The Dentist with Blood-Borne Viral Infection: What are the Risks to Patients and What is an Appropriate Approach to the Dentist?

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Executive Summary

The risk of a dentist transmitting a blood-borne viral (BBV) infection to a patient is low and has fallen in the past two decades as increasingly effective methods of prevention and treatment have been developed and utilized. However, there are multiple documented cases in which dentists have transmitted hepatitis B virus to patients, and one dentist transmitted HIV to six patients. To date, there is no documented case of transmission of hepatitis C virus (HCV) from a dentist to a patient, but it is a possibility, given that other health care workers have transmitted HCV to patients during exposure-prone procedures (EPPs).

Recommendation 1: *The policies governing dentist screening for BBV and the management of BBV-infected dentists should be evidence-based.*

Recommendation 2: *Dental regulatory bodies should develop policies that encourage a safe working environment and maximize the use of measures to prevent BBV transmission. Some of these opportunities include but are not limited to 1) mandating the use of Standard Precaution; 2) reporting all occupational blood exposures to and from patients; and 2) identifying additional financial resources to support BBV-infected dentists who face practice restrictions.*

Recommendation 3: *When dentist-to-patient blood exposure occurs during an EPP, the involved dentist and patient should both be tested for BBVs. If a patient is exposed to blood from a BBV-infected dentist, the patient should be told about the exposure as well as the specific BBV, and the estimated risk of transmission. Appropriate follow-up of the patient and the dentist should be provided. Both the patient and the dentist should be offered baseline and follow-up testing, and where appropriate, postexposure prophylaxis, ideally at no cost to the patient or dentist.*

Recommendation 4: *The available evidence does not support mandatory testing for BBVs for dentists who do not perform EPPs.*

Recommendation 5: *Current data support mandatory testing of dentists who perform EPPs for immunity to HBV (presence of anti-HBs).*

Recommendation 6: *Current data do not support mandatory HIV testing of dentists who perform EPPs.*

Recommendation 7: *Current data do not support mandatory HCV testing of dentists who perform EPPs.*

Recommendation 8: *For BBV-infected dentists who do not perform EPPs, there are no grounds to restrict their practice on account of the BBV infection, provided that they adhere to Standard Precautions.*

Recommendation 9: *HIV-infected dentists should not perform EPPs, until they are on antiretroviral therapy (ART) and their plasma HIV RNA is undetectable. Once documented to have undetectable plasma HIV RNA on ART, HIV-infected dentists should be permitted to perform EPPs using double gloves with the*

proviso that their personal physician provides regular (every 6 months) confirmation to the dental regulatory agency that his/her plasma HIV RNA is consistently undetectable.

Recommendation 10: *HBV-infected dentists with plasma HBV DNA over 2000 IU/mL should not perform EPPs, except on patients who are HBV immune (anti-HBs positive) or HBV infected (HBsAg positive), until or unless their infectivity status changes- whether by natural immunity or from antiviral therapy. HBV-infected dentists with plasma HBV DNA consistently below 2000 IU/mL should be permitted to perform EPPs using double gloves and Standard Precautions, regardless of their HBeAg status, with the proviso that their personal physician provides regular (every 6 months) confirmation that his/her plasma HBV DNA is consistently suppressed below this level to their dental regulatory agency.*

Recommendation 11: *HCV RNA positive dentists should not perform EPPs. They may resume EPPs once an HCV RNA test done at least 12 weeks after completion of treatment is confirmed to be negative.*

Introduction

The recommendations for the management of health care workers (HCWs) with blood-borne viral (BBV) infections are evolving. In 1998, Health Canada published the proceedings of a Canadian consensus conference on infected HCWs and risk for transmission [1]. Their recommendations were subsequently modified by the Canadian Dental Association and the Canadian Medical Association. Since that time, there have been significant advances in knowledge about BBVs and changes in the dental licensing environment. To guide policy development in this evolving area, the authors of this paper, a panel of specialists from three relevant medical and dental specialties was convened by the Royal College of Dental Surgeons of Ontario (RCDSO). The authors undertook a comprehensive literature review to create evidence-based recommendations for the management of dentists infected with hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). The authors developed the recommendations independent of the RCDSO. The RCDSO provided background information outlining the need for such guidelines and logistical support.

Background

The risk of dentists transmitting BBV infections to patients is exceptionally low and will continue to fall as more effective methods of prevention and treatment are identified**.** To date, there are no documented cases of transmission of any BBV from Canadian dentists to patients, and also no documented transmissions of either HIV or HCV from Canadian physicians to patients. There is only one report of a Canadian physician (an orthopedic surgeon) implicated in transmitting HBV to two patients; these infections occurred prior to the implementation of Standard Precautions (formerly known as universal precautions) and before the availability of modern antiviral therapy for HBV [2]. There is also a

well-documented case of a Canadian electroencephalogram technologist who transmitted HBV to multiple patients [3].

Paradoxically, despite evidence that the risk of transmission of BBVs by HCWs is low and falling, a growing number of Canadian provincial dental, medical and nursing licensing bodies have started to collect information about the HBV, HIV and HCV status of dentists, physicians and nurses at the time of initial licensure and/or at the time of license renewal. These licensing changes have occurred despite the expert opinion of the United States Centers for Disease Control and Prevention (CDC) that "infected HCWs who adhere to universal precautions and who do not perform exposure-prone procedures (EPPs) pose no risk for transmitting HIV or HBV to patients" [4]. EPPs are broadly defined as those in which access for surgery is difficult, where needlestick injuries (NSIs) are likely to occur, typically in closed or unvisualized operating spaces. Traditionally, many routine dental procedures were considered EPPs. However, in 2012, the CDC, in consultation with multiple stakeholders, reclassified the majority of dental procedures as low or no risk for percutaneous injury (Category II procedures), reserving only major oral or maxillofacial surgery as known or likely to pose an increased risk of percutaneous injury to dentists and placed in Category I (5). The 2012 CDC document describes Category I procedures as "the simultaneous presence of a health care provider's fingers and a needle in a poorly visualized or highly confined anatomic site" (5), yet specifically excludes routine dental procedures from Category I, even though it is common practice for dentists to inject local anesthesia with a needle adjacent to their finger inside the patient's mouth.

Many changes have contributed to a deceased incidence of the transmission of BBVs in the health care setting. The implementation of Standard Precautions substantially reduced the risk of transmission of BBVs both to and from HCWs by reducing exposures to patient blood and body fluids [6, 7, 8]. Also, a majority of HCWs, as well as a growing number of patients, have now received hepatitis B vaccine [9,

10]. Likely as a result of these two factors, between 1976 and 1993, the annual incidence of HBV infection decreased from 3.0% to 0.1% among hemodialysis patients and from 2.6% to 0.02% among hemodialysis staff in the United States [11]. Similarly, there has been an 85% reduction in cases of symptomatic acute hepatitis B in the United States from the early 1990s to 2009 [5]. Additionally, there have been significant advances in antiviral therapy for the three BBVs. Indeed, the majority of HBV and HIV infected patients receiving modern antiviral therapy have plasma viral loads (pVL) below the limit of detection in highly sensitive nucleic acid amplification tests, such as polymerase chain reaction (PCR). HCV infection can be cured in approximately 80% of patients with HCV genotypes 2 and 3 infection treated with pegylated interferon alfa plus ribavirin [12], and in about 75% of patients with HCV genotype 1 infection with the addition of HCV NS3/NS4A protease inhibitors [13], and cure rates may be even higher in the future with combination therapy with multiple directly acting antiviral drugs. Finally, we have entered an era with an increased focus on patient safety. There is an acknowledged need to reduce risks to patients. However, as discussed below, some of the measures recently undertaken by some licensing bodies with respect to BBV-infected HCWs appear to contravene the just culture component of the patient safety movement and may result in increased patient risk [14].

HCWs can acquire BBV infections as a result of a parenteral exposure to an infected patient's blood. The estimated risk per needlestick injury (NSI) from an infected, untreated source patient to a susceptible recipient is 30% for HBV [4], 1.8% for HCV [15] and 0.3% for HIV [16]. Studies conducted prior to the availability of HBV vaccine clearly demonstrated that the prevalence of antibodies to HBV was higher in dentists and physicians than the general population [17, 18], and that the prevalence of serologic markers of HBV infection in dentists and physicians increased with the number of years in practice, as well as being higher in specialties with more exposure to patient blood [17, 18, 19]. In contrast, the prevalence of HCV antibody is not higher among dentists than the general population in

almost all studies [18, 20, 21, 22, 23], likely reflecting the considerable lower infectivity of HCV relative to HBV, possibly supplemented by the efficacy of Standard Precautions. Nevertheless, exposure to BBVs is an occupational hazard that HCWs must face, and in addition to HBV, there are well-documented cases of HCWs acquiring HCV [24] or HIV [25] infection from occupational parenteral exposures. However, it is considered unethical for HCWs to refuse to provide medically required care simply because the patient has a BBV [26]. While HCWs should practice Standard Precautions [27] and receive hepatitis B vaccine to protect them from HBV [4, 15], it is recognized that some persons are HBV vaccine non-responders, and there are no vaccines for either HIV or HCV, nor is it likely that they will become available any time soon.

The risk of a non-immune patient acquiring HBV from an infected dentist or physician during an EPP is significant. There have been many documented cases in which HBV-infected dentists (including oral surgeons) or physicians (always surgeons or obstetricians-gynecologists) have transmitted HBV to patients [4]; most of these cases occurred prior to the practice of Standard Precautions. Recognition of the risk of transmission of infections from HCWs to patients led to the development of guidelines to identify those dentists and physicians at risk for transmitting HBV by ascertaining the degree of infectivity, best assessed by pVL, and the specific procedures performed by that practitioner [15, 28-31]. Thus, HBV-infected dentists and physicians with high plasma levels of HBV DNA are appropriately advised to refrain from performing EPPs [4, 28-31].

The risk of a patient acquiring a HCV or HIV infection from an infected HCW is very low. The vast majority of patients receive care from HCV-infected HCWs without acquiring HCV infection [31, 32, 33, 34], although there have been a few cases of documented transmission of HCV from physicians to patients [31, 35, 36]. There have been no documented cases of HCV transmission from a dentist to a patient, but there is a risk that such transmission could occur.

To date, 31 years into the HIV/AIDS epidemic, there have been only 4 HCWs documented to transmit HIV to patients. One of the implicated HCWs was a dentist, who transmitted HIV to six patients [37]. This dentist was unaware of his diagnosis and was not receiving antiretroviral therapy. Two were physicians, both of whom were surgeons who were unaware of their HIV infection and were not receiving antiretroviral therapy [38, 39]. The fourth implicated HCW was a HIV-HCV co-infected nurse who transmitted HIV but not HCV to a patient [40]. This nurse did not perform EPPs, and the circumstances are suspicious for unprofessional activity. In contrast, there have been over 22,000 patients who have received care from HIV-infected dentists or physicians with no documented HIV transmission [41].

