



## **HEPATITIS C November 2003**

1: Br J Dermatol. 2003 Aug;149(2):390-4.

Hyperpigmentation during interferon-alpha therapy for chronic hepatitis C virus infection.

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Many types of skin disorders concomitantly occur with hepatitis C virus infection. These skin lesions may be induced or worsened during antiviral therapy with interferon-alpha (IFN). To our knowledge, hyperpigmentation of the skin--and especially of the tongue--has not been reported so far. We describe two dark-skinned patients who developed hyperpigmented skin and tongue lesions during combination therapy with IFN and ribavirin. Immunohistochemical analysis of tongue biopsies confirmed the suspicion of melanin deposits in these areas of hyperpigmentation. We hypothesize that during interferon therapy, melanocytes may produce more melanin pigment in the presence of alpha-melanocyte stimulating hormone and sufficient amounts of tyrosine, leading to melanin deposits and clinical hyperpigmentation.

PMID: 12932249 [PubMed - indexed for MEDLINE]

2: Clin Liver Dis. 2003 Aug;7(3):585-602.

Natural history of hepatitis C and outcomes following liver transplantation.

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Hepatitis C-associated liver failure is the most common indication for liver transplantation and the infection recurs nearly universally following transplantation. Histologic evidence of recurrence is apparent in approximately 50% of HCV-infected recipients in the first postoperative year. Approximately 10% of HCV-infected recipients will die or lose their allograft secondary to hepatitis C-associated allograft failure in the medium term. HCV-infected recipients who undergo retransplantation experience 5-year patient and graft survival rates that are similar to recipients undergoing retransplantation who are not HCV-infected. While the choice of calcineurin inhibitor or the use of azathioprine have not been clearly shown to affect histologic recurrence of hepatitis C or the frequency of rejection in HCV-infected recipients, cumulative exposure to corticosteroids is associated with increased mortality, higher levels of HCV viremia, and more severe histologic recurrence. In contrast to non-HCV-infected recipients, treatment for acute cellular rejection is associated with attenuated patient survival among recipients with hepatitis C. The development of steroid-resistant rejection is associated with a greater than 5-fold increased risk of mortality in HCV-infected liver transplant recipients. In lieu of large studies in a posttransplant population, therapy with pegylated

IFN (+/- ribavirin) should be considered in recipients with histologically apparent recurrence of hepatitis C before total bilirubin exceeds 3 mg/dl. The role of hepatitis C immunoglobulin and new immunosuppression agents in the management of posttransplant hepatitis C infection is still evolving.  
PMID: 14509528 [PubMed - indexed for MEDLINE]

3: Clin Liver Dis. 2003 Aug;7(3):573-84, vi.

The use of virologically compromised organs in liver transplantation.

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The present organ donor crisis has led to accepted use of organs from donors infected with hepatitis C virus (HCV) and hepatitis B virus (HBV). Although capable of transmitting disease, these grafts offer opportunities to expand the donor pool for certain populations. Anti-HBc positive grafts can be used if care is taken to provide prophylaxis. Good quality grafts from HCV+ donors may be used in recipients who are themselves HCV+ with good outcomes.

PMID: 14509527 [PubMed - indexed for MEDLINE]

4: Clin Liver Dis. 2003 Aug;7(3):603-14.

Factors that influence the severity of recurrent hepatitis C virus following liver transplantation.

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Poor outcomes following OLT for HCV disease have been associated with several host, viral, and non-host/non-viral factors. As is evident from the literature, there is confounding data in favor of and against these factors in the pathogenesis of severe recurrent HCV. Nevertheless, from a viral perspective, the patient most likely to achieve a good outcome following OLT is someone with low-level (< or = 10(9) copies/mL) HCV RNA viremia both pre- and post-OLT and a genotype other than 1b. In terms of host factors, the patients with best outcomes are: whites, men, less than 49 years of age, receiving a donor liver less than 40 years of age, not coinfecting with CMV, and have low HAI or histologic activity indices during the early stage of follow-up. Host recipient immune homology may or may not be a major factor in outcomes. A non-host, non-viral factor favoring less severe recurrence of HCV is a shorter warm ischemia time. Finally, features that may influence outcomes over which there is no control include: recipient age, recipient gender, and donor age (in the case of cadaveric donors). Unfortunately, the best-case scenario is uncommon.

