ISSN : 0974 - 7532 Volume 6 Issue 1

Trade Science Inc.

Research & Reviews in

BioSciences

Review

RRBS, 6(1), 2012 [22-34]

Infectious disease associated with blood donation

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Received: 27th December, 2011 ; Accepted: 13th January, 2012

ABSTRACT

Blood transfusion is a vitally important practice for emergency and sustaining health care administration. However blood donation incurs risk of infectious disease transmission that is not insignificant. Increased risks to hepatitis B, hepatitis C, HIV and other microbial infections is measurable. It is estimated that up to 10% of worldwide HIV infections is due to transfusion of contaminated blood and blood products. Effective screening methods for blood donors is vital is order to avoid transmission of disease. Laboratory methods for screening include enzyme immunoassays, chemiluminescent immunoassays, nucleic acid amplification assays, and particle agglutination assays. Incidents have been reported where donors not identified as HIV positive at time of donation but with high risk activity did indeed transmit HIV to blood product recipients. Hemolytic transfusion reactions are also a source of transfusion fatalities. The microbes Babesia microti and Escherichia coli have been associated with fatal transfusion outcome from recipients receiving red blood cells and pooled platelets, respectively. Other emerging pathogens in blood banks include hepatitis E, erythrovirus B19, and plasmodium. Previous studies have shown that Babesia microti and Escherichia coli accounts for 31% and 20% of transfusion fatalities that are due to microbial infection. Studies have revealed that donors having same sex activity entail additional risks of disease transmission which includes HIV, hepatitis A, hepatitis B, hepatitis C, and other infectious diseases. A small titer of Creutzfeldt-Jakob prion is still able to present a disease risk in blood transfusion. Calls for elevated blood screening methodologies in Caribbean nations to curtail prolific hepatitis C virus transmission by blood donation has been determined to be vital. Other disease conditions occurring by blood transfusion are discussed.

KEYWORDS

Transfusion;
HIV;
Needle stick;
Blood.

SCREENING TECHNIQUES

Blood transfusions are a vital practice for healthcare practice and facilities. Donor selection is of the utmost importance so that transfusion-transmissible infections (TTIs) are avoided. It is crucial to minimize the number of inappropriate blood transfusions so that risks of TTIs and adverse reactions are avoided. Correct blood grouping and compatibility of donor to recipient is implicit in the administration of screening blood, this being

the concept of good laboratory practice. Other factors that influence the safety of transfusable blood include[1]: 1) Lack of safe donors; 2) Lack of safe donations; 3) Lack of screening; and 4) Blood used inappropriately.

World wide there are up to 4 million blood donations which are not evaluated for HIV or hepatitis B virus (HBV), with few being tested for hepatitis C virus (HCV). Blood substitutes such as colloids and crystalloids are thought not to transmit infections, they are cheaper than whole blood, and therefore have significant advantages.

Various analytical methodologies are applied as screening assays, each having limitations that must be understood to ensure effectiveness of screening. The main types of screening include the following[1]: 1) Immunoassays (enzyme immunoassays (EIAs), chemiluminescent immunoassays (CLIAs), haemagglutination, and rapid tests); and 2) Nucleic acid amplification technology or NAT assays. Large number of samples can be screened by use of EIAs and CLIAs, either manually or by an automated assay processing systems. Advantages of rapid tests are simplicity, results obtained within minutes, have disposable nature, they are discrete, and can be applied to be individual. However as disadvantages, the reading and interpretation of rapid tests can be subjective with no ability for permanent record keeping. NAT screening detects the presence of viral nucleic acid which can be either RNA or DNA, or even simultaneously. NAT type tests can be applied for the simultaneous detection of multiple viruses[1].

Currently the American Red Cross utilizes tests for multiple infectious diseases and steadfastly upgrades to more sensitive technologies when possible. Methods for screening potentially harmful infection includes[2, 3]: 1) Chagas disease; 2) Hepatitis B virus; 3) Hepatitis C virus; 4) HIV types 1 and 2; 5) Human T-lymphotropic virus; 6) Syphilis; and 7) West Nile Virus.

