Background document

"Burden and prevention of Viral Hepatitis in Portugal."

Viral Hepatitis Prevention Board Meeting
Lisbon, Portugal, 18-19 November 2010.

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Content

This pre-meeting document is a list of selected abstracts/ references from a Pubmed MEDLINE search on different search terms. The references are ranged by publication year (most recent first) and for each year in alphabetical order of the first author's name.

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1. Hepatitis in Portugal

Pubmed MEDLINE search on {(**Portugal** OR **Portugees**) AND (**Hepatitis** OR **HAV** OR **HBV** OR **HCV** OR **HDV** OR **HEV)**} in all fields and published **from 2007** on**,** was performed. A second search on these results was performed in Endnote with {'**Epidemiology**' or '**Prevalence**' or '**Prevention**' or '**vaccin***' or '**control**' or ''**Diagnostic***' or '**surveillanc**e'or '**screening**'}. After a manual search only the references and the abstracts really related to Prevention and control in Portugal were selected. In total 43 out of 252 references are mentioned in this background document, the references are ranged by publication year (most recent first) and for each year in alphabetical order of the first author's

Gyarmathy VA, Giraudon I, Hedrich D, Montanari L, Guarita B, and Wiessing L.
Drug use and pregnancy - challenges for public health.
Euro Surveill 14: 33-36, 2009.

Involving pregnant drug users in drug treatment is likely to decrease the chances of pre- and perinatal complications related to drug use and to increase access to prenatal care. Timely medical intervention can effectively prevent vertical transmission of human immunodeficiency virus, hepatitis B virus as well as certain other sexually transmitted diseases, and would allow newborns infected with hepatitis C virus during birth to receive immediate treatment.

Machado MV, and Cortez-Pinto H.
Insulin resistance and steatosis in chronic hepatitis C.
Ann Hepatol 8 Suppl 1: S67-75, 2009.

In chronic hepatitis C, insulin resistance (IR) and type 2 diabetes mellitus (DM) are more prevalent than in healthy controls or in chronic hepatitis B patients. HCV infection promotes IR mainly through increased TNF-a and cytokine suppressor (SOCS-3) production. Both events inhibit insulin receptor and IRS-1 (insulin receptor substrate) tyrosine phosphorylation. Hepatic steatosis is also 2.5 fold more frequent in hepatitis C virus (HCV) infected patients as compared to the general population. Metabolic factors play a crucial role in the etiology of hepatic steatosis genotype non-3 related, which are also the genotypes with a greater association to IR. However, genotype 3, and particularly 3a, has a greater direct steatogenic capacity, and consequently, in those patients, the association with metabolic factors is weaker. Instead, in genotype 3, steatosis associates with viral factors like viral load. Those metabolic factors influence not only the natural history of HCV infection, as well as associate to an accelerated hepatic fibrosis progression, to a worse prognosis when hepatic cirrhosis is present, namely an increased risk of hepatocellular carcinoma, and to a lower sustained viral response rate. On the other hand, in patients who achieve viral eradication, IR and hepatic steatosis may regress, and return if viral infection recurs, which once again indicates an intrinsic steatosis and IR promoter action by HCV.

Mota A, Guedes F, Areias J, Pinho L, and Cardoso MF.
Epidemiological study of genotypes of hepatitis B virus in northern Portugal.
J Med Virol 81: 1170-1176, 2009.

While the overall prevalence of hepatitis B virus (HBV) infection in Portugal is around 1%, there are no published studies examining HBV genotypes in this country. This

study aimed to survey HBV genotypes in the northern Portugal and to examine the possible associations between genotypes and gender, viral transmission routes, viral markers, viral load, and biochemical tests of liver function. The study sample consists of 340 patients with HBV infection of whom 42.9% were women. Tests were carried out for HBV genotypes and biochemical liver function while demographic information, including alcohol intake, was obtained from the patient files. The results indicate the predominance of genotype D (60.3%) and genotype A (31.5%). Intrafamilial transmission was predominant in female patients, while males were infected in equal proportions by perinatal, sexual, and intrafamilial transmission. Absence of HBeAg was found in a significantly smaller proportion of female patients with genotype D as compared to A (56.6% vs. 82.1%, P = 0.028). High viral load was associated significantly and independently with genotype D and HBeAg. Both alanine and aspartate aminotransferases (ALT and AST) were associated with gender and HBeAg. Thus, genotypes A and D were found to be the most prevalent in the north of Portugal. Patients infected with genotype D had higher levels of HBV DNA. HBeAg was associated with genotype D, viral load, and ALT and AST.

Quelhas R, and Lopes A.
Psychiatric problems in patients infected with hepatitis C before and during antiviral treatment with interferon-alpha: a review.
J Psychiatr Pract 15: 262-281, 2009.

OBJECTIVE: Neuropsychiatric symptoms are common in patients with chronic hepatitis C (CHC) and can potentially be exacerbated by interferon-alpha treatment. Such symptoms can contribute to problems with treatment adherence, which can significantly compromise epidemiological virus control. This review summarizes current knowledge about the etiology, course, and management of neuropsychiatric symptoms in patients with CHC. METHOD: Studies were identified using computerized searches, with further references obtained from the bibliographies of the reviewed articles. RESULTS: Psychopathological syndromes that occur during interferon-alpha treatment frequently have atypical features that may complicate their recognition using standard diagnostic criteria. In addition, prospective studies in this area often exclude patients with psychiatric disorders and have methodological disparities that make it difficult to develop guidelines for management of psychiatric side effects induced by interferon-alpha. Despite the high prevalence of chronic hepatitis C virus (HCV) infection in patients with psychiatric and substance use disorders, neuropsychiatric concerns often lead to the exclusion of such patients from interferon-alpha treatment, inappropriately depriving them of the potential benefits of this therapy. CONCLUSION: Consultation-liaison psychiatrists should become familiar with the clinical spectrum of presentations associated with HCV infection as well as with related neuropsychiatric symptoms in order to promote the creation of multidisciplinary teams who specialize in the care of patients with HCV infections. More studies are needed to define neuropsychiatric syndromes that can be induced by interferon-alpha and to clarify best assessment and treatment procedures for these syndromes. It is also important to create and evaluate psychoeducational programs for all patients with chronic HCV infections, even those with low risk of complications, in order to promote adherence to therapy and optimize patients' quality of life.

Santos L, Alves R, Macario F, Parada B, Campos M, and Mota A.
Impact of hepatitis B and C virus infections on kidney transplantation: a single center experience.
Transplant Proc 41: 880-882, 2009.