PMID: 14509529 [PubMed - indexed for MEDLINE]

5: Clin Liver Dis. 2003 Aug;7(3):667-81.

Immunosuppression in hepatitis B virus and hepatitis C virus transplants: special considerations.

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The management of the immunosuppression treatment must take account its consequences on viral replication. Such treatment operates on the emerging balance between the recurrence of the virus on the graft and the immune response of the host. Randomized and prospective trials are currently ongoing with the purpose of determining the opportunity and relevance of each immunosuppressive agent in the treatment. In HBV patients, good control of HBV reinfection by prophylactic strategies using HBIG, lamivudine, or both have decreased the impact of immunosuppression on HBV recurrence. In contrast, HCV recurrence is now a major problem. The mechanisms of viral recurrence need to be deepened thus

requiring new studies. The absence of in vitro and in vivo systems to study HCV reinfection is a lack in the comprehension of the relation between HCV and immunosuppression. It will allow adapting the effectiveness of the immunosuppression treatment. The treatment's primary target is to avoid graft rejection, and its secondary objective is to limit the risk of viral recurrence. PMID: 14509533 [PubMed - indexed for MEDLINE]

6: Clin Liver Dis. 2003 Aug;7(3):615-29.

To transplant or not to transplant recurrent hepatitis C and liver failure. Forman LM.

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In summary, re-OLT accounts for 10% of all OLTs performed and is associated with significantly increased resource use, and decreased survival compared with primary OLT. After transplantation into an HCV-infected recipient, infection of the allograft by HCV is invariable. As patients survive longer after liver transplantation, it is likely that allograft failure related to HCV recurrence will occur. Results of re-OLT for HCV are inferior to those of primary grafting, paralleling the results for retransplantation for other indications. Many studies have demonstrated that HCV infection significantly impairs patient and allograft survival after liver retransplantation, regardless of etiology of allograft failure. Patient survival rates with HCV infection are 57% to 65% at 1 year, as compared with 65% to 82% among patients without HCV infection. Experience with retransplantation is limited, however, and studies are difficult to interpret because of small sample sizes and lack of uniform definitions of survival, HCV recurrence, and allograft failure. Similar to outcomes after retransplantation for non-HCV related indications, the most common causes of death are sepsis and multi-organ failure. The high mortality associated with retransplantation has not universally been caused by recurrent disease, however recent studies have demonstrated that re-recurrent HCV occurs and the natural history is similar, if not more accelerated, after the second transplant. HCV infection may, in fact, increase mortality in a group of patients already predisposed to an inferior outcome. Preoperative serum creatinine and bilirubin have been consistently associated with survival after retransplantation and favorable results are attainable with strict selection criteria. The increasing use of expanded donor criteria, in particular, LRLT, raises important practical and ethical issues with regards to the HCV-positive transplant recipient and will become a challenge to the transplant community as a whole. With the donor morbidity and mortality associated with LRLT currently estimated at 32% and 0.3%, respectively, one must determine how much risk is acceptable to the donor in relation to the outcome in the recipient. This is especially true in HCV-infected recipients, in whom HCV re-recurrence may occur in the second allograft and lead to accelerated failure. LRLT, however, would not deplete the organ pool and would lead to the use of scarce cadaveric organs to patients who are awaiting primary liver transplantation. Despite inferior outcomes, a better tactic may be to consider retransplantation for recurrent HCV in those whose primary transplant was a LDLT, as the initial allograft did not deplete the donor pool. Given the shortage of donor organs and the increasing number of patients with HCV-induced allograft cirrhosis, identifying ways to improve allograft survival in HCV-infected patients represents an important focus for further research. Additional studies are needed to further explore the mechanisms underlying the reduction in survival and to identify which HCV-positive individuals are at greatest risk for poor survival. Studies are beginning to emerge that demonstrate that HCV recurrence can be modified with combination antiviral therapy and that the HCV virus can be eliminated. Additional longitudinal prospective studies are needed to assess the exact impact of HCV on survival after retransplantation, the effects of the newer

immunosuppressive agents such as sirolimus and mycophenolate mofetil on HCV, the use of preemptive antiviral therapy on HCV eradication and fibrosis modification, and the appropriateness of expanded donor criteria. Until we have longer follow-up and greater experience with the HCV-positive recipient with allograft failure, retransplantation should be considered a viable option for highly selected patients, particularly in patients in whom renal failure and severe hyperbilirubinemia have not occurred.  
PMID: 14509530 [PubMed - indexed for MEDLINE]

