
(2) Bird SM. Trial size, HIV pre-exposure prophylaxis, and breastfeeding. Lancet 2016 May 21;387(10033):2090-2091


IMPORTANCE: Screening for syphilis infection is currently recommended for high-risk individuals, including those with previous syphilis infection, an infected sexual partner, HIV infection, or more than 4 sex partners in the preceding year. OBJECTIVE: To update a 2004 systematic review of studies of syphilis screening effectiveness, test accuracy, and screening harms in nonpregnant adults and adolescents. DATA SOURCES: Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews through October 2015 and Ovid MEDLINE (January 2004 to October 2015), with updated search through March 2016. STUDY SELECTION: English-language trials and observational studies of screening effectiveness, test accuracy, and screening harms in nonpregnant adults and adolescents. DATA EXTRACTION AND SYNTHESIS: One investigator abstracted data, a second checked data for accuracy, and 2 investigators independently assessed study quality using predefined criteria. MAIN OUTCOMES AND MEASURES: Transmission of disease, including HIV; complications of syphilis; diagnostic accuracy; and harms of screening. RESULTS: No evidence was identified regarding the effectiveness of screening on clinical outcomes or the effectiveness of risk assessment instruments; the harms of screening; or the effectiveness of screening in average-risk, nonpregnant adolescents or adults or high-risk individuals other than men who have sex with men (MSM) or men who are HIV positive. Four non-US studies indicated higher rates of syphilis detection with screening every 3
months vs 6 or 12 months for early syphilis in HIV-positive men or MSM. For example, there was an increased proportion of asymptomatic, higher-risk MSM in Australia (n=6789 consultations) receiving a diagnosis of early syphilis when tested every 3 months vs annually (53% vs 16%, P=.001), but no difference among low-risk MSM. Treponemal and nontreponemal tests were accurate in asymptomatic individuals (sensitivity >85%, specificity >91%) in 3 studies but required confirmatory testing. Reverse sequence testing with an initial automated treponemal test yielded more false reactive test results than with rapid plasma reagin in 2 studies, one with a low-prevalence US population (0.6% vs 0.0%, P=.03) and another in a higher-prevalence Canadian population (0.26% vs 0.13%). CONCLUSIONS AND RELEVANCE: Screening HIV-positive men or MSM for syphilis every 3 months is associated with improved syphilis detection. Treponemal or nontreponemal tests are accurate screening tests but require confirmation. Research is needed on the effect of screening on clinical outcomes; effective screening strategies, including reverse sequence screening, in various patient populations; and harms of screening.

(4) Clement ME, Hicks CB. *Syphilis on the Rise: What Went Wrong?*. JAMA 2016 Jun 7;315(21):2281-2283


BACKGROUND: Most persons living with HIV smoke cigarettes and tend to be highly dependent, heavy smokers. Few such persons receive tobacco treatment, and many die from tobacco-related illness. Although advancements in antiretroviral therapy (ART) have increased the quality and quantity of life, the health harms from tobacco use diminish these gains. Without cessation assistance, thousands will benefit from costly ART, only to suffer the consequences of tobacco-related disease and death. A study was conducted to examine in detail inpatient tobacco treatment for smokers with HIV. METHODS: Data collected at hospital admission and data collected by tobacco treatment specialists were examined retrospectively for all inpatients with HIV who were admitted to an academic medical center for a five-year period. Specifically, the prevalence of cigarette smoking, factors predictive of referral to tobacco treatment, referral for tobacco treatment, treatment participation, and abstinence at six months posttreatment were measured. Differences in referral and treatment participation between all smokers and smokers with HIV were also assessed. RESULTS: Among the 422 admitted persons with HIV, 54.5% smoked and 21.7% were referred to inpatient tobacco treatment services. Substance abuse and tobacco-related diagnoses were predictive of referral to inpatient tobacco treatment specialists. Among the 14 treatment participants reached for follow-up, 11 (78.6%) made quit attempts and 3 (21.4%) reported abstinence. Smokers with HIV were less likely to be referred to and treated by tobacco treatment services than all smokers admitted during the same time frame. CONCLUSIONS: Although tobacco is a major cause of mortality, few smokers with HIV are offered treatment during...
hospitalization. Those who are treated attempt to quit. Hospitalization offers a prime opportunity for initiating smoking cessation among those with HIV.


(10) Jin J. JAMA PATIENT PAGE. Screening for Syphilis. JAMA 2016 Jun 7;315(21):2367


BACKGROUND: Few data are available regarding the use of tenofovir disoproxil fumarate (TDF) during pregnancy for the prevention of mother-to-child transmission of hepatitis B virus (HBV). METHODS: In this trial, we included 200 mothers who were positive for hepatitis B e antigen (HBeAg) and who had an HBV DNA level higher than 200,000 IU per milliliter. Participants were randomly assigned, in a 1:1 ratio, to receive usual care without antiviral therapy or to receive TDF (at an oral dose of 300 mg per day) from 30 to 32 weeks of gestation until postpartum week 4; the participants were followed until postpartum week 28. All the infants received immunoprophylaxis. The primary outcomes were the rates of mother-to-child transmission and birth defects. The secondary outcomes were the safety of TDF, the percentage of mothers with an HBV DNA level of less than 200,000 IU per milliliter at delivery, and loss or seroconversion of HBeAg or hepatitis B surface antigen at postpartum week 28. RESULTS: At delivery, 68% of the mothers in the TDF group (66 of 97 women), as compared with 2% in the control group (2 of 100), had an HBV DNA level of less than 200,000 IU per milliliter (P<0.001). At postpartum week 28, the rate of mother-to-child transmission was significantly lower in the TDF group than
in the control group, both in the intention-to-treat analysis (with transmission of virus to 5% of the infants [5 of 97] vs. 18% [18 of 100], P=0.007) and the per-protocol analysis (with transmission of virus to 0 vs. 7% [6 of 88], P=0.01). The maternal and infant safety profiles were similar in the TDF group and the control group, including birth-defect rates (2% [2 of 95 infants] and 1% [1 of 88], respectively; P=1.00), although more mothers in the TDF group had an increase in the creatine kinase level. After the discontinuation of TDF, alanine aminotransferase elevations above the normal range occurred more frequently in mothers in the TDF group than in those in the control group (45% [44 of 97 women] vs. 30% [30 of 100], P=0.03). The maternal HBV serologic outcomes did not differ significantly between the groups.