OBJECTIVE: The impacts of hepatitis C virus (HCV) and hepatitis B virus (HBV) infections on patient and renal graft survivals are controversial. This study sought to evaluate the effects of pretransplantation HCV and HBV infections on renal transplant patients and their grafts at our center. PATIENTS AND METHODS: We retrospectively examined 1224 renal transplantations performed between 1992 and 2006, including 28 HBsAg positive; 64, anti-HCV; 9, anti-HCV plus HBsAg positive; and 1123, negative for anti-HCV and HBsAg. The mean posttransplantation follow-up was 5.6 +/- 4.1 years. RESULTS: The prevalences of HBV infection were 6.2% in 1994 and 2.3% in 2006 and those of HCV infection were 6.8% in 1998 and 5.2% in 2006. The rejection rate was higher among HBV+ (46.4%) and HCV+ (40.6%) groups than the negative groups (31.5%), but it was not significant. There were no significant differences in patient and graft survivals among the groups. The major cause of patient death was liver failure among patients with concomitant HBV+ and HCV+ infections and cardiovascular disease among HCV+ and negative patients. CONCLUSIONS: There has been a decrease in the prevalence of recipients with hepatitis virus infections over the last 15 years. Patient and graft survivals were not affected by HCV or HBV infection.

Barros H, Ramos E, and Lucas R.
A survey of HIV and HCV among female prison inmates in Portugal.
Cent Eur J Public Health 16: 116-120, 2008.

HIV and hepatitis C virus (HCV) monitoring among prison inmates is instrumental in countries with concentrated HIV/AIDS epidemics. Knowledge on these dynamics in imprisoned women in Portugal is scarce. The HIV and HCV prevalence was estimated among inmates in the largest Portuguese prison for women, which holds 57% of all female inmates in Portugal, according to sociodemographic and behavioural variables and characterised attitudes towards HIV/AIDS according to serological status. Collected variables included age, education, country of birth, penal status, and accumulated time in prison. Drug injection and sharing of injection material were inquired, as well as age at first sexual intercourse. Inmates also characterised their attitudes towards HIV/AIDS. A venous blood sample was collected and tested for anti-HIV and anti-HCV antibodies. In this sample of 445 female inmates, 10% were HIV-positive, while 11% were HCV-positive. Longer imprisonment periods were associated with relatively higher HCV prevalence and women with later ages at first sexual intercourse were less frequently HIV-positive, regardless of drug injecting behaviour. HIV prevalence was 44% in women who had ever injected drugs and 6% in those who had never injected. HCV frequency was 69% among injecting drug users (IDUs) and 4% among non-IDUs. In women who injected drugs both HIV and HCV were more frequent when the number of injections was higher and when women reported sharing of injection material. Similar attitudes towards HIV/AIDS were found for HIV-positive and negative women, but those living with HIV had more tolerant positions. This study emphasizes the role of injecting drug use in the transmission of HIV and HCV in women in Portuguese prisons and reinforces the need for the systematic adoption of harm reduction measures.

Carneiro de Moura M, and Marinho R.
[Natural history and clinical manifestations of chronic hepatitis B virus.].
Enferm Infecc Microbiol Clin 26 Suppl 7: 11-18, 2008.

Hepatitis B virus (HBV) infection is a serious public health problem worldwide. In the last few decades, major advances have been achieved that have contributed to

greater understanding of the natural history and clinical manifestations of this infection. The fluctuation between viral replication and the host's immune response has implications in the pathogenesis and progression of the hepatic lesion. In immunocompetent adults, most HBV infections resolve spontaneously in contrast with progression to chronic infection in most infants. Patients with chronic hepatitis due to HBV or chronic hepatitis B can present at four phases: 1) the immune tolerance phase, 2) HBeAg-positive chronic hepatitis B, 3) inactive HBsAg carrier state, and 4) HBeAg-negative chronic hepatitis. HBeAg-positive or -negative chronic hepatitis can progress to cirrhosis, liver failure and hepatocellular carcinoma. Progression to these complications is more frequent in HBeAg-negative forms, associated with mutations that affect the pre-core region and maintain active viral replication. Risk factors are HBV-DNA positive serum levels, an increase in serum transaminase levels and some genotypes. These factors highlight the need to evaluate and monitor all HBV carriers to identify those who could benefit from early antiviral treatment, thus avoiding progression to more advanced forms of liver disease. These measures could improve prevention and treatment of hepatitis B.

Abreu C.
[Viral hepatitis in travellers].
Acta Med Port 20: 557-566, 2007.

Considering the geographical asymmetric distribution of viral hepatitis A, B and E, having a much higher prevalence in the less developed world, travellers from developed countries are exposed to a considerable and often underestimated risk of hepatitis infection. In fact a significant percentage of viral hepatitis occurring in developed countries is travel related. This results from globalization and increased mobility from tourism, international work, humanitarian and religious missions or other travel related activities. Several studies published in Europe and North America shown that more than 50% of reported cases of hepatitis A are travel related. On the other hand frequent outbreaks of hepatitis A and E in specific geographic areas raise the risk of infection in these restricted zones and that should be clearly identified. Selected aspects related with the distribution of hepatitis A, B and E are reviewed, particularly the situation in Portugal according to the published studies, as well as relevant clinical manifestations and differential diagnosis of viral hepatitis. Basic prevention rules considering enteric transmitted hepatitis (hepatitis A and hepatitis E) and parenteral transmitted (hepatitis B) are reviewed as well as hepatitis A and B immunoprophylaxis. Common clinical situations and daily practice "pre travel" advice issues are discussed according to WHO/CDC recommendations and the Portuguese National Vaccination Program. Implications from near future availability of a hepatitis E vaccine, a currently in phase 2 trial, are highlighted. Potential indications for travellers to endemic countries like India, Nepal and some regions of China, where up to 30% of sporadic cases of acute viral hepatitis are caused by hepatitis E virus, are considered. Continued epidemiological surveillance for viral hepatitis is essential to recognize and control possible outbreaks, but also to identify new viral hepatitis agents that may emerge as important global health issues.

Bosetti C, Levi F, Lucchini F, Zatonski WA, Negri E, and La Vecchia C.
Worldwide mortality from cirrhosis: an update to 2002.
J Hepatol 46: 827-839, 2007.

BACKGROUND/AIMS: Cirrhosis mortality has registered large changes over the last few decades. METHODS: Age-standardized (world standard) cirrhosis mortality rates per 100,000 were computed for 41 countries worldwide over the period 1980-2002

using data from the WHO mortality database. RESULTS: In the early 1980s, the highest rates were in Mexico, Chile (around 55/100,000 men and over 14/100,000 women), France, Italy, Portugal, Austria, Hungary and Romania (around 30-35/100,000 men and 10-15/100,000 women). Mortality from cirrhosis has been steadily declining in most countries worldwide since the mid or late 1970s (annual percent change, APC, between -5% and -1.5% in the last decade only for both sexes). In southern Europe, rates in the early 2000s were less than halved compared to earlier decades. In contrast, rates have been rising in Eastern European countries to reach extremely high values in the mid 1990s, and declined only thereafter. In the UK rates were still steadily rising (APC around +7% in men and +3% in women from England and Wales, and +9% in men and +7% in women from Scotland). CONCLUSIONS: Mortality from cirrhosis shows favourable trends in most countries of the world, following the reduction in alcohol consumption and hepatitis B and C virus infection. The steady upward trends observed over more recent calendar periods in the UK and central and eastern European countries are attributed to the persistent increase in the prevalence of alcohol consumption.

