Blood borne viruses
August – September 2014

(1) Urge primary care physicians to test. AIDS Policy Law 2014 Sep;29(10):4
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(2) Adult circumcision does not lead to risky behaviors. AIDS Policy Law 2014 Sep;29(10):3
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(3) Treatment. Allowing ART initiation in the home increases participation. AIDS Policy Law 2014 Sep;29(10):3
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(4) Behavior. Certain youth demographics fall short on HIV prevention efforts. AIDS Policy Law 2014 4; Sep;29(10):1
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(5) UW creates tampon-like HIV prevention option. AIDS Policy Law 2014 Sep;29(10):1
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OBJECTIVES: We examined HIV, hepatitis B virus (HBV), and HCV seroprevalence in an interim analysis and the potential risk factors associated with these infections among injection drug users (IDUs) residing in nonurban communities of southwestern Connecticut. METHODS: We recruited and interviewed active adult IDUs about their injection-associated risk and conducted serological tests for HIV, HBV, and HCV. Regression analyses were performed to identify risk

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factors for infection and coinfection. RESULTS: Among 446 participants, 51.6% carried at least 1 infection, and 16.3% were coinfected. Infection risk was associated with longer duration of injection use, overdose, substance abuse treatment, depression, and involvement with the criminal justice system. Coinfection was associated with longer injection drug use, lower education, overdose, and criminal justice involvement. Multivariate models identified injection drug use duration, substance abuse treatment, and criminal justice involvement as the most significant predictors of infection; injection drug use duration and education were the most significant predictors of coinfection. CONCLUSIONS: Suburban IDUs are at significant risk for acquiring single and multiple viral infections. Effective harm reduction strategies are needed to reach users early. There might be roles for interventions in the treatment and justice systems in which IDUs interact.


OBJECTIVES: To determine the prevalence of eosinophilia among antiretroviral therapy (ART)-naive patients infected with human immunodeficiency virus (HIV) and to identify variables associated with eosinophilia. METHODS: We included all ART-naive HIV-infected patients entering into care at the Thomas Street Health Center (Houston, Texas) between February 2007 and January 2009. Eosinophilia was defined as absolute eosinophil count > 400 cells per cubic millimeter. Patients with eosinophilia (cases) at baseline were matched to patients without baseline eosinophilia (controls). Clinical and laboratory data were collected for cases and controls. Variables associated with eosinophilia were evaluated by univariate and multivariate analyses. RESULTS: Sixty-five (9.7%) of 671 ART-naive patients had eosinophilia. There was no difference in age, sex, race, or baseline CD4 count between patients with and without eosinophilia; however, patients with eosinophilia were more likely to have higher HIV RNA viral loads (5.05 vs 4.82 log10 copies per milliliter; P = 0.019). A total of 52 (80%) of 65 patients with eosinophilia (cases) had at least two follow-up clinic visits. They were matched to 104 controls. Skin rash was the only variable associated with eosinophilia (odds ratio 2.16, 95% confidence interval 1.04-4.47) in our multivariate analysis. Of eight cases tested, only one, from Central America, had a parasitic infection (hookworm). Thirty-eight (73.1%) patients experienced resolution of their eosinophilia by the end of the study (mean follow-up 1019 days). Resolution of eosinophilia did not differ between patients with and without HIV viral suppression. CONCLUSIONS: Eosinophilia is not an infrequent occurrence among ART-naive HIV-infected patients. Patients with eosinophilia are more likely than patients without eosinophilia to present with a skin rash. HIV RNA viral suppression did not necessarily result in the resolution of eosinophilia. Extensive workup for eosinophilia may not be necessary in most cases.

BACKGROUND & AIMS: The interferon-free regimen of ABT-450 (a protease inhibitor), ritonavir, ombitasvir (an NS5A inhibitor), dasabuvir (a non-nucleoside polymerase inhibitor), and ribavirin has shown efficacy in patients with hepatitis C virus (HCV) genotype 1b infection-the most prevalent sub-genotype worldwide. We evaluated whether ribavirin is necessary for ABT-450, ritonavir, ombitasvir, and dasabuvir to produce high rates of sustained virologic response (SVR) in these patients. METHODS: We performed a multicenter, open-label, phase 3 trial of 179 patients with HCV genotype 1b infection, without cirrhosis, previously treated with peginterferon and ribavirin. Patients were assigned randomly (1:1) to groups given ABT-450, ritonavir, ombitasvir, and dasabuvir, with ribavirin (group 1) or without (group 2) for 12 weeks. The primary end point was SVR 12 weeks after treatment (SVR12). We assessed the noninferiority of this regimen to the rate of response reported (64%) for a similar population treated with telaprevir, peginterferon, and ribavirin. RESULTS: Groups 1 and 2 each had high rates of SVR12, which were noninferior to the reported rate of response to the combination of telaprevir, peginterferon, and ribavirin (group 1: 96.6%; 95% confidence interval, 92.8%-100%; and group 2: 100%; 95% confidence interval, 95.9%-100%). The rate of response in group 2 was noninferior to that of group 1. No virologic failure occurred during the study. Two patients (1.1%) discontinued the study owing to adverse events, both in group 1. The most common adverse events in groups 1 and 2 were fatigue (31.9% vs 15.8%) and headache (24.2% vs 23.2%), respectively. Decreases in hemoglobin level to less than the lower limit of normal were more frequent in group 1 (42.0% vs 5.5% in group 2; P < .001), although only 2 patients had hemoglobin levels less than 10 g/dL. CONCLUSIONS: The interferon-free regimen of ABT-450, ritonavir, ombitasvir, and dasabuvir, with or without ribavirin, produces a high rate of SVR12 in treatment-experienced patients with HCV genotype 1b infection. Both regimens are well tolerated, as shown by the low rate of discontinuations and generally mild adverse events. ClinicalTrials.gov number: NCT01674725. Copyright 2014 AGA Institute. Published by Elsevier Inc. All rights reserved.
grade (25.8% versus 17.6%) and high-grade lesions (8.3% versus 4.8%) were comparable in HIV-positive and HIV-negative group. Thirteen (20%) smears were p16-positive with a sensitivity and specificity for anal dysplasia of 72.3% and 100%, respectively. Anal cytology may be used to screen for anal dysplasia in MSM irrespective of HIV status. Furthermore, the addition of p16, with greater specificity for high-grade lesions, may improve diagnostic accuracy especially for high-grade lesions. A larger study to further corroborate these observations is warranted. The Author(s) 2014 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav.


UNLABELLED: HIV-1 modulates key host cellular pathways for successful replication and pathogenesis through viral proteins. By evaluating the hijacking of the host ubiquitination pathway by HIV-1 at the whole-cell level, we now show major perturbations in the ubiquitinated pool of the host proteins post-HIV-1 infection. Our overexpression- and infection-based studies of T cells with wild-type and mutant HIV-1 proviral constructs showed that Vpr is necessary and sufficient for reducing whole-cell ubiquitination. Mutagenic analysis revealed that the three leucine-rich helical regions of Vpr are critical for this novel function of Vpr, which was independent of its other known cellular functions. We also validated that this effect of Vpr was conserved among different subtypes (subtypes B and C) and circulating recombinants from Northern India. Finally, we establish that this phenomenon is involved in HIV-1-mediated diversion of host ubiquitination machinery specifically toward the degradation of various restriction factors during viral pathogenesis.

IMPORTANCE: HIV-1 is known to rely heavily on modulation of the host ubiquitin pathway, particularly for counteraction of antiretroviral restriction factors, i.e., APOBEC3G, UNG2, and BST-2, etc.; viral assembly; and release. Reports to date have focused on the molecular hijacking of the ubiquitin machinery by HIV-1 at the level of E3 ligases. Interaction of a viral protein with an E3 ligase alters its specificity to bring about selective protein ubiquitination. However, in the case of infection, multiple viral proteins can interact with this multienzyme pathway at various levels, making it much more complicated. Here, we have addressed the manipulation of ubiquitination at the whole-cell level post-HIV-1 infection. Our results show that HIV-1 Vpr is necessary and sufficient to bring about the redirection of the host ubiquitin pathway toward HIV-1-specific outcomes. We also show that the three leucine-rich helical regions of Vpr are critical for this effect and that this ability of Vpr is conserved across circulating recombinants. Our work, the first of its kind, provides novel insight into the regulation of the ubiquitin system at the whole-cell level by HIV-1. Copyright 2014, American Society for Microbiology. All Rights Reserved.


UNLABELLED: Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) cause substantial mortality, especially in persons chronically infected with both viruses. HIV infection raises plasma HCV RNA levels and diminishes the response to
exogenous alpha interferon (IFN). The degree to which antiretroviral therapy (ART) control of infection overcomes these HIV effects is unknown. Participants with HIV-HCV coinfection were enrolled in a trial to measure HCV viral kinetics after IFN administration (HCVIFN) twice: initially before (pre-ART) and then after (post-ART) HIV RNA suppression. Liver tissue was obtained 2-4 hours before each IFN injection to measure interferon stimulated genes (ISGs). Following ART, the HCVIFN at 72 hours (HCVIFN,72) increased in 15/19 (78.9%) participants by a median (interquartile range [IQR]) of 0.11 log10 IU/mL (0.00-0.40; P<0.05). Increases in HCVIFN,72 post-ART were associated with decreased hepatic expression of several ISGs (r=-0.68; P=0.001); a 2-fold reduction in a four-gene ISG signature predicted an increase in HCVIFN,72 of 0.78 log10 IU/mL (95% confidence interval [CI] 0.36,1.20). Pre- and post-ART HCVIFN,72 were closely associated (r=0.87; P<0.001). HCV virologic setpoint also changed after ART (HCVART): transient median increases of 0.28 log10 IU/mL were followed by eventual median decreases from baseline of 0.21 log10 IU/mL (P=0.002). A bivariate model of HIV RNA control (P<0.05) and increased expression of a nine-gene ISG signature (P<0.001) predicted the eventual decreased HCVART. CONCLUSION: ART is associated with lower post-IFN HCV RNA levels and that change is linked to reduced hepatic ISG expression. These data support recommendations to provide ART prior to IFN-based treatment of HCV and may provide insights into the pathogenesis of HIV-HCV coinfection. 2014 by the American Association for the Study of Liver Diseases.


The pattern recognition molecules of the lectin complement pathway are important components of the innate immune system with known functions in host-virus interactions. This paper summarizes current knowledge of how these intriguing molecules, including mannose-binding lectin (MBL), Ficolin-1, -2 and -3, and collectin-11 (CL-11) may influence HIV-pathogenesis. It has been demonstrated that MBL is capable of binding and neutralizing HIV and may affect host susceptibility to HIV infection and disease progression. In addition, MBL may cause variations in the host immune response against HIV. Ficolin-1, -2 and -3 and CL-11 could have similar functions in HIV infection as the ficolins have been shown to play a role in other viral infections, and CL-11 resembles MBL and the ficolins in structure and binding capacity. Copyright 2014 Elsevier Inc. All rights reserved.


OBJECTIVE: To assess procreative outcomes for HIV-positive men and women with seronegative partners. DESIGN: Systematic review and meta-analysis. SETTING: Not applicable. PATIENT(S): Twenty-four studies with extractable data for HIV-serodiscordant couples undergoing intrauterine insemination (IUI) or in vitro fertilization (IVF). INTERVENTION(S): None. MAIN OUTCOME MEASURE(S): PRIMARY OUTCOMES: HIV transmission to a seronegative partner and per cycle fecundability; secondary outcomes: analysis of multiple gestation rates, miscarriage
rates, and cancellation rates. RESULT(S): For serodiscordant couples, HIV-positive men or women undergoing IUI and IVF treatment had a 17%, 30%, 14%, and 16% per cycle fecundability, respectively. Multiple gestation rates were 10%, 33%, 14%, and 29%, respectively. Miscarriage rates were 19%, 25%, 13%, and 20%, respectively. No HIV transmission was observed in 8,212 IUI and 1,254 IVF cycles, resulting in 95% confidence that the true rate is 4.5 transmissions per 10,000 IUI cycles or less. CONCLUSION(S): In serodiscordant couples, IUI and IVF seem effective and safe based on the literature. Evidence-based practice and social justice suggest that our field should increase access to care for HIV-serodiscordant couples. Published by Elsevier Inc.