Analysis for cytomegalovirus (CMV) is not a routine assay screening for blood donation[1]. However the prevalence of the CMV antibody ranges from 50% to 80% of whole population. Blood donated that is contaminated with CMV can cause serious problems in neonates and immunocompromised patients.

Beside viruses such as HHV-8, erythrovirus B19, and hepatitis A, emerging arbovirus diseases such as West Nile virus, dengue, and chikungunya[2] that threaten to occur in the French metropolitan areas following the implantation in Europe of the mosquito Aedes albopictus, also threaten the blood donation paradigm. Unique blood-linked risks gaining prominance, notably in United Kingdom and France, is the prion agent responsible for the variant form of the Creutzfeldt-Jakob disease[2]. Toxoplasmosis is a protozoan infection that causing similar symptoms to infectious mononucleosis (with immuno-compromised patients this infection can induce serious neurological symptoms and may cause fetal death in pregnant women). Other agents the fall into the broad definition of emerging blood-transmitted infections, including Plasmodium spp. (Malaria transfusion-transmitted cases is steadily increasing as donors travel to high risk malaria areas should be deferred from donating blood for six months), parvovirus B19, and prions that cause variant Creutzfeld-Jacob disease (vCJD)[3].

NEEDLE STICK INJURIES

A percutaneous piercing wound (needle stick injury) by needle point or other sharp object is an occupational hazard within the medical community and is associated with blood donation utilizing hypodermic needles. There are significant risks in these events for the transmission of hepatitis B, hepatitis C, and HIV. The risks include the patient if the health care worker is infected. It is believed that 3.5 million individuals are affected by this occupational hazard worldwide[4], with nurses and physicians especially at risk[4]. The infectiousness of hepatitis C virus and HIV decrease over a period of 2 hours, however hepatitis B virus infectiousness remains for more than seven days and even after desiccation[5].

A needle stick injury does have the capability to transfer protozoa, bacteria, viruses, as well as prions[6]. From needle stick events the seroconversion to HIV, hepatitis C, and hepatitis B, are 0.3%, 1.8%, and 31%, respectively (see Figure 1). Clearly the greatest threat for infection among these three is hepatitis B. The actual risk of being infected with HIV from a single prick with a needle that has been used on an HIV-infected person is thought to be about 1 in 150, however the outcome depends on the nature of the injury (ie. Depth of penetration and amount of blood contained on

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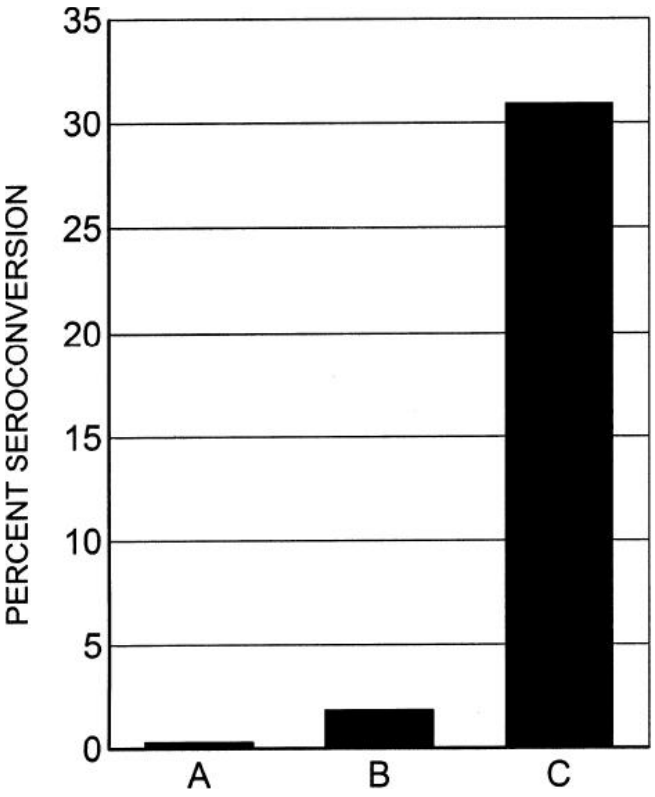

Figure 1 : Needle stick events can induce seroconversion to HIV, hepatitis C, and hepatitis B. These rates are: (A) 0.3%; (B) 1.8%; and (C) 31%, respectively.

needle). Post-exposure prophylaxis with anti-HIV drugs such as zidovudine has been found to reduce this risk[7, 8].