Blood Exposures In Dental Practice

Frequency and Mechanisms

Dentists can acquire BBV infections through exposure to patient blood during procedures. Dentists can transmit BBV infection when patients are exposed to the blood of the dentist; these exposures are more common than many dentists appreciate. In 1986, US dentists reported an average of one percutaneous injury per month [42]. In 1991, the main causes of percutaneous injury in dentistry were burs (31%), syringe needles (30%), sharp instruments including laboratory knives (21%), and orthodontic wire (6%) [43]. Fortunately, the frequency of percutaneous injury by dentists appears to have declined to about 0.28 injuries per month, or 3.35 per year [44], likely as a result of Standard Precautions (see later). However, it is likely that many percutaneous injuries are unrecognized, since surgeons perceive only 30-66% of glove perforations [45, 46]. Patients are exposed to the dentist's or surgeon's blood when the sharp object that caused the injury re-contacts the patient; one study reported that this happened in 32% of sharp object injuries to surgeons [47].

Exposure Prone Procedures (EPPs)

In 1998, the CDC defined an EPP as follows: 1) Digital palpation of a needle tip in a body cavity (a hollow space within the body or one of its organs) or the simultaneous presence of the HCW's fingers and a needle or other sharp instrument or object in a blind or highly confined anatomic site (e.g., during major abdominal, cardiothoracic, vaginal and/or orthopaedic operations), or 2) Repair of major traumatic injuries, or 3) Manipulation, cutting or removal of any oral or perioral tissue, including tooth structures, during which blood from a HCW has the potential to expose the patient's open tissue to a blood-borne pathogen. Hence, according to the 1998 definition of an EPP, nearly all dentists and dental specialists perform EPPs. However, as noted above, in 2012, the CDC concluded that most dentists do not perform EPPs according to the updated definition [5]. In contrast, oral surgeons do perform EPPs according to the updated definition.

Risk Reduction Measures

Standard Precautions are the most important measure to ensure that HCWs are not exposed to a patient's blood (and conversely, to also ensure that a patient is not exposed to a HCW's blood) [27]. In a study by Panlilio et al., 81 (74%) of the 110 blood contacts among surgeons were potentially preventable by additional barrier precautions, such as face shields and fluid-resistant gowns [48]. Immunization is a highly effective method to prevent the transmission of HBV [4]. All HCWs who perform EPPs should be immunized for HBV and tested to confirm the presence of an effective antibody response [4].

Double-gloving could also be used routinely by BBV-infected dentists, and ideally by all dentists, since the BBV infection status of most patients is unknown. Double-gloving reduces total glove perforation rates by 50% and reduces the exposure to blood by up to six-fold [49, 50, 51]. Because glove perforations are more likely to occur in cases lasting more than one hour [47], changing gloves during long cases is a prudent practice. One concern about implementation of preventive measures in dental practice could be the cost, which is borne by the practitioner, in contrast to hospitals where it is borne

by the taxpayers. In a survey of general dentists in Ontario conducted in 1994, 31% reported that necessary infection control procedures are a financial burden to their practice [52].

As discussed above, handling tissues with fingers is associated with higher rates of glove perforations [47]. While different surgical techniques have not been evaluated in a prospective fashion, the available data strongly suggest that handling tissues and sharp objects with instruments only is likely another effective method of reducing the risks of NSIs.

When sharp object injuries occur, it should be mandatory to report the injury to an occupational health and safety program and seek appropriate medical follow-up and treatment, if necessary. Self-reporting of blood exposures is a critical step in preventing disease transmission to dentists (and subsequent transmission to patients). Postexposure prophylaxis for HBV (in those who are both HBsAg and anti-HBs negative) with hepatitis B immune globulin plus HBV vaccine is safe and effective. Most acute HCV infections can be cured with treatment started within 12 weeks of infection [12] and most HIV infections can be prevented with early postexposure prophylactic treatment [53]. Unfortunately, only a small fraction of sharp object injuries are currently being reported [54]. The reasons for the low rate of reporting of parenteral exposures have not been well investigated. Knowledge of the benefits of early detection of BBV infection ought to promote reporting. On the other hand, concern about a punitive response to the identification of BBV-infected dentists and surgeons is a potential explanation for underreporting.

Human Immunodeficiency Virus

Occupational Transmission in the Absence of Antiretroviral Therapy

The HIV epidemic was first described in June 1981 [55]. The causative virus was initially characterized in 1983 [56], but serologic testing was not widely available until 1985. Nevertheless, the first documented case of patient to HCW transmission of HIV from a NSI was published in 1984 [57]. Subsequent studies prior to the era of modern antiretroviral therapy (ART) found that the risk of HIV transmission following a NSI from an infected person is about 0.3% per exposure [16]. A case-control study conducted from 1987 to 1994 identified 4 factors associated with an increased risk of HIV transmission following percutaneous exposure: a deep injury, visible blood on the device, a procedure involving a needle in an artery or vein, and death of the source patient within two months following the parenteral exposure [58]. Of note, in the same study, the use of post exposure prophylaxis with zidovudine alone was associated with a statistically significant 81% reduction in transmission, underscoring the need for prompt reporting of occupational NSIs.

As of September 1997, 94 documented and 170 possible cases of occupational patient to HCW transmissions of HIV infection had occurred worldwide [59]. That number has undoubtedly increased in the intervening 15 years.

It was not until 1990 that the first cases of occupational transmission of HIV from an infected HCW to patients were reported from a dentist in Florida [60]. Subsequent investigation revealed that the same dentist infected six patients [37]. The circumstances that led to multiple infections in that practice are still poorly understood. The most likely explanation is a combination of a very high pVL in the dentist plus egregious disregard to infection control and prevention practices. In the early 1990s, the practices of many HIV-infected physicians and a few dentists were investigated for possible occupational transmission of HIV infection [61-70]. As of January 1, 1995, over 22,000 patients treated by 64 HIV-infected HCWs had been evaluated and no occupationally transmitted cases of HIV infection were found outside the single dental practice noted above [41].

It was not until 1999 that first case of physician-to-patient transmission of HIV infection was reported [38]. The source of infection was an orthopedic surgeon in France and the surgery associated with HIV transmission lasted 10 hours. The surgeon was unaware that he was HIV-infected until after he retired from performing surgery. No other cases of occupationally transmitted HIV infection were found in this surgeon's practice after another 982 patients were evaluated [38]. Seven years later in 2006, the second case of physician-to-patient transmission of HIV infection was described following caesarean section by a Spanish obstetrician who had sustained a NSI during the surgery [39]. The obstetrician was also unaware that he was HIV-infected at the time of surgery.

The only other case of HCW to patient transmission of HIV infection occurred in France where there was a close genetic match of the patient's HIV isolate and one of the patient's nurses [40] who had unrecognized advanced HIV infection with HCV co-infection. The nurse had contact with the patient on two night shifts only, but the published report does not describe any EPPs performed by the nurse nor does it exclude non-occupational routes of transmission. The fact that the nurse was co-infected with HCV raises the distinct possibility that she abused intravenous drugs, since injection drug use is the leading mode of acquisition of HCV in developed countries [71]. Intravenous drug abusing HCWs have been documented to negligently transmit BBVs to patients by "sharing" the patients' intravenous narcotic medication [72-77]; however, according to the report, the nurse denied a history of injection drug use [78].

Shortly after the report of the occupational transmission of HIV from the Florida dentist to patients, Bell and colleagues described a model to estimate the probability of transmission of HIV from an infected surgeon to patients [79]. Risk was estimated as the product of three probabilities: (i) that the surgeon will sustain a percutaneous injury during an invasive procedure (probability 2.5%), (ii) that the sharp object causing the injury and now contaminated with the surgeon's blood will contact the patient's

wound (probability 32%); and (iii) that infection would be transmitted to the patient after such an exposure (probability 0.3%). It should be noted that the 0.3% estimated probability was derived from parenteral exposures from HIV-infected persons not receiving ART. These three individual probabilities (2.5%, 32% and 0.3%, respectively) would give a total estimated probability of occupational transmission of 0.0024%, or 1 in 42,000 procedures. However, since the use of double surgical gloves is associated with up to a 10-fold reduction in the amount of blood transferred [80], Bell et al. noted that the risk might be as low as 0.00024% or 1 in 420,000 procedures.

HIV Viral Load Testing and Combination Antiretroviral Therapy

In 1996, it became standard practice to quantify HIV RNA in the plasma of HIV-infected patients, commonly called pVL, because of its ability to predict a more rapid clinical progression to AIDS [81]. In patients not receiving ART, pVL is the chief determinant of infectivity for sexual transmission [82] and for mother-to-child transmission [82-86]. It is highly probable that pVL is also the major determinant of occupational transmission, but the studies evaluating the risks for occupational HIV transmission were undertaken prior to the availability of pVL testing.

The year 1996 also heralded the modern era of combination ART. PVL testing demonstrated that single and even double therapy with two nucleoside HIV reverse transcriptase inhibitors had only a modest effect on reducing pVL, and almost never reduced it to below the lower limit of detection (at the time 400-500 RNA copies/mL). However, triple therapy with a combination of two nucleoside reverse transcriptase inhibitors plus an HIV protease inhibitor could suppress the pVL to undetectable in about 70% of patients, resulting in the introduction of the term “highly active antiretroviral therapy” (HAART), ergo - an admission that previous ART was *not* very active [87]. The introduction of HAART resulted in dramatic reductions in HIV-related mortality and morbidity [88, 89]. HIV infection has now become a

chronic controllable, yet incurable disease [90], considered by many to be not unlike diabetes mellitus, Crohn's disease, and rheumatoid arthritis, just to name three chronic medical illnesses. As of 2012, 24 distinct antiretroviral drugs are approved in Canada, several of which are available in fixed-dose combinations to reduce pill burden and enhance patient adherence. Additional investigational antiretroviral drugs are under clinical development. Furthermore, antiretroviral resistance testing is readily available to assist in the selection of appropriate antiretroviral regimens. It is now possible to suppress the pVL of nearly all HIV-infected patients to below the lower limit of detection of current tests (20-50 RNA copies/mL).

Role of pVL in Mother-to-Child Transmission of HIV

The obstetrical literature provides compelling evidence that ART markedly reduces infectivity. First, zidovudine monotherapy reduced the risk of mother-to-child transmission (MTCT) of HIV from 25.5% to 8.3% [91] despite the fact that zidovudine monotherapy decreases maternal pVL by less than 1 $\log_{10}$ [84]. The use of combination ART in pregnant HIV-infected women has further decreased the risk of MTCT to less than 1% [92,93] and in women with pVL below 50 copies/mL at delivery, the risk is about 0.4% [94]. Nevertheless, a small number of cases of MTCT of HIV have been documented despite low maternal pVL [95, 96]. These cases of MTCT can be explained by two factors; (i) while maternal pVL is the dominant determinant of MTCT, it is not the only one [97]; and (ii) some cases of MTCT occur *in utero* prior to the pregnant woman initiating ART. A recent analysis of cases of MTCT despite maternal pVL below 500 copies/mL at the time of delivery found that predictors of MTCT were lack of receipt of ART at conception, and viremia at weeks 14, 28 and 32 of gestation [96]. Assuming a background rate of MTCT in the absence of ART of 25.5% [91] and noting that the rate of MTCT observed with maximal virologic suppression (pVL < 50 copies/mL) in the ANRS French perinatal cohort was 0.4% [87], ART with a suppressed pVL results in a 64-fold reduction in transmission.