The aim of this study was to compare outcomes (self-esteem, coping self-efficacy, and internalized stigma) across time in HIV-infected women living in the Deep South who received a stigma reduction intervention (n=51) with those of a control group (n=49) who received the usual care at baseline, and at 30 and 90 days. We recruited 99 women from clinics and an AIDS service organization; they were randomized by recruitment site. A video developed from the results of a qualitative metasynthesis study of women with HIV infection was loaded onto iPod Touch devices. Participants were asked to watch the video weekly for 4 weeks, and to record the number of times they viewed it over a 12-week period. We examined the trajectory model results for efficacy outcomes for the intent-to-treat and the supplemental completers groups. There was a treatment-by-time effect for improved self-esteem (intent-to-treat: p=0.0308; completers: p=0.0284) and decreases in internalized stigma (intent-to-treat: p=0.0036; completers: p=0.0060), and a treatment-by-time-by-time effect for improved coping self-efficacy (intent-to-treat: p=0.0414; completers: p=0.0321). A medium effect of the intervention in terms of improving self-esteem was observed when compared with the control condition in those who completed the study. The magnitude of the intervention effect, however, was large with regard to reducing overall stigma, improving social relationships, and decreasing stereotypes in both groups.


We describe here the case of a 13-month-old boy who acquired HIV infection postnatally through breastfeeding in a developed country in 2012. His mother had regular pregnancy follow-up and was found to be seronegative for HIV on 2 consecutive screening tests (during pregnancy and just after delivery). However, 1 year later, diagnosis of HIV infection arose in both of them after a pediatric
emergency department visit for bronchitis when unexplained hepatosplenomegaly and inflammatory syndrome were noted. The negative maternal viral load found just after delivery confirmed that the mother's seroconversion occurred postnatally, which allowed for active HIV transmission during lactation and lack of the efficient preventive measures that have implemented in Belgium for years. We discuss this uncommon but still existing mode of HIV transmission in industrialized countries and highlight the importance of implementing new targeted health education interventions in addition to constant clinicians’ awareness. Copyright 2014 by the American Academy of Pediatrics.


Summary HIV transmission risk is increased during antiretroviral therapy (ART) use if individuals are not virologically suppressed and engage in high risk transmission behaviour. Baseline data of HIV-infected men who have sex with men (MSM) with recent history of risky behaviour on ART for >3 months (n=139) were evaluated to assess predictors of detectable viraemia and HIV transmission risk-taking behaviour. Twenty-four subjects had viral load (VL) >75 copies/mL and 12 had VL >1000 copies/mL. In multivariable regression analyses, subjects with VL >75 copies/mL were more likely to be Black (OR=4.48, p=0.007), have lower CD4 cell counts (OR=0.727, p=0.005) and have used methamphetamines in the last month (OR=6.64, p=0.019). Subjects with VL >1000 copies/mL were more likely to have lower CD4 cell counts (OR=0.494, p=0.004), report 75 copies/mL with the greatest transmission risk behaviour (n=14) were more likely to be Black (OR=8.00, p=0.006), have lower CD4 cell counts (OR=0.657, p=0.009) and have used methamphetamines in the last month (OR=5.20, p=0.042). High risk HIV transmission behaviour with viraemia occurred in 10% of the cohort. Future efforts to reduce HIV transmission among MSM on ART will require combined interventions that target risk-taking behaviours and substance use. The Author(s) 2014 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav. **Order via Shelcat**


**UNLABELLED:** Tenofovir (TDF) is considered the ideal treatment for patients coinfected with human immunodeficiency virus (HIV) and hepatitis B virus (HBV). However, certain coinfected patients exhibit incomplete viral suppression, with persistent, and sometimes transient, bouts of HBV replication. The reasons for this, including clinical effect, are unclear. A total of 111 HIV-HBV-infected patients undergoing TDF-containing antiretroviral therapy were prospectively followed. Serum HBV-DNA viral load, hepatitis surface (HBsAg) and e antigen (HBeAg) status were obtained at baseline and every 6-12 months. Amino acid (aa) changes on the polymerase gene were assessed using direct sequencing after nested polymerase chain reaction in patients with persistent viremia (PV). After a median of 74.7 months (interquartile range: 33.4-94.7), virological response (VR; 2,000 IU/mL) was rare (4 of 111; 3.6%) and was associated with nonadherence. At TDF initiation, patients with
stabilized VR had significantly higher nadir CD4(+) count, compared to those with transient PV (P=0.006) or LL-PV (P=0.04). No consistent aa changes, other than those associated with lamivudine resistance, were observed in patients with persistent viremia. Importantly, HBeAg loss, HBeAg seroconversion, and HBsAg loss only occurred in patients with stabilized VR. Two patients with stabilized VR developed hepatocellular carcinoma and 2 with LL PV died, 1 of a liver-related cause. CONCLUSION: Suboptimal HBV control during TDF treatment has a negative effect on serological outcomes, but not necessarily clinical events. Immunoregulation may provide more insight into this phenomenon. 2014 by the American Association for the Study of Liver Diseases.

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INTRODUCTION: The CDC estimates that there are currently over 1million people living with human immunodeficiency virus (HIV-1) in the United States, with new cases increasing by approximately 50,000 each year. HIV-1 consists of four distinct groups: the major M group, and the rare N, O, and P groups, each comprising of various subtypes. Without proper care, HIV-1 can lead to cardiovascular, kidney, and liver diseases, cancer, and rapid progression into acquired immune deficiency syndrome (AIDS). Here, we describe a novel, rapid, and highly sensitive assay for the detection of HIV-1 using intercalating dye based RT-PCR and melt curve analysis. MATERIALS AND METHODS: We designed an RT-PCR assay for the detection of the major M subtypes in addition to the rare (O, N, and P) HIV-1 groups, as well as an extraction/RT-PCR control, using melt curve analysis. Viral RNA was extracted using the automated Qiagen EZ1 robotic system (Qiagen, Valencia, CA). To establish the limit of detection (LOD) for this assay, we diluted the AcroMetrix HIV-1 panel (LifeTechnologies, Grand Island, NY) to concentrations ranging from 25 to 500 copies/ml. Armored RNA BCR/ABL b3/a2 (Asuragen, Austin, Texas) was used as our extraction and RT-PCR control. Specificity and accuracy were assessed by testing plasma specimens from 48 anonymized patients negative for HIV-1. RESULTS: This assay has a turnaround time of less than 2.5h and has a limit of detection of 50 copies/ml of plasma. Our assay also demonstrated 100% concordance with 53 previously quantified plasma patient specimens, including 48 negative samples and 5 positive samples. HIV-1 and our extraction/RT-PCR control were consistently identified at 79 degreeC and 82.5 degreeC, respectively. CONCLUSIONS: We developed a comprehensive, easy to use assay for the detection of HIV-1 in human plasma. Our assay combines a rapid and cost-effective method for molecular diagnostics with the versatility necessary for widespread laboratory use. These performance characteristics make this HIV-1 detection assay highly suitable for use in a clinical laboratory. Copyright 2014 Elsevier Inc. All rights reserved. Order via Shelcat

UNLABELLED: Hepatitis B virus (HBV) quasispecies contain a large number of variants that serve as a reservoir for viral selection under antiviral treatment and the immune response, leading to the acute exacerbation and subsequent development of liver failure. However, there is no clear experimental evidence for a significant role of HBV quasispecies in viral pathogenesis. In the present study, HBV sequences were amplified from a patient with severe liver disease and used for construction of HBV replication-competent plasmids. Western blotting, enzyme-linked immunosorbent assay (ELISA), and immunofluorescence staining were performed to analyze the expression, secretion, and subcellular localization of viral proteins in vitro. Viral replication intermediates were detected by Southern blotting. HBV gene expression and replication and the induction of specific immune responses in an HBV hydrodynamic injection (HI) mouse model were investigated. The results demonstrated that two naturally occurring HBV variants, SH and SH-DPS, were identified. The variant SH-DPS expressed only a nonexportable hepatitis B virus surface antigen (HBsAg) with abnormal intracellular accumulation. The coexistence of the HBV variants at a ratio of 1 to 4 (SH to SH-DPS) increased HBV replication. Significantly stronger intrahepatic cytotoxic T lymphocyte (CTL) responses and antibody responses specific to HBsAg were induced in mice by the HBV variants when coapplied by HI. These findings uncovered an unexpected aspect of HBV quasispecies: the coexistence of different variants can significantly modulate specific host immune responses, representing a novel mechanism for the immunopathogenesis of HBV infection. IMPORTANCE: Hepatitis B virus (HBV) is an important human pathogen. HBV quasispecies with genetically heterogenous variants are thought to play a role in the progression of HBV-associated liver diseases. So far, direct evidence is available in only a few cases to confirm the proposed role of HBV variants in the pathogenesis. We report here that the coexistence of two naturally occurring HBV variants at a ratio of 1 to 4 increased HBV replication and induced significantly stronger intrahepatic cytotoxic T lymphocyte responses and antibody responses specific to HBV surface antigen (HBsAg) in mice. Our discovery uncovered an unexpected aspect of HBV quasispecies: the coexistence of different variants can significantly modulate specific host immune responses and may enhance immune-mediated liver damage under some circumstances, representing a novel mechanism for the immunopathogenesis of HBV infection. Copyright 2014, American Society for Microbiology. All Rights Reserved.


We assessed the decisional capacity (DC) of 72 youth with HIV, ages 13-24, using the MacArthur Competence Tool for Treatment, a structured interview that assesses DC along the following dimensions: understanding, appreciation, reasoning, and the ability to express a choice. Using previously established cutoff
scores, results suggested 100% of youth were competent in the area of appreciation, but only 62% and 60% were competent in the areas of understanding and reasoning, respectively. Additional descriptive analyses reveal more detailed information regarding specific strengths and weaknesses within each of the dimensions of decisional capacity. These findings have important implications for health literacy initiatives, medical education, and treatment for youth with HIV, and support the need for adherence and secondary prevention interventions that include a decisional capacity component. Order via Shelcat


TNF-alpha is a proinflammatory cytokine, dramatically elevated during pathogenic infection and often responsible for inflammation-induced disease pathology. SOCS proteins are inhibitors of cytokine signaling and regulators of inflammation. In this study, we found that both SOCS1 and SOCS3 were transiently induced by TNF-alpha and negatively regulate its NF-B-mediated signal transduction. We discovered that PBMCs from HCV-infected patients have elevated endogenous SOCS3 expression but less TNF-alpha-mediated IB degradation and proinflammatory cytokine production than healthy controls. HCV protein expression in Huh7 hepatocytes also induced SOCS3 and directly inhibited TNF-alpha-mediated IL-8 production. Furthermore, we found that SOCS3 associates with TRAF2 and inhibits TRAF2-mediated NF-B promoter activity, suggesting a mechanism by which SOCS3 inhibits TNF-alpha-mediated signaling. These results demonstrate a role for SOCS3 in regulating proinflammatory TNF-alpha signal transduction and reveal a novel immune-modulatory mechanism by which HCV suppresses inflammatory responses in primary immune cells and hepatocytes, perhaps explaining mild pathology often associated with acute HCV infection. 2014 Society for Leukocyte Biology. Order via Shelcat


We report the case of 47-year-old man with HIV and hepatitis C virus-associated cirrhosis who, following discontinuation of his antiretroviral therapy (ART), rapidly developed hepatic decompensation. On restarting his ART there was a noticeable improvement in his liver function, which was attributed to regaining good HIV virus control. Further data on the effects of restarting ART after ART cessation-associated hepatic decompensation are needed. The Author(s) 2014 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav. Order via Shelcat
Vaccines are critical components for protecting HIV-infected adults from an increasing number of preventable diseases. However, missed opportunities for vaccination among HIV-infected persons persist, likely due to concerns regarding the safety and efficacy of vaccines, as well as the changing nature of vaccine guidelines. In addition, the optimal timing of vaccination among HIV-infected adults in regards to HIV stage and receipt of antiretroviral therapy remain important questions. This article provides a review of the current recommendations regarding vaccines among HIV-infected adults and a comprehensive summary of the evidence-based literature of the benefits and risks of vaccines among this vulnerable population.


