# Hospital Infection Control and Bloodborne Infective Agents

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Bloodborne infections are a worldwide health care burden. Many of these infections are acquired during a medical procedure and could be prevented by an appropriate preventive strategy in the health care setting. The purpose of this article is to review the current status of hospital infection control practices for well-recognized and emerging bloodborne viral infections. The prevention of bloodborne infections in the health care setting involves two main strategies: to decrease the risk of infection in patients who receive blood products and to avoid the transmission of potential pathogens between health care providers and patients. Significant evidence exists to suggest that not adhering to some form of consistently applied bloodborne pathogen protocol results in exposure to bloodborne pathogens from patient to health care worker (HCW), from HCW to patient, and from patient to patient[1,2].

## Hospital infection control

The *Infection Control Guideline Series*[3], published by Health Canada, provides a comprehensive set of evidenced-based recommendations for hospitals and other health care facilities to adapt and implement in order to prevent and control infections that can be transmitted during the provision of health care. Infection control practices are continually evolving as new knowledge and new technology develop.

Historically, three forms of body fluid precautions have been practised in Canada. Before 1987, facilities used blood labeling precautions[4]; then, Universal Precautions (UP)[5] and Body Substance Isolation (BSI)[6] were developed. In 1997, new integrated bloodborne pathogen protocols were introduced with the publication of *Preventing the Transmission of Bloodborne Pathogens in Health Care and Public Service Settings*[7]. This was quickly followed in 1999 by the introduction of Routine Practices[8] (known as Standard Precautions in the United States[9]), a complete integration of bloodborne pathogen protocols with other critical infection prevention and control protocols. In the past 4 years most health care facilities in Canada have moved to adapt the new protocols.

UP and BSI address the problem of bloodborne pathogens from different perspectives. UP have an occupational health orientation focusing primarily on minimizing HCW exposure to bloodborne pathogens. BSI focuses on minimizing cross-infection risk from all pathogens for both patients and staff. The confusion between the two systems has led to frequent inconsistent, unsafe applications, often resulting in both underprotection of staff and overisolation of patients[10-12].

The principle of UP was that a single standard of blood and body fluid precaution be used with all patients at all times, i.e. it was assumed that all blood or visibly blood-contaminated body fluids were potentially infectious. UP were specifically intended to prevent transmission of bloodborne pathogens from patients to occupational groups that have the potential for exposure to blood in the line of duty. UP applied to blood and other body fluids containing visible blood, semen and

vaginal secretions, and cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids[13].

BSI, a strategy intended to prevent transmission of potential pathogens between patients, was introduced in 1987 as an alternative to UP[6]. Although BSI was implemented in a number of large Canadian and U.S. institutions, it was never embraced by government bodies in Canada or the U.S. BSI expanded the principles of UP to all body fluids. Unlike UP, BSI replaced all other traditional isolation strategies, with the exception of isolation for airborne infections and multiple drug-resistant organisms.

Routine Practices builds on the 1997 integration of the key elements of UP and BSI and then enables consistent application of key infection prevention and control protocols (including bloodborne pathogen protocols) to all patients at all times. Appropriately applied Routine Practices also enhance the safety of staff caring for patients.

The recent introduction of new needlestick prevention technology may offer additional protection from needlestick injuries when used in conjunction with Routine Practices.