March JC, Oviedo-Joekes E, and Romero M.
Factors associated with reported hepatitis C and HIV among injecting drug users in ten European cities.
Enferm Infecc Microbiol Clin 25: 91-97, 2007.

BACKGROUND: To analyze self-reported prevalence of HCV and HIV in a sample of socially excluded injecting drug users, as well as factors associated with the presence of these diseases. METHODS: Cross-sectional study. Data were collected with a structured, face-to-face questionnaire by outreach workers and privileged access interviewers in 1131 participants who had injected heroin and/or cocaine over the past year (71.5% men; mean age, 30 years) from Seville and Granada, Spain; Cologne, Germany; Vienna, Austria; Brussels, Belgium; Athens, Greece; Dublin, Ireland; London, England; Lisbon, Portugal and Perugia, Italy. RESULTS: Among the total sample, 595 (52.6%) participants reported HCV-positive status and 143 (12.6%) HIV-positive status. Multivariate analysis for HCV showed that women are at less risk than men, and that longer drug use, injecting while in prison, sharing needles, and reported positive status for tuberculosis, HBV, HIV or sexually-transmitted disease are positively associated with HCV. Participants reporting positive HIV status were generally older, had injected drugs while in prison, had completed less than 8 years of schooling, were divorced, had no regular employment, and declared infection with tuberculosis, sexually-transmitted disease and HCV. CONCLUSIONS: The highest incidences of HCV and HIV were reported by participants in a poorer social and health situation. Drug addicts must cope not only with their addiction but also with the process of social exclusion they are immersed in. To the greatest extent possible, any course of action for this group should be built into integrated, coordinated plans that take a broad approach to the main issues involved.

Mendez-Sanchez N, Villa AR, Zamora-Valdes D, Morales-Espinosa D, and Uribe M.
Worldwide mortality from cirrhosis.
Annals of Hepatology 6: 194-195, 2007.

Background/Aims: Cirrhosis mortality has registered large changes over the last few decades. Aim: To report worldwide mortality due to cirrhosis over the period 1980-2002. Methods: Age-standardized (world standard) cirrhosis mortality rates per 100,000 were computed for 41 countries worldwide over the period 1980-2002 using

data from WHO mortality database. Results: In the early 1980s, the highest rates were in Mexico, Chile (around 551100,000 men and 14/100,000 women), France, Italy, Portugal, Austria, Hungary and Romania (around 30-351100,000 men and 10-15/100,000 women). Mortality from cirrhosis has been steadily declining in most countries worldwide since the mid or late 1970s (annual percent change, APC, between -5 % and -1.5 % in the last decade only for both sexes). In southern Europe, rates in the early 2000s were less than halved compared to earlier decades. In contrast, rates have been rising in Eastern European countries to reach extremely high values in the mid 1990s, and declined only thereafter. In the UK rates were still steadily rising (APC around +7% in men and +3% in women from England and Wales, and +9% in men and +7% in women from Scotland). Conclusions: Mortality from cirrhosis shows favourable trends in most countries of the world, following the reduction in alcohol consumption and hepatitis B and C virus infection. The steady upward trends observed over more recent calendar periods in the UK and central and eastern European countries are attributed to the persistent increase in the prevalence of alcohol consumption.

Rodrigues L, Pista A, Oliveira A, Agua-Doce I, Manita C, and Paixao MT.
Molecular epidemiology of hepatitis A virus in a group of Portuguese citizens living in Lisbon area.
J Med Virol 79: 483-487, 2007.

Hepatitis A virus (HAV) is the most important cause of acute infectious hepatitis worldwide. In Portugal, due to improvements in sanitation epidemic outbreaks of HAV infection have become less frequent. This report is the first, to our knowledge that characterized HAV in Portugal. For the detection and molecular characterization of HAV cases in a group of Portuguese individuals in the Lisbon area, 31 serum samples were tested: 8 from symptomatic children from an acute hepatitis A outbreak in a Roma (Gipsies) community (2004-2005), and 22 from patients with acute HAV from sporadic cases (2005-2006). A sample of CSF involved in a case of meningitis was also included. IgM anti-HAV detection and nested reverse transcription (RT-PCR), with primers located at the VP1-P2a region, was undertaken to detect HAV genome. In positive samples, molecular characterization was followed by phylogenetic analysis. All samples (n = 31) were positive for IgM anti-HAV. HAV RNA was found in 96.7% of cases. All isolates were classified as genotype I: 22 belonged to sub-genotype IA (73.3%), and 8 to sub-genotype IB (26.7%). All strains obtained from an acute HAV outbreak had sub-genotype IA, in which seven isolates (87.5%) had identical sequences. In HAV sporadic cases sub-genotypes IA and IB were identified, and this may reflect the co-circulation of these two sub-genotypes in Portugal. Molecular epidemiology of HAV infection in this group of Portuguese appears to be similar to other European countries. HAV phylogenetic studies can provide important information for the design of appropriate public health measures.

Tavora-Tavira L, Teodosio R, Seixas J, Prieto E, Castro R, Exposto F, and Atouguia J.
Sexually transmitted infections in an African migrant population in Portugal: a base-line study.
J Infect Dev Ctries 1: 326-328, 2007.

BACKGROUND: For geographical and recent historic reasons, Portugal is a gateway and home for immigration from sub-Saharan countries. Misconceptions related to these populations often lead to consider them as high-frequency clusters for dissemination of sexually transmitted infections (STIs). Epidemiological evidence-

based data is needed to elucidate these issues and baseline prevalence studies are the starting point for this. METHODOLOGY: A prospective study was conducted in 220 African migrants (171 men and 49 women), recently arrived in Portugal, at the time of their first consultation. The presence of STIs was evaluated using a clinical syndromic approach and biological confirmation for gonorrhoea, Chlamydia trachomatis genital infection, syphilis, Hepatitis B and Human Immunodeficiency Virus (HIV) infection. RESULTS: Global prevalence of the targeted infections were 1.8% for gonorrhoea, 0 % for Chlamydia infection, 4.1% for Syphilis, 5.9% for HBsAg presence and 7.3% for HIV infection. Globally, 16.4% of the studied persons had at least one sexually transmitted infection. CONCLUSIONS: We concluded that prevalence rates encountered in this population is similar to that of non-migrant Portuguese populations with a high risk for sexually transmitted diseases. Therefore migration from sub-Saharan Africa doesn't seem to constitute a particularly critical isolated factor for public health risk of STIs in the community.

Vicente J, and Wiessing L.
European Monitoring Centre for Drugs and Drug Addiction annual report 2007: positive assessment of HIV in IDUs though hepatitis C still very high.
Euro Surveill 12: E071122 071126, 2007.

Chodick G, Ashkenazi S, and Lerman Y.
The risk of hepatitis A infection among healthcare workers: a review of reported outbreaks and sero-epidemiologic studies.
J Hosp Infect 62: 414-420, 2006.