BACKGROUND & AIMS: Cyclophilin inhibitors are being developed for treatment of hepatitis C virus (HCV) infection. They are believed to inhibit the HCV replication complex. We investigated whether cyclophilin inhibitors interact with interferon (IFN) signaling in cultured cells infected with HCV. METHODS: We used immunoblot assays to compare expression of IFN-stimulated genes (ISGs) and of components of IFN signaling in HCV-infected and uninfected cells. RESULTS: Incubation with IFN alfa induced expression of ISGs in noninfected cells and, to a lesser extent, in HCV-infected cells; addition of the cyclophilin inhibitor SCY-635 restored expression of ISG products in HCV-infected cells. SCY-635 reduced phosphorylation of double-strand RNA-dependent protein kinase (PKR) and its downstream factor eIF2alpha; the phosphorylated forms of these proteins are negative regulators of ISG translation. Cyclophilin A interacted physically with PKR; this interaction was disrupted by SCY-635. SCY-635 also suppressed PKR-mediated formation of stress granules. Cyclophilin inhibitors were found to inhibit PKR phosphorylation and stress granule formation in HCV-infected and uninfected cells. CONCLUSIONS: In cultured cells, cyclophilin inhibitors reverse the attenuation of the IFN response by HCV, in addition to their effects on HCV replication complex. Cyclophilin A regulation of PKR has been proposed as a mechanism for observed effects of cyclophilin inhibitors on IFN signaling. We found that cyclophilin inhibitors reduce phosphorylation of PKR and eIF2alpha during HCV infection to allow for translation of ISG products. Proteins in this pathway might be developed as targets for treatment of HCV infection.


UNLABELLED: The Japanese fulminant hepatitis-1 (JFH1)-based hepatitis C virus (HCV) infection system has permitted analysis of the complete viral replication cycle in vitro. However, lack of robust infection systems for primary, patient-derived isolates limits systematic functional studies of viral intrahost variation and vaccine
development. Therefore, we aimed at developing cell culture models for incorporation of primary patient-derived glycoproteins into infectious HCV particles for in-depth mechanistic studies of envelope gene function. To this end, we first constructed a packaging cell line expressing core, p7, and NS2 based on the highly infectious Jc1 genotype (GT) 2a chimeric genome. We show that this packaging cell line can be transfected with HCV replicons encoding cognate Jc1-derived glycoprotein genes for production of single-round infectious particles by way of trans-complementation. Testing replicons expressing representative envelope protein genes from all major HCV genotypes, we observed that virus production occurred in a genotype- and isolate-dependent fashion. Importantly, primary GT 2 patient-derived glycoproteins were efficiently incorporated into infectious particles. Moreover, replacement of J6 (GT 2a) core, p7, and NS2 with GT 1a-derived H77 proteins allowed production of infectious HCV particles with GT 1 patient-derived glycoproteins. Notably, adaptive mutations known to enhance virus production from GT 1a-2a chimeric genomes further increased virus release. Finally, virus particles with primary patient-derived E1-E2 proteins possessed biophysical properties comparable to Jc1 HCVcc particles, used CD81 for cell entry, were associated with ApoE and could be neutralized by immune sera. CONCLUSION: This work describes cell culture systems for production of infectious HCV particles with primary envelope protein genes from GT 1 and GT 2-infected patients, thus opening up new opportunities to dissect envelope gene function in an individualized fashion. 2014 by the American Association for the Study of Liver Diseases.


Osteitis is an under-recognised clinical manifestation of early syphilis, especially in patients with HIV. We report here a case of syphilitic osteitis of the skull and review its clinical presentation, diagnosis and management. The Author(s) 2014 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav. Order via Shelcat


In vitro studies in primary or immortalized cells continue to be used to elucidate the essential principles that govern the interactions between HIV-1 and isolated target cells. However, until recently, substantial technical barriers prevented this information from being efficiently translated to the more complex scenario of HIV-1 spread in the host in vivo, which has limited our understanding of the impact of host physiological parameters on the spread of HIV-1. In this Review, we discuss the recent development of imaging approaches to visualize HIV-1 spread and the adaptation of these approaches to organotypic ex vivo models and animal models. We focus on new concepts, including the mechanisms and in vivo relevance of cell-
cell transmission for HIV-1 spread and the function of the HIV-1 pathogenesis factor Nef, which have emerged from the application of these integrative approaches in complex cell systems.


There is an international epidemic of hepatitis C virus (HCV) infection among human immunodeficiency virus-infected men who have sex with men. Transmission of HCV variants that are resistant to recently approved direct-acting antivirals (DAAs) could be an important clinical and public health problem. We document a case of transmission of a DAA-resistant variant of HCV from a patient who was treated with telaprevir to his sexual partner. The transmission of HCV DAA-resistant variants could impair therapeutic regimens that include DAAs. Copyright 2014 AGA Institute. Published by Elsevier Inc. All rights reserved.


OBJECTIVES: The aim of this study was to explore sodium taurocholate co-transporting polypeptide (NTCP) exerting its function with hepatitis B virus (HBV) and its targeted candidate compounds, in HBV therapy. MATERIALS AND METHODS: Identification of NTCP as a novel HBV target for screening candidate small molecules, was used by phylogenetic analysis, network construction, molecular modelling, molecular docking and molecular dynamics (MD) simulation. In vitro virological examination, q-PCR, western blotting and cytotoxicity studies were used for validating efficacy of the candidate compound. RESULTS: We used the phylogenetic analysis of NTCP and constructed its protein-protein network. Also, we screened compounds from Drugbank and ZINC, among which five were validated for their authentication in HepG 2.2.15 cells. Then, we selected compound N4 (azelastine hydrochloride) as the most potent of them. This showed good inhibitory activity against HBsAg (IC50 = 7.5 mum) and HBeAg (IC50 = 3.7 mum), as well as high SI value (SI = 4.68). Further MD simulation results supported good interaction between compound N4 and NTCP. CONCLUSIONS: In silico analysis and experimental validation together demonstrated that compound N4 can target NTCP in HepG2.2.15 cells, which may shed light on exploring it as a potential anti-HBV drug. 2014 John Wiley & Sons Ltd. Order via Shelcat


Testing for HIV is one of the cornerstones in the fight against HIV spread. The 2014 European Guideline on HIV Testing provides advice on testing for HIV infection in individuals aged 16 years and older who present to sexually transmitted infection, genito-urinary or dermato-venereology clinics across Europe. It may also be applied
in other clinical settings where HIV testing is required, particularly in primary care settings. The aim of the guideline is to provide practical guidance to clinicians and laboratories that within these settings undertake HIV testing, and to indicate standards for best practice. The Author(s) 2014 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav. Order via Shelcat.

(36) Gouda HM, El-Saadany ZA, Foad NB, Salama RM. Interleukin 28B polymorphisms and therapy response in Egyptian hepatitis C genotype-4 patients. DNA & Cell Biology 2014 Sep;33(9):642-646

Hepatitis C infection represents a major health problem in Egypt; only 20% of patients undergo spontaneous clearance of the virus and around 25% of all patients progress to develop cirrhosis. More than 90% of Egyptian patients have hepatitis C virus (HCV) genotype-4. Combined pegylated interferon and oral ribavirin are the current standard therapies for HCV-4. The aim of the work is to evaluate the predictive power of the rs12979860 IL28B SNP and rs12980275 IL28B SNP for treatment response in Egyptian patients infected with HCV genotype 4. One hundred eleven HCV patients receiving combined treatment were studied for rs12979860 and rs12980275 polymorphisms by the restriction fragment length polymorphism technique. The rs12979860 CC and rs12979860 AA genotypes were significantly associated with sustained virological response (p=0.001). Our results suggest that studying IL28B polymorphisms contribute to proper prediction of response to standard therapies in Egyptian patients, optimizing cost effectiveness, and minimizing unneeded adverse effect of therapy. Order via Shelcat.


OBJECTIVES: To evaluate clinician adherence to guidelines for documentation of sexual history and screening for sexually transmitted infection (STI)/HIV infection during routine adolescent well visits. Secondary objectives were to determine patient and clinician factors associated with sexual history documentation and STI/HIV testing. STUDY DESIGN: Retrospective, cross-sectional study of 1000 randomly selected 13- to 19-year-old routine well visits at all 29 pediatric primary care practices affiliated with a children's hospital. We evaluated frequency of documentation of sexual history and testing for gonorrhea (GC)/chlamydia (CT) and HIV testing. Multivariable logistic regression was performed to identify factors associated with documentation and testing. RESULTS: Of the 1000 patient visits reviewed, 212 (21.2%; 95% CI, 18.7-23.7) had a documented sexual history, of which 45 adolescents’ (21.2%; 95% CI, 15.7-26.8) encounters were documented as being sexually active. Overall, 26 (2.6%; 95% CI, 1.6-3.6) patients were tested for GC/CT and 16 (1.6%; 95% CI, 0.8-2.4) were tested for HIV infection. In multivariable analyses, factors associated with sexual history documentation included older patient age, non-Hispanic black race/ethnicity, nonprivate insurance status, and care by female clinician. Factors associated with GC/CT testing included male gender, non-Hispanic black race/ethnicity, and nonprivate insurance. HIV testing was more likely to be performed on older adolescents, those of non-Hispanic black race/ethnicity, and those with nonprivate insurance. CONCLUSIONS: Pediatric...
primary care clinicians infrequently document sexual histories and perform STI and HIV testing on adolescent patients. Future studies should investigate provider beliefs, clinical decision-making principles, and perceived barriers to improve the sexual health care of adolescents and evaluate interventions to increase rates of adolescent sexual health screening. Copyright 2014 Elsevier Inc. All rights reserved.