The risk of HIV infection following needle stick event is associated with viral load and increases as the volume of blood carried increases, accordingly with increased titer of HIV within the source blood[7]. Factors that increase the risk of HIV seroconversion include the following[8]: 1) Visible blood on the needle; 2) Increased depth of puncture incision; 3) Needle applied in vein or artery of patient; 4) The source patient being terminal HIV. Speed of action is crucial following a needle stick event. It has been determined that the hepatitis B virus vaccine is effective, as well as prophylaxis with anti-HIV drug zidovudine[8]. There is evidence of increased risk in cases where larger volumes of blood from the source patient occurs or high titer is present[9]. As of the year 2000 a successful approach for prophylaxis treatment for this occupational derived exposure to HIV utilized three drugs that included two nucleoside analogues (such as zidovudine and lamivudine) with a protease inhibitor (indinavir)[9]. However, there is minimal data concerning the long term effects of this triple therapy on the body. Previous studies have observed that hepatitis C virus is transferred through needle stick injury, resulting in symptoms that include dry cough, headaches, nausea, myalgia, and fever[10]. Hepatitis B incurs the greatest risk of infection.

Needle stick injuries are a substantial problem for many areas of health care operations. The drawing of blood during blood donation operations presents a significant opportunity for job related infection. Over 50% of health care workers in Khartoum, Sudan, utilizing needles or sharp objects as part of their function reported needle stick or sharp injuries[11]. In Alexandria, Egypt, it is reported that 67.9% of care workers in a teaching hospital suffered at least one needle stick injury in 12 months and high risk patients (having history of HIV, HBV, HCV) were involved in 8.2% of those incidents[12]. Studies in Indonesia found that in 2005 there were 1445 infections of HBV, 399 with HCV, and 18 with HIV in health care workers of which 44%, 47%, and 11%, respectively, were due to sharps injuries[13]. Vaccinations for HBV and access to HIV-post-exposure prophylaxis were found to be of utmost importance in a German University Hospital[14]. The significant hazard of sharps and needle stick injuries, particularly in blood handling scenarios, exposes the health care worker to risk of infection by serious disease and steadfast training and fast reaction are paramount in effective management of this vector of infection[15, 16, 17].

FATALITIES FOLLOWING BLOOD COLLECTION AND TRANSFUSION

Up to 3000 platelet units were found to be contaminated with bacteria, these among almost 9 million platelet units transfused within the United States in 2004[18]. Because fatal bacterial sepsis can result from contamination, authorities have insisted that health care providers be able to diagnose transfusion associated infections. Transfusion associated bacterial sepsis is the second most common cause of transfusion related fatalities and accounts for 46% of transfusion fatalities (in the United States) from the time period 1990 to 1998[18]. Life threatening sepsis with immediate fatal outcome results in one in total of 500,000 recipients of this blood product, and this conclusion is believed to be

underreported[18]. Platelets are particularly vulnerable to bacterial infections due to their storage at room temperature for five days.

The most common bacterial contaminants of platelet units are also those found on the skin and are Gram-positive bacteria (ie. Staphylococcus species)[18]. Also determined to be contaminants, albeit to a lesser extent, are Gram-negative bacteria such as Serratia, Enterobacter, and Salmonella species. However these Gram-negative bacteria account for much more severe and fatal infections[18].

Two fatalities post transfusion were reported to the United States FDA (Food and Drug Administration) in the year 2010, in which Babesia microti was involved and associated with RBC transfusion[19, 20], and Escherichia coli which was associated with transfusion of platelets[19, 20]. Infection by Babesia microti accounted for 31% of reported deaths due to microbial infection (for years 2004 to 2010), with Staphylococcus aureus accounting for 20% of the fatalities. The trend for reported fatalities due to bacterial infection that are reported to the FDA have been generally decreasing (see Figure 2).