7: Clin Liver Dis. 2003 Aug;7(3):631-50, vii.  
Treatment strategies for hepatitis C: intervention prior to liver transplant, pre-emptively or after established disease.  
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Cirrhosis secondary to chronic hepatitis C virus (HCV) infection accounts for most liver transplants performed in the United States and European transplant centers. Given the high prevalence of HCV infection in the general population, the lack of consistently effective antiviral therapy, and the eventual progression to cirrhosis of a subset of those infected, predictions for the future are that the number of patients in need of transplantation will increase in the coming decade. In addition, viral infection recurs nearly universally leading to the development of chronic HCV in most recipients and progression to cirrhosis after a median of 9 to 12 years in a significant proportion of these recipients.  
PMID: 14509531 [PubMed - indexed for MEDLINE]

8: Clin Liver Dis. 2003 Aug;7(3):651-65, viii.  
Living donor liver transplantation and hepatitis C.  
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Preliminary results indicate that living donor liver transplantation patients infected with hepatitis C virus (HCV) develop earlier and more severe recurrence than their cadaveric counterparts. The mechanisms underlying this observation are unknown, but could include hepatic regeneration, differences in living donor liver transplantation recipient demographics, immune homology between donor and recipients, or other factors not previously considered. The optimum clinical approach is to only consider living donor liver transplantation in HCV-infected recipients as a life-saving procedure and to attempt to eradicate HCV before transplantation to prevent recurrent infection.  
PMID: 14509532 [PubMed - indexed for MEDLINE]

9: Clin Liver Dis. 2003 Aug;7(3):683-714.  
Rising incidence of hepatocellular carcinoma: the role of hepatitis B and C; the impact on transplantation and outcomes.  
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Hepatocellular carcinoma caused by hepatitis B and hepatitis C are global scourges but are likely to peak in incidence in the next 2 decades and then decline. Universal vaccination has been effective in stemming the incidence of chronic hepatitis B and early-onset HCC in regions of high endemicity where implemented, but preventive measures in HCV are not yet available. After the attrition of older affected generations, the incidence of HCC will likely decline rapidly. While no vaccine is currently available for hepatitis C, cases are projected to peak and decline because of a marked reduction in transmission as a result of behavioral modification and safeguarding of blood supplies. Until

these epidemiologic projections come to pass, management of hepatocellular carcinoma will continue to become a progressively more frequently encountered clinical challenge. Therapy for chronic hepatitis may ameliorate but will not eliminate the development of tumors. The demand for orthotopic liver transplantation will continue to climb, and palliative therapies for non-resectable cases will require studies aimed at optimization of benefit. LDLT may remain an option for high-risk patients affording tumor-free survival for some otherwise terminal patients.

PMID: 14509534 [PubMed - indexed for MEDLINE]

10: Hawaii Med J. 2003 Aug;62(8):163-4.

Adverse response to pegylated interferon therapy in two patients with chronic hepatitis C. Thomas WL Jr, Ramos F, Hospenhal DR.

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Pegylated interferons have recently been approved for treatment of hepatitis C. The safety of these formulations is reported to be similar to that of non-pegylated interferon. We present two patients who experienced exacerbations of their liver disease following administration of pegylated interferon alfa-2b. Vigilant monitoring of patients treated with these new agents is recommended. PMID: 14533347 [PubMed - indexed for MEDLINE]

11: J Clin Microbiol. 2003 Aug;41(8):3955-9.

Vertical transmission of the hepatitis C virus to infants of anti-human immunodeficiency virus-negative mothers: molecular evolution of hypervariable region 1 in prenatal and perinatal or postnatal infections.