Role of pVL in Sexual Transmission of HIV

The risk of sexual transmission of HIV depends on the specific sexual activity. The per episode risk of acquiring HIV infection from sex with an infected partner is estimated at 0.5% for receptive anal intercourse, 0.1% for receptive vaginal intercourse, 0.65% for insertive anal intercourse and 0.05% for insertive vaginal intercourse [16, 98, 99]. In untreated HIV-infected subjects, pVL is the major predictor of infectivity via heterosexual intercourse [82]. Quinn et al. found no instances of HIV transmission among the 51 serodiscordant heterosexual couples in which the HIV-infected partner had a pVL below 1500 copies/mL [82]. A systematic review of 5021 heterosexual couples and 461 HIV transmissions found no transmissions from an infected partner with a pVL below 400 copies/mL receiving ART [100]. However, sexual transmission from a patient with an undetectable pVL (<50 copies/mL) on ART has now been reported in a gay male couple [101] and in a heterosexual couple [102]. These rare cases of sexual transmission despite aviremia may be explained by the observation that some patients can have detectable HIV RNA in semen when it is undetectable in plasma [103].

Risk of Occupational HIV Infection in the Era of Combination Antiretroviral Therapy

To date, there has not been a single documented case of occupational transmission of HIV from an infected HCW receiving ART and there are no published risk estimates. A reasonable estimate of the risk of occupational transmission of HIV from an HIV-infected surgeon who is receiving ART and has an undetectable pVL may be calculated by taking the risk of transmission from an HIV-infected surgeon not receiving ART (calculated by Bell et al. [79] as 1 in 42,000 to 1 in 420,000 procedures) and dividing by the 64-fold reduction in HIV transmission observed by the ANRS French perinatal cohort in pregnant HIV-infected women receiving ART who had pVL below 50 copies/mL at the time of delivery [94]. This calculation results in an estimated risk of 1 in 2,688,000 to 1 in 26,880,000 procedures, a risk slightly

lower than the current risk of 1 in 2 million of acquiring HIV infection from a single unit of blood, despite screening for both HIV antibody and HIV RNA [104], and slightly lower than the risk of mortality from general anesthesia of about 1.1 per million [105]. The above calculation may be an underestimate of the protection provided by suppressive ART in the occupational setting, since MTCT is affected not only by HIV maternal pVL at the time of delivery, but also by maternal pVL at conception, weeks 14, 28 and 32 [96], and other factors, such as the use of invasive fetal monitoring [97]. Similarly, the two documented cases of sexual transmission of HIV from persons on ART with a suppressed pVL are explainable by detectable HIV RNA in semen. Unlike sexual transmission or MTCT, only the concentration of virus in blood and the volume of blood exposed at the time of the parenteral exposure are relevant for one-time parenteral exposures. Thus, it is likely that the pVL of an infected HCW will be a stronger predictor of infectivity for parenteral exposure than it is for either sexual transmission or MTCT.

The greatest risk of HCW-to-patient transmission of HIV (and this risk is still extremely small) is from HCWs who are unaware that they are HIV-infected. These HCWs would obviously not be taking ART and would be unlikely to be routinely double-gloving. Indeed, the only three documented cases of dentist or physician-to-patient transmission of HIV occurred in exactly this setting [37, 38, 39]. It is estimated that 21% of all cases of HIV infection in adults and adolescents in the United States are undiagnosed [106]. If the same proportion of dentists and surgeons with HIV infection were undiagnosed (about 1 in 5), and if the 4 in 5 with known HIV infection were receiving ART with undetectable pVL and were permitted to perform EPPs using double-gloves, and finally assuming that there is a 64-fold reduction in HIV transmission in the latter group, it is estimated that 94% of all HIV transmissions would occur from the 20% of HIV-infected dentists and surgeons unaware of their HIV infection. Expressed differently, one

would expect 16 transmissions from dentists and surgeons unaware of their HIV infection for every case from HIV-infected dentists and surgeons receiving ART with an undetectable pVL.

Hepatitis B Virus

Epidemiology

HBV is an important human pathogen with an estimated 350 million chronic carriers worldwide. Most infections worldwide are transmitted from mother-to-child, usually during parturition or in early childhood. An estimated 500,000 persons die annually from the complications of chronic HBV infection, such as primary liver cancer (hepatocellular carcinoma), esophageal variceal bleeding or liver failure, with the greatest burden of disease in Asia. Acute HBV infection in immune competent adults is usually cleared spontaneously, but up to 5% can develop chronic HBV infection and approximately 1% can develop fulminant liver failure. Although Canada is considered a low-endemic area for HBV, there are certain populations and geographic regions in which the prevalence of HBV is significantly higher, especially immigrants to Canada from HBV endemic areas. Currently there are an estimated 350,000 chronic HBV carriers in Canada [107]. Since 1982, a safe and effective HBV vaccine has been available and widely used. The initial vaccine formulation produced from human plasma containing high titres of hepatitis B surface antigen (HBsAg), and whilst very effective, has since been replaced by a "synthetic" recombinant HBsAg vaccine which is equally safe and effective but more widely accepted than the human plasma derived formulation. All Canadian provinces have adopted a policy of publicly funded HBV vaccination either in infancy or pre-adolescence. Most (>95%) immunocompetent children and adults will develop protective antibodies to HBsAg (anti-HBs) and a robust, long-lasting memory B cell response to the HBV, despite waning of anti-HBs titres over time (15-20 years), hence revaccination or booster shots are not routinely recommended [108]. Vaccine non-response can occur, particularly in older, heavier and immunodeficient persons. All dental and medical schools in Canada require

immunization against HBV for students before entry, and overall, a growing proportion of patients and HCWs [8, 9] will have received HBV vaccine. However, there are still cases of HBV-infected HCWs that were infected vertically (mother-to-child) or via early horizontal childhood transmission prior to the era of screening pregnant women for HBV in Canada. In addition, it is recognized that internationally trained HCWs moving from HBV endemic areas to low prevalence countries such as Canada and the United States may represent another potential group of infected HCWs [109].

Hepatitis B Diagnosis and Monitoring

Over the last two decades there has been exponential progress in the clinical management and concomitant understanding of the natural history of chronic hepatitis B, both of which have been facilitated by the availability of sensitive diagnostic assays and potent anti-HBV antiviral therapies [110]. The definition of chronic HBV infection is persistence of serum HBsAg for greater than 6 months. The detection of hepatitis B e antigen (HBeAg) was historically used as a surrogate marker of high level HBV viremia [111], and loss of HBeAg with anti-HBe antibodies, an indicator of quiescent, "nonreplicative" or inactive disease. However it is now well-recognized that in some patients, seroconversion to anti-HBe seropositive status, can occur along with ongoing moderate levels of HBV replication and active liver disease due to a mutation in the HBV core gene that abolishes production of HBeAg (i.e., precore or basal core promoter mutant HBV) [112]. The presence of antibodies to hepatitis B surface antigen (anti-HBs) is indicative of either prior vaccination against HBV or natural immunity from prior infection (which is frequently asymptomatic). Prior HBV infection is typically confirmed by the concomitant presence of antibodies to hepatitis B core antigen (anti-HBc), which do not develop in response to HBV vaccine.

As noted above, the presence of HBeAg had been used as a surrogate marker of HBV viremia. First generation molecular testing for HBV DNA relied on a slot-blot HBV DNA hybridization assay with a

lower limit of detection (i.e., sensitivity) of 5 pg/mL or approximately 1,000,000 virus copies per mL. In the early 2000s, the advent of sensitive PCR-based assays for detection of HBV DNA has significantly lowered the detection limit of HBV DNA. Due to wide variation and poorly standardized HBV DNA assays in use, the World Health Organization has adopted the convention of international units per mL (IU/mL), which is estimated to equal 5.2 virus copies per mL. The current "gold standard" for detection of HBV DNA is a sensitive real-time PCR-based assay that has a lower limit of detection of 20 IU/mL– at least 5 $\log_{10}$ greater sensitivity than the first generation slot-blot hybridization assay. Hence, an important end-point of current anti-HBV therapy, along with liver enzyme normalization and HBeAg seroconversion (in patients initially HBeAg positive), is undetectable plasma HBV DNA according to a highly sensitive PCR assay, equal to < 20 IU/mL [107].

HBV Therapy

The goal of anti-HBV therapy is durable virological suppression and avoidance of antiviral resistance to prevent the development of progressive liver disease [113, 114]. Approved anti-HBV therapies include several formulations of interferon given by subcutaneous injection. However, interferon is often poorly tolerated due to its significant side effect profile [107, 113, 114]. In 1998, lamivudine was the first oral nucleoside analogue approved for treatment of HBV, although it had been used as an anti-HIV agent for several years previously. Lamivudine is well tolerated, has an excellent safety profile and moderate antiviral potency; however prolonged therapy results in high rates of antiviral resistance development – up to 70% after 3 years, so that it is no longer a preferred first-line agent [114]. Over the past 5 years, an increasing number of newer nucleoside/nucleotide analogues have become available for management of HBV. Entecavir, approved for use in Canada in June 2006, was the first HBV antiviral that could reliably suppress pVL to below the limit of detection in sensitive PCR assays with minimal side effects and minimal risk for treatment failure due to resistance. Tenofovir, approved in Canada in

September 2008, was the second very potent antiviral, but the first that could also reliably control HBV variants that were resistant to lamivudine [107, 114, 115, 116].

Occupational Transmission of HBV from Infected Health Care Workers to Patients

As noted in the introduction, since the availability of serologic testing for HBV infection in the early 1970s, there have been a number of reported cases of HBV-infected HCWs transmitting HBV to their patients during invasive procedures. Figure 1 provides a summary of cases. In 1991, the CDC reviewed 20 clusters of over 300 patients who were infected with HBV in association with treatment by an HBV-infected HCW [4]. In 12 of 20 of these "clusters", the implicated HCW did not practice Standard Precautions, such as routinely wearing gloves; several had open skin lesions that may have facilitated transmission. HBeAg status was assessed in 17 of the 20 HCWs and all were positive. All of these transmissions occurred before the advent of sensitive PCR-based HBV DNA assays. In 1991, the CDC recommended restricting HBeAg positive HCWs from performing EPPs [4].