BACKGROUND: The effect of HIV pre-exposure prophylaxis (PrEP) depends on uptake, adherence, and sexual practices. We aimed to assess these factors in a cohort of HIV-negative people at risk of infection. METHODS: In our cohort study, men and transgender women who have sex with men previously enrolled in PrEP trials (ATN 082, iPrEx, and US Safety Study) were enrolled in a 72 week open-label extension. We measured drug concentrations in plasma and dried blood spots in seroconverters and a random sample of seronegative participants. We assessed PrEP uptake, adherence, sexual practices, and HIV incidence. Statistical methods included Poisson models, comparison of proportions, and generalised estimating equations. FINDINGS: We enrolled 1603 HIV-negative people, of whom 1225 (76%) received PrEP. Uptake was higher among those reporting condomless receptive anal intercourse (416/519 [81%] vs 809/1084 [75%], p=0003) and having serological evidence of herpes (612/791 [77%] vs 613/812 [75%] p=003). Of those receiving PrEP, HIV incidence was 18 infections per 100 person-years, compared with 26 infections per 100 person-years in those who concurrently did not choose PrEP (HR 051, 95% CI 026-101, adjusted for sexual behaviours), and 39 infections per 100 person-years in the placebo group of the previous randomised phase (HR 049, 95% CI 031-077). Among those receiving PrEP, HIV incidence was 47 infections per 100 person-years if drug was not detected in dried blood spots, 23 infections per 100 person-years if drug concentrations suggested use of fewer than two tablets per week, 06 per 100 person-years for use of two to three tablets per week, and 00 per 100 person-years for use of four or more tablets per week (p<00001). PrEP drug concentrations were higher among people of older age, with more schooling, who reported non-condom receptive anal intercourse, who had more sexual partners, and who had a history of syphilis or herpes. INTERPRETATION: PrEP uptake was high when made available free of charge by experienced providers. The effect of PrEP is increased by greater uptake and adherence during periods of higher risk. Drug concentrations in dried blood spots are strongly correlated with protective benefit. FUNDING: US National Institutes of Health. Copyright 2014 Elsevier Ltd. All rights reserved.


OBJECTIVES: To estimate the effectiveness of candidate microbicides BufferGel
and 0.5% PRO 2000 Gel (P) (PRO 2000) for prevention of non-ulcerative sexually transmitted infections (STIs). METHODS: Between 2005 and 2007, 3099 women were enrolled in HIV Prevention Trials Network (HPTN) protocol 035, a phase II/IIb evaluation of the safety and effectiveness of BufferGel and PRO 2000 for prevention of STIs, including Neisseria gonorrhoeae (NG), Chlamydia trachomatis (CT) and Trichomonas vaginalis (TV). Incidences of STIs were determined by study arm, and HRs of BufferGel and PRO 2000 versus placebo gel or no gel control groups were computed using discrete time Andersen-Gill proportional hazards model. RESULTS: The overall incidence rates were 1.6/100 person-years at risk (PYAR) for NG, 3.9/100 PYAR for CT and 15.3/100 PYAR for TV. For BufferGel versus placebo gel, HRs were 0.99 (95% CI 0.49 to 2.00), 1.00 (95% CI 0.64 to 1.57) and 0.95 (95% CI 0.71 to 1.25) for prevention of NG, CT and TV, respectively. For PRO 2000, HRs were 1.66 (95% CI 0.90 to 3.06), 1.16 (95% CI 0.76 to 1.79) and 1.18 (95% CI 0.90 to 1.53) for prevention of NG, CT and TV, respectively. CONCLUSIONS: The incidence of STIs was high during HIV Prevention Trials Network 035 despite provision of free condoms and comprehensive risk-reduction counselling, highlighting the need for effective STI prevention programmes in this population. Unfortunately, candidate microbicides BufferGel and PRO2000 had no protective effect against gonorrhoea, chlamydia or trichomoniasis. TRIAL REGISTRATION NUMBER: NCT00074425. Published by the BMJ Publishing Group Limited.


Access to oral health care for vulnerable populations is one of the concerns addressed by the U.S. Health Resources and Services Administration HIV/AIDS Bureau's Community-Based Dental Partnership Program (CBDPP). The program introduces dental students and residents at several dental schools to care for vulnerable patients through didactic and clinical work in community-based dental settings. This study of the dental students and residents in this program answered three questions: 1) What are their HIV knowledge, attitudes, and behaviors? 2) How has participation in the CBDPP impacted their knowledge, attitudes, and behaviors? 3) Has the intervention affected their work placement decisions and attitudes after graduation, particularly with respect to treating people living with HIV and other underserved populations? A total of 305 first- through fourth-year dental students and first- and second-year residents at five dental schools across the United States completed surveys before and after a community-based rotation and following graduation. Response rates at each of the five schools ranged from 82.4 to 100 percent. The results showed an increase in the participants' knowledge and positive attitudes regarding treatment for patients with HIV and other vulnerable populations post-rotation compared to pre-rotation. Results after graduation found that most respondents were practicing in private settings or in academic institutions as residents but were willing to treat a diverse patient population. These findings support the role of training programs, such as the CBDPP, for expanding the dental workforce to treating vulnerable populations including people living with HIV/AIDS.

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BACKGROUND: Given recent advances in hepatitis C virus (HCV) treatment, health systems must ensure that patients with a positive HCV antibody receive timely determination of their HCV status through viral testing. At the Louis Stokes Cleveland Department of Veterans Affairs Medical Center, viral testing was completed within six months of the first instance of a positive HCV antibody test for only 45% of patients. Beginning in 2008, three sequential improvements were implemented to close this care gap. METHODS: The three sequential improvements phases were as follows: (1) improving patient-centeredness of screening process in ambulatory patients, (2) local implementation of the Department of Veterans Affairs national HCV reflex testing policy, and (3) local evaluation of the efficiency and effectiveness of local implementation of reflex testing. RESULTS: From 2005 through 2013, 40 to 150 unique patients/quarter required viral testing following a positive antibody test. The firsts and second-phase improvements resulted in a 68% and 96% completion rate for timely viral testing during respective improvement phases. In the third improvement phase, remaining process problems related to the reflex testing process were identified using a locally developed electronic HCV population management application, resulting in a sustained rate of 100% completion of timely viral testing. Interrupted time series analysis revealed that the implementation of HCV reflex testing had the largest impact on the ability to complete timely viral testing. CONCLUSIONS: A continuous quality improvement approach, supported by an HCV population management application, achieved the complete closure of an important HCV care gap. Reflex testing should be initiated at facilities that have yet to adopt this approach.


Over the past decade, landmark collaboration between regulatory agencies, pharmaceutical companies, academia, and patient community representatives has enabled the development and approval of new hepatitis C virus (HCV) treatment regimens with unprecedented speed. By providing a neutral platform for cross-sector engagement, the Forum for Collaborative HIV Research's(1) HCV Drug Development Advisory Group played a critical role in fostering this collaboration and expediting drug development. The applicability of this model to other therapeutic areas should be explored.


OBJECTIVES: 1) To describe autoimmune diseases (AD) in HIV-infected people; and 2) to perform a literature review concerning this issue. DESIGN: 52 HIV-infected patients that presented an AD in 14 medical departments in Paris and Ile-de-France area were retrospectively included in this study. RESULTS: The ADs were vasculitis...
immune cytopenias (8), rheumatic diseases (8), lupus (7), sarcoidosis (7), thyroid diseases (6), hepatic diseases (5), and antiphospholipid syndrome (4). Four patients presented 2 ADs. In 5 patients the AD preceded HIV infection, in 14 HIV infection was diagnosed at the same time as the AD and 34 were HIV-infected when they developed an AD. 40 ADs (80%) occurred in patients with a CD4 T lymphocyte count of more than 200/mm(3). Cases of autoimmune hemolytic anemia occurred only in patients severely immunodepressed. In five patients (a vasculitis case, a sarcoidosis case, three thyroid disease cases) the AD presented as a form of immune restoration inflammatory syndrome (IRIS). Some ADs allowed HIV-infection diagnosis at a stage of moderate immune deficiency (vasculitis, antiphospholipid syndrome, immune thrombocytopenia). 37 patients received immunosuppressant treatments with good tolerance. These results confirm in a large series of patients previous data concerning autoimmune diseases occurrence in HIV-infected people. CONCLUSION: In the HAART era, when HIV-infected people are treated more and more early, autoimmune diseases can occur, mainly at the phase of immunological recovery. HIV infection should not limit immunosuppressant treatment use. Copyright 2014 Elsevier B.V. All rights reserved.


The aim of this study was to estimate the prevalence of total antibodies to hepatitis A virus (anti-HAV-T) in the group of HIV-positive adults in Lodz region of Poland, and to evaluate the response and long-term immunity after vaccination against hepatitis A virus. In the group of 234 HIV-infected patients, 72 persons (30.8%) were anti-HAV-T positive (>20IU/L). In multivariate analysis, two independent factors associated with the presence of anti-HAV-T were identified: the age of patients (OR=1.07) and the presence of antibodies to hepatitis C virus (OR=2.87). Vaccination was completed in 83 patients. Good response (anti-HAV-T >20IU/L one month after the booster dose) was obtained in 79.5% of patients. In patients with CD4 >200 cells/L in multivariate analysis only presence of antibodies to hepatitis C virus was a prognostic factor for the response to vaccination (OR=0.13). Among responders available for the follow-up, 82% (50 out of 61) had detectable anti-HAV-T at 1 year and 75.5% (37 out of 49) at 5 years. Our results demonstrate that most of the studied HIV-positive patients were susceptible to hepatitis A virus infection. Most HIV-infected adults with high CD4 counts had a durable response even up to 5 years after vaccination. Patients with a HIV/hepatitis C virus coinfection displayed a worse response to vaccination. The Author(s) 2014 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav.


UNLABELLED: Increasing data suggest that NK cells can mediate antiviral activity in HIV-1-infected humans, and as such, novel approaches harnessing the anti-HIV-1 function of both T cells and NK cells represent attractive options to improve future HIV-1 immunotherapies. Chronic progressive HIV-1 infection has been associated with a loss of CD4(+) T helper cell function and with the
accumulation of anergic NK cells. As several studies have suggested that cytokines produced by CD4(+) T cells are required to enhance NK cell function in various infection models, we hypothesized that reconstitution of HIV-1-specific CD4(+) T-cell responses by therapeutic immunization would restore NK cell activity in infected individuals. Using flow cytometry, we examined the function of CD4(+) T cells and NK cells in response to HIV-1 in subjects with treated chronic HIV-1 infection before and after immunization with an adjuvanted HIV-1 Gp120/NeFtAt subunit protein vaccine candidate provided by GlaxoSmithKline. Vaccination induced an increased expression of interleukin-2 (IL-2) by Gp120-specific CD4(+) T cells in response to HIV-1 peptides ex vivo, which was associated with enhanced production of gamma interferon (IFN-) by NK cells. Our data show that reconstitution of HIV-1-specific CD4(+) T-cell function by therapeutic immunization can enhance NK cell activity in HIV-1-infected individuals. IMPORTANCE: NK cells are effector cells of the innate immune system and are important in the control of viral infection. Recent studies have demonstrated the crucial role played by NK cells in controlling and/or limiting acquisition of HIV-1 infection. However, NK cell function is impaired during progressive HIV-1 infection. We recently showed that therapeutic immunization of treated HIV-1-infected individuals reconstituted strong T-cell responses, measured notably by their production of IL-2, a cytokine that can activate NK cells. The current study suggests that reconstitution of T-cell function by therapeutic vaccination can enhance NK cell activity in individuals with chronic HIV-1 infection. Our findings provide new insights into the interplay between adaptive and innate immune mechanisms involved in HIV-1 immunity and unveil opportunities to harness NK cell function in future therapeutic vaccine strategies to target HIV-1. Copyright 2014, American Society for Microbiology. All Rights Reserved. 