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In a prospective study of 33 infants born to hepatitis C virus (HCV)-positive human immunodeficiency virus-negative mothers the vertical transmission of HCV occurred in 6.8%. The evolution of HCV infection in two babies was studied from birth up to 5 or 6 years of age, and the sequencing of the hypervariable region (HVR) of the putative envelope-encoding E2 region of the HCV genome was performed. The HVR1 sequence variability and the different serological profiles during follow-up could reflect the differences in HCV transmission routes, HCV genotypes, and clinical evolution of infection.

PMID: 12904428 [PubMed - indexed for MEDLINE]

12: J Clin Microbiol. 2003 Aug;41(8):3881-4.

Monitoring response to antiviral therapy for patients with chronic hepatitis C virus infection by a core-antigen assay.

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A recently released immunoassay detecting total serum hepatitis C virus (HCV) core antigen was used to prospectively monitor virological responses to antiviral treatment in patients with chronic HCV infection. Sustained responders cleared core protein from serum within the first month of therapy and maintained stably negative values for the entire duration of follow-up after treatment discontinuation. However, patients who relapsed or failed to respond showed transient negative values and could not be accurately discriminated either because of the intrinsic lower sensitivity of the core-antigen assay than those of molecular assays or because of differentially regulated secretion of immunoreactive core protein from infected hepatocytes.

PMID: 12904409 [PubMed - indexed for MEDLINE]

13: J Clin Microbiol. 2003 Aug;41(8):3615-22.

Significance of pretreatment analysis of hepatitis C virus genotype 1b hypervariable region 1 sequences to predict antiviral outcome.

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The heterogeneity of hypervariable region 1 (HVR1), located at the amino terminus of the E2 envelope, may be involved in resistance to alpha interferon (IFN-alpha) treatment. We investigated whether peculiar HVR1 domain profiles before treatment were associated with the maintenance of sensitivity or the appearance of resistance to treatment. Fifteen patients infected with hepatitis C virus genotype 1b and treated with IFN with or without ribavirin were selected. Ten responded to treatment (groups R1 and R2) and five did not (group NR). The amino acid sequences of 150 naturally occurring HVR1 variants present in the serum before therapy were compared in relation to treatment outcome. HVR1 variants from the NR group contained a constant nonantigenic amino acid segment that was not found in HVR1 variants from the R groups.

PMID: 12904364 [PubMed - indexed for MEDLINE]

14: J Clin Microbiol. 2003 Aug;41(8):3503-8.

Evaluation of the MagNA pure LC instrument for extraction of hepatitis C virus RNA for the COBAS AMPLICOR Hepatitis C Virus Test, version 2.0.

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The COBAS AMPLICOR system has played a major role in the transition of molecular diagnostics from research to routine clinical laboratory use by automating the nucleic acid amplification and detection processes. However, sample preparation remains a labor-intensive portion of the procedure. In this study, we evaluated the performance of the COBAS AMPLICOR Hepatitis C Virus Test, version 2.0 (Roche Molecular Systems, Branchburg, N.J.) following manual hepatitis C virus (HCV) RNA extraction versus automated extraction with the MagNA Pure LC instrument (Roche Applied Science, Indianapolis, Ind.). Parallel replicate testing was performed with standard dilutions of 100, 75, 60, and 0 HCV IU/ml and 153 clinical specimens. An analytical sensitivity of 75 IU/ml was achieved with either the manual or the standard-volume (200 microl) automated extraction methodologies (25 of 26 [96.2%]; 95% confidence interval [95% CI], 80.4 to 99.9), whereas the clinical sensitivity and specificity were both 100% with either extraction method. A large-volume (1 ml) automated extraction method was also evaluated with standard dilutions of 40, 25, 10, and 0 IU/ml and the same 153 clinical specimens. The analytical sensitivity of the COBAS AMPLICOR assay with the large-volume extraction method was 25 HCV IU/ml (26 of 26 [100%]; 95% CI, 86.8 to 100), whereas the clinical sensitivity and specificity were both 100%. The MagNA Pure LC instrument is a versatile, labor-saving platform capable of integration with minimal modification of the existing assay procedure. The increased sensitivity of the COBAS AMPLICOR Hepatitis C Virus Test, version 2.0 performed in conjunction with large-volume HCV RNA extraction may be important in HCV diagnostic testing as new therapeutic strategies evolve.