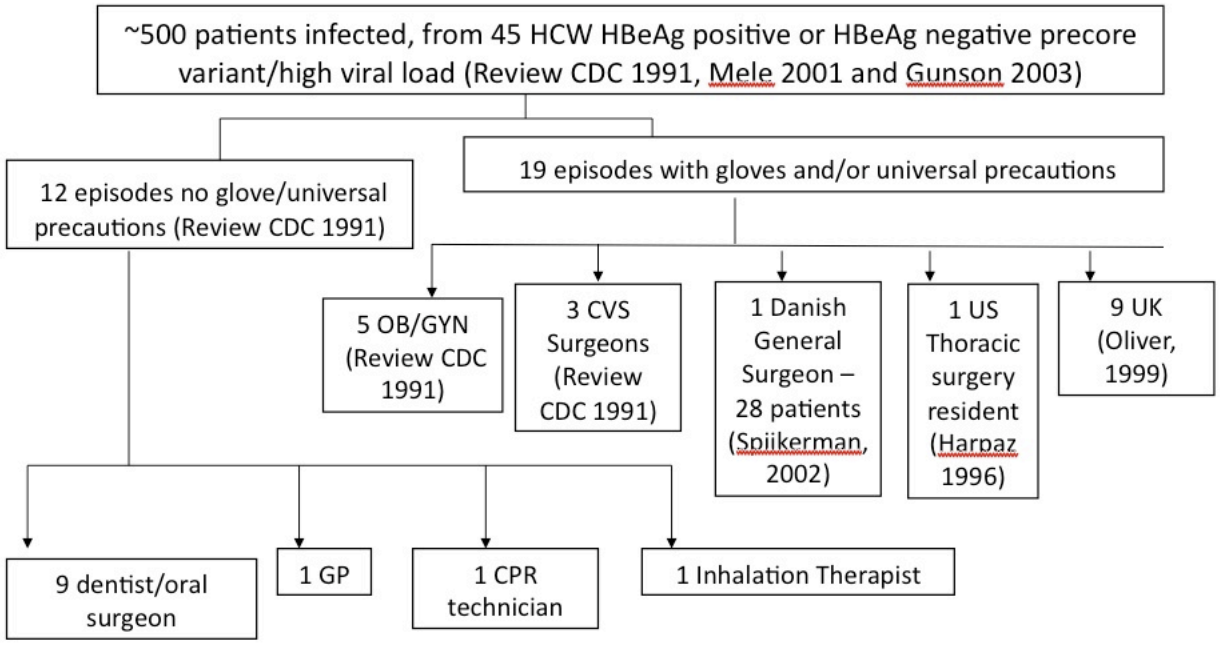
Since 1991, 11 episodes of HBV transmission to patients from infected surgeons have been reported, nine from the United Kingdom [117, 118, 119], one from the Netherlands [120], and one from the United States [121]. In several cases, the surgeons were HBeAg positive, but unaware of their diagnosis [118, 120, 121]. However, in 1997, the first reports of HBV transmission from HBeAg negative surgeons were published [122]. The four HBeAg negative surgeons implicated in transmission had plasma HBV DNA concentrations ranging from 250,000 to 10 million copies/mL (50,000 to 2 million IU/mL). By 2003, a total of 7 HBeAg negative HBV-infected surgeons had been implicated in HBV transmission to patients [29], including the 4 surgeons described above [122]. Plasma HBV DNA was quantified in 6 of the 7, and the lowest value was 40,000 copies/mL (~8000 IU/mL), with all others above 200,000 copies/mL (40,000

IU/mL). The lowest value of 40,000 copies/mL (~8000 IU/mL) was from a blood sample collected more than 3 months after transmission.

On the basis of these data, the European Consensus Group in 2003, prior to the availability of potent HBV antiviral therapy, proposed a pVL cut-off of <10,000 copies/mL (2000 IU/mL) for HBV-infected HCWs performing EPPs, as a balance between risk of HBV transmission and loss of HCWs [29]. The Netherlands has chosen to permit HBV-infected surgeons to perform EPPs as long as their pVL is below 100,000 copies/mL (~20,000 IU/mL), regardless of their HBeAg status [29]. From 2000 to 2008, the Dutch Committee for the Prevention of Iatrogenic Hepatitis B evaluated 99 HBV-infected HCWs and noted that of 36 HBV-infected Dutch physicians performing EPPs, 11 (31%) had pVL > 100,000 copies/mL (~20,000 IU/mL) without antiviral therapy and were required to stop performing EPPs [123]. Dutch authorities have attempted to keep HBV-infected surgeons in surgical practice by offering anti-HBV therapy to HBV-infected HCWs with pVL >100,000 copies/mL (~20,000 IU/mL) who perform EPPs [124]. When last evaluated in 2009, no cases of HCW-to-patient transmission of HBV have been recognized in Holland since this pVL cutoff of was implemented in the year 2000 [123].

In contrast, the United Kingdom (UK) has chosen to prohibit HBeAg positive physicians from performing EPPs regardless of pVL or whether they are receiving antiviral therapy, and to prohibit HBeAg negative physicians from performing EPPs if their pVL is >1000 copies/mL (200 IU/mL) [125]. If the Dutch used this pVL cutoff as used in the UK, then 32 of 36 (89%) of their HBV-infected HCWs performing EPPs would be restricted from performing EPPs [123]. In 2010, the Society for Healthcare Epidemiology of America (SHEA) recommended the same pVL cut-off of <10,000 copies/mL (2000 IU/mL) for HBV-infected HCWs performing EPPs as chosen by the European Consensus Group [31]. In 2012, the CDC recommended a pVL cut-off of 1000 IU/mL [5].

Figure 1: Summary of Reported Cases of HBV transmission from Infected Health Care Workers. Many cases of transmission occurred before the introduction of Standard Precautions and before the advent of sensitive diagnostic tests for HBV viral load and availability of suppressive antiviral therapy for HBV.



Hepatitis C

Epidemiology

The existence of HCV was inferred in the mid-1970s, when a parenterally transmitted form of non-A, non-B hepatitis was described [126]. In 1989, collaboration between scientists at the CDC and the Chiron

Corporation led to the “discovery” of HCV by molecular cloning [127]. HCV has an incubation period averaging 2 months. Most acute HCV infections are asymptomatic or result in anicteric disease [128]. Approximately 25% of cases of HCV infection are cleared spontaneously whereas about 75% become chronic [128]. Chronic HCV infection can lead to cirrhosis, liver failure and hepatocellular carcinoma [129]. Excess alcohol consumption [130] and HIV or HBV co-infection [131] increase the rate of progression of HCV liver disease. Hepatitis C is a global public health problem, with about 170 million people chronically infected [71]. Hepatitis C is the leading cause of chronic liver disease and hepatocellular carcinoma in North America and Europe, and is the leading indication for liver transplantation [129].

HCV Therapy

Current antiviral therapy for chronic hepatitis C depends on the HCV genotype. The combination of pegylated interferon alfa-2a or 2b administered subcutaneously once weekly plus ribavirin administered orally twice daily, is given for 24 weeks for HCV genotypes 2 or 3, and for 48 weeks for HCV genotypes 4, 5 and 6 [12]. For HCV genotype 1, the most prevalent genotype, telaprevir or boceprevir is added to pegylated interferon and ribavirin, with the treatment duration varying from 24 to 48 weeks, depending on the time to clearance of viremia and the presence of cirrhosis [13, 132]. The goal of therapy is a sustained virologic response (SVR), defined as HCV RNA negativity in serum or plasma 6 months following completion of therapy, although recent data indicate that HCV RNA negativity 12 weeks after completion of therapy, referred to as SVR12, has 99.7% accuracy in predicting SVR [133], and is now accepted by the United States Food and Drug Administration. SVR appears to be equivalent to virologic cure and is achieved in about 75% in genotype 1, 85% in genotype 2, 75% in genotype 3 and 65% in genotype 4. However, if antiviral therapy is administered to patients with acute hepatitis C, SVR rates are high (57 to 94%), and ribavirin is probably unnecessary [128]. The high SVR rate with acute HCV

infection underscores the need for prompt reporting to the occupational health program when HCWs sustain NSIs.

HCV Transmission

Over 90% of HCV infections are transmitted via a parenteral exposure. In developed countries, most cases of HCV infection are acquired from illicit injecting drug use [71], but in developing countries, many cases are acquired from inadequately sterilized reused needles and syringes used in health care [71]. Transmission through blood products has virtually disappeared in the developed world since blood banks began screening donated blood for both HCV antibody and HCV RNA [104]. Unfortunately, other (non blood transfusion) healthcare related transmissions of HCV continue to occur via breaches in infection control measures [134, 135, 136].

Heterosexual transmission of HCV can occur, but is rare [71, 137]. Male homosexual transmission via unprotected receptive anal intercourse is increasingly reported, mainly among those co-infected with HIV [138]. Mother-to-child transmission occurs in about 4-7% of pregnancies in HCV-infected women, with the higher rates noted in women co-infected with HIV [139].

Occupational Transmission of HCV from Patients to Healthcare Workers

The first evidence that HCV can be transmitted via a NSI was the recognition in 1980 that non-A, non-B hepatitis could be transmitted from a patient to a HCW [140]. In 1990, it was confirmed that HCV could be transmitted from a single NSI [24, 141].

The risk of HCV transmission following a NSI from an HCV-infected source is about 1.8% [142]. A source needle that had been placed in a patient's vein or artery carries about a 100-fold increased risk of HCV

transmission compared with needles not placed in a blood vessel [143]. A deep puncture and male sex of the injured HCW were also found to increase the risk of HCV transmission following occupational exposure [143]. Furthermore, the HCV viral load of the source patient also influences the risk of transmission. Specifically, the risk of HCV transmission was 11-fold greater from source patients with HCV RNA > 6 $\log_{10}$ copies/mL compared with those with HCV RNA < 4 $\log_{10}$ copies/mL [143].

Occupational Transmission of HCV from Healthcare Workers to Patients

Surgeons and Dentists

To date there have been 33 documented instances of HCV transmissions from 9 HCV-infected surgeons [32]. The per patient transmission probability from these 9 surgeons ranged from 0.0004% to 0.0225% (or one in 4,444 to one in 250,000 cases) [32]. However, this overestimates the risk of surgeon-to-patient transmission of HCV, since it only includes surgeons implicated in transmission. A look-back exercise of patients operated upon by an HCV-infected general surgeon in Germany found no cases of HCV transmission in 1192 patients [34]. To date, there has been no documented physician to patient transmission of HCV in Canada, and a look-back investigation of 231 patients who had undergone EPPs by an HCV-infected Canadian general surgeon failed to demonstrate HCV transmission [32]. To date, there have been no documented cases of occupational transmission of HCV from dentists to patients.

Anesthesiologists

Regrettably, there are three well documented cases in which narcotic addicted anesthesiologists caused multiple cases of HCV infection in patients by self-injecting the patients' narcotic and then using the same syringe on the patient [72, 73, 76, 77]. Similar cases have been described in a nurse anesthetist [74] and a surgical technician [75].

In 2000, Ross et al. reported a case in which an anesthesiology assistant acquired HCV infection from a patient and then transmitted the identical HCV strain to 5 patients [144]. In 2002, a single case of HCV transmission from an anesthesiologist to a patient was described [145]. No evidence of HCV transmission was found in 343 other patients treated by this anesthesiologist and who were tested. In 2005, Mawdsley et al. reported a single case of HCV transmission from an anesthetist to a patient [146]. It is impossible to determine if any of the above cases may also be attributable to illicit drug diversion. The fact that there have been no documented cases of transmission of HBV from anesthetists to patients, despite the fact that HBV carries a substantially higher risk per NSI, increases the suspicion that the above cases were also related to drug diversion [31].

RECOMMENDATIONS

General Principles

Recommendation 1: The policies governing dentist screening for BBV and the management of BBV-infected dentists should be evidence-based. Mandatory testing of dentists and/or practice restrictions for BBV-infected dentists are costly and an intrusion of privacy. There should be evidence of benefit in order to justify these costs and intrusion of privacy.

Recommendation 2: Provincial/territorial dental regulating authorities (Colleges) should develop policies that encourage a safe working environment and maximize the use of measures to prevent BBV transmission. Some of these opportunities include but are not limited to: 1) mandating the use of Standard Precautions; 2) reporting occupational blood exposures to and from patients; and 3) identifying additional financial resources to support BBV-infected dentists who face practice

restrictions. Colleges are encouraged to explore measures that will encourage reporting of occupational exposures and contribute to a culture of patient and dentist safety.