In Ireland the incidence of sexually transmitted infections (STIs) is steadily increasing while the number of new HIV-diagnoses in men who have sex with men has more than doubled in the past decade. This study investigated the prevalence of STIs in asymptomatic HIV-infected men who have sex with men (MSM) attending a clinic for routine HIV care in the largest HIV-centre in Ireland. Fifty HIV-infected MSM were included in the study (mean age [SD] 38 years [9], 66% Irish). Sixteen per cent of HIV-infected MSM screened were diagnosed with a STI. Thirty-eight per cent reported always using condoms while 4% reported never using condoms, 46% used condoms inconsistently and 10% reported no sexual contacts in the preceding 12 months. Recognising the need to optimise STI screening, a pilot self-screening programme was subsequently introduced to our HIV clinic as a quality improvement initiative. Asymptomatic MSM attending for routine HIV care were invited to have an opportunistic STI screen either provider performed or by self-screening. Seventy-one patients were included in the pilot. Sixty-five (92%) opted for self-collected rectal swabs. Ten STIs were detected in eight patients. This study supports guidelines recommending routine screening for STIs in the care of HIV-infected patients and highlights opportunities to provide relevant screening and education interventions targeting unsafe sexual behaviours. The Author(s) 2011 Reprints and permissions:

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BACKGROUND: We present an analysis of the first 2 years of hepatitis B virus (HBV) nucleic acid testing (NAT) of the Australian donor population. STUDY DESIGN AND METHODS: Between July 5, 2010, and July 4, 2012, all blood donations were screened for HBV DNA and hepatitis B surface antigen (HBsAg). Donors who tested HBsAg negative but HBV NAT positive were assessed as occult hepatitis B infections (OBI) if reactive for antibodies to HBV core antigen (anti-HBc). Donors who were anti-HBc reactive but with nonrepeatable or nondiscriminated NAT results were assessed as HBV inconclusive pending follow-up testing. RESULTS: During the study period a total of 2,673,521 donations were screened for HBV. Forty-two chronic OBI infections (5.55/100,000 donors) were identified compared to eight acute serologic window period infections (1.06/100,000 donors). Of the 42 OBI cases, 23 (54.8%) were detected the first time they were screened for HBV DNA while 19 (45.2%) gave one or more HBV NAT-nonreactive results before detection. Of 68 donors initially assessed as HBV inconclusive and available for follow-up, 10 later confirmed as OBI cases while 51 were NAT nonreactive but remained anti-HBc reactive and OBI could not be excluded. CONCLUSION: This study demonstrated a substantially higher prevalence of OBI compared to acute serologic window period HBV infections in Australian blood donors. Follow-up testing of OBI cases indicates that HBV DNA is often only intermittently detectable in OBI, highlighting the importance of including anti-HBc to optimize the HBV testing algorithm. 2014 The Authors. Transfusion published by Wiley Periodicals, Inc. on behalf of AABB.


Treatment of sexually transmitted infections (STIs) has been hypothesised to decrease HIV transmission. Although observational studies show an association between STIs and HIV, only one prospective randomised controlled trial (RCT) has confirmed this. Female genital schistosomiasis can cause genital lesions, accompanied by bloody discharge, ulcers or malodorous discharge. Genital schistosomiasis is common, starts before puberty and symptoms can be mistaken for STIs. Three observational studies have found an association between schistosomiasis and HIV. Genital lesions that develop in childhood are chronic. This paper sought to explore the possible effects of schistosomiasis on the RCTs of STI treatment for HIV prevention. In the study sites, schistosomiasis was a likely cause of genital lesions. The studies recruited women that may have had genital schistosomal lesions established in childhood. Schistosomiasis endemic areas with different prevalence levels may have influenced HIV incidence in intervention and control sites differently, and some control group interventions may have influenced the impact of schistosomiasis on the study results. Schistosomiasis is a neglected cause of genital tract disease. It may have been an independent cause of HIV incidence in the RCTs of STI treatment for HIV prevention and may have obscured the findings of these trials. The Author(s) 2011 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav. Order via Shelcat
(49) Kusumoto S, Tanaka Y, Mizokami M, Ueda R. **Strategy for preventing hepatitis B reactivation in patients with resolved hepatitis B virus infection after rituximab-containing chemotherapy.** Hepatology 2014 Aug;60(2):765-766

(50) Landovitz RJ, Coates TJ. **Moving HIV PrEP from research into practice.** The Lancet Infectious Diseases 2014 Sep;14(9):781-783


HIV-related stigma has a major impact on quality of life and health among people living with HIV and AIDS (PLWHA). This study examines demographic, mental health, behavioral, contextual, and HIV care-related correlates of HIV stigma among 503 substance abusing PLWHA. Stigma was measured with the HIV Internalized Stigma Measure which has four subscales: stereotypes about HIV, self-acceptance, disclosure concerns, and social relationships. Severe substance dependence (55.3%) and depression (54.7%) were associated with higher HIV stigma across all domains. 49.9% of the sample reported antiretroviral (ARV) medication diversion (the unlawful sale and trading of ARV medications); diverters endorsed significantly higher stigma related to disclosure. 54.1% of the sample reported >95% ARV adherence; these individuals reported significantly lower stigma for self-acceptance, disclosure, and social relationships. Multivariate linear regression showed that depression and social support demonstrated significant main effects across stigma domains. Findings suggest that interventions to decrease HIV related stigma may be an important component of initiatives to increase engagement in HIV care.

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(53) Li C, Lu L, Murphy DG, Negro F, Okamoto H. **Origin of hepatitis C virus genotype 3 in Africa as estimated through an evolutionary analysis of the full-length genomes of nine subtypes, including the newly sequenced 3d and 3e.** J.Gen.Virol. 2014 Aug;95(Pt 8):1677-1688

We characterized the full-length genomes of nine hepatitis C virus genotype 3 (HCV-3) isolates: QC7, QC8, QC9, QC10, QC34, QC88, NE145, NE274 and 811. To the best of our knowledge, NE274 and NE145 were the first full-length genomes for confirming the provisionally assigned subtypes 3d and 3e, respectively, whereas 811 represented the first HCV-3 isolate that had its extreme 3' UTR terminus sequenced. Based on these full-length genomes, together with 42 references representing eight assigned subtypes and an unclassified variant of HCV-3, and 10 sequences of six other genotypes, a timescaled phylogenetic tree was reconstructed after an evolutionary analysis using a coalescent Bayesian procedure. The results indicated that subtypes 3a, 3d and 3e formed a subset with a common ancestor dated to
~202.89 [95% highest posterior density (HPD): 160.11, 264.6] years ago. The analysis of all of the HCV-3 sequences as a single lineage resulted in the dating of the divergence time to ~457.81 (95% HPD: 350.62, 587.53) years ago, whereas the common ancestor of all of the seven HCV genotypes dated to ~780.86 (95% HPD: 592.15, 1021.34) years ago. As subtype 3h and the unclassified variant were relatives, and represented the oldest HCV-3 lineages with origins in Africa and the Middle East, these findings may indicate the ancestral origin of HCV-3 in Africa. We speculate that the ancestral HCV-3 strains may have been brought to South Asia from Africa by land and/or across the sea to result in its indigenous circulation in that region. The spread was estimated to have occurred in the era after Vasco da Gama had completed his expeditions by sailing along the eastern coast of Africa to India. However, before this era, Arabians had practised slave trading from Africa to the Middle East and South Asia for centuries, which may have mediated the earliest spread of HCV-3. 2014 The Authors.


Research in the past two decades has generated unequivocal evidence that host genetic variations substantially account for the heterogeneous outcomes following human immunodeficiency virus type 1 (HIV-1) infection. In particular, genes encoding human leukocyte antigens (HLA) have various alleles, haplotypes, or specific motifs that can dictate the set-point (a relatively steady state) of plasma viral load (VL), although rapid viral evolution driven by innate and acquired immune responses can obscure the long-term relationships between HLA genotypes and HIV-1-related outcomes. In our analyses of VL data from 521 recent HIV-1 seroconverters enrolled from eastern and southern Africa, HLA-A*03:01 was strongly and persistently associated with low VL in women (frequency = 11.3 %, P 0.50). In a reduced multivariable model, age, sex, geography (clinical sites), previously identified HLA factors (HLA-B*18, B*45, B*53, and B*57), and the interaction term for female sex and HLA-A*03:01 collectively explained 17.0 % of the overall variance in geometric mean VL over a 3-year follow-up period (P < 0.0001). Multiple sensitivity analyses of longitudinal and cross-sectional VL data yielded consistent results. These findings can serve as a proof of principle that the gap of "missing heritability" in quantitative genetics can be partially bridged by a systematic evaluation of sex-specific associations.


UNLABELLED: Generalized immune activation during HIV infection is associated with an increased risk of cardiovascular disease, neurocognitive disease, osteoporosis, metabolic disorders, and physical frailty. The mechanisms driving this immune activation are poorly understood, particularly for individuals effectively treated with antiretroviral medications. We hypothesized that viral characteristics such as sequence diversity may play a role in driving HIV-associated immune activation. We therefore sequenced proviral DNA isolated from peripheral blood
mononuclear cells from HIV-infected individuals on fully suppressive antiretroviral therapy. We performed phylogenetic analyses, calculated viral diversity and divergence in the env and pol genes, and determined coreceptor tropism and the frequency of drug resistance mutations. Comprehensive immune profiling included quantification of immune cell subsets, plasma cytokine levels, and intracellular signaling responses in T cells, B cells, and monocytes. These antiretroviral therapy-treated HIV-infected individuals exhibited a wide range of diversity and divergence in both env and pol genes. However, proviral diversity and divergence in env and pol, coreceptor tropism, and the level of drug resistance did not significantly correlate with markers of immune activation. A clinical history of virologic failure was also not significantly associated with levels of immune activation, indicating that a history of virologic failure does not inexorably lead to increased immune activation as long as suppressive antiretroviral medications are provided. Overall, this study demonstrates that latent viral diversity is unlikely to be a major driver of persistent HIV-associated immune activation. IMPORTANCE: Chronic immune activation, which is associated with cardiovascular disease, neurologic disease, and early aging, is likely to be a major driver of morbidity and mortality in HIV-infected individuals. Although treatment of HIV with antiretroviral medications decreases the level of immune activation, levels do not return to normal. The factors driving this persistent immune activation, particularly during effective treatment, are poorly understood. In this study, we investigated whether characteristics of the latent, integrated HIV provirus that persists during treatment are associated with immune activation. We found no relationship between latent viral characteristics and immune activation in treated individuals, indicating that qualities of the provirus are unlikely to be a major driver of persistent inflammation. We also found that individuals who had previously failed treatment but were currently effectively treated did not have significantly increased levels of immune activation, providing hope that past treatment failures do not have a lifelong "legacy" impact. Copyright 2014, American Society for Microbiology. All Rights Reserved. Order via Shelcat


BACKGROUND & AIMS: MK-5172 is an inhibitor of the hepatitis C virus (HCV) nonstructural protein 3/4A protease; MK-5172 is taken once daily and has a higher potency and barrier to resistance than licensed protease inhibitors. We investigated the efficacy and tolerability of MK-5172 with peginterferon and ribavirin (PR) in treatment-naive patients with chronic HCV genotype 1 infection without cirrhosis. METHODS: We performed a multicenter, double-blind, randomized, active-controlled, dose-ranging, response-guided therapy study. A total of 332 patients received MK-5172 (100, 200, 400, or 800 mg) once daily for 12 weeks in combination with PR. Patients in the MK-5172 groups received PR for an additional 12 or 36 weeks, based on response at week 4. Patients in the control group (n = 66) received a combination of boceprevir and PR, dosed in accordance with boceprevir's
US product circular. RESULTS: At 24 weeks after the end of therapy, sustained virologic responses were achieved in 89%, 93%, 91%, and 86% of the patients in the groups given the combination of PR and MK-5172 (100, 200, 400, or 800 mg), respectively, vs 61% of controls. In the MK-5172 group receiving 100 mg, 91% of patients had undetectable levels of HCV RNA at week 4 and qualified for the short duration of therapy. The combination of MK-5172 and PR generally was well tolerated. Transient increases in transaminase levels were noted in the MK-5172 groups given 400 and 800 mg, at higher frequencies than in the MK-5172 groups given 100 or 200 mg, or control groups. CONCLUSIONS: Once-daily MK-5172 (100 mg) with PR for 24 or 48 weeks was highly effective and well tolerated among treatment-naive patients with HCV genotype 1 infection without cirrhosis. Studies are underway to evaluate interferon-free MK-5172-based regimens. ClinicalTrials.gov number: NCT01353911. Copyright 2014 AGA Institute. Published by Elsevier Inc. All rights reserved.