All reports of hepatitis A (HA) outbreaks in healthcare settings published between 1975 and 2003 were studied to determine the background immunity or susceptibility of healthcare workers (HCWs) to HA. Twenty-six reports were found. The number of infected personnel ranged from one to 66 and, in most outbreaks, nurses accounted for the majority of personnel infected, reflecting high attack rates reaching 15-41%. In addition, we found 23 sero-epidemiological studies for HA among HCWs that had been performed in 13 different countries. Seroprevalence rates of HCWs with anti-HA antibody ranged between 4% among paramedical workers in Germany to 88% among hospital maintenance workers in Portugal. Effective infection control of HA outbreaks in hospitals demands early recognition, including awareness of atypical presentations of the infection, and strict adherence to universal infection control measures. Education programmes are of special importance for HCWs in neonatal, paediatric and intensive care units. The findings of the current study suggest that a pre-employment screening policy and administration of active vaccination to susceptible HCWs, particularly nurses, should be seriously considered in high-risk settings.

Cruz Neves A, Dickens C, and Xavier M.
[Comorbidity between hepatitis C and depression. Epidemiological and etiopathogenic aspects].
Acta Med Port 19: 21-28, 2006.

Neuropsychiatric symptoms are commonly associated with chronic hepatitis C virus infection (HCV). The aim of this review of the literature was to evaluate the prevalence of depression in patients with hepatitis C, as well as the proposed etiopathogenic models. A review of the literature was undertaken using the complete

search strategy devised by the Cochrane Collaboration Review Group for Depression, Anxiety and Neurosis. All studies but one have shown that major depression in chronic HCV patients is significantly more common than in the general population (reported rates from 5.7% and 45%), being related with illness perception, functional disability, impaired quality of life, fatigue severity, and the presence of psychiatric comorbidity. The mechanism by which depression is related to Hepatitis C is still poorly understood. Authors address some possible mechanisms, such as the psychological impact of the knowledge that one has been infected with HCV and the direct effects of the virus itself on the Central Nervous System (eg. cytoquines).

Leite FJ, Dias F, Ferreira C, Oliveira F, Mota A, and Marques A.
Seroprevalence of human immunodeficiency virus, hepatitis B and C virus and syphilis infections in a blood donor population of Portugal.
Transfusion 46: 101A-101A, 2006.

Mossong J, Putz L, Patiny S, and Schneider F.
Seroepidemiology of hepatitis A and hepatitis B virus in Luxembourg.
Epidemiol Infect 134: 808-813, 2006.

A prospective seroepidemiological survey was carried out in Luxembourg in 2000-2001 to determine the antibody status of the Luxembourg population against hepatitis A virus (HAV) and hepatitis B virus (HBV). One of the objectives of this survey was to assess the impact of the hepatitis B vaccination programme, which started in May 1996 and included a catch-up campaign for all adolescents aged 12-15 years. Venous blood from 2679 individuals was screened for the presence of antibodies to HAV antigen and antibodies to hepatitis B surface antigen (anti-HBs) using an enzyme immunoassay. Samples positive for anti-HBs were tested for antibody to hepatitis B core antigen (anti-HBc) using a chemiluminiscent microparticle immunoassay to distinguish between individuals with past exposure to vaccine or natural infection. The estimated age-standardized anti-HAV seroprevalence was 42.0% [95% confidence interval (CI) 39.8-44.1] in the population >4 years of age. Seroprevalence was age-dependent and highest in adult immigrants from Portugal and the former Yugoslavia. The age-standardized prevalence of anti-HBs and anti-HBc was estimated at 19.7% (95% CI 18.1-21.3) and 3.16% (95% CI 2.2-4.1) respectively. Anti-HBs seroprevalence exceeding 50% was found in the cohorts targeted by the routine hepatitis B vaccination programme, which started in 1996. Our study illustrates that most young people in Luxembourg are susceptible to HAV infection and that the hepatitis B vaccination programme is having a substantial impact on population immunity in children and teenagers.

Pedroso S, Martins L, Fonseca I, Dias L, Henriques AC, Sarmento AM, and Cabrita A.
Impact of hepatitis C virus on renal transplantation: association with poor survival.
Transplant Proc 38: 1890-1894, 2006.

Data concerning the effect of hepatitis C virus (HCV) infection on the long-term outcome of patient and allograft survival are conflicting. We performed a retrospective study including all renal transplant recipients who underwent the procedure at our center between July 1983 and December 2004. We compared HCV-positive (n = 155) versus HCV-negative (n = 1044) recipients for the prevalence of anti-HCV, patient/donor characteristics, and graft/patient survival. The prevalence

of HCV-positive patients was 12%. The anti-HCV positive recipients displayed a longer time on dialysis (P < .001), more blood transfusions prior to transplant (P < .001), and a higher number of previous transplants (P < .001). There were no differences in the incidence of acute rejection between the two groups. Patient (P = .006) and graft survival (P = .012) were significantly lower in the HCV-positive than the HCV-negative group. Graft survival censored for patient death with a functioning kidney did not differ significantly between HCV-positive and HCV-negative recipients (P = .083). Death from infectious causes was significantly higher among the HCV-positive group (P = .014). We concluded that HCV infection had a significant detrimental impact on patient and renal allograft prognosis. Death from infectious causes was significantly more frequent among HCV-positive than the non-HCV population.

Sargento SS, Almeida AM, Ferreira C, Silva E, Neto P, and Colaborators C.
Molecular epidemiology of HCV in Portugal.
Vox Sanguinis 91: 63-63, 2006.

Teixeira JN, Henggeler F, Diniz R, Caldeira B, Mateus N, and Goncalves H.
NAT screening for HIV/HCV (Procleix, Chiron) in single donation in Coimbra, Portugal (2000-2006).
Vox Sanguinis 91: 88-88, 2006.

Wiessing L, and Nardone A.
Ongoing HIV and viral hepatitis infections in IDUs across the EU, 2001-2005.
Euro Surveill 11: E061123 061122, 2006.

Zampieron A, Jayasekera H, Elseviers M, Lindley E, DeVos JY, Visser R, and Harrington M.
European study on epidemiology and management of hepatitis C virus (HCV) infection in the haemodialysis population. Part 3: prevalence and incidence.
Edtna Erca J 32: 42-44, 2006.

An analysis of the literature showed a high prevalence of HCV in the European dialysis population in the nineties. The prevalence was similar in most countries in northern Europe, but infection was more common in France, Italy, Spain, Portugal and Greece (1) and in Eastern European countries (2). The reported prevalence of anti-HCV-positive patients in the EDTA registry was 21% in 1992 and 18% in 1993 (3) ranging from 1% in Finland to 42% in Egypt (4). The incidence of HCV, in new patients starting renal replacement therapy, ranged from 3% to 7% (5,6) and reported seroconversion rates during dialysis treatment varied between 1% (7) and 16% (8) per year.

Araujo F, Henriques I, Monteiro F, Meireles E, Cruz A, Tavares G, and Mota-Miranda A.
Evaluation of NucliSens-AmpliScreen methodology to detect subtypes G of HIV-1 and 4c/4d of HCV in the screening of blood donors.
Transfus Clin Biol 12: 331-335, 2005.