## Prevalence of bloodborne infections

Although little relevant information exists in Canada, the risk of transmission of bacterial infections via transfusion is now thought to be equal to or greater than the risk of viral infection. Bacterial infections account for > 10% of transfusion-related deaths reported to the Food and Drug Administration[14]. The risk of HCWs' exposure to bloodborne pathogens varies according to the prevalence of each potential infectious agent. The prevalence of bloodborne viral infections among people admitted to Canadian hospitals varies institutionally and provincially. The reported prevalence of hepatitis C seropositivity in the general population in the Yukon is 275 per 100,000[15]. In one Ontario community survey, 62 of 6,055 patients (1%) were seropositive for hepatitis C[16]. The prevalence rates of hepatitis B surface antigen, and antibodies to HIV and the hepatitis C virus (HCV) among people admitted to a Toronto hospital were 2.1%, 0.6%, and 0.5% respectively[17]. In a retrospective examination of donor records at the Eye Bank of Canada (Ontario), the prevalence of hepatitis B virus (HBV) was 0.25%, of HCV was 0.93%; and of HIV was 0.031%[18]. A seroprevalence survey of more than 6,000 individuals attending an Alberta STD clinic demonstrated HIV in 1.5% and HCV in 3.5% of the subjects[19]. In Vancouver, the prevalence rates of HIV-1 and HCV among intravenous drug users were 23% and 88% respectively[20]. The observed seroprevalence rates of these Canadian studies support the use of a proactive prevention strategy to curtail the transmission of bloodborne pathogens in the health care setting.

## Nosocomial sharp injuries

HCWs may be exposed to bloodborne pathogens during the course of their work, and percutaneous injuries are the main risk of exposure. Preliminary results from the new Canadian Needle Stick Surveillance Network (CNSSN) indicate that for the first 6 months of data collection, HCWs in 12 centres were exposed to 497 known sources. Forty-eight of the known sources tested positive for a bloodborne pathogen; more than half were from patients with hepatitis C, 15 % from patients with hepatitis B, and 20% from patients with HIV. Three exposures were from source patients positive for HIV and HCV (unpublished data).

Phlebotomy causes 13%-62% of the injuries reported to hospital occupational health services in North America[21,22]. CNSSN reports that phlebotomists have a rate of 14.5 exposures per full time employee equivalent (FTE), nurses have 2.21 exposures per FTE, and medical residents have 6.2 exposures per FTE (unpublished data) . There are more than 50 documented episodes of occupationally acquired HIV infection reported in the U.S., of which almost 40% occurred during phlebotomy[23,24]. In Canada, there has been only one documented case of HIV transmission to a health care worker, who had a needle stick injury[25]. The estimated risk of infection after sustaining a sharp injury for HIV, HBV, and HCV is 0.3%, 10%-35%, and 2.7% respectively[23,26,27].

## Recognized bloodborne pathogens

Guidelines have been published on hepatitis B (as well as hepatitis C and HIV) postexposure prophylaxis for health care workers[28]. Hepatitis B immunization of health care workers at occupational risk reduces transmission in the health care setting. It is estimated that 5% to 8% of individuals are poor responders to HBV vaccination[29], but the rate of non-responders among Canadian HCWs is unknown. Individuals at high risk of exposure will benefit from confirmation of immunologic response to HBV vaccination by a test for anti-HB surface antigen. In addition, there is a small number of reported hepatitis B infections that have been contracted from health care providers who are chronic hepatitis B carriers[30]. It has been estimated that the risk of hepatitis B infection contracted from a physician or dentist is in the order of 240-2,400 per 1 million procedures. The *Proceedings of the Consensus Conference on Infected Health Care Workers* were published in July 1998[31]. More than 70 recommendations were accepted at the meeting, including mandatory hepatitis B immunization

and testing for health care workers (supported by 70% of participants). However, responses from the Canadian Medical Association and the Canadian Dental Association indicate that there is still strong controversy concerning maintenance of individuals' rights[31]. All hospitals in Canada have a voluntary immunization and testing policy for hepatitis B. To date, there are no Canadian data on the number of patients who have contracted infections from health care workers.

HCV is now rarely transmitted by blood transfusion. During 1985-1990, cases of transfusion-associated non-A, non-B hepatitis declined by greater than 50% because of screening policies that excluded donors with HIV infection and donors with surrogate markers for non-A, non-B hepatitis[32]. By 1990, the risk of transfusion-associated HCV infection was approximately 1.5% per recipient or approximately 0.02% per unit transfused[33]. In May 1990, routine testing of donors for evidence of HCV infection was initiated, and in July 1992 more sensitive multi-antigen testing was implemented, which further reduced the risk of infection to 0.001% per unit transfused[34]. Albumin or immune serum globulins have not been associated with viral transmission in Canada.