Oral HIV pre-exposure prophylaxis (PrEP) is a promising new biomedical prevention approach in which HIV-negative individuals are provided with daily oral antiretroviral medication for the primary prevention of HIV-1. Several clinical trials have demonstrated efficacy of oral PrEP for HIV prevention among groups at high risk for HIV, with adherence closely associated with level of risk reduction. In the United States (US), three groups have been prioritized for initial implementation of PrEP—injecting drug users, men who have sex with men at substantial risk for HIV, and HIV-negative partners within serodiscordant heterosexual couples. Numerous demonstration projects involving PrEP implementation among MSM are underway, but relatively little research has been devoted to study PrEP implementation in HIV-serodiscordant heterosexual couples in the US. Such couples face a unique set of challenges to PrEP implementation at the individual, couple, and provider level with regard to PrEP uptake and maintenance, adherence, safety and toxicity, clinical monitoring, and sexual risk behavior. Oral PrEP also provides new opportunities for serodiscordant couples and healthcare providers for primary prevention and reproductive health. This article provides a review of the critical issues, challenges, and opportunities involved in the implementation of oral PrEP among HIV-serodiscordant heterosexual couples in the US. Order via Shelcat


Antiretrovirals (ARVs) decrease the infectiousness of treated HIV-infected persons and can reduce the acquisition of HIV infection when taken by uninfected persons. Coformulated emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) is approved in the United States for the preexposure prophylaxis (PrEP) indication, changing the regulatory landscape for new prophylactic agents. We describe the challenge of conducting rigorous clinical end-point trials for prophylactic agents and
point to alternatives that leverage new information about correlates of HIV risk and protection.


Know Your Status (KYS), a novel, student-run program offered free HIV-testing at a private university (PU) and community college (CC). Following completion of surveys of risk behaviors/reasons for seeking testing, students were provided with rapid, oral HIV-testing. We investigated testing history, risk behaviors, and HIV prevalence among students tested during the first three years of KYS. In total, 1408 tests were conducted, 5 were positive: 4/408 CC, 1/1000 PU (1% vs. 0.1%, p=0.01). Three positives were new diagnoses, all black men-who-have-sex-with-men (MSM). Over 50% of students were tested for the first time and 59% reported risk behaviors. CC students were less likely to have used condoms at last sex (a surrogate for risk behavior) compared to PU (OR 0.73, CI [0.54, 0.98]). Race, sexual identity, and sex were not associated with condom use. These results demonstrate that KYS successfully recruited large numbers of previously untested, at-risk students, highlighting the feasibility and importance of testing college populations.


OBJECTIVE: This guideline reviews the evidence relating to the care of pregnant women living with HIV and the prevention of perinatal HIV transmission. Prenatal care of pregnancies complicated by HIV infection should include monitoring by a multidisciplinary team with experts in this area. OUTCOMES: OUTCOMES evaluated include the impact of HIV on pregnancy outcome and the efficacy and safety of antiretroviral therapy and other measures to decrease the risk of vertical transmission. EVIDENCE: Published literature was retrieved through searches of PubMed and The Cochrane Library in 2012 and 2013 using appropriate controlled vocabulary (HIV, anti-retroviral agents, pregnancy, delivery) and key words (HIV, pregnancy, antiretroviral agents, vertical transmission, perinatal transmission). Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies published in English or French. There were no date restrictions. Searches were updated on a regular basis and incorporated in the guideline to June 2013. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies. VALUES: The quality of evidence in this document was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1).; Publisher: Abstract available from the publisher. Language: French
(62) Moragianni VA. Why are we still, 20 years later, depriving human immunodeficiency virus-serodiscordant couples of equal access to fertility care?. Fertility & Sterility 2014 Aug;102(2):352-353
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BACKGROUND: Influenza A has been described in association with hepatitis. We present a case of complicated influenza A hepatitis in a pregnant woman, adding to the broad differential of liver disease in pregnancy. CASE: A 32-year-old woman, gravida 3 para 2002, at 31 4/7 weeks of gestation had influenza A diagnosed and subsequent development of severe pruritis and elevated liver enzymes (aspartate aminotransferase 659 international units/L, normal 15-46 micromoles/L; alanine aminotransferase 933 international units/L, normal 13-69 micromoles/L; and total bile acids 249.7 micromoles/L, normal 4.5-19.2 micromoles/L). She was treated supportively, and fetal surveillance was normal. Her symptoms resolved over the subsequent 2 weeks, and she delivered a healthy term newborn. CONCLUSION: Influenza A infection can be associated with hepatitis in pregnancy, which in our case resolved spontaneously over 10 to 14 days with favorable maternal and perinatal outcomes.


OBJECTIVES: We estimated the seroprevalence of both acute and chronic HIV infection by using a random sample of emergency department (ED) patients from a region of the United States with low-to-moderate HIV prevalence. METHODS: This cross-sectional seroprevalence study consecutively enrolled patients aged 18 to 64 years within randomly selected sampling blocks in a Midwestern urban ED in a region of lower HIV prevalence in 2008 to 2009. Participants were compensated for providing a blood sample and health information. After de-identification, we assayed samples for HIV antibody and nucleic acid. RESULTS: There were 926 participants who consented and enrolled. Overall, prevalence of undiagnosed HIV was 0.76% (95% confidence interval [CI] = 0.30%, 1.56%). Three participants (0.32%; 95% CI = 0.09%, 0.86%) were nucleic acid-positive but antibody-negative and 4 (0.43%; 95% CI = 0.15%, 1.02%) were antibody-positive. CONCLUSIONS: Even when the absolute prevalence is low, a considerable proportion of undetected HIV cases in an ED population are acute. Identification of acute HIV in ED settings should receive increased priority.


BACKGROUND: Buruli Ulcer (BU)-HIV co-infection is an important emerging management challenge for BU disease. Limited by paucity of scientific studies, guidance for management of this co-infection has been lacking. METHODS: Initiated by WHO, a panel of experts in BU and HIV management developed guidance principles for the management of BU-HIV co-infection based on review of available scientific evidence, current treatment experience, and global recommendations established for management of HIV infection and tuberculosis. RESULTS: The expert panel agreed that all BU patients should be offered quality provider-initiated HIV testing and counselling. In areas with high prevalence of malaria and/or bacterial infections, all patients with HIV co-infection should be started on cotrimoxazole preventative therapy. Combination antibiotic treatment for BU should be commenced before starting antiretroviral therapy (ART) and provided for 8 weeks duration. The suggested combination is rifampicin (10 mg/kg daily up to a maximum of 600 mg/day) plus streptomycin (15 mg/kg daily). An alternative regimen is rifampicin plus clarithromycin (7.5 mg/kg twice daily up to a maximum of 1000 mg daily) although due to drug interactions with antiretroviral drugs this regimen should be used with caution. ART should be initiated in all BU-HIV co-infected patients with symptomatic HIV disease (WHO clinical stage 3 or 4) regardless of CD4 cell count and in asymptomatic individuals with CD4 count <500 cells/mm(3). If CD4 count is not available, BU-HIV co-infected individuals with category 2 or 3 BU disease should be offered ART. For eligible individuals, ART should be commenced as soon as possible within 8 weeks after commencing BU treatment, and as a priority in those with advanced HIV disease (CD4 < 350 cells/mm(3) or WHO stage 3 or 4 disease). All co-infected patients should be actively screened for tuberculosis before commencing BU treatment and before starting ART. Programmes should implement a monitoring and reporting system to document the outcomes of BU-HIV interventions. CONCLUSIONS: Knowledge of the clinical and epidemiological interactions between BU and HIV disease is limited. While awaiting more urgently needed evidence, current management practice of both diseases has been useful to build simple 'common sense' preliminary guidance on how to manage BU-HIV co-infection. 2014 John Wiley & Sons Ltd.

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(69) Pearlman BL, Lim TH. **You’re not the one: treating subjects co-infected with hepatitis C genotypes 2 and 3 and human immunodeficiency virus.** Digestive Diseases & Sciences 2014 Aug;59(8):1681-1683


UNLABELLED: Polyadenylated mature mRNAs are the focus of standard transcriptome analyses. However, the profiling of nascent transcripts, which often include nonpolyadenylated RNAs, can unveil novel insights into transcriptional regulation. Here, we separately sequenced total RNAs (Total RNAseq) and mRNAs (mRNAseq) from the same HIV-1-infected human CD4(+) T cells. We found that many nonpolyadenylated RNAs were differentially expressed upon HIV-1 infection, and we identified 8 times more differentially expressed genes at 12 h postinfection by Total RNAseq than by mRNAseq. These expression changes were also evident by concurrent changes in introns and were recapitulated by later mRNA changes, revealing an unexpectedly significant delay between transcriptional initiation and mature mRNA production early after HIV-1 infection. We computationally derived and validated the underlying regulatory programs, and we predicted drugs capable of reversing these HIV-1-induced expression changes followed by experimental confirmation. Our results show that combined total and mRNA transcriptome analysis is essential for fully capturing the early host response to virus infection and provide a framework for identifying candidate drugs for host-directed therapy against HIV/AIDS. IMPORTANCE: In this study, we used mass sequencing to identify genes differentially expressed in CD4(+) T cells during HIV-1 infection. To our surprise, we found many differentially expressed genes early after infection by analyzing both newly transcribed unprocessed pre-mRNAs and fully processed mRNAs, but not by analyzing mRNAs alone, indicating a significant delay between transcription initiation and mRNA production early after HIV-1 infection. These results also show that important findings could be missed by the standard practice of analyzing mRNAs alone. We then derived the regulatory mechanisms driving the observed expression changes using integrative computational analyses. Further, we predicted drugs that could reverse the observed expression changes induced by HIV-1 infection and showed that one of the predicted drugs indeed potently inhibited HIV-1 infection. This shows that it is possible to identify candidate drugs for host-directed therapy against HIV/AIDS using our genomics-based approach. Copyright 2014, American Society for Microbiology. All Rights Reserved. **Order via Shelcat**


OBJECTIVES: We sought to determine the prevalence of HCV infection and identify risk factors associated with HCV infection among at-risk clients presenting to community-based health settings in Hawaii. METHODS: Clients from 23 community-based sites were administered risk factor questionnaires and screened for HCV antibodies from December 2002 through May 2010. We performed univariate and multivariate logistic regression analyses. RESULTS: Of 3306 participants included in...
the analysis, 390 (11.8%) tested antibody positive for HCV. Highest HCV antibody prevalence (17.0%) was in persons 45 to 64 years old compared with all other age groups. Significant independent risk factors were current or prior injection drug use (P<.001), blood transfusion prior to July 1992 (P=.002), and having an HCV-infected sex partner (P=.03). Stratification by gender revealed sexual exposure to be significant for males (P=.001). CONCLUSIONS: Despite Hawaii’s ethnic diversity, high hepatocellular carcinoma incidence, and a statewide syringe exchange program in place since the early 1990s, our HCV prevalence and risk factor findings are remarkably consistent with those reported from the mainland United States. Hence, effective interventions identified from US mainland population studies should be generalizable to Hawaii.

(72) Reynolds KS. **Combining forces to combat infectious diseases.** Clinical Pharmacology & Therapeutics 2014 Aug;96(2):123-126

Because the threat of infectious diseases can cause widespread fear in a community, these diseases receive much public attention. Collaborations that bring together industry, academia, regulators, and the public can lead to improved and accelerated drug development. The collaborations must be grounded in strong science and expertise in clinical trials. Development of drugs to treat infections caused by resistant bacteria, drugs to treat hepatitis C virus (HCV), and drugs to prevent HIV is taking advantage of these collaborations.