Recommendation 3: When dentist-to-patient blood exposure occurs during a procedure, the involved dentist and patient should both be tested for BBVs. If a patient is exposed to blood from a BBV-infected dentist, the patient should be told about the exposure as well as the specific BBV, and the estimated risk of transmission. Appropriate follow-up of the patient and the dentist should be provided. The patient should be offered baseline and follow-up testing, and where appropriate, the HCW or patient should be offered postexposure prophylaxis at no cost.

Screening of Dentists for BBV

Dentists Who Do Not Perform EPPs

Recommendation 4: The available evidence does not support mandatory testing for BBVs for dentists who do not perform EPPs. To date, BBV infections transmitted by HCWs have only occurred during EPPs. Thus, there are no data to justify either the cost or the intrusion of privacy associated with mandatory testing of dentists who do not perform EPP. However, voluntary anti-HBs testing is strongly encouraged to determine each dentist's HBV immune status in light of the known effectiveness of HBV vaccination. Dentists not performing EPP, but at increased risk for one or more BBV for non-work related reasons are also encouraged to undergo testing, for their personal health benefit.

Dentists Who Perform EPPs

HBV Testing

Recommendation 5: Current data support mandatory testing of dentists who perform EPPs for immunity to HBV (presence of anti-HBs). This recommendation is based on the significant number of documented dentist-to-patient transmissions of HBV, the widespread use of HBV vaccine among HCWs and the recognition that most dentists will test anti-HBs positive and only require testing once. Those testing anti-HBs positive are considered immune and no further testing is required. Those testing anti-HBs negative should be tested for HBV infection (HBsAg and anti-HBc), and if positive for HBsAg, should be managed as below. Those testing negative for all three tests, HBsAg, anti-HBc and anti-HBs, i.e. vaccine non-responders, and those who never received vaccine, should receive another series of HBV vaccine and be retested for anti-HBs following immunization. In those in whom HBsAg, anti-HBs and anti-HBc remain negative after repeat immunization, annual testing for HBsAg is recommended. Those who test positive for anti-HBc but negative for HBsAg have likely been infected with HBV in the past but the infection has resolved. As such, further vaccination is not required.

HIV Testing

Recommendation 6: Current data do not support mandatory HIV testing of dentists who perform EPPs. This recommendation is based on the negligible risk of dentist-to-patient transmission (one implicated dentist worldwide in 31 years; two from surgeons, one of which occurred after a recognized NSI, which would result in testing and reporting under recommendation 3), and, taking into account observed risk, the lack of any evidence of not only cost-effectiveness, but also effectiveness. Even prior to the HAART era, screening surgeons for HIV infection was found not to be cost-effective [147]. Specifically, annual screening was estimated to cost 1.1 million 1995 U.S. dollars per life-year saved [147]. The cost per life-year saved in the HAART era would be markedly higher. Furthermore, if HIV

testing of dentists were to be implemented, there are no data on which to base a recommendation for the frequency of such testing.

HCV Testing

Recommendation 7: Current data do not support mandatory HCV testing of dentists who perform EPPs. The infectivity of HCV is intermediate between that of HBV and HIV, and the risk estimates for HCW-to-patient transmission of HCV are wide. It is recognized that there have been a few documented cases of HCW-to-patient transmission of HCV. However, 22 years after the availability of HCV testing, there have been no documented cases of occupational transmission of HCV from any dental health care worker anywhere in the world. Furthermore, if screening of dentists for HCV infection were implemented, there are no data to guide the frequency of repeat HCV testing of the ~99% of dentists who test negative. The rarity of dentist-to-patient transmission of HCV in the era of Standard Precautions does not justify mandatory screening of dentists for HCV.

Approach to the Dentist with BBV Infection

General Principles

The overall approach to a BBV-infected dentist should not differ from the approach to dentists with any other chronic illness. The dentist should receive appropriate medical care and should be permitted to continue to practice dentistry as long as his/her health permits and as long as the risk to the patient is not disproportionate. The BBV-infected dentist should have a personal physician qualified in the

management of the particular BBV infection that he/she has. As with any patient, the BBV-infected dentist is entitled to confidentiality.

BBV-Infected Dentists Who Do Not Perform EPPs

Recommendation 8: For BBV-infected dentists who do not perform EPPs, there are no grounds to restrict their practice on account of the BBV infection, provided that they adhere to Standard Precautions. The criteria for initiating antiviral therapy in BBV-infected HCWs who do not perform EPPs should not differ from BBV-infected patients who are not HCWs.

BBV-Infected Dentists Who Perform EPPs

Dentists who perform EPPs and who know that they are infected with a BBV should report that information to their regulatory authority as soon as possible. The approach to BBV-infected dentists who perform EPPs is based on assessing the risk of transmission and reducing it as much as possible. Since the risk of transmission of BBVs is related to the amount of virus to which a patient is exposed, the pVL of the infected HCW is critical in assessing infectivity. When the pVL of the BBV-infected dentist is high, prohibiting EPPs in susceptible patients is appropriate. In individual cases, it is reasonable to consider antiviral therapy in the BBV-infected dentist who performs EPPs, even if that dentist doesn't meet the conventional criteria for antiviral therapy, since antiviral therapy can reduce pVL to very low levels, allowing the dentist to continue practice. This approach is similar to treating HIV-infected pregnant women with ART even if they have high CD4 counts. In the latter case, ART is given to prevent transmission, rather than for direct maternal benefit.

As there are some differences with each of the three BBVs, the recommendations for each will be discussed separately.

HIV-Infected Dentists Who Perform EPPs

The risk of transmitting HIV during EPPs from HIV-infected surgeons NOT receiving ART is estimated at 1 in 42,000 to 1 in 420,000 procedures [79]. It is estimated that this risk can be reduced to 1 in 2.7 to 1 in 27 million procedures if the surgeon is receiving ART and has an undetectable pVL and wears double gloves. A policy which prohibits all HIV-infected dentists from performing EPPs possibly increases the risk to patients. Since only dentists known to be HIV-infected are subject to restrictions on their practice, there is a clear disincentive against voluntary testing of dentists who perform EPPs. Furthermore, a dentist who leads a lifestyle which places him/her at increased risk of contracting HIV-infection, might be even more inclined to avoid testing when a positive test means that his/her livelihood is at risk. Mandatory testing of dentists who perform EPPs would potentially overcome this problem, but we do not believe it to be an appropriate response, given the incredibly low risk.

A better approach, we believe, is one that achieves the dual benefits of protecting more patients from occupational HIV infection and allowing more HIV-infected dentists to remain in practice, and is congruent with the just culture of the patient safety movement. We encourage dentists to undergo voluntary HIV testing, especially if they are at increased risk by lifestyle or previous residence in an endemic country.

Recommendation 9: HIV-infected dentists who perform EPPs should be started on ART as soon as possible. HIV-infected dentists should not be able to perform EPPs until they are on ART and their pVL is undetectable. Once documented to have an undetectable pVL on ART, they should be permitted to perform EPPs using double gloves, as was recently permitted for an Israeli cardiothoracic surgeon [148], with the proviso that their personal physician provides regular (every 6 month) confirmation to the regulatory agency that his/her pVL is persistently suppressed. If dentists experience loss of income

during the time that they are not permitted to perform EPPs, efforts should be made to supplement the income loss, possibly through insurance, since any disincentive to identifying HIV-infected dentists puts patients at increased risk of HIV infection. In the event that public health officials choose to pursue a look-back study when an HIV-infected dentist is newly identified, and it is recognized that this is not routinely required [31], it is important that the identity of the infected dentist not be disclosed publicly, because of the need to respect his/her confidentiality [31, 149].

HBV-Infected Dentists Who Perform EPPs

The vast majority of transmissions of BBVs from HCW to patient have been with HBV. There are four probable explanations. The first, and likely most important, is that HBV is the most infectious of the three, on a per exposure basis, possibly because the pVL of untreated hepatitis B can be exceedingly high, a thousand to a million fold higher than either HIV or HCV. The risk per parenteral exposure is about 10-fold higher than HCV and about 100-fold higher than HIV. Second, there have been many more years to identify HBV outbreaks. Testing for HBV has been available since the early 1970s. In contrast, testing for HIV became available in 1985 and testing for HCV in late 1989. The third factor is that most of the HCW-to-patient transmissions occurred in a period of time when infection control practices were much more lax than the present era of Standard Precautions. For example, most dentists did not wear gloves in the 1970s. Fourth, the global prevalence of chronic HBV infection is about 350 million, in comparison with 170 million for HCV and 33 million for HIV.

There are several reasons why the incidence of HCW-to-patient transmission of HBV appears to be diminishing. First, Standard Precautions substantially reduce risk [5, 6, 7, 8]. Second, a growing proportion of both HCWs and patients have been immunized against HBV [9, 10]. Third, policies, such as those put forward by the CDC in 1991 [4] have led to restrictions of some HBV-infected HCWs (that

particular document recommended prohibiting HBeAg positive HCWs from performing EPPs). Fourth, many dental schools have been screening students for HBV infection after acceptance and not permitting HBeAg positive students to complete training, since it is considered impossible to train a dentist without teaching him/her to perform EPPs.

When the CDC guidelines were published in 1991 [4], sensitive PCR based assays for HBV DNA were not yet available, but it was known that the presence of HBeAg was predictive of increased infectivity [109]. Hence, the state of knowledge in 1991 supported the recommendation to prohibit HBeAg positive HCWs from performing EPPs.

It has become recognized that some untreated HBeAg negative patients have moderately high levels of viremia due to mutations in the precore gene [150]. Thus, it is not surprising that a few transmissions of HBV were subsequently documented from HBeAg negative surgeons with precore mutant virus [122]. Similarly, it is also known that a minority of HBeAg positive persons have low levels of plasma HBV DNA. Furthermore, HBeAg positive patients who start on antiviral therapy typically experience marked reductions in pVL (often below the limit of detection of sensitive PCR assays) before HBeAg is cleared. It is not unusual for such patients to have undetectable pVL by currently available assays on antiviral therapy but remain HBeAg positive for months to years. For example, of 354 HBeAg positive patients with a median baseline pVL of 9.63 $\log_{10}$ copies/mL who were treated with entecavir, 67% had HBV DNA below 300 copies/mL (<50 IU/mL) at week 28, but only 22% were HBeAg negative at that time [151]. Long term therapy safely and effectively suppresses pVL consistently in the majority and leads to resolution of HBV infection (loss of HBsAg) in a few. For these reasons, it no longer makes sense to assess HBV infectivity on the basis of HBeAg status alone. Plasma HBV DNA measured by a sensitive PCR assay appears to be the most appropriate measure of infectivity.

The evidence supports a pVL cut-off of 10,000 copies/mL (2000 IU/mL) chosen by the European Consensus Group in 2003 [29] and SHEA in 2010 [31], which is four times lower than the lowest pVL documented from an infected HCW who transmitted HBV to a patient, is an appropriate cut-off for the performance of EPPs. It is acknowledged that in 2012, the CDC selected a slightly lower cut-off of 1000 IU/mL [5].