PMID: 12904346 [PubMed - indexed for MEDLINE]

15: J Clin Virol. 2003 Aug;27(3):247-51.

Cell-associated, non-replicating strand(+) hepatitis C virus-RNA shedding in cervicovaginal secretions from chronically HCV-infected women.

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BACKGROUND: Lack of mucosal hepatitis C virus (HCV) transmission may be due to fairly low infectivity of body fluids in HCV-infected individuals in association

with yet unknown innate or acquired resistance factors in individuals exposed to the virus. OBJECTIVE: To evaluate HCV excretion patterns in cervicovaginal secretions obtained from chronically HCV-infected women. STUDY DESIGN: Fifteen chronically HCV-infected women of childbearing age hospitalized for chronic hepatitis were prospectively recruited. Cervicovaginal secretions were obtained by vaginal washing with 3 ml phosphate-buffered saline (PBS). All cervicovaginal secretions were free of hemoglobin traces and also free of semen traces. Free HCV-RNA and cell-associated HCV-RNA were examined in acellular part and cellular part of the cervicovaginal secretions, respectively, by in-house qualitative PCR for 5'-HCV-non-coding region (NCR). Negative strand HCV-RNA, a marker of HCV replication, was searched by using tag-RT-nested PCR (tag-RT-NPCR). RESULTS: HCV-RNA could not be detected in the acellular fractions of the 15 evaluated cervicovaginal secretions. In contrast, HCV-RNA could be detected in the cellular fractions of four of 15 (27%) cervicovaginal secretions. None of the cervicovaginal secretions, including the four positive cell-associated HCV-RNA, contained negative strand, replicating HCV-RNA. CONCLUSIONS: Our results suggest that positive strand HCV-RNA may be present outside the menstruation periods as cell-associated virus in the cervicovaginal secretions of a minority of untreated HCV-seropositive, HCV-RNA-viremic women, and that the lower female genital tract does not constitute a reservoir where HCV replicates. These observations thus provide the basis for the low risk of female-to-male sexual transmission of HCV infection.

PMID: 12878088 [PubMed - indexed for MEDLINE]

16: J Clin Virol. 2003 Aug;27(3):276-85.

Genotyping of hepatitis C virus-comparison of three assays.

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BACKGROUND: Genotyping of hepatitis C virus (HCV) is clinically relevant to epidemiology, prognosis, and therapeutical management of HCV infection.

OBJECTIVES: Accuracy and specificity of three assays for HCV genotyping/subtyping were determined. The TruGene HCV 5'NC Genotyping Kit (TruGene), which is a direct sequencing test and two assays based on reversed hybridization, Inno-LiPA HCV II assay and ViennaLab HCV Strip Assay, were compared. Amplification products generated by the Cobas Amplicor HCV Test were used. STUDY DESIGN: A total of 100 consecutive HCV RNA positive samples derived from patients with chronic hepatitis C were examined for their genotypes/subtypes by the three assays. RESULTS: Identification of genotypes and subtypes by the TruGene assay as reference test for the Inno-LiPA HCV II assay and the ViennaLab HCV Strip Assay or Inno-LiPA HCV II assay as reference test for the TruGene and the ViennaLab HCV Strip Assay showed similar results for overall accuracies (TruGene as reference test for Inno-LiPA HCV II and ViennaLab HCV Strip Assay, genotypes/subtypes: 100%/95.5% and 97%/92%; Inno-LiPA HCV II as reference test for TruGene and ViennaLab HCV Strip Assay, genotypes/subtypes: 99%/85.9% and 97%/87.9%) and specificities (TruGene as reference test for Inno-LiPA HCV II and ViennaLab HCV Strip Assay, genotypes/subtypes: 100%/97.8% and 99%/97.7%; Inno-LiPA HCV II as reference test for TruGene and ViennaLab HCV Strip Assay, genotypes/subtypes: 100%/99.4% and 99.7%/98%). CONCLUSIONS: The three assays were found to be reliable for the detection and discrimination of all HCV genotypes common in Europe and in North America and to be suitable for the routine diagnostic laboratory.