The burden of HIV is disproportionate for Guatemalan sexual minorities (e.g., gay and bisexual men, men who have sex with men [MSM], and transgender persons). Our bi-national partnership used authentic approaches to community-based participatory research (CBPR) to identify characteristics of potentially successful programs to prevent HIV and promote sexual health among Guatemalan sexual minorities. Our partnership conducted Spanish-language focus groups with 87 participants who self-identified as male (n=64) or transgender (n=23) and individual in-depth interviews with ten formal and informal gay community leaders. Using constant comparison, an approach to grounded theory, we identified 20 characteristics of potentially successful programs to reduce HIV risk, including providing guidance on accessing limited resources; offering supportive dialogue around issues of masculinity, socio-cultural expectations, love, and intimacy; using Mayan values and images; harnessing technology; increasing leadership and advocacy skills; and mobilizing social networks. More research is clearly needed, but participants reported needing and wanting programming and had innovative ideas to prevent HIV exposure and transmission.

Initial descriptions of the HIV engagement continuum are limited by short-term follow-up and incomplete data. We evaluated engagement in a newly HIV-diagnosed cohort. Our goals were to assess long-term engagement-in-care, evaluate the effects of out-of-state migration on engagement estimates, and determine whether engagement has improved in more recently diagnosed individuals. This is a retrospective cohort study of individuals newly HIV-diagnosed at two large HIV care centers in the Denver metropolitan area from 2005 to 2009. Clinical data were obtained from three public HIV providers and two clinical trial groups. For statewide evaluation, we used mandated laboratory reporting databases for CD4 lymphocyte counts and HIV-1 RNA levels. From 2005 to 2009, 615 individuals were diagnosed with HIV. By 18 months after HIV diagnosis, 84% of the cohort had linked to care, 73% were retained in care, 49% were prescribed antiretroviral therapy, and 36% had viral suppression. By 5 years after HIV diagnosis, 55% of the cohort were retained in care, 37% had viral suppression, 15% had moved out of state, and 3% were deceased. When censoring for outmigration and death, 66% of the cohort were retained in care and 45% of the cohort had viral suppression 5 years after HIV diagnosis. Engagement-in-care 18 months after diagnosis was better in individuals diagnosed more recently. Retention in care declined while viral suppression increased over time after HIV diagnosis. Accounting for outmigration and death significantly increased estimates of engagement-in-care. Performance in the engagement continuum 18 months after diagnosis improved significantly in individuals more recently diagnosed with HIV.


The HIV-1 restriction factor SAM domain- and HD domain-containing protein 1 (SAMHD1) is proposed to inhibit HIV-1 replication by depleting the intracellular dNTP pool. However, phosphorylation of SAMHD1 regulates its ability to restrict HIV-1 without decreasing cellular dNTP levels, which is not consistent with a role for SAMHD1 dNTPase activity in HIV-1 restriction. Here, we show that SAMHD1 possesses RNase activity and that the RNase but not the dNTPase function is essential for HIV-1 restriction. By enzymatically characterizing Aicardi-Goutieres syndrome (AGS)-associated SAMHD1 mutations and mutations in the allosteric dGTP-binding site of SAMHD1 for defects in RNase or dNTPase activity, we identify SAMHD1 point mutants that cause loss of one or both functions. The RNase-positive and dNTPase-negative SAMHD1D137N mutant is able to restrict HIV-1 infection, whereas the RNase-negative and dNTPase-positive SAMHD1Q548A mutant is defective for HIV-1 restriction. SAMHD1 associates with HIV-1 RNA and degrades it during the early phases of cell infection. SAMHD1 silencing in macrophages and CD4(+) T cells from healthy donors increases HIV-1 RNA stability, rendering the cells permissive for HIV-1 infection. Furthermore, phosphorylation of SAMHD1 at T592 negatively regulates its RNase activity in cells and impedes HIV-1 restriction. Our results reveal that the RNase activity of SAMHD1 is responsible for preventing HIV-1 infection by directly degrading the HIV-1 RNA.
OBJECTIVES: The current surveillance system in The Netherlands cannot differentiate recent HIV infections from established infections, which is crucial for estimating the HIV incidence; this information is needed for assessing trends of the HIV epidemic and the impact of prevention interventions. We determined the proportion of recent HIV infections (RI) and estimated HIV incidence using a recent infection testing algorithm (RITA) among men who have sex with men (MSM) newly diagnosed as having HIV attending sexually transmitted infection (STI) clinics.

METHODS: Plasma samples collected between 2009 and 2011 were tested for RI with the Architect HIV Ag/Ab Combo immunoassay. Data on viral load, CD4 count and previous HIV testing were incorporated into the RITA. HIV incidence and 95% CIs were estimated. Logistic regression was used to identify factors associated with RI.

RESULTS: Of the 251 samples tested for RI, 78/251 (31%) infections were determined as recent by the RITA. No significant change over time was observed. The estimated HIV incidence in this high-risk MSM population was 3.3 per 100 person-years (95% CI 2.5 to 4.1). The only factor associated with RI in the multivariable model was being tested for HIV > 3 times in the past (aOR=7.4; 95% CI 2.0 to 27.8).

CONCLUSIONS: The proportion of RIs was comparable to studies in similar settings in Europe. Implementation of the RITA for routine surveillance in The Netherlands to assess trends in RIs over time, to study the infections in other groups and to inform public health actions, is being planned. Published by the BMJ Publishing Group Limited.

OBJECTIVE: Male-to-female transgender women (transwomen) have a disproportionate burden of HIV. We sought to estimate HIV treatment cascade indicators among transwomen in San Francisco. METHODS: We conducted a respondent driven sampling (RDS) study of 314 transwomen from August to December 2010. The study tested participants for HIV and collected self-reported data on linkage and access to care, viral load and antiretroviral treatment (ART). We derived population-based estimates and 95% CIs of cascade indicators using sampling weights based on established RDS methods. We conducted RDS-weighted logistic regression analyses to evaluate correlates of being on ART and being virologically suppressed (viral load < 200 copies/mL).

RESULTS: The RDS-weighted population-based estimate of HIV prevalence was 39% (95% CI 32% to 48%) among transwomen tested for HIV. Among HIV-positive transwomen, 77% (95% CI 70% to 93%) reported being linked to care within 3 months of diagnosis and 87% (95% CI 76% to 98%) accessed care in the past 6 months. In addition, 65% (95% CI 54% to 75%) were on ART, and less than half (44%; 95% CI 21% to 58%) were virologically suppressed. Housing instability was associated with lower odds of being on ART and being virologically suppressed. CONCLUSIONS: We observed a high prevalence of HIV in our population-based estimates of transwomen in San Francisco, coupled with modest ART use and low virological suppression rates, indicating high potential
Poor HIV treatment outcomes were consistently associated with housing instability. These data suggest that multi-level efforts, including efforts to address housing insecurity, are urgently needed to ameliorate disparities in HIV clinical outcomes among transwomen and reduce secondary HIV transmission to their partners.


In 2013, researchers announced that a newborn child from Mississippi, USA might have been functionally cured of HIV by being given combination antiretroviral therapy within hours of birth. Public and media attention has since been captured by the possibility of finding a cure for HIV transmitted from mother to child. Research into the strategy used for the Mississippi patient is crucially important to establish whether it can be replicated and shown to work in diverse populations. At the same time, any ethical issues likely to arise in such studies should be addressed and not ignored in the pursuit of a functional cure. In this Personal View we identify ethical issues that could arise in research towards achievement of a functional cure for HIV in neonates, including difficult trade-offs associated with choosing the study population and questions about the broader social implications of the research, and propose ways to resolve them. Copyright 2014 Elsevier Ltd. All rights reserved.


Hepatocystin/80K-H is known as a causative gene for autosomal dominant polycystic liver disease. However, the role of hepatocystin in hepatitis B virus-related liver disease remains unknown. Here, we investigated the role of hepatocystin on the cytokine-mediated antiviral response against hepatitis B virus infection. We investigated the antiviral effect and mechanism of hepatocystin by ectopic expression and RNAi knockdown in cell culture and mouse livers. Hepatocystin suppressed the replication of hepatitis B virus both in vitro and in vivo. This inhibitory effect was HBx-independent and mediated by the transcriptional regulation of viral genome via the activation of exogenous signal-regulated kinase 1/2 and the reduced expression of hepatocyte nuclear factor 4alpha, a transcription factor essential for hepatitis B virus replication. The amino-terminal region of hepatocystin was essential for regulation of this antiviral signaling pathway. We also found that hepatocystin acts as a critical component in interferon-mediated mitogen-activated protein kinase signaling pathway, and the interferon-induced antiviral activity against hepatitis B virus is associated with the expression levels of hepatocystin. We demonstrated that hepatocystin plays a critical role in modulating the susceptibility of hepatitis B virus to interferon, suggesting that the modulation of hepatocystin expression is important for...

OBJECTIVES: We sought to describe HIV diagnoses among men who have sex with men and women (MSMW), who have the potential to bridge HIV transmission risk from men who have sex with men (MSM) to women. METHODS: Applying National HIV Surveillance System data for persons aged 13 years and older, we examined estimated numbers and percentages of HIV diagnoses among MSMW and MSM only (MSMO) from 2008 to 2011, and estimated the annual percentage change and 95% confidence intervals, by age and race/ethnicity. RESULTS: In 2011, 26.4% of 30,896 MSM diagnosed with HIV infection also had had sex with women. A larger percentage of MSMW were Black/African American (44.5%) compared with MSMO (36.0%), and fewer MSMW were White (26.4%) compared with MSMO (36.2%); similar percentages were classified as either MWMW or MSMO among other racial/ethnic groups. Among MSMW, HIV diagnoses were relatively stable and MSMO increased more than 6% annually among those aged 13 to 29 years. CONCLUSIONS: Many MSM diagnosed with HIV infection had also had sex with women. Intensified interventions are needed to decrease HIV infections overall for MSMW and reverse the increasing trends among young MSMO.


OBJECTIVES: We sought to assess the prevalence and correlates of seroadaptive behaviours (i.e., sexual history incorporating some unprotected anal intercourse (UAI)) and conventional risk reduction behaviours (i.e., consistent condom use or no anal intercourse) among men who have sex with men (MSM) in San Francisco in 2011. We compared the prevalence of seroadaptive behaviours between serial cross-sectional surveys from 2004, 2008 and 2011. METHODS: We analysed data from the 2011 wave of the National HIV Behavioral Surveillance system in San Francisco. We categorised men’s self-reported sexual behaviour history in the past 6 months into a schema of seroadaptive behaviours and conventional risk reduction behaviours. We compared the prevalence of behaviour categories by self-reported HIV serostatus, HIV testing history, awareness of pre-exposure HIV prophylaxis (PrEP) and diagnosis of a sexually transmitted infection (STI). RESULTS: Seroadaptive behaviours remained common in San Francisco MSM, with a 2011 prevalence of 46.6%, up from 35.9% in 2004. Consistent condom use or no anal intercourse was more common than seroadaptive behaviours in HIV-negative MSM, men who had not heard of PrEP and men without an STI diagnosis. Seroadaptive behaviours increased from 2004 to 2011. CONCLUSIONS: HIV seroadaptive behaviours remain common in San Francisco MSM, have increased in the last decade and are practiced differently by MSM with different sexual health knowledge and outcomes. Public health researchers and officials should continue to document the prevalence, intentionality, efficacy and safety of seroadaptive
behaviours among diverse communities of MSM. Published by the BMJ Publishing Group Limited.