Recommendation 10: HBV-infected dentists with pVL over 2000 IU/mL should not perform EPPs, except on patients who are HBV immune (anti-HBs positive) or HBV infected (HBsAg positive), until or unless their infectivity status changes- whether by natural immunity or from antiviral therapy. HBV-infected dentists with pVL consistently below 2000 IU/mL should be permitted to perform EPPs using double gloves and Standard Precautions, regardless of their HBeAg status, with the proviso that their personal physician provides regular (every 6 months) confirmation that his/her pVL is suppressed below this level to the regulatory agency as long as HBsAg remains positive on annual testing.

HCV-Infected Dentists Who Perform EPPs

The infectivity of HCV is intermediate between HBV and HIV. However, unlike HBV, where the range of pVL in untreated subjects is extremely wide (undetectable to 1 trillion IU/mL), there is much less variability in HCV, with a mean pVL of about 2 million IU/mL using the TaqMan PCR assay. A European study has confirmed what would be logically predicted, in that pVL predicts risk of transmission of HCV following parenteral exposures [143], as it does MTCT [152]. However, a transmission threshold has not been established. The UK prohibits all HCV viremic HCWs from performing EPPs [153], whereas SHEA recommends that those with pVL below 10,000 copies/mL may perform EPPs with double gloves and universal precautions [31]. In practice, few HCV-infected persons have pVLs below this cut-off. For

example, in a recent study of 3070 patients with HCV genotype 1 infection, only 18% had pVL below 600,000 IU/mL [154].

Recommendation 11: HCV RNA positive dentists should not perform EPPs. If HCV RNA done at least 12 weeks after completion of treatment is negative [133], they can resume EPPs.

Efforts should be make to supplement any income loss related to the time that the HCV-infected dentist was unable to practice, possibly from an insurance plan.

Conclusions

Dentists are at much greater risk of acquiring BBVs from patients than patients are of acquiring them from dentists. Nevertheless, there are multiple documented cases of HBV transmission from infected, but untreated dentists to patients during EPPs, most of which occurred prior to the use of Standard Precautions in infection prevention. One untreated HIV-infected dentist transmitted HIV to six patients, but there have been no other documented cases of dentist-to-patient transmission of HIV. There have been no documented cases of dentist-to-patient transmission of HCV, but there is a risk of such transmission, given that surgeons have rarely transmitted HCV to patients. Standard Precautions have substantially decreased the number of blood exposures throughout health care, protecting both patients and HCWs from BBVs. The risk of HBV infection has additionally been reduced by the increasing use of hepatitis B vaccine, especially among HCWs. Nucleic acid amplification tests can accurately quantify the amount of BBVs in plasma, and pVL has proven to be an accurate measure of infectivity. Current antiviral therapy can cure about 75% of HCV infections and can suppress the level of viremia in

HBV and HIV infection to below the level of detection in sensitive PCR assays in most patients, reducing transmission risks to minimal levels.

BBV-infected dentists who do not perform EPPs require no restriction of their practice, but are expected to practice Standard Precautions, as all HCWs should. BBV-infected dentists who perform EPPs should be assessed on a case-by case basis. Antiviral therapy may be indicated to allow performance of EPPs even if no other clinical indication for treatment exists. HBV-infected dentists with plasma HBV DNA consistently <2000 IU/mL, whether naturally (i.e. the immune control/inactive phase of chronic HBV infection) or because of antiviral therapy should be permitted to perform EPPs, regardless of their HBeAg status. HIV-infected dentists should not perform EPPs until they are receiving ART and have consistently undetectable pVL, at which time they should be permitted to perform EPPs. HCV viremic dentists should not perform EPPs, but they should be encouraged to undergo anti-HCV therapy and may resume EPPs if they become aviremic.

References

1. Health Canada. Proceedings of the consensus conference on infected health care workers: risk for transmission of bloodborne pathogens. *Can Commun Dis Rep* 1998;24(Suppl 4):I,III,1-25,i-iii,1-28.

2. Johnston BL, Macdonald S, Lee S, LeBlanc JC, Gross M, Schlech WF, Chaudhary R, Langille D. Nosocomial hepatitis B associated with orthopedic surgery--Nova Scotia. *Can Commun Dis Rep* 1992;18:89-90.

3. Hepatitis B Outbreak Investigation Team. An outbreak of hepatitis B associated with reusable subdermal electroencephalogram electrodes. *CMAJ* 2000;162:1127-31.

4. Recommendations for preventing transmission of human immunodeficiency virus and hepatitis B virus to patients during exposure-prone invasive procedures. *MMWR Morbid Mort Wkly Rep* 1991;40(RR08):1-9.

5. Updated CDC recommendations for the management of hepatitis B virus-infected health-care providers and students. *MMWR Morbid Mort Wkly Rep* 2012;61 (3):1-12.

6. Wong ES, Stotka JL, Chinchilli VM, Williams DS, Stuart G, Markowitz SM. Are universal precautions effective in reducing the number of occupational exposures among health care workers? A prospective study of physicians on a medical service. *JAMA* 1991;265:1123-8.

7. Beekmann SE, Vlahov D, Koziol DE, Mc Shalley ED, Schmitt JM, Henderson DK. Temporal association between implementation of universal precautions and a sustained, progressive decrease in percutaneous exposures to blood. *Clin Infect Dis* 1994;18:562-9.

8. Haiduven DJ, DeMaio TM, Stevens DA. A five-year study of needlestick injuries: significant reduction associated with communication, education, and convenient placement of sharps containers. *Infect Control Hosp Epidemiol* 1992;13:265-71.

9. Mahoney FJ, Stewart K, Hu H, Coleman P, Alter MJ. Progress toward the elimination of hepatitis B virus transmission among health care workers in the United States. *Arch Intern Med* 1997;157:2601-5.

10. Cleveland JL. Hepatitis B vaccination and infection among US dentists, 1983-1992. *JADA* 1996;127:1385-90.

11. Tokars JI, Alter MJ, Favero MS. National surveillance of dialysis-associated diseases in the United States, 1993. Centers for Disease Control and Prevention, Atlanta, Ga. 1995.

12. Sherman M, Shafran S, Burak K, Doucette K, Wong W, Girgrah N, et al. Management of chronic hepatitis C: consensus guidelines. *Can J Gastroenterol* 2007;21(Suppl C):25C-34C.

13. Jacobson IM, McHutchison JG, Dusheiko G, Di Bisceglie AM, Reddy KR, Bzowej NH, et al. Telaprevir for previously untreated chronic hepatitis C infection. *N Engl J Med* 2011;364:2405-16.

14. Khatri N, Brown GD, Hicks LL. From a blame culture to a just culture in health care. *Health Care Manage Rev* 2009;34:312-22.

15. Recommendations for postexposure interventions to prevent infection with hepatitis B virus, hepatitis C virus, or human immunodeficiency virus, and tetanus in persons wounded during bombings and other mass-casualty events-United States, 2008. *MMWR Morbid Mort Wkly Rep* 2008;57(RR06):1-19.

16. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States. Recommendations from the U.S. Department of Health and Human Services. *MMWR Morbid Mort Wkly Rep* 2005;54(RR02):1-10.

17. West DJ. The risk of hepatitis B infection among health professionals in the United States: a review. *Am J Med Sci* 1984;287:26-33.

18. Thomas DL, Gruninger SE, Siew C, Joy ED, Quinn TC. Occupational risk of hepatitis C infections among general dentists and oral surgeons in North America. *Am J Med* 1996;100:41-5.

19. Segal HE, Llewellyn CH, Irwin G, et al. Hepatitis B antigen and antibody in the U.S. army: prevalence in health care personnel. *Am J Public Health* 1976;66:667-71.

20. Zuckerman J, Clewley G, Griffiths P, Cockroft A. Prevalence of hepatitis C antibodies in clinical health-care workers. *Lancet* 1994;343:1618-20.

21. Kuo MY, Hahn LJ, Hong CY, et al. Low prevalence of hepatitis C virus infection among dentists in Taiwan. *J Med Virol* 1993;40:10-3.

22. Ammon A, Reichart PA, Pauli G, Petersen LR. Hepatitis B and C among Berlin dental personnel: incidence, risk factors, and effectiveness of barrier prevention measures. *Epidemiol Infect* 2000;125:407-13.

23. Ashkenazi M, Fisher N, Levin L, Littner MM. Seroepidemiology of hepatitis C antibodies among dentist and their self-reported use of infection control measures. *Community Dent Health* 2009;26:99-103.

24. Vaglia A, Nicolin R, Puro V, et al. Needlestick hepatitis C virus seroconversion in a surgeon. *Lancet* 1990;336:1315-6.

25. Do AN, Ciesielski CE, Metler RP, at al. Occupationally acquired human immunodeficiency virus (HIV) infection: national case surveillance data during 20 years of the HIV epidemic in the United States. *Infect Control Hosp Epidemiol* 2003;24:86-96.

26. Halevy A., Brody B. Acquired immunodeficiency syndrome and the Americans with Disabilities Act: a legal duty to treat. *Am J Med* 1994;96:282-8; discussion 289-91.

27. Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. *MMWR* 1988;37:377-82,387-8.

28. Schalm SW, Buster EHCJ. Management of hepatitis B virus infected health care workers based on HBV DNA levels. *J Clin Virol* 2003;27:231-4.

29. Gunson RN Shouval D, Roggendorf, et al. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections in health care workers (HCWs): guidelines for prevention of HBV and HCV from HCW to patients. *J Clin Virol* 2003;27:213-30.

30. Reitsma AM, Closen ML, Cunningham M, et al. Infected physicians and invasive procedures: safe practice management. *Clin Infect Dis* 2005;40:1665-72.

31. Henderson DK, Dembry L, Fishman NO, et al. SHEA guideline for management of healthcare workers who are infected with hepatitis B virus, hepatitis C virus, and/or human immunodeficiency virus. *Infect Control Hosp Epidemiol* 2010;31:203-32.

32. Dawar M, Stuart TL, Sweet LE, Neatby AM, Abbott LP, Andonov AP, et al. Canadian hepatitis C look-back investigation to detect transmission from an infected general surgeon. *Can J Infect Dis Med Microbiol* 2010;21(1);e6-e11.

33. Ross RS, Viazov S, Thormählen M, et al. Risk of hepatitis C virus transmission from an infected gynecologist to patients: results of a 7-year retrospective investigation. *Arch Intern Med* 2002;162:805-10.

34. Ross RS, Steinbrückner B, Böhm S, at al. Outcome of an exercise to notify patients treated by a general surgeon infected by the hepatitis C virus. *J Clin Virol* 2008;41:314-7.

35. Estebal JI, Gómez J, Martell M, et al. Transmission of hepatitis C virus by a cardiac surgeon. *N Engl J Med* 1996;334:555-60.

36. Ross RS, Viazof S, Roggendorf M. Phylogenetic analysis indicates transmission of hepatitis C virus from an infected orthopedic surgeon to a patient. *J Med Virol* 2002;66:461-7.

37. Ciesielski CA, Marianos D, Ou CY, et al. Transmission of human immunodeficiency virus in a dental practice. *Ann Intern Med* 1992;116:798-805.