Approximately 30% of transfused patients are unaware that they have undergone transfusion of blood products. In one study, only 6.3% of patients transfused before 1990 had undergone testing for hepatitis C[35]. Notification programs have had success in convincing patients to undergo testing for HIV and HCV.

Several prevention strategies have been successful in decreasing the incidence of new hepatitis C infections. Blood screening and perhaps needle exchange programs have helped in reducing the rates of infection. Unfortunately, little improvement has been made in postexposure prophylaxis. The use of interferon alpha early during exposure is controversial, and there is no consensus recommendation. At present, the only licensed treatment for hepatitis C is interferon alpha and ribavirin, which are given as combination therapy[36]. Efforts are now directed to developing more effective antiviral agents for treatment. High affinity antibodies could be used in the future after liver transplantation of hepatitis C positive recipients. A vaccine is not likely to be available in the short term because of the inherent difficulty of developing a protective response to a virus with a rapid mutation rate and multiple genotypes.

Few HIV seroprevalence studies of HCWs have been published. These studies are important, because they may assist in estimating the extent of occupational risk of HIV infection. In one survey of HIV seroprevalence among 3,420 surgeons, 87.4% reported a blood-skin contact and 39.2% reported a percutaneous blood contact in the previous month, but none was positive for HIV antibody[37]. Extensive reviews and postexposure guidelines have been published recently[31,38-44].

The combined administration of three antiviral drugs is recommended in cases of high risk exposure when the HCW has been exposed to a large volume of blood, a source patient with high HIV viral titre, or a patient suspected of having a multi-drug resistant HIV strain[42].

Nucleic acid testing (NAT) has been used to screen for blood or blood products potentially contaminated with HIV or HCV. The advantage of this method is that it can detect viral infections during the window period (from when a donor's blood is capable of transmitting HIV until detectable antibody appears). It is difficult, however, to assess the impact of NAT on the safety of the blood supply. The incidence of HIV and HCV associated with transfusion is already extremely low. The estimated risk of HIV infection per blood unit in Canada is 1 in 913,000[44]. In a recent review, Leparc found two donations in the U.S. that were reactive by HCV-NAT and one by HIV-NAT that were not detected by serologic tests. Since several blood components are prepared from each blood donation, the number of preventable transmissions may represent 2 to 3 times the number of rejected donations[45]. Therefore, the impact of NAT testing may be assessed from the rate of rejected donations, rather than through serology studies of blood recipients. In addition, it is difficult to determine the rate of infection transmission after a transfusion because of the short shelf life of some of the blood products, such as platelets, which could be transfused before results are available.

Since viremia precedes seroconversion by several days in the case of HIV and several weeks for HCV, tests that detect viral nucleic acids are considered a significant technologic advance and an additional step in our quest to achieve the goal of zero risk for blood transfusion recipients.

Currently, two test systems are being used by about 20 testing sites that test all blood collected in the U.S.: a combined HIV-1/HCV RNA in a single tube in a multiplex format (Genprobe/Chiron) and a single-probe system for HCV (Roche).

In Canada, HCV NAT was implemented first because it has a bigger impact on safety. Mathematical models indicate that NAT for HCV would detect an additional 4-6 cases of HCV a year in Canada, whereas NAT for HIV is predicted to detect 1 additional case of HIV every 18-24 months. (This is because the window period is significantly longer for HCV than HIV, and the reduction of this window period by NAT has a much greater impact on HCV detection). There are no data suggesting that human T-cell lymphotropic virus (HTLV) type

II or I is transmitted in the health care setting, and the seroprevalence rates in the population are extremely low. A recent survey of transfused patients found no cases of HTLV infection in 5,939 recipients[46].

