. Tassopoulos, G. Papaevangelou, A. Roumeliotou-Karayannis, P. Kalafatas, R. Engle, J. Gerin and R. H. Purcell. Double infections with hepatitis A and B viruses. *Liver*, 1985; 5: 6: 348-53

Ten (2.8%) asymptomatic carriers of HBsAg and four (1.1%) patients with acute hepatitis B virus (HBV) infection were detected among 356 adults with acute viral hepatitis A (HAV)

consecutively admitted to the Athens Hospital for Infectious Diseases from May 1981 to March 1984. These patients did not differ in clinical, epidemiologic (except in age), biochemical or serologic characteristics from patients acutely infected with HAV alone. Transient suppression of the HBV replication and disappearance of the HBV DNA accompanied by seroconversion from HBeAg positive to anti-HBe positive were detected in one and two carriers respectively. The titer of non-class-specific anti-HBc was low (less than or equal to 10^{-2}) in all cases. These data suggest that superinfection of HBsAg carriers with HAV does not cause more severe disease or influence adversely the course of chronic hepatitis B disease. However, accurate diagnosis of double infections is necessary for prognosis of the liver disease and appropriate management of the patient's environment. This is quite important in areas with a high prevalence of HBV infections, like Greece, where double infections are relatively common.

A. Roumeliotou-Karayannis, G. Papaevangelou, N. Tassopoulos, S. C. Richardson and S. Krugman. Post-exposure active immunoprophylaxis of spouses of acute viral hepatitis B patients. *Vaccine*, 1985; 3: 1: 31-4

Post-exposure efficacy of hepatitis B vaccine was evaluated in susceptible sexual partners of acute hepatitis B patients in a randomized double-blind, placebo-controlled trial in Greece. Vaccine (20 micrograms dose) or placebo was repeated one and six months after initial administration. Nine months' follow-up was completed by 146/160 entrants. Vaccinated (16.0%) and control spouses (18.3%) showed similar attack rates for all infections. The vaccine group had fewer clinical infections (2.7% against 7.0%) and fewer infections occurring more than one month after first vaccination (8.7% against 14.7%). These differences are not statistically significant, but suggest modification of infection. Overall, the attack rate was lower (p less than 0.01) for male spouses (6.4%) than for females (22.4%). It may be necessary to complement hepatitis B vaccination with hepatitis B immunoglobulin to protect this high-risk group.

G. Papaevangelou, A. Roumeliotou-Karayannis, N. Tassopoulos, S. C. Richardson, P. Stathopoulou, N. Papadoyannakis, N. Tsantoulis, K. Politi and A. Tassiopoulou. Evaluation of methods of pre-vaccination screening for markers of hepatitis B infection. *Eur J Epidemiol*, 1985; 1: 2: 100-3

The prevalence of serologic evidence of hepatitis B virus infection in various populations in Greece was examined to provide data for formulating cost-effective strategies for prevaccination screening. Markers were detected in 17.5% of 320 healthy persons, 73.3% of 273 multiply transfused patients and 61.0% of 146 haemodialysis patients. In multiply transfused patients, antibody to hepatitis B surface antigen (anti-HBs) was significantly more common than antibody to core antigen (anti-HBc) (67.0%, 44.3%), while the opposite was true for haemodialysis patients (43.8%, 57.5%). These data suggest that it may be most cost-effective to screen only for anti-HBs in multiply transfused patients and only anti-HBc in haemodialysis patients. Vaccination without screening may be more cost-effective for healthy persons. Anti-HBs and anti-HBc were detected with similar frequencies (14.7%, 15.9%), thus neither offers an advantage in screening healthy persons, although use of anti-HBc may facilitate detection of chronic carriers. These data indicate that the choice of marker for pre-vaccination screening should depend on the population under consideration.

G. Papaevangelou, A. Roumeliotou-Karayannis, G. Kallinikos and K. Politou. Lack of antibodies to LAV/HTLV-III in hepatitis B vaccine recipients. *Eur J Epidemiol*, 1985; 1: 4: 323-5

There is no evidence up to now that the currently available plasma hepatitis B vaccine transmits the agent of AIDS. To support further the safety of this vaccine we examined 137 vaccinees for the presence of antibodies to LAV/HTLV-III. Three groups had received Merck, Sharp and Dohme hepatitis B vaccine (two groups of 25 Air Force cadets vaccinated with investigational lots and 18 multiply transfused children vaccinated with a commercial lot); another two groups (50 Air Force cadets and 19 multiply transfused) were vaccinated with two commercial lots of Institut Pasteur vaccine. Sera were collected before inoculation, 7 and 24 months later. Enzyme linked immunosorbent assay was used for the detection of antibodies to LAV/HTLV-III. Positive sera were tested again by Western Blot and Radioimmune Precipitation Assay to exclude non-specific binding. Antibodies to LAV/HTLV-III were not detected in any of the sera examined, providing evidence for safety. We believe that these data increase the acceptance of hepatitis B vaccine.