BACKGROUND AND OBJECTIVES: Albeit, the NucliSens Extractor combined with the Ampliscreen was validated for application in NAT minipool screening, a study to evaluate the reliability of the procedure in relation to subtypes G of human immunodeficiency virus (HIV)-1 RNA and 4c/4d of hepatitis C virus (HCV) RNA should be performed, due to their genetic differences and the high frequency in our country. STUDY DESIGN: Samples from patients infected with subtypes G of HIV-1 RNA and 4c/4d of HCV RNA were diluted with negative plasma and tested eight times for each concentration. For nucleic acid extraction we used an automated silica-based extraction method (NucliSens Extractor) and for amplification and detection the AmpliScreen HIV-1 version 1.5 and AmpliScreen HCV version 2.0 (Roche Diagnostic Systems) were applied. RESULTS: The sensitivity for HIV-1 RNA genotype G using the NucliSens-AmpliScreen method-95% detection limit (95% CI) of 25 (18-50) copies per ml-is comparable with those described for genotypes B and E and to that obtained by the Multiprep procedure. In the case of HCV, the sensitivity of the method was also similar, when we compared the detection limits obtained for genotype 4c/4d-95% detection limit (95% CI) of 34 (24-71) IU/ml-with the genotype 1 published. CONCLUSIONS: The data presented here suggest that these infections will not be missed because of genetic variation, as the platform exhibited similar limits of detection for the subtypes evaluated, meeting the sensitivity requirements set by the regulatory bodies.

Henriques I, Monteiro F, Meireles E, Cruz A, Tavares G, Ferreira M, and Araujo F.
Prevalence of Parvovirus B19 and Hepatitis A virus in Portuguese blood donors. *Transfus Apher Sci* 33: 305-309, 2005.

INTRODUCTION: In recent years, concern about the safety of blood in regard to the transmission of blood-borne viruses has been decreased. Safety has been achieved with a combination of different strategies, such as careful selection of donors, screening for relevant virological markers and viral inactivation/removal methods. More recently, the implementation of the nucleic acid amplification technologies for the detection of HIV-1, HCV and HBV, has increased safety by reducing the "window period" of the infections. Other viruses, such as Parvovirus B19 (PB19) and Hepatitis A virus (HAV), can cause problems for blood safety. These infections could provoke serious complications in some risk groups, such as pregnant women, patients with hematological problems, children and patients with immunodeficiencies. MATERIALS AND METHODS: An observational study was performed to determine the prevalence of PB19 and HAV in Portuguese blood donors. We gathered, during four months, 5025 plasma donations and made them into 505 pools with no more than 10 donations each. The nucleic acids were isolated using MagNA Pure LC (Roche, Mannheim, Germany). A "Real Time PCR" (LightCycler, Roche) was used to perform the nucleic acid amplification and detection, using kits from the manufacturer. RESULTS: We found a prevalence of 0.12% for PB19 and 0% for HAV. Viraemia levels found in the positive donations range from 7.1x10(4) to 2.1x10(12)IU/ml. DISCUSSION: This study demonstrates the possibility of performing these tests in routine blood banks. We found a similar prevalence of PB19 when compared with other European and USA countries. In the case of HAV, we predict a maximum risk of 0.06% for a donor to be infected. It is necessary to perform other studies, including cost/benefit analysis to evaluate the risks and profits of implementing these methodologies in Transfusion Medicine.

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Sobrinho G, Ferreira ME, Albino JP, Gomes H, and Capitao LM.

Acute ischemic hepatitis in aortocaval fistula.
Eur J Vasc Endovasc Surg 29: 239-243, 2005.

OBJECTIVES: To characterise liver dysfunction in patients with aortocaval fistula. DESIGN: Retrospective study. MATERIALS: All four patients operated on for aortocaval fistula between 1999 and 2003. Three were males with ruptured abdominal aortic aneurysm (AAA). One was a female who underwent lumbar disk surgery. Four patients operated on for ruptured AAA were used as controls. METHODS: Measurement of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and creatinine from the preoperative period until full recovery. RESULTS: The median delay between the presumed formation of the fistula and surgery was 2 days (range 1-3 days). High levels of AST, ALT and LDH were observed in all patients, starting from the preoperative period, reaching the maximum on the first two postoperative days and normalising thereafter. Median peak values were: AST=4256 IU/l (range 816-7779), ALT=2487 IU/l (range 960-5645) and LDH=15165 IU/l (range 3122-32361). Serum creatinine also sustained alterations with a similar time course. Median peak values were: 256 micromol/l (range 230-468). All the patients survived. CONCLUSIONS: Acute ischemic hepatitis appears to be a consistent or, at least, a common complication of aortocaval fistula. Although a concern during the perioperative period, its course is benign and fully resolves upon successful surgery.

Valadas E, Ribeiro C, and Antunes F.
Is there a gender shift in HCV infection?
Int J Infect Dis 9: 230-231, 2005.

Antunes H, Macedo M, and Estrada A.
[Hepatitis B virus vaccination rate with immunization].
Acta Med Port 17: 303-308, 2004.

The hepatitis B virus is an important cause of morbidity and mortality in humans, thus making it a serious public health issue. The purpose of this study was to determine the hepatitis B virus vaccination rate with immunization, the risk of this population group becoming infected before vaccination and the prevalence of hepatitis B virus infection. The study involved randomly analyzing the serum of 311 adolescents of both sexes aged 14 from a total population of 536 adolescents attending schools in Braga, Portugal. A questionnaire was administered to the adolescents and asked them if they had received the Hepatitis B vaccine, how many doses they received, if they had a history of acute hepatitis, drug abuse, whether or not they had had sexual intercourse and if so, if they had used protection. The determination of the hepatitis B surface antigen (HbsAg), the antibody to HbsAg and the antibody to hepatitis B core antigen was carried out using the chemoluminiscence method. The vaccination rate with immunization was 85.8 %, [95% CI 81.9-89.7%]. The prevalence of hepatitis B virus infection was 0.6%, [95% CI 0-1.5%]. Conclusions: The prevalence of hepatitis B virus infection was low in this adolescent population of Braga. The vaccination rate with immunization is satisfactory, but does not reach 100%, which means that the risk of transmission is still present in this age group.

Antunes H, Macedo M, and Estrada A.
[Hepatitis A virus prevalence: Portuguese first results of low endemicity].
Acta Med Port 17: 219-224, 2004.