PMID: 12878092 [PubMed - indexed for MEDLINE]

17: J Clin Virol. 2003 Aug;27(3):235-41.

Quantitation of HCV RNA with the microwell plate and COBAS Amplicor HCV Monitor assays.

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BACKGROUND: We performed the Roche Amplicor Monitor hepatitis C virus (HCV) v2.0 microwell plate (MWP) assay for 2 years prior to bringing a COBAS instrument into the lab. Before reporting any results from the automated COBAS Amplicor Monitor HCV v2.0, we compared quantitative data with results on the same specimens from the manual Amplicor Monitor HCV. OBJECTIVE: To determine if the COBAS Amplicor Monitor assay yielded quantitative results that were comparable with those given by the manual Amplicor Monitor HCV. STUDY DESIGN: We tested 145 specimens with both assays. Specimens were chosen on the basis of having fallen within the linear range of the first assay. RESULTS: The log(10) mean (+/-standard deviation) for all 145 specimens was 5.976 (+/-0.597) for the COBAS and 6.142 (+/-0.597) for the MWP assay. When plotted as 145 pairs of numbers (log MWP result vs. log COBAS result), the linear regression line was displaced slightly downward from the line of equivalence by 0.1 log at the lower end and by 0.2 log at the upper end indicating the COBAS result was somewhat lower than the MWP result across the full range of the assay. The mean of the difference of the manual method and the COBAS for all 145 specimens was 0.166 log(10). A subset of 45 specimens for which we had HCV genotype data was analyzed separately. This set of specimens (of which 33 were genotype 1) also showed excellent concordance between the automated and manual methods. The two trendlines, one for genotype 1 and the other for genotypes 2, 3 and 4, were superimposable and thus the quantitative results were apparently not influenced by the genotypes, although the numbers were small (six HCV genotype 2, five HCV genotype 3 and one HCV genotype 4). CONCLUSIONS: We conclude that the automated Roche COBAS Amplicor Monitor v2.0 yields results that are comparable with the manual Amplicor Monitor assay for HCV genotype 1 and possibly also for genotypes 2, 3 and 4.  
PMID: 12878086 [PubMed - indexed for MEDLINE]

18: J Clin Virol. 2003 Aug;27(3):213-30.

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections in health care workers (HCWs): guidelines for prevention of transmission of HBV and HCV from HCW to patients.

Gunson RN, Shouval D, Roggendorf M, Zaaier H, Nicholas H, Holzmann H, de Schryver A, Reynders D, Connell J, Gerlich WH, Marinho RT, Tsantoulas D, Rigopoulou E, Rosenheim M, Valla D, Puro V, Struwe J, Tedder R, Aitken C, Alter M, Schalm SW, Carman WF; European Consensus Group.

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The transmission of viral hepatitis from health care workers (HCW) to patients is of worldwide concern. Since the introduction of serologic testing in the 1970s there have been over 45 reports of hepatitis B virus (HBV) transmission from HCW to patients, which have resulted in more than 400 infected patients. In addition there are six published reports of transmissions of hepatitis C virus (HCV) from HCW to patients resulting in the infection of 14 patients. Additional HCV cases are known of in the US and UK, but unpublished. At present the guidelines for preventing HCW to patient transmission of viral hepatitis vary greatly between countries. It was our aim to reach a Europe-wide consensus on this issue. In order to do this, experts in blood-borne infection, from 16 countries, were questioned on their national protocols. The replies given by participating countries formed the basis of a discussion document. This paper was then discussed at a meeting with each of the participating countries in order to reach a Europe-wide consensus on the identification of infected HCWs, protection of susceptible HCWs, management and treatment options for the infected HCW. The results of that process are discussed and recommendations formed. The guidelines produced aim to reduce the risk of transmission from infected HCWs to patients. The document is designed to complement existing guidelines or form the basis for the development of new guidelines. This

guidance is applicable to all HCWs who perform EPP, whether newly appointed or already in post.

PMID: 12878084 [PubMed - indexed for MEDLINE]

19: Nurs Times. 2003 Aug 5-11;99(31):24-5.