CONCLUSIONS: In a cohort of HBeAg-positive mothers with an HBV DNA level of more than 200,000 IU per milliliter during the third trimester, the rate of mother-to-child transmission was lower among those who received TDF therapy than among those who received usual care without antiviral therapy. (Funded by Gilead Sciences; ClinicalTrials.gov number, NCT01488526.)


Despite the identification and characterization of four opioid receptor subtypes and the genes from which they are encoded, pharmacological data does not conform to the predications of a four opioid receptor model. Instead, current studies of opioid pharmacology suggest the existence of additional receptor subtypes; however, no additional opioid receptor subtype has been identified to date. It is now understood that this discrepancy is due to the generation of multiple isoforms of opioid receptor subtypes. While several mechanisms are utilized to generate these isoforms, the primary mechanism involves alternative splicing of the pre-mRNA transcript. Extensive alternative splicing patterns for opioid receptors have since been identified and discrepancies in opioid pharmacology are now partially attributed to variable expression of these isoforms. Recent studies have been successful in characterizing the localization of these isoforms as well as their specificity in ligand binding; however, the regulation of opioid receptor splicing specificity is poorly characterized. Furthermore, the functional significance of individual receptor isoforms and the extent to which opioid- and/or HIV-mediated changes in the opioid receptor isoform profile contributes to altered opioid pharmacology or the well-known physiological role of opioids in the exacerbation of HIV neurocognitive dysfunction is unknown. As such, the current review details constitutive splicing mechanisms as well as the specific architecture of opioid receptor genes, transcripts, and receptors in order to highlight the current understanding of opioid receptor isoforms, potential mechanisms of their regulation and signaling, and their functional significance in both opioid pharmacology and HIV-associated neuropathology. Copyright © 2015 Wiley Periodicals, Inc.


BACKGROUND: Acute human immunodeficiency virus type 1 (HIV-1) infection is a major contributor to transmission of HIV-1. An understanding of acute HIV-1
infection may be important in the development of treatment strategies to eradicate HIV-1 or achieve a functional cure. METHODS: We performed twice-weekly qualitative plasma HIV-1 RNA nucleic acid testing in 2276 volunteers who were at high risk for HIV-1 infection. For participants in whom acute HIV-1 infection was detected, clinical observations, quantitative measurements of plasma HIV-1 RNA levels (to assess viremia) and HIV antibodies, and results of immunophenotyping of lymphocytes were obtained twice weekly. RESULTS: Fifty of 112 volunteers with acute HIV-1 infection had two or more blood samples collected before HIV-1 antibodies were detected. The median peak viremia (6.7 log10 copies per milliliter) occurred 13 days after the first sample showed reactivity on nucleic acid testing. Reactivity on an enzyme immunoassay occurred at a median of 14 days. The nadir of viremia (4.3 log10 copies per milliliter) occurred at a median of 31 days and was nearly equivalent to the viral-load set point, the steady-state viremia that persists durably after resolution of acute viremia (median plasma HIV-1 RNA level, 4.4 log10 copies per milliliter). The peak viremia and downslope were correlated with the viral-load set point. Clinical manifestations of acute HIV-1 infection were most common just before and at the time of peak viremia. A median of one symptom of acute HIV-1 infection was recorded at a median of two study visits, and a median of one sign of acute HIV-1 infection was recorded at a median of three visits. CONCLUSIONS: The viral-load set point occurred at a median of 31 days after the first detection of plasma viremia and correlated with peak viremia. Few symptoms and signs were observed during acute HIV-1 infection, and they were most common before peak viremia. (Funded by the Department of Defense and the National Institute of Allergy and Infectious Diseases.).


(19) 't Hoen EFM. Indian hepatitis C drug patent decision shakes public health community. Lancet 2016 Jun 4;387(10035):2272-2273


IMPORTANCE: In 2014, 19,999 cases of syphilis were reported in the United States. Left untreated, syphilis can progress to late-stage disease in about 15% of persons who are infected. Late-stage syphilis can lead to development of inflammatory lesions throughout the body, which can lead to cardiovascular or organ dysfunction. Syphilis infection also increases the risk for acquiring or transmitting HIV infection. OBJECTIVE: To update the 2004 US Preventive Services Task Force (USPSTF) recommendation on screening for syphilis infection in nonpregnant adults. Screening for syphilis in pregnant women was updated in a separate recommendation statement in 2009 (A recommendation). EVIDENCE REVIEW: The USPSTF reviewed the evidence on screening for syphilis infection in asymptomatic, nonpregnant adults and adolescents, including patients coinfected with other sexually transmitted infections (such as HIV). FINDINGS: The USPSTF found convincing evidence that screening for syphilis infection in asymptomatic, nonpregnant persons at increased risk for infection provides substantial benefit.
Accurate screening tests are available to identify syphilis infection in populations at increased risk. Effective treatment with antibiotics can prevent progression to late-stage disease, with small associated harms, providing an overall substantial health benefit. CONCLUSIONS AND RECOMMENDATION: The USPSTF recommends screening for syphilis infection in persons who are at increased risk for infection. (A recommendation).

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