The prevalence of the hepatitis A virus in a population determines the degree of morbidity associated with this illness, that is, the higher the morbidity, the lower the prevalence. This study aims to obtain the prevalence of total antibody to the hepatitis A virus in children, 5 and 8 years of age, and in adolescents, 14 years of age. The study was based on two samples: the serum of 64 healthy five-year-olds and 76 healthy eight-year-olds living in the proximity of the Sao Marcos Hospital in Braga and the serum of 311 adolescents, aged 14, from a total population of 536 adolescents attending schools in Braga, North of Portugal. The samples were collected in 1999 for the adolescent group, in 2000 and 2001 for the group of the five-year-olds and in 2002 and 2003 for the group of the eight-year-olds. None of the persons involved had been vaccinated with the hepatitis A virus vaccine. The Enzyme Linked Fluorescent Assay method was used to measure the serum total antibody to the hepatitis A virus. The prevalence of total antibody to the hepatitis A virus was 1.6% at 5 years of age, [95% confidence intervals (CI), 0-4.7%]; 3.9% at 8 years of age, [95% CI, 0-8,4%]; and 32.5% at 14 years of age +/- 6 months, [95% CI, 27.3-37.7%]. The prevalence of total antibody to the hepatitis A virus in this population revealed lower natural immunity. The results obtained for the five and eight-year-olds were the first Portuguese results of low endemicity to the hepatitis A virus.

Dourado M, Alves V, Mesquita L, Ramos I, Pinto AM, and Rosa MS.
CD26/DPPIV and response to hepatitis B vaccination.
Pathophysiology 11: 147-152, 2004.

The prevention of hepatitis B is important, since it is responsible for significant morbidity and mortality around the world. Unfortunately, hepatitis B vaccine does not always induce protective immunity. The lack of immune response to vaccine (non-responders) can depend on individual characteristics. The objective of this study was to correlate the CD26/DPPIV cellular expression and DPPIV serum activity with HBV vaccine response and its possible role as an indicator of immune competence acquisition. We also determined the cellular expression of CD3, CD19, CD56 and CD25 in peripheral blood T lymphocytes. Blood samples were obtained from 28 healthy human volunteers who were enrolled with a vaccination program. There were "responders" (RM = 13) and "non-responders" (NRM = 15), after vaccination. The lymphocyte populations were identified by flow cytometry. DPPIV serum activity was measured fluorimetrically. CD26 expression in responders (55.9 +/- 7.7%) versus in non-responders (51.9 +/- 7.0%) did not show a significant difference. The DPPIV serum activity in responders compared to in non-responder subgroup (59.9 +/- 8.4/50.3 +/- 10.6U/L) showed, however, a significant difference ($P < 0.05$). The expression of CD3, CD19 and CD56 on peripheral lymphocytes was similar between responders and non-responders. The expression of CD3CD26 (52.2 +/- 8.6%) and CD3CD25 (10.9 +/- 3.8%) in responders versus the expression of CD3CD26 (48.0 +/- 5.7%) and CD3CD25 (8 +/- 4.6%) in non-responders did not show statistically significant difference. CD25 referred as a marker of T lymphocyte activation was increased in responders (15.8 +/- 4.5%) versus in non-responders (10.1 +/- 4.8%), showing a significant difference ($P = 0.003$). It was, however, impossible to demonstrate an increase in CD3CD25 and CD3CD26 in the responder subgroup. This suggests that different lymphocyte subsets other than T cells are implicated in the response to hepatitis B vaccination.

Marinho RT, Pinto R, Santos ML, Lobos IV, and Moura MC.
Effects of interferon and ribavirin combination therapy on CD4+ proliferation,

lymphocyte activation, and Th1 and Th2 cytokine profiles in chronic hepatitis C.
J Viral Hepat 11: 206-216, 2004.

We studied the relationship between immunological markers such as CD4+ proliferation, cytokines profile and lymphocyte activation markers in patients with chronic hepatitis C, having different responses to interferon (IFN) and ribavirin (RBV) treatment. A prospective study of 20 patients was conducted, six had received IFN-alpha-2b alone and 14 IFN in combination with RBV. The proliferative immune responses of peripheral blood mononuclear cells to hepatitis C virus peptides and the lymphocyte activation markers (CD25+, CD38+ and CD69+) were assessed before treatment, at 1 week, and 1, 3 and 6 months of treatment. Cytokines interleukin (IL)-2, IFN-gamma, IL-4 and IL-10 were determined in supernatants before onset of treatment and at 1 and 6 months thereafter. Stimulation indices (SI) were higher in the sustained responders (SR), in comparison with those with no response (NR), before treatment (5.2 +/- 3.7 to 3.3 +/- 1.9, P = 0.028) and also at 6 months (7.8 +/- 1.9 to 4.1 +/- 1.2, P = 0.021). Patients with SR also had high SI to NS3 when compared with those with transitory response or no response (NR) (4.9 +/- 2.5 and 3.3 +/- 1.1, P = 0.033). At 1 month, SR had higher supernatant IL-2 than those with NR (133.8 +/- 119.2 to 56.0 +/- 89.3 pg/mL, P = 0.023) and lower levels of IL-10 (13.8 +/- 10.1 and 167.1 +/- 272.0 pg/mL, P = 0.023) in response to NS3. Combination therapy induced a higher percentage of the lymphocyte activation markers CD69+ and CD38+. In conclusion, we found that SR is associated with higher CD4+ proliferation particularly in response to the NS3 region, promoting a T-helper (Th)1/Th0 profile of cytokines, and that combination therapy induced a higher percentage of lymphocyte activation than therapy with IFN alone.

Passadouro R.
[Prevalence infections and risk factors due to HIV, Hepatitis B and C in a prison establishment in Leiria].
Acta Med Port 17: 381-384, 2004.

The present study emerged due to HIV, Hepatitis B and C test samples that have been taking place in a prison establishment in Leiria. The samples were taken from 788 (77%) of the 1019 prisoners that entered the prison during the periods between February of 1999 to September 2003. A questionnaire was carried to the transmission of HIV, Hepatitis B and C infections and blood samples were also taken to determine the immunologic situation in relationship to the same viruses. Of the 788 prisoners that participated, 699 (89%) were male and 89(11%) were female. The average age was 32.3, the oldest person was 70 and the youngest was 16 years old. 294 (40%) prisoners admitted using injectable drugs and 606 (84%) confirmed they had more than one sexual partner. HIV infection were found in 47 (6%) of the prisoners, HCV infection in 326 (42%), HBsAg in 21 (3%), HBsAc in 309 (40%) and HBcAc in 312 (40%) of the prisoners. Statistics confirm a significant relationship between injectable drugs and the presence of HIV infection and HBcAc and between sexual relationships with an infected partner and the presence of HBcAc, anti-HCV and HIV infection. The prevalence of infected prisoners with HIV was 6%, with HBV 40% and with HCV 42%. Hepatitis B and C infected 70% of the prisoner who used injectable drugs. The prevalence of hepatitis B and C and HIV infection that were found compel for the continuation of prevention.

Araujo FM, Henriques I, Monteiro F, Meireles E, Koch MC, Celeste R, and Cunha-Ribeiro LM.
The first case of HCV seroconversion in Portugal after the introduction of HCV NAT

screening.
Transfusion 41: 848-849, 2001.

Cunha I, and Antunes H.
[Prevalence of antibodies against hepatitis A virus in a population from northern Portugal].
Acta Med Port 14: 479-482, 2001.