The epidemiology and control of hepatitis C infection.

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Hepatitis C is a global public health problem, and a major cause of chronic hepatitis. The virus can cause cirrhosis, liver failure and primary liver cancer. Combination therapy is effective in 50-60 per cent of patients with chronic infection. Prevention initiatives should target high-risk groups, such as injecting drug users.

PMID: 13677115 [PubMed - indexed for MEDLINE]

20: Optometry. 2003 Aug;74(8):517-23.

Hepatitis C: a review of diagnosis, management, and ocular complications from treatment.

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BACKGROUND: Chronic hepatitis C is a serious condition that can lead to cirrhosis of the liver, and may progress to life-threatening hepatocellular carcinoma. Timely diagnosis and treatment of patients at risk for severe liver disease from the chronic hepatitis C virus is imperative to prevent life-threatening illness. Current combination therapy of interferon alpha and ribavirin is the most successful treatment. However, patients must be monitored closely, as this therapy may produce serious ocular and systemic side effects. CASE REPORT: A 53-year-old white man, who was undergoing treatment for chronic hepatitis C with peginterferon alpha-2b and ribavirin, came to the eye clinic for routine examination. Dilated funduscopy was clear O.D., but revealed flame-shaped hemorrhages and one cotton-wool spot in the superior/temporal arcade O.S. The retinopathy was attributed to peginterferon treatment and resolved completely with no recurrences over the rest of the treatment period.

CONCLUSION: Patients in need of treatment for chronic hepatitis C should have a baseline fundus examination before initiating treatment to identify any pre-existing retinopathy. Patients with pre-existing retinopathy from diabetes or hypertension should be monitored monthly for progression throughout the course of treatment for chronic hepatitis C. Patients without pre-existing retinopathy in whom mild interferon retinopathy develops should be monitored monthly until the retinopathy resolves. Patients in whom proliferative retinopathy develops must be re-evaluated by their internists to determine whether treatment for chronic hepatitis C should be continued. These patients should also be referred for consultation for pan-retinal photocoagulation.

PMID: 12926825 [PubMed - indexed for MEDLINE]

21: Rev Esp Enferm Dig. 2003 Aug;95(8):568-74, 561-7.

Therapeutic advantages of pegylation of interferon alpha in chronic hepatitis C.

[Article in English, Spanish]

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Modification of the pharmacokinetic profile of interferon-alfa (IFNalfa) through pegylation (addition of a polyethylenglicol molecule) has resulted in a marked improvement of drug efficacy for the treatment of infection due to hepatitis C virus. Two pegylated derivatives of IFNalfa are available: PEG-IFNalfa-2a, with

a 40 kDa polyethylenglicol molecule of branched structure, and PEG- IFNalpha- 2b, with a 12kDa linear PEG. Both compounds have slower absorption, more reduced distribution and lower elimination rate than the respective non- pegylated IFNalpha, which assures that concentrations appropriate to inhibit viral replication are maintained during longer periods of time, thus allowing administration once a week, In addition to achieving greater therapeutic efficacy, the adverse effects related to excessive Cmax are reduced, the risk of therapeutic failure is decreased by eliminating the intervals of inefficient plasma levels, and the uncomfortable thrice weekly injection regimens are avoided. The current recommendations include the use of a combination therapy with pegylated IFNalpha and ribavirin as the standard treatment. However, further research is required to achieve dosage optimization of pegylated IFN and rebavirin according to the patients characteristics and to evaluate the efficacy and safety of this combined therapy for difficult- to- treat patients.  
PMID: 14510631 [PubMed - indexed for MEDLINE]

22: Trends Immunol. 2003 Aug;24(8):456-64.

Hepatitis C virus infection: when silence is deception.

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Hepatitis C virus (HCV) uses complex and unique mechanisms to prevent, evade or subvert innate and adaptive immune responses and to establish persistent infection and chronic hepatitis. Recently developed experimental systems have significantly facilitated the analysis of HCV replication, virus-host interaction and pathogenesis of chronic hepatitis and have provided new insights into the mechanisms of HCV clearance and persistence.  
PMID: 12909460 [PubMed - indexed for MEDLINE]