G. Papaevangelou, N. Tassopoulos, A. Roumeliotoukarayannis and C. Richardson. Etiology of Fulminant Viral-Hepatitis in Greece. *Hepatology*, 1984; 4: 3: 369-372

G. Papaevangelou, A. Roumeliotou-Karayannis, N. Tassopoulos and P. Stathopoulou. Diagnostic value of anti-HBc IgM in high HBV prevalence areas. *J Med Virol*, 1984; 13: 4: 393-9

The diagnostic value of an anti-mu-capture immunoassay for the detection of IgM antibody against hepatitis B core antigen (anti-HBc) was evaluated. Strongly positive results were obtained from the acute phase sera of the 25 acute hepatitis B patients who were hepatitis B surface antigen (HBsAg) positive and of the 18 confirmed acute hepatitis B patients who had already cleared HBsAg when symptoms developed. Negative results were obtained in 5 hepatitis A patients, 20 non-A, non-B acute hepatitis patients serologically susceptible to HBV, 22 patients with chronic hepatitis B liver disease, 15 asymptomatic HBsAg carriers, and 10 healthy patients immune from past HBV infection. Fourteen of the acute hepatitis patients remained HBsAg positive for a follow-up period of at least 6 months, and 12 of these were found consistently anti-HBc IgM negative. These were considered as chronic HBsAg carriers with a superimposed form of acute liver injury. These data show that this assay can differentiate between acute from chronic (HBsAg positive) and recent from old (HBsAg negative) hepatitis B virus infection. Thus, it should be very useful in the complex diagnostic situations encountered commonly in areas with high prevalence of HBV infections.

G. Papaevangelou, A. Roumeliotou-Karayannis, N. Tassopoulos, N. Kolaitis and P. Stathopoulou. Source of infection due to hepatitis B virus in Greece. *J Infect Dis*, 1983; 147: 6: 987-9

The possible source of infection due to hepatitis B virus (HBV) was investigated in 260 hospitalized adult patients with acute infections. Blood transfusions (30 patients, 11.5%), illicit drug use (16 patients, 6.2%), homosexuality (five patients, 1.9%), and possible

iatrogenic transmission (77 patients, 29.6%) accounted for less than 50% of the cases of hepatitis. Thirty (29.4%) of 102 sexual partners were the most probable source of infection of the patients; three (2.9%) had a history of acute HBV infection two to six months before their partners were admitted to the hospital, and the remaining 27 (26.5%) were characterized as asymptomatic, chronic carriers of hepatitis B surface antigen (HBsAg). The HBsAg carrier rate was higher in men (47.5%) than women (12.9%) and in unmarried (31.6%) than married (25.3%) sexual partners. Hepatitis B e antigen and abnormal serum glutamic pyruvic transaminase levels were detected more frequently in sexual partners who were HBsAg carriers (29.6% and 48.1%, respectively) than in comparable control partners (2.6% and 5.4%, respectively).

G. Papaevangelou, A. Roumeliotou-Karayannis, N. Tassopoulos, N. Kolaitis, P. Contoyannis and S. Krugman. Post-exposure hepatitis B vaccination of sexual partners of acute viral hepatitis patients. *J Infect*, 1983; 7 Suppl 1: 63-7

Sexual transmission of HBV was studied in a sample of 350 sporadic acute viral hepatitis type B adult patients hospitalised in the Infectious Diseases Hospital of Athens, Greece. Spouses with acute viral hepatitis type B (six in number) or asymptomatic HBsAg carriership (80 in number) were considered as the most likely sources of infection in 86 (24.6 per cent) of the 350 patients. Only 164 (46.8 per cent) spouses were susceptible to HBV and 149 agreed to participate in a double-blind, placebo-controlled, randomised trial of hepatitis B vaccine. The Merck Sharp and Dohme vaccine (20 micrograms per dose) or placebo were administered as soon as possible and repeated one and six months later. Vaccinees were interviewed, clinically examined and bled one, three, six and nine months after the first injection. HBV events (clinical hepatitis type B in seven or serological evidence of HBV infection in 15) were diagnosed in 22 vaccinees. We anticipate completing the required sample to establish the possible protective efficacy of the hepatitis B vaccine by the end of November 1982. Final results of the trial will be available early next year.