AIM: To find the prevalence of antibody to hepatitis A virus in the population of the North of Portugal. MATERIAL AND METHODS: Ten General Practitioners were asked to provide blood samples from patients who would need blood tests for any reason other than acute hepatitis, during January and February 1996. In this way, 381 samples were obtained for assessment of anti hepatitis A virus antibodies using a commercial radioimmunassay ELISA. All subjects gave their informed consent and answered to a protocol regarding age, sex, geographic area, number of people per household and sewage systems. The statistics were performed using SPSS. RESULTS: The 381 subjects were distributed into eight age groups: I (1-4 years)--57; II (5-9 years)--57; III (10-14 years)--26; IV (15-19 years)--41; V (20-29 years)--55; VI (30-39 years)--51; VII (40-49 years)--41; VIII--(equal or more than 50 years)--53. The prevalence of anti HAV antibodies per group-percentage (number), (confidence intervals), were: I--7.0% (4) (3-17%); II--15.8% (9), (9-27%); III--26.9% (7) (14-46%); IV--51.2% (21) (37-66%); V--85.5% (47) (74-92%); VI--72.5% (37) (59-83%); VII--87.8% (36) (75-95%); VIII--88.7% (47) (80-93%). CONCLUSION: The comparison with previous data (Lecour et al.) shows improvement in sanitary conditions of population, with associated lower prevalence of anti hepatitis A virus antibody.

Marinho RT, Moura MC, Giria JA, and Ferrinho P.
Epidemiological aspects of hepatitis C in Portugal.
J Gastroenterol Hepatol 16: 1076-1077, 2001.

Van Damme P.
Hepatitis B: vaccination programmes in Europe--an update.
Vaccine 19: 2375-2379, 2001.

In the eight years since the Global Advisory Group of the Expanded Program on Immunisation set 1997 as the target for integrating hepatitis B (HB) vaccination into national immunisation programs world-wide, more than 116 countries have included HB vaccine as part of their routine infant or adolescent immunisation programs. Meanwhile, many countries have performed economic evaluation studies, while others have initiated sero-epidemiological studies to generate input data for burden of disease calculation. These studies have indicated that epidemiological and economic arguments cannot be used to delay the implementation of universal hepatitis B vaccination. Some countries have improved their surveillance system and included viral hepatitis in the surveillance programs. Other have put hepatitis B vaccination on the political agenda. By the year 2000, following countries of the WHO European Region (51 countries) have implemented a universal hepatitis B immunisation programme: Andorra, Albania, Austria, Belarus, Belgium, Bulgaria, Estonia, France, Germany, Greece, Italy, Israel, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Luxembourg, Malta, Moldova, Monaco, Poland, Portugal, parts of the Russian Federation, Romania, Slovakia, Slovenia, San Marino, Spain, Switzerland,

Turkey and Uzbekistan. The Netherlands and some other European countries are seriously studying the issues or are making budgetary provisions for introduction of HB vaccine into their vaccination programme. Most of the European countries, which now use the vaccine routinely, have started with adolescent or infant immunisation. Belgium (1999), France (1994) and Italy (1991) have begun with both adolescent and infant HB immunisation. France continues since 1st October 1998 with the infant immunisation programme only. The rewards of effective implementation of the programmes in these countries are becoming apparent; and their success offers an exemplary model for other countries. The deadline was 1997. Globally, work still remains to be done to support and implement interventions that will bring us closer to the WHO goal and to control, eliminate and eradicate hepatitis B in the coming generations at large. If all the 145 million infants born in 1991 had been vaccinated in this way, the number of chronic carriers would have been reduced by 7.5 million, and 1.8 million deaths prevented.

Aires S, Carvalho A, Aires E, Calado E, Aragao I, Oliveira J, Polonia A, and Vasconcelos C.
[Evaluation of the knowledge and attitudes to the standard precautions for infection control of the healthcare workers of a Portuguese central and university hospital].
Acta Med Port 23: 191-202.

INTRODUCTION: The Standard Precautions are measures to prevent healthcare workers' exposure to infectious agents, like HIV, HBV and HCV, through the routine use of techniques and appropriate barriers that reduce the exposure probability. These measures intend to prevent contact with blood and other fluids, potentially infected, contributing to the reduction of nosocomial infection. OBJECTIVES: To evaluate the knowledge, attitudes and adherence to the standard precautions for infection control among the healthcare workers of the Hospital Geral de Santo Antonio, through the application of a questionnaire. To identify the gaps of each professional group and clinical departments, in order to better define the needs to planning future education. RESULTS: Of the total of 172 questionnaires, 7% did not know about the standard precautions, the majority from medical staff. Importantly 21% affirm recapping needles. Globally, a low level knowledge about the ways HIV, HBV and HCV is transmitted was verified, mostly regarding the possibility of transmission from dishes and other material necessary to give food to the patients. About 95% considered it important to wash the hands in several different situations but 21% are unaware of alternative alcoholic solutions. CONCLUSIONS: There is a precarious knowledge of these measures, enhancing the risk of nosocomial infection and pointing to the need of specific education for all different health professionals.

Branco C, Esteves A, Piedade J, and Parreira R.
A new genotype 2 subcluster identified among GBV-C strains circulating in the Lisbon metropolitan area of Portugal.
J Med Virol 82: 452-459.

The rate of infection by the GBV-C virus was investigated in a group of 214 individuals at high risk of infection with parenterally transmitted viruses, and all living in the Lisbon metropolitan area (Portugal). RNA was extracted from plasma samples, and a fragment of the 5'-UTR was amplified by RT-PCR, disclosing a high prevalence of infection (40.7%). Most probably due to similar modes of viral transmission, the majority of GBV-C (+) individuals were found to be coinfected with HIV and/or HCV. A genomic region covering part of the E1/E2 glycoprotein coding sequence was amplified from approximately half of the GBV-C positive samples (44/87).

Phylogenetic analysis of nucleotide sequences showed segregation of Portuguese GBV-C strains with genotype 1 (G1, n = 10) and genotype 2 (G2, n = 24) references. Genotype 1 was significantly associated with the African descent of those infected. Curiously, some of the strains assigned to genotype 2 were shown to form a separate cluster (designated G2*) in both neighbor-joining and Bayesian phylogenetic trees, which was confirmed by multivariate principal coordinate analysis. However, analysis of the distribution of intra- and intergenotype genetic distances support the hypothesis that rather than corresponding to a new viral genotype, G2* is a geographical subcluster within the genotype 2 radiation. J. Med. Virol. 82:452-459, 2010. (c) 2010 Wiley-Liss, Inc.

de Sousa BC, and Cunha C.
Development of mathematical models for the analysis of hepatitis delta virus viral dynamics.
PLoS One 5.