38. Lot F, Séguier J-C, Fégueux S, at al. Probable transmission of HIV from an orthopedic surgeon to a patient in France. *Ann Intern Med* 1999;130:1-6.

39. Mallolas J, Arnedo M, Pumarola T. Transmission of HIV-1 from an obstetrician to a patient during a caesarean section. *AIDS* 2006;20:285-7.

40. Goujon CP, Schneider VM, Grofti J, et al. Phylogenetic analyses indicate an atypical nurse-to-patient transmission of human immunodeficiency virus type 1. *J Virol* 2000;74:2525-32.

41. Robert LM, Chamberland ME, Cleveland JL, et al. Investigations of patients of health care workers infected with HIV. The Centers for Disease Control and Prevention Database. *Ann Intern Med* 1995;122:653-7.

42. Cleveland JL, Gooch BF, Lockwood SA. Occupational blood exposures in dentistry: a decade in review. *Infect Control Hosp Epidemiol* 1997;18:717-21.

43. Siew C, Chang S, Gruninger S, Verrusio C, Neidle E. Self-reported percutaneous injuries in dentists: implications for HBV, HIV transmission risk. *JADA* 1992;123:37-44.

44. Siew C, Gruninger SE, Miaw C, Neidle EA. Percutaneous injuries in practicing dentists. *JADA* 1995;126:1227-34.

45. Sullivan S, et al. Blunt needles for the reduction of needlestick injuries during cesarean delivery: a randomized controlled trial. *Obstet Gynecol* 2009;114(2 Pt 1):211-6.

46. Faisal-Cury A, Rossi Menezes P, Kahhale S, Zugaib M. A study of the incidence and recognition of surgical glove perforation during obstetric and gynecological procedures. Arch Gynecol Obstet 2004;270:263–4.

47. Tokars JI, Bell DM, Culver DH, et al. Percutaneous injuries during surgical procedures. *JAMA* 1992;267:2899-904.

48. Panlilio AL, Foy DR, Edwards JR, et al. Blood contacts during surgical procedures. *JAMA* 1991;265:1533-7.

49. Jagger J, Bentley M, Tereskerz P. A study of patterns and prevention of blood exposure in OR personnel. *AORN J* 1998; 67: 979-81, 983-4, 986-7 passim.

50. Wittmann A, Kralj N, Köver J, Gasthaus K, Hofmann F.. Study of blood contact in simulated surgical needlestick injuries with single or double latex gloving. *Infect Control Hosp Epidemiol* 2009;30:53-6.

51. Lefebvre DR, Strande LF, Hewitt CW. An enzyme-mediated assay to quantify inoculation volume delivered by suture needlestick injury: two gloves are better than one. *Am Coll Surg* 2008;206:113-22

52. McCarthy GM, MacDonald JK. The infection control practices of general dental practitioners. *Infect Control Hosp Epidemiol* 1997;18:699-703.

53. Cleveland JL, Barker L, Gooch BF, et al. Use of HIV postexposure prophylaxis by dental health care personnel. An overview and updated recommendations. *JADA* 2002;133:1619-26.

54. Au E, Gossage JA, Bailey SR. The reporting of needlestick injuries sustained in theatre by surgeons: are we under-reporting*? J Hosp Infect* 2008;70:66-70.

55. *Pneumocystis* pneumonia- Los Angeles. *MMWR* 1981;30:250-2.

56. Chermann JC, Barré-Sinoussi F, Dauguet C, et al. Isolation of a new retrovirus in a patient at risk for acquired immunodeficiency syndrome. *Antibiot Chemother* 1983;32:48-53.

57. Needlestick transmission of HTLV-III from a patient in Africa*. Lancet* 1984;2:1376-7.

58. Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure*. N Engl J Med* 1997;337:1485-90.

59. Ippolito G, Puro V, Heptonstall J, et al. Occupational human immunodeficiency virus infection in health care workers: worldwide cases through September 1997. *Clin Infect Dis* 1999;28:365-83.

60. Possible transmission of human immunodeficiency virus to a patient during an invasive dental procedure. *MMWR Morbid Mort Wkly Rep* 1990;39:489-93.

61. Armstrong FP, Miner JC, Wolfe WH. Investigation of a health care worker with symptomatic human immunodeficiency virus infection: an epidemiological approach. *Milit Med* 1987;152:414-8.

62. Mishu B, Schaffner W, Horan JM, et al. A surgeon with AIDS: lack of evidence of transmission to patients. *JAMA* 1990;264:467-70.

63. Porter JD, Cruickshank JG, Gentle PH, et al. Management of patients treated by a surgeon with HIV infection. *Lancet* 1990;335:113-4.

64. Danila RN, MacDonald K, Rhame F, et al. A look-back investigation of patients of an HIV-infected physician: public health implications. *N Engl J Med* 1991;325:1406-11.

65. Smith Rogers A, Froggatt JW III, Townsend T, et al. Investigation of potential HIV transmission to the patients of an HIV-infected surgeon. *JAMA* 1993;269:1795-801.

66. Dickinson GM, Morhart RE, Klimas NG, et al. Absence of HIV transmission from an infected dentist to his patients. An epidemiologic and DNA sequence analysis. *JAMA* 1993;269:1802-6.

67. Fordham von Reyn C, Gilbert TT, Shaw FE Jr, et al. Absence of HIV transmission from an infected orthopedic surgeon. A 13 year look-back study. *JAMA* 1993;269:1807-11.

68. Babinchak TJ, Renner C. Patients treated by a thoracic surgeon with HIV. A review. *Chest* 1994;106:681-3.

69. Jaffe HW, McCurdy JM, Kalish ML, et al. Lack of HIV transmission in the practice of a dentist with AIDS. *Ann Intern Med* 1994;121:855-9.

70. Longfield JN, Brundage J, Badger G, et al. Look-back investigation after human immunodeficiency virus seroconversion in a pediatric dentist. *J Infect Dis* 1994;169:1-8.

71. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis* 2005;5:558-67.

72. Bosch X. Hepatitis C outbreak astounds Spain. *Lancet* 1998;351:1415.

73. Bosch X. Newspaper apportions blame in Spanish hepatitis C scandal. *Lancet* 2000;355:818.

74. Roche WF. Nurse accused of spreading hepatitis C at a military hospital. Los Angeles Times 2008. Available at: http://articles.latimes.com/2008/mar/12/nation/na-nurse12. Accessed April 3, 2010.

75. Sehulster L, Taylor J, Hendriks K, VanEgdom M, Whiteley S, Manning S. Hepatitis C outbreak linked to narcotic tampering in an ambulatory surgical center. In: Abstracts of the 1997 Interscience Conference on Antimicrobial Agents and Chemotherapy. Washington, DC: American Society for Microbiology Press, 1997:293.

76. Shemer-Avni Y, Cohen M, Keren-Naus A, et al. Iatrogenic transmission of hepatitis C virus (HCV) by an anesthesiologist: comparative molecular analysis of the HCV-E1 and HCV-E2 hypervariable regions. *Clin Infect Dis* 2007;45:e32-8.

77. ProMED. Hepatitis C, physician-related cluster – Australia (03): (Victoria). May 31, 2010

78. Astagneau P, Lot F, Bouvet E, Labascle K, Baffoy N, Aggoune N, Brückner G. Lookback investigation of patients potentially exposed to HIV type 1 after a nurse-to-patient transmission. *Am J Infect Control* 2002;30:242-5.

79. Bell DM, Shapiro CN, Culver DH, et al. Risk of hepatitis B and human immunodeficiency virus transmission to a patient from an infected surgeon due to percutaneous injury during an invasive procedure: estimates based on a model. *Infectious Agents Dis* 1992;1:263-9.

80. Mast ST, Woolwine, JD, Gerberding JL. Efficacy of gloves in reducing blood volumes transferred during simulated needlestick injury. *J Infect Dis* 1993;168:1589-92.

81. Mellors JW, Kingsley LA, Rinaldo CR Jr, et al. Quantitation of HIV-1 RNA in plasma predicts outcome after seroconversion. *Ann Intern Med* 1995;122:573-9.

82. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med* 2000;342:921-9.

83. Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. *N Engl J Med* 1996;335:1621-9.

84. Dickover RE, Garratty EM, Herman SA, et al. Identification of levels of maternal HIV-1 RNA associated with risk of perinatal transmission. Effect of zidovudine treatment on viral load. J*AMA* 1996;275:599-605.

85. Thea DM, Steketee RW, Pliner V, et al. the effect of maternal viral load on the risk of perinatal HIV-1 transmission of HIV-1. *AIDS* 1997;11:437-44.

86. Garcia PM, Kalish LA, Pitt J, et al. Maternal levels of human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. *N Engl J Med* 1999;341:394-402.

87. Shafran SD, Conly JM. Ya gotta have HAART. *Can J Infect Dis* 1997; 8:130-2.

88. Pallela FJ Jr, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med* 1998;338:853-60.

89. Forrest DM, Seminari E, Hogg RS, et al. The incidence and spectrum of AIDS-defining illnesses in persons treated with antiretroviral drugs. *Clin Infect Dis* 1998;27:1379-85.

90. Antiretroviral Therapy Cohort Collaboration. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. *Lancet* 2008;372:293-9.

91. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Engl J Med,* 1994. 331:1173-80.

92. Cooper ER, Charurat M, Mofenson L, et al. Combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. *J Acquir Immune Defic Syndr* 2002;29:484-94.

93. Townsend CL, Cortina-Borja M, Peckham CS, et al. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. *AIDS* 2008;22:973-81.

94. Warszawski J, Tubiana R, Le Chenadec J, et al. Mother-to-child HIV transmission despite antiretroviral therapy in the ANRS French perinatal cohort. *AIDS* 2008;22:289-99.

95. Ioannidis JP, Abrams EJ, Ammann A, et al. Perinatal transmission of human immunodeficiency virus type 1 by pregnant women with RNA virus loads < 1000 copies/ml. *J Infect Dis* 2001;183:539-45.

96. Tubiana R, Le Chenadec J, Rouzioux C, et al. Factors associated with mother-to-child transmission of HIV-1 despite a maternal viral load < 500 copies/ml at delivery: a case-control study nested in the French perinatal cohort (EPF-ANRS CO1). *Clin Infect Dis* 2010;50:585-96.

97. The European Collaborative Study. Maternal viral load and vertical transmission of HIV-1: an important factor but not the only one. *AIDS* 1999;13:1377-85.

98. European Study Group on Heterosexual Transmission of HIV. Comparison of female to male and male to female transmission of HIV in 563 stable couples. *BMJ* 1992;304:809-13.

99. Varghese B, Maher JE, Peterman TA, Branson BM, Steketee RW. Reducing the risk of sexual HIV transmission: quantifying the per-act risk for HIV on the basis of choice of partner, sex act, and condom use. *Sex Transm Dis* 2002;29:38-43.

100. Attia S, Egger M, Müller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systemic review and meta-analysis. *AIDS* 2009;23:1397-404.

101. Stürmer M, Doerr HW, Berger A, Gute P. Is transmission of HIV-1 in non-viraemic serodiscordant couples possible? *Antivir Ther* 2008;13:729-32.