N. Matsaniotis, C. Kattamis, S. Laskari, E. Dionysopoulou and C. Liapaki. Immunogenicity and efficacy of hepatitis B vaccine in normal children and in patients with thalassaemia. *J Infect*, 1983; 7 Suppl 1: 57-61

S. Hadziyannis, A. Hatzakis, C. Anastassakos and P. Papadopoulos. Hepatitis B vaccination strategy for health-care workers in a country of intermediate hepatitis B endemicity. *J Infect*, 1983; 7 Suppl 1: 93-4

G. Papaevangelou, A. Roumeliotoukarayannis and P. Contoyannis. Changing Epidemiological Characteristics of Acute Viral-Hepatitis in Greece. *Infection*, 1982; 10: 1: 1-4

G. J. Papaevangelou, K. P. Gourgouli-Fotiou and H. G. Vissoulis. Epidemiologic characteristics of hepatitis A virus infections in Greece. *Am J Epidemiol*, 1980; 112: 4: 482-6

The major epidemiologic characteristics of hepatitis A virus (HAV) infections in Greece were studied in a sample of 877 Air Force recruits, 19-25 years old coming from every geographic region of Greece. Antibodies to HAV (anti-HAV) were detected by solid phase

radioimmunoassay in 83.8% of the recruits. Antibody frequency varied significantly in the various geographic regions of Greece and was inversely related to the size of the community. It was further shown that the prevalence of HAV infection was highly related to the recruit's social class and years of education as well as number of siblings and number of persons per room. These findings in accordance with previous reported data show that hepatitis A is hyperendemic and should be regarded as a childhood infection in Greece. Prevailing socioeconomic, hygienic living and housing conditions should be considered as the main epidemiologic determinants of HAV infections.

L. R. Mathiesen, G. Papaevangelou, R. H. Purcell, D. Grammatikopoulos, P. Contoyannis and D. Wong. Etiological characterization of hepatitis B surface antigen-negative hepatitis among adult patients in Athens, Greece. *J Clin Microbiol*, 1980; 11: 3: 297-300

In a 4-month period, 216 cases of acute viral hepatitis were diagnosed in adults at the Infectious Diseases Hospital, Athens, Greece. Twenty-six percent of these were hepatitis B surface antigen negative. A full set of clinical specimens was obtained from 19 of these patients, who were studied in depth for the etiology of their hepatitis. A total of 7 of the 19 patients had serological evidence of hepatitis A virus infection, and 2 had evidence of recent hepatitis B virus infection. The remaining 10 patients lacked evidence of hepatitis A virus, hepatitis B virus, cytomegalovirus, or Epstein-Barr virus infection related to their illness and were classified as having type non-A, non-B hepatitis. Types A and non-A, non-B hepatitis were clinically similar in these adults patients. However, patients with type non-a, non-B hepatitis were, on the average, older and more likely to have received parenteral inoculations during the 6 months before contracting hepatitis. Approximately 76% of the 216 consecutive cases of acute viral hepatitis were probably type B, approximately 10% were probably type A, and approximately 14% were probably type non-A, non-B, although the latter two types may be underestimated because of the possibility of superinfection with these viruses in asymptomatic hepatitis B surface antigen carriers. Thus, all three types of viral hepatitis appear to be important in the etiology of liver disease in Athens, Greece.

D. Schenzle, K. Dietz and G. G. Frosner. Antibody against hepatitis A in seven European countries. II. Statistical analysis of cross-sectional surveys. *Am J Epidemiol*, 1979; 110: 1: 70-6

The age-specific prevalence of hepatitis A antibodies has been analyzed using a catalytic epidemic model for populations in seven European countries: West Germany, Norway, Greece, Switzerland, Holland, France and Sweden. The results indicate a significant decline in the force of infection in recent decades. However, there are substantial differences between the countries, especially between the Scandinavian countries and Greece. The incidence of hepatitis A in Norway and Sweden has declined since 1930, while a downward trend in incidence in Greece may have started only recently.

G. G. Frosner, G. Papaevangelou, R. Butler, S. Iwarson, A. Lindholm, A. Courouce-Pauty, H. Haas and F. Deinhardt. Antibody against hepatitis A in seven European countries. I. Comparison of prevalence data in different age groups. *Am J Epidemiol*, 1979; 110: 1: 63-9

Using a solid phase radioimmunoassay, antibody to hepatitis A virus (anti-HAV) was determined in 3890 sera from populations in seven European countries. Prevalence of anti-

HAV was lowest in Scandinavian countries and highest in Greece and France. Antibodies were found in 77 (13%) of 602 blood donors in Sweden, in 29 (17%) of 175 blood donors and women taking birth control pills in Norway, in 273 (39%) of 700 blood donors in Switzerland, in 262 (52%) of 505 blood donors in Holland, in 365 (55%) of 661 accident patients in West Germany, in 452 (75%) of 600 blood donors in France and in 530 (82%) of 647 persons in Greece. Prevalence of anti-HAV increased with age in all populations tested, indicating nearly total exposure to HAV in persons over 19 years of age in Greece and in persons over 39 years of age in West Germany, Holland and France. Antibody was found more frequently in rural than in urban populations in Greece and Switzerland. Calculation of the age-specific incidence of HAV infections suggests a remarkable decline in the exposure rate in the last few decades.