BACKGROUND: Mathematical models have shown to be extremely helpful in understanding the dynamics of different virus diseases, including hepatitis B. Hepatitis D virus (HDV) is a satellite virus of the hepatitis B virus (HBV). In the liver, production of new HDV virions depends on the presence of HBV. There are two ways in which HDV can occur in an individual: co-infection and super-infection. Co-infection occurs when an individual is simultaneously infected by HBV and HDV, while super-infection occurs in persons with an existing chronic HBV infection. METHODOLOGY/PRINCIPAL FINDINGS: In this work a mathematical model based on differential equations is proposed for the viral dynamics of the hepatitis D virus (HDV) across different scenarios. This model takes into consideration the knowledge of the biology of the virus and its interaction with the host. In this work we will present the results of a simulation study where two scenarios were considered, co-infection and super-infection, together with different antiviral therapies. Although, in general the predicted course of HDV infection is similar to that observed for HBV, we observe a faster increase in the number of HBV infected cells and viral load. In most tested scenarios, the number of HDV infected cells and viral load values remain below corresponding predicted values for HBV. CONCLUSIONS/SIGNIFICANCE: The simulation study shows that, under the most commonly used and generally accepted therapy approaches for HDV infection, such as lamivudine (LMV) or ribavirine, peggylated alpha-interferon (IFN) or a combination of both, LMV monotherapy and combination therapy of LMV and IFN were predicted to more effectively reduce the HBV and HDV viral loads in the case of super-infection scenarios when compared with the co-infection. In contrast, IFN monotherapy was found to reduce the HDV viral load more efficiently in the case of super-infection while the effect on the HBV viral load was more pronounced during co-infection. The results suggest that there is a need for development of high efficacy therapeutic approaches towards the specific inhibition of HDV replication. These approaches may additionally be directed to the reduction of the half-life of infected cells and life-span of newly produced circulating virions.

Machado MV, Oliveira AG, and Cortez-Pinto H.
Hepatic steatosis in patients coinfected with human immunodeficiency virus/hepatitis C virus: a meta-analysis of the risk factors.
Hepatology 52: 71-78.

Hepatic steatosis (HS) is frequent in patients with hepatitis C virus (HCV) infection, occurring in 40%-80%, associating with metabolic and virus-related factors, namely,

genotype 3 and viral load. Human immunodeficiency virus (HIV) infection and antiretroviral treatment seem to be risk factors for HS. Several studies addressed this issue in coinfected patients, with discrepant results. A meta-analysis was performed on the HS risk factors in coinfected patients. Eligible studies were identified through structured keywords including coinfection, HCV, HIV, and steatosis in relevant databases including PubMed. Pooled odds ratios (ORs) and confidence limits (CIs) were obtained with the random-effects model and the DerSimonian-Laird method. Twelve studies, including 1,989 coinfected patients, were selected. Twenty percent were infected with HCV genotype 3. The overall prevalence of HS was 50.8% (23%-72%). Four studies also included 1,540 HCV monoinfected patients, not showing an increased risk for HS in coinfected patients (OR 1.61, 95% CI 0.84-3.10, P = 0.151). In coinfected patients, HS was associated with higher body mass index (OR 1.13, 95% CI 1.07-1.19, P < 0.001), diabetes mellitus (OR 2.32, 95% CI 1.32-4.07, P = 0.003), elevated alanine aminotransferase levels (OR 1.28, 95% CI 1.02-1.61, P = 0.035), necroinflammatory activity (OR 1.72, 95% CI 1.11-2.67, P = 0.016), and fibrosis (OR 1.67, 95% CI 1.20-2.34, P = 0.003). No associations were found between HS and gender, other metabolic factors (dyslipidemia, glucose, metabolic syndrome), HCV-related factors (genotype, viral load), or HIV-related factors (viral load, CD4 count, antiretroviral therapy, and class of medication). CONCLUSION: In coinfected patients, HS does not seem to be more frequent than in HCV monoinfected patients and is mostly associated with metabolic factors, such as increased weight, diabetes mellitus, and more severe liver disease. The fact that no associations with HCV factors were found may be due to the small percentage of genotype 3-infected patients.

Mota A, Guedes F, Areias J, Pinho L, and Cardoso MF.
Alcohol consumption among patients with hepatitis B infection in northern Portugal considering gender and hepatitis B virus genotype differences.
Alcohol 44: 149-156.

Alcohol abuse is an important public health problem. In Portugal with a population of 10 millions of inhabitants, there are around 10% of alcoholics or excessive alcohol drinkers and 1% of chronically infected patients with hepatitis B virus (HBV). To examine the characteristics of patients with higher levels of alcohol consumption and to investigate the association between alcohol consumption and liver damage a total of 298 chronically infected individuals, with HBV genotyped and submitted to liver biopsy, were classified with Child's grading and separated by habits of alcohol intake, less and greater than 20g/day. No significant differences were observed about genotype but genotypes A and D were predominant in both of them. A higher percentage of males (P<.001) were observed in the group with alcohol intake above 20g/day, as well a lower proportion of patients with HBeAg negativity (P< or =.035). In this group, biochemistry parameters, such as alanine aminotransferase (P=.006), aspartate aminotransferase (P=.001), gamma-glutamyl transferase (P<.001) were elevated in a significantly higher proportion than in the other group. The analysis of hematological parameters showed significantly lower values of platelets (P=.042) and mean corpuscular volume (P<.001) and significantly higher values of prothrombin time (P<.001) in the group with higher levels of alcohol consumption. The characteristics of biopsy (P<.001) and Child-Phug's classification (P=.002) revealed more severe results in this group. Logistic regression showed a positive association between liver damage and alcohol intake, increasing with age. In female patients, a strong positive association between alcohol intake and liver damage was also found (odds ratio: 9.379; 95% confidence interval: 0.859-468.422; P = .037); however, the most severe cases were only observed in women older than 45 years. In patients with HBV infection, alcohol is associated with a more severe liver disease. No

evidence was found concerning association with HBV genotype.

Silva AM, Vieira H, Martins N, Granja AT, Vale MJ, and Vale FF.
Viral and bacterial contamination in recreational waters: a case study in the Lisbon bay area.
J Appl Microbiol 108: 1023-1031.

AIMS: To assess the presence of viral pathogens in bathing water samples and to evaluate the interdependency of bacterial indicator counts and viral detection. METHODS AND RESULTS: Bathing water samples of 16 beaches collected along a Portuguese Coastal area were screened for the hepatitis A virus (HAV) and norovirus genogroup I (NVGI) using RT-PCR technique. Bacteriological water quality was also assessed, according to European regulations. HAV and NVGI were detected in 95% and 27% of the water samples, respectively, whereas bacteriological quality was good in all but one sample, according to current water quality regulations. CONCLUSIONS: All water samples would be considered of excellent quality according to the most recent European regulations. No relationship between viral detection and regulatory-based bacterial indicators was found. SIGNIFICANCE AND IMPACT OF THE STUDY: The current results reinforce the importance of increased surveillance for pathogenic viruses in bathing waters.

Teixeira M, Henggeler F, Castro R, Mateus N, Jeronimo S, and Goncalves M.
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VHPB

2. Hepatitis Bibliography of the Speakers

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If speakers complete the 'speakers form' than the their publication list was copied

Francisco George, Chief Medical Officer, DGS

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Gonçalo Cordeiro Ferreira, Head of Depart. Pediatrics, Hospital D. Estefânia, Lisbon

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Armando Carvalho, Internal Medicine, University Hospital, Coimbra Vice-President, Portuguese Association for Study of the Liver

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