102. Donnell D, Baeten JM, Kiarie J, Thomas KK, Stevens W, Cohen CR, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: A prospective cohort analysis. *Lancet* 2010; epublished May 27, 2010

103. Lorello G, la Porte C, Pilon R, et al. Discordance in HIV-1 viral loads and antiretroviral drug concentrations comparing semen and blood plasma. *HIV Med* 2009;10:548-54.

104. Stramer SL, Glynn SA, Kleinman SH, at al. Detection of HIV-1 and HCV infections among antibody-negative blood donors by nucleic acid-amplification testing. *N Engl J Med* 2004;351:760-8.

105. Li G, Warner M, Lang BH, Huang L, Sun LS. Epidemiology of anesthesia-related mortality in the United States, 1999-2005. *Anesthesiology* 2009;110:759-65.

106. Campsmith ML, Rhodes PH, Hall HI, Green TA. Undiagnosed HIV prevalence among adults and adolescents in the United States at the end of 2006; *J Acquir Immune Defic Syndr* 2010;53:619-24.

107. Sherman M, Shafran S, Burak K, Doucette K, Wong W, Girgrah N, et al. Management of chronic hepatitis B: Consensus guidelines. *Can J Gastroenterol* 2007;21(Suppl C):5C-24C.

108. Mackie CO, Buxton JA, Tadwalkar JS, Patrick DM. Hepatitis B immunization strategies: timing is everything. *CMAJ* 2009; 180:196-202.

109. Kim WR. Epidemiology of hepatitis B in the United States. *Hepatology* 2009;49 (5 suppl):S28-34.

110. Rotman Y, Brown TA, Hoofnagle JH. Evaluation of the patient with hepatitis B. *Hepatology* 2009;49 (5 suppl):S22-7.

111. Alter HJ, Seeff LB, Kaplan PM, McAuliffe VJ, Wright EC, Gerin JL, Purcell RH, Holland PV, Zimmerman HJ. Type B hepatitis: the infectivity of blood positive for e antigen and DNA polymerase after accidental needlestick exposure. *N Engl J Med* 1976;295:909-13.

112. Carman WF, Jacyna MR, Hadziyannis S, et al. Mutation preventing formation of hepatitis B e antigen in patients with chronic hepatitis B infection. *Lancet* 1989;2:588-91.

113. Sorrell MF, Belongia EA, Costa J, et al. National Institutes of Health consensus development conference statement: management of hepatitis B. *Hepatology* 2009;49 (5 suppl):S4-12.

114. Lok ASLF, McMahon BJ. Chronic hepatitis B: Update 2009. *Hepatology* 2009;50:1-35.

115. Coffin CS, Lee SS. Treatment of HBeAg-positive patients with nucleos/tide analogues. *Liver Int* 2009;29 Suppl 1:116-24.

116. van Bömmel F, de Man RA, Wedemeyer H, Deterding K, Petersen J, Buggish P, et al. Long-term efficacy of tenofovir monotherapy for hepatitis B virus-monoinfected patients after failure of nucleoside/nucleotide analogues. *Hepatology* 2010;51:73-80.

117. Sundkvist T, Hamilton GR, Rimmer D, Evans BG, Teo CG. Fatal outcome of transmission of hepatitis B from an e antigen negative surgeon. *Commun Dis Public Health* 1998;1:48-50.

118. Oliver SE, Woodhouse J, Hollyoak V. Lessons from patient notification exercises following the identification of hepatitis B e antigen positive surgeons in an English health region. *Commun Dis Public Health* 1999;2:130-6.

119. Molyneaux P, Reid TM, Collacott I, McIntypre PG, Dillon JF, Laing RB. Acute hepatitis B in two patients transmitted from an e antigen negative cardiothoracic surgeon. *Commun Dis Public Health* 2000;3:250-2.

120. Spijkerman IJ, van Doorn LJ, Janssen MH, et al. Transmission of hepatitis B virus from a surgeon to his patients during high-risk and low-risk surgical procedures during 4 years. *Infect Control Hosp Epidemiol* 2002;23:306–312.

121. Harpaz R, von Seidlein L, Averhoff FM, et al. Transmission of hepatitis B virus to multiple patients from a surgeon without evidence of inadequate infection control. *N Engl J Med* 1996;334:549-54.

122. Incident Investigation Teams and others. Transmission of hepatitis B to patients from four infected surgeons without hepatitis B e antigen. *N Engl J Med* 1997;336:178-84.

123. Daha TJ, Bilkert-Mooiman MA, Ballemans C, Frijstein G, Keeman JN, de Man RA, van Steenbergen JE, Weers-Pothoff G, Zaaijer HL. Hepatitis B virus infected health care workers in The Netherlands, 2000-2008. *Eur J Clin Micobiol Infect Dis* 2009;28:1041-4.

124. Buster EH, van der Eijk AA, de Man RA, Janssen HL, Schalm SW. Prolonged antiviral therapy for hepatitis B virus-infected health care workers: a feasible option to prevent work restriction without jeopardizing patient safety. *J Viral Hepat* 2007;14:350-4.

125. Van der Eijk AA, de Man RA, Niesters HGM, Schalm SW, Zaaijer HL. Hepatitis B virus (HBV) DNA levels and the management of HBV-infected health care workers. *J Viral Hepat* 2006;13:2-4.

126. Prince AM, Brotman B, Grady GF, Kuhns WJ, Hazzi C, Levine RW, Miller SJ. Long-incubation post-transfusion hepatitis without serological evidence of exposure to hepatitis-B virus. *Lancet* 1974;2:241-6.

127. Kuo G, Choo Q-L, Alter HJ, Gitnick GL, Redecker AG, Purcell RH, et al. An assay for circulating antibodies to a major etiologic virus of human nonA, nonB hepatitis. *Science* 1989;244:362-4.

128. Santantonio T, Wiegand J, Gerlach JT. Acute hepatitis C: current status and remaining challenges. J *Hepatol* 2008;49:625-33.

129. Perz JF, Armstrong G, Farrington LA, Hutin YJF, Bell BP. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. *J Hepatol* 2006;45:529-38.

130. Wiley TE, McCarthy M, Breidi L, McCarthy M, Layden TJ. Impact of alcohol on the histological and clinical progression of hepatitis C infection. *Hepatology* 1998:28:805-9

131. Graham CS, Baden LR, Yu E, Mrus JM, Carnie J, Heern T, Koziel MJ. Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. *Clin Infect Dis* 2001;33:562-9.

132. Poordad F, McCone J, Bacon BR, Bruno S, Manns MP, Sulkowski MS, et al. Boceprevir for untreated chronic HCV genotype 1 infection. *N Engl J Med* 2011;364:1195-206.

133. Martinot-Peignoux M, Sren C, Maylin S, Ripault M-P, Boyer N, Leclere L, et al. Twelve weeks posttreatment follow-up is as relevant as 24 weeks to determine the sustained virologic response in patients with hepatitis C virus receiving pegylated interferon and ribavirin. *Hepatology* 2010;51:1122-6.

134. de Oliveira AM, White KL, Leschinsky DP, Beecham BD, Vogt TM, Moolenaar RL, Perz JF, Safranek TJ. An outbreak of hepatitis C virus infections among outpatients at a hematology/oncology clinic. *Ann Intern Med* 2005;142:898-902.

135. Centers for Disease Control and Prevention. Acute hepatitis C virus infections attributed to unsafe injection practices at an endoscopy clinic--Nevada, 2007. *MMWR Morbid Mort Wkly Rep* 2008;57:513-7;

136. Thompson ND, Perz JF, Moorman AC, Holmberg SD. Nonhospital healthcare-associated hepatitis B and C virus transmission: United States, 1998-2008. *Ann Intern Med* 2009;150:33-9.

137. Bessa M, Rodart IF, Menezes GB, Carmo TM, Athanazio DA, Reis MG. Limited evidence of HCV transmission in stable heterosexual couples from Bahia, Brazil. *Braz J Infect Dis* 2009;13:262-5.

138. van de Laar T, Pybus O, Bruisten S, Brown D, Nelson M, Bhagani S, et al. Evidence of a large, international network of HCV transmission in HIV-positive men who have sex with men. *Gastroenterol* 2009;136:1609-17.

139. Roberts EA, Yeung L. Maternal-infant transmission of hepatitis C virus infection. *Hepatology* 2002;36 (Suppl 1):S106-13.]

140. Ahtone J, Francis D, Bradley D, Maynard J. NonA, nonB hepatitis in a nurse after percutaneous needle exposure. *Lancet* 1980;1:1142.

141. Schlipköter U, Roggendorf M, Cholmakow K, Weise A, Deinhatdt F. Transmission of hepatitis C virus (HCV) from a haemodialysis patient to a medical staff member. *Scand J Infect Dis* 1990;22:757-8

142. Centers for Disease Control and Prevention. Recommendations for follow-up of health-care workers after occupational exposure to hepatitis C virus. *MMWR Morbid Mort Wkly Rep* 1998; 47:603–606.

143. Yazdanpanah Y, Ce Carli G, Migueres B, Lot F, Campins M, Columbo C, et al. Risk factors for hepatitis C transmission to health care workers after occupational exposure: A European case-control study. *Clin Infect Dis* 2005; 41:1423–30.

144. Ross RS, Viazov S, Gross T, Hofmann F, Seipp H-M, Roggendorf M. Transmission of hepatitis C virus from a patient to an anesthesiology assistant to five patients. *N Engl J Med* 2000;343:1851-4.

145. Cody SH, Nainam OV, Garfein RS, Myers H, Bell BP, Shapiro CN, et al. Hepatitis C virus transmission from an anesthesiologist to a patient. *Arch Intern Med* 2002;162:345-50.

146. Mawdsley J, Teo CG, Kyi M, Anderson M. Anesthetist to patient transmission of hepatitis C virus associated with non exposure-prone procedures. *J Med Virol* 2005; 75:399–401.

147. Owens DK, Harris RA, Scott PM, Nease RF Jr. Screening surgeons for HIV infection. A cost-effectiveness analysis. *Ann Intern Med* 1995;122:641-52.

148. Investigation of patients treated by an HIV-infected cardiothoracic surgeon-Israel, 2007. *MMWR Morbid Mort Wkly Rep* 2009;57(53):1413-5.

149. Pell J, Gruer L, Christie P, Goldberg D. Management of HIV infected health care workers: lessons from three cases. *BMJ* 1996;312:1150-2.

150. Corden S, Ballard AL, Ijaz S, Barbara JA, Gilbert N, Gilson RJ, Boxall EH, Tedder RS. HBV DNA levels and transmission of hepatitis B by health care workers. *J Clin Virol* 2003;27:52-8.

151. Chang T-T, Gish RG, deMan R, Gadano A, Sollano J, Chao Y-C, et al. A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. *N Engl J Med* 2006;354:1001-10.

152. Okamoto M, Nagata I, Murakami J, Kaji S, Iitsuka T, Hoshika T, et al. Prospective reevaluation of risk factors in mother-to-child transmission of hepatitis C virus: high virus load, vaginal delivery, and negative anti-NS4 antibody. *J Infect Dis* 2000; 182:1511–4.

153. UK Department of Health. Hepatitis C infected health care workers.

2002. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/

PublicationsPolicyAndGuidance/DH_4010554.

154. McHutchison JG, Lawitz EJ, Shiffman ML, Muir AJ, Galler GW, McCone J, et al. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection. *N Engl J Med* 2009;360:580-93.