Due to an unexpected technical error, patients at a dialysis unit who were seronegative for hepatitis C virus (HCV) were temporarily transferred to another dialysis unit next to a ward reserved for HCV-seropositive patients. In the following 7 months, 17 patients were diagnosed as anti-HCV positive. The aim of the study was to reveal the cause of this nosocomial infection. Anti-HCV-positive sera were further tested by molecular methods. Data collection and on-site epidemiologic inspections were carried out. The source of the nosocomial infection proved to be a seropositive patient treated at the unit, who died before the outbreak was recognized. The exact date of the infection was determined.


Hepatocellular carcinoma (HCC) is a common cancer associated with chronic hepatitis B virus (HBV) infection. Conventional interferon-alpha (IFN-alpha) and pegylated IFNs (PEG-IFNs) approved for chronic HBV infection treatment can reduce the risk of HCC but are not suitable for the majority of patients and cause significant side effects. IFN-1 is a type III IFN with antiviral, antiproliferative, and immunomodulatory functions similar to type I IFNs but with fewer side effects. However, the tolerability and antitumor activity of PEG-IFN-1 in HCC xenograft mice are unknown. In vitro IFN-1 treatment of Hep3B and Huh7 human hepatoma cell lines increased MHC class I expression, activated JAK-STAT signaling pathways, induced IFN-stimulated gene expression, and inhibited hepatitis B surface antigen (HBsAg) expression. IFN-1 treatment also caused 23.2 and 19.9% growth inhibition of Hep3B and Huh7 cells, respectively, and promoted cellular apoptosis. PEG-IFN-1, but not IFN-1 treatment, significantly suppressed tumor growth (P=0.002) and induced tumor cell apoptosis in a Hep3B cell xenograft mouse model without significant weight loss or toxicity. PEG-IFN-1 also significantly inhibited (P=0.000) serum HBsAg secretion from Hep3B xenograft tumors in vivo. Thus, PEG-IFN-1 can suppress Hep3B xenograft tumor growth and inhibit HBsAg production and may be a potential treatment for HBV-related HCC. FASEB. Order via Shelcat


OBJECTIVES: We estimated the proportions of persons living with HIV/AIDS (PLWHA) in New York City (NYC) retained in care and virally suppressed. METHODS: We used routinely reported laboratory surveillance data to measure trends in retention in care and viral suppression in PLWHA in NYC from 2006...
through 2010. Our denominator excluded persons lacking any HIV-related laboratory tests during the 5 years prior to the year of analysis. RESULTS: The proportion of patients retained in care (> 1 care visit in a calendar year) was stable, at 82.5% in 2006 and 81.8% in 2010. However, the proportion of persons with evidence of viral suppression increased significantly, from 44.3% to 59.1%. Blacks were least likely to have viral suppression (adjusted prevalence ratio [APR] = 0.89; 95% confidence interval [CI] = 0.87, 0.90). A U-shaped relationship between age and viral suppression was observed, with the 20- to 29-year age group least likely to have a suppressed viral load. CONCLUSIONS: Higher and more plausible proportions retained in care and virally suppressed than national estimates may reflect the difference in methodology and our comprehensive HIV-related laboratory reporting system.


OBJECTIVES: To characterize migration patterns among people diagnosed as having and who died of acquired immunodeficiency syndrome (AIDS) from 1993 to 2007 because migrating to a new community can disrupt human immunodeficiency virus/AIDS care delivery and patients' adherence to care and affect migrants' social services and healthcare needs. METHODS: Florida AIDS surveillance data were used to describe patterns of migration among people diagnosed as having and who died of AIDS from 1993 to 2007. Individual and community characteristics were compared between residence at the time of AIDS diagnosis and residence at the time of death by type of migration. RESULTS: Of 31,816 people in the cohort, 2510 (7.9%) migrated to another county in Florida and 1306 (4.1%) migrated to another state. Interstate migrants were more likely to be men, 20 to 39 years old, non-Hispanic white, and born in the United States, to have had a transmission mode of injection drug use (IDU) or men who have sex with men with IDU (MSM&IDU), and to have been diagnosed before 1999. Intercounty migrants were more likely to be non-Hispanic white, younger than 60 years, have had a transmission mode of MSM, IDU, or MSM&IDU, have higher CD4 counts/percentages, and to have lived in areas with low levels of poverty or low physician density. There was a small net movement from urban to rural areas within the state. CONCLUSIONS: A sizable percentage of people, particularly younger people and people with a transmission mode of IDU and IDU&MSM, migrated at least once between the time of their AIDS diagnosis and death. This has important implications for care and treatment, as well as efforts to prevent the disease. Further research is needed to explore barriers and facilitators to access to care upon migration and to assess the need for programs to help people transfer their human immunodeficiency virus/AIDS care, ensuring continuity of care and adherence.

(87) Urry K, Mardis C. Current considerations of HIV and HCV testing and the risks of vertical transmission during pregnancy. Mlo: Medical Laboratory Observer 2014 10; Aug;46(8):8

The heavy burden of maternal HIV infection has resulted in a high prevalence of premature birth and associated necrotizing enterocolitis (NEC). Human milk oligosaccharides (HMOs) were recently associated with HIV infection and transmission through breastfeeding and were also shown to reduce NEC in an animal model, particularly the HMO disialyllacto-N-tetraose (DSLNT). The primary aim of this study was to verify differences in HMO composition between HIV-infected and HIV-uninfected women. The secondary aim was to assess whether the HMO composition in the milk of mothers whose infants were diagnosed with NEC differs from that of mothers whose infants did not develop NEC. This study forms part of a larger clinical trial conducted at the Tygerberg Children's Hospital, Cape Town, South Africa, which recruited HIV-infected and HIV-uninfected mothers and their preterm infants (500 and <1250 g). Eighty-two mother-infant pairs were selected for the substudy. Mother-infant pairs were stratified according to the mother's HIV (infected/uninfected) and secretor status (secretor/nonsecretor). HMOs in 4- and 28-d postpartum milk samples were analyzed by HPLC and compared between groups. Our results confirm previous reports that HIV-infected mothers have higher relative abundances of 3'-sialyllactose in their milk compared with HIV-uninfected mothers (10.7% vs. 6.8%; P < 0.01). Most intriguingly, the data also indicated that low concentrations of DSLNT in the 4-d milk samples in the mother's milk increased the infant's risk of NEC (200 + 126 vs. 345 + 186 mug/mL; P < 0.05), which is in accordance with results from previously published animal studies and warrants further investigation. This trial was registered at clinicaltrials.gov as NCT01868737. 2014 American Society for Nutrition.


(90) Wapner J. The solid-gold wonder drug. A long, difficult and costly research effort gives doctors a new cure for hepatitis C. Sci.Am. 2014 34; Sep;311(3):32


OBJECTIVES: We sought to validate previous reports of HCV prevalence in jails, identify HCV risk factors prevalence, and identify risk factors associated with HCV infection in this population. METHODS: Inmates at the Buzz Westfall Justice Center (BWJC) in St. Louis, Missouri, were offered risk factor screening for HCV and anti-HCV antibody testing from December 2012 through May 2013. Demographic and risk factor information were assessed for significant associations with positive HCV antibody results. Risk factors that were significantly associated in univariate analysis were assessed using binary logistic regression to model the relationship between positive HCV results and the risk factors and demographics. RESULTS: Fifty of 304
inmates were positive for HCV, with a prevalence of 16.4%. The risk factors significantly associated with increased risk for positive HCV antibody were age (odds ratio [OR] = 1.09; 95% confidence interval [CI] = 1.04, 1.15 for each year), injection drug use (OR = 53.87; 95% CI = 17.78, 163.21), sex with HCV-positive partner (OR = 7.35; 95% CI = 1.41, 38.20), and tattoos by a nonlicensed provider (OR = 2.62; 95% CI = 1.09, 6.33). Prevalence for women was 3 times that of men (38% vs 12%).

CONCLUSIONS: Prevalence of HCV at BWJC was similar to previous jail studies, which is lower than reported prison rates and higher than the general population.


Tailored health interventions have been found to be effective in various areas of health promotion because of their delivery of customized content, which focuses the prevention messages more closely on the individual's risk behavior. However, the use of tailored interventions in the prevention of STD/HIV has been limited, and there is a void in the literature on translating tailored interventions into practice. This paper discusses the process of translating a tailored, self-help, technology-driven STD/HIV prevention intervention from research-to-practice. Three agencies were selected during the translation process to test the intervention materials and provided valuable lessons learned for translating a tailored intervention into practice. A racially diverse group of more than 250 women in six states participated in the intervention during this pilot test. Lessons learned for research-to-practice efforts for tailored interventions are presented, including expanding the reach of such interventions by making them more compatible for mobile technology.


BACKGROUND: Current guidelines recommend that interferon-based treatment of hepatitis C (HCV) genotype 2 or 3 in those with HIV coinfection should be for 48 weeks, especially if HCV PCR remains positive after 4 weeks of treatment. AIM: To examine a single-center experience using response-guided therapy (RGT) using pegylated interferon (PegIFN) and weight-based ribavirin (RBV) for treating HCV genotype 2 or 3 in those with HIV coinfection. METHODS: Electronic medical records were used to identify patients with HCV genotype 2 or 3 HIV coinfection seen at the Toronto General Hospital Immunodeficiency Clinic from February 2003 to December 2012. HCV PCR was tested after every 4 weeks of treatment until it was negative (<50 IU/mL). RGT protocol was as follows: Those with HCV PCR first negative after 4 weeks (VR4) were treated 24 weeks; first negative after 8 weeks (VR8) treated 36 weeks and VR12 treated 48 weeks. RESULT: Database search identified 35 individuals with HCV genotype 2 or 3. Twelve were excluded. Total 23 patients completed the treatment and were included for data analysis. Eleven of 23 (48 %) achieved VR4 and eleven of 23 (48 %) achieved VR8. Only one individual had detectable viremia to week 12 and required 48 weeks of treatment. The majority (96 %) were successfully treated with <48 weeks of PegIFN-RBV therapy. One hundred percent achieved SVR with a response-guided HCV therapy.
CONCLUSION: The use of response-guided therapy allows therapy to be shortened in the majority of individuals. HCV PCR testing should be performed every 4 weeks during the first 12 weeks of therapy until HCV PCR is negative.


Restriction factors are host cell proteins that inhibit retroviral infection. A new study using mutants of human HIV-1 restriction factor SAMHD1 suggests that it inhibits infection through degradation of viral RNA rather than through its dNTPase activity as previously suggested.

(96) Young SD, Holloway I, Jaganath D, Rice E, Westmoreland D, Coates T. Project HOPE: online social network changes in an HIV prevention randomized controlled trial for African American and Latino men who have sex with men. Am.J.Public Health 2014 Sep;104(9):1707-1712

OBJECTIVES: We examined whether and how an HIV prevention diffusion-based intervention spread throughout participants' online social networks and whether changes in social network ties were associated with increased HIV prevention and testing behaviors. METHODS: We randomly assigned 112 primarily racial/ethnic minority men who have sex with men (MSM) to receive peer-delivered HIV (intervention) or general health (control) information over 12 weeks through closed Facebook groups. We recorded participants' public Facebook friend networks at baseline (September 2010) and follow-up (February 2011), and assessed whether changes in network growth were associated with changes in health engagement and HIV testing. RESULTS: Within-group ties increased in both conditions from baseline to follow-up. Among the intervention group, we found a significant positive relation between increased network ties and using social media to discuss sexual behaviors. We found a positive trending relationship between increased network ties and likelihood of HIV testing, follow-up for test results, and participation in online community discussions. No significant differences were seen within control groups. CONCLUSIONS: Among high-risk MSM, peer-led social media HIV prevention interventions can increase community cohesion. These changes appear to be associated with increased HIV prevention and testing behaviors.
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