## Potential bloodborne infective agents

### *Herpesviruses*

Transmission of human herpesvirus 6 (HHV-6), HHV-7, Epstein-Barr virus (EBV), cytmomegalovirus (CMV), and other herpesviruses, such as HHV-8, require close contact between mucous membranes and direct inoculation of mucous membranes with fresh secretions. The viruses are found in genital secretions and blood. Removal of lymphocytes may decrease the transmission of CMV through blood transfusion and likely also EBV and HHV-8, as these are also cell-associated viruses[47-49]. HHV-8 is associated with Kaposi's sarcoma in 80% of cases. Its prevalence (0%-20%) varies, depending on the country[50]. Kaposi's sarcoma has never been reported after blood transfusion. Viral DNA searches based on polymerase chain reaction (PCR) have yielded negative results for HHV-8 in 19 poly-transfused subjects. Continual monitoring is required for recipients at risk (e.g. those who are immunosuppressed). The practice of lymphocyte removal from blood products has decreased the risk of transmission of CMV, and it may likely also decrease the risk of transmission for other pathogens in susceptible populations[51,52].

### *Parvovirus*

In Canada, the rate of parvovirus infection among adults is around 40%. Most infections occur in childhood between the ages of 4 and 12. The spectrum of parvovirus disease varies widely. The most distinctive presentation is that of fifth disease or erythema infectiosum, which is characterized by a rash mainly in the cheeks. Parvovirus can also cause arthritis, a frequent presentation when the infection occurs in adult women. Patients with an underlying hemoglobinopathy or immunodeficiency may have severe anemia during parvovirus infections. In addition, transplacental spread of infection may result in intrauterine infection and the onset of hydrops fetalis. Parvovirus is an infrequent cause of infection transmitted during blood transfusions[53-56].

### *Hepatitis G*

Hepatitis G virus (HGV), also known as GB virus C (~9,392 nucleotides), is a newly discovered flavivirus that is transmissible by blood transfusion and other possible routes. It has been detected in 2%-4% of blood donors[57]. Hepatitis G virus is not an accurate name for this bloodborne agent, as it is not a cause of hepatitis[58]. Ten percent of patients with chronic non-A-E hepatitis are HGV RNA positive. The incidence of HGV infection is higher than expected from PCR studies, and HGV has a high prevalence in the world. Among 220 cases of needle-stick injuries, 21 employees were contaminated with HGV[59]. Initially, none of the 21 recipients was HGV positive. Fourteen of them were followed up and further tested for HGV RNA and serum anti-envelope (E2) specific antibody. None of the 21 recipients exposed to HGV developed liver function abnormalities, but one of the 14 recipients who were followed up became positive for HGV RNA after the injury[59].

### *TTV*

Transfusion transmitted virus (TTV) is a novel family of parvo-like non-enveloped DNA viruses recently classified in the family *Circinovidae*[60]. TTV is an agent in search of a disease association. Its prevalence varies from 2% to 80%, and although infections are found in the general population they are more common in patients who have received multiple transfusions with blood products. TTV was found in approximately 10% of U.S. volunteer blood donors, 13% of commercial blood donors, and 17% of intravenous drug abusers. As well, the rate of TTV infection among non-A, non-E hepatitis patients in the U.S. was only 2%[61]. There are no published studies of TTV prevalence in Canadian populations.

### *SEN-V*

Discovered in 1999, SEN-V is a single-stranded DNA virus without an envelope. As with TTV, it is highly variable in nucleic acid sequence and comprises at least eight viral subtypes or genotypes. It is approximately 3,340 base pairs in length and contains at least three open reading frames (ORFs) that code for one protein each[62]. None of the SEN-V ORF sequences hybridizes specifically to that of TTV.

Some strains of this virus are reportedly associated with acute and chronic hepatitis. Between 80% and 90% of viral hepatitis cases are caused by hepatitis viruses A, B, C, D, and E; up to 20% are caused by unknown agents, hence, the acronym non-A non-E hepatitis, or NANE. Because SEN-V is present in 80% of such cases, it is believed to play a role in these illnesses. Although the presence of the virus does not imply that it causes illness, some scientists are optimistic that they

have found a cause of hepatitis that had previously gone unnoticed. Before the discovery of SEN-V, TTV had been a promising candidate for NANE causation because it was present in a large proportion (55%) of NANE patients. It was later shown, however, that TTV is also present in a relatively large proportion (5%-7%) of healthy donors[63,64].

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