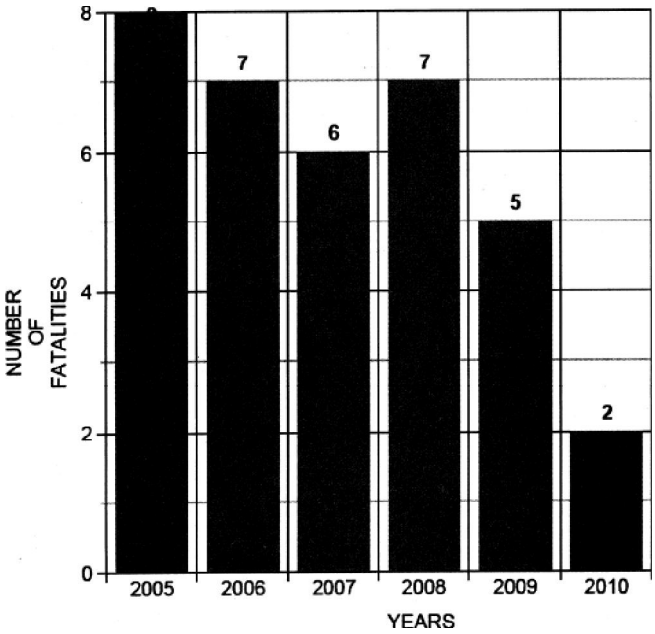

Figure 2 : Microbial infection causing fatalities post transfusion event by year.

Babesiosis is an intraerythrocytic parasitic infection caused from the bite of the infected Ixodes tick. Babesiosis significantly affects the hematological system, causing hemolytic anemia, thrombocytopenia, and atypical lymphocyte formation[19]. The parasite only infects red blood cells, in which it alters the cell membranes causing decreased conformability, but increased red cell adherence. The red cell adherence anomaly may lead to acute respiratory distress syndrome (ARDS). Babesia parasites actually invade and do survive within erythrocytes. Babesiosis parasites remain viable even under Blood bank storage conditions. However transfusion transmitted Babesia microti can be significant in the cause of transfusion associated morbidity and mortality, particularly among infants, elderly, and asplenic blood recipients[19]. Infections of the intraerythrocytic parasites of the genus Babesia can occur with high levels of regional proximity, when transfusion of blood products is a determinant[20]. There is a reported increase in transfusion related infections of Babesia microti where the parasite is endemic, such as in Connecticut, U.S.A.[21]. In that study it was found that 0.9% of 3490 bood donations were confirmed seropositive for Babesia microti, with the majority of those cases coming from areas that are endemic in Babesia microti. Babesia microti is usually transmitted by tick bite and endemic to the North Eastern and upper Midwestern United States, however a fatal case of this parasite has been documented in Delaware, resulting in the detection of a very high titer blood donor as the potential source[22].

Although endemic to Latin America, Chagas disease or American human trypanosomiasis (caused by Trypanosoma cruzi), is a parasitic disease that is potentially fatal is becoming a significant problem in non-endemic regions of the world, in consideration of blood donations, and is increasing in incidence due to immigration rates[23]. Chagas disease is essentially a parasitic infection that is similar to Lyme disease by some characteristics and it is able to cause substantial destruction of the heart and digestive tract if it progresses to the chronic stage and is a leading cause of chronic heart disease in areas where it is endemic. Immigration is increasing the number of incidence within the United States with as many as 100,000 people living in the United States potentially infected and the majority of infected individuals not showing symptoms[24, 25]. This disease is well documented as a transfusion associated disease, as a result, the American Red Cross screens for Chagas disease.

Previous investigations have shown that the use of

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questionnaires to exclude donors at higher risk for HIV infection and the use of highly sensitive laboratory screening tests to identify infected blood donations has greatly reduced transfusion associated HIV infections[26]. Also documented is the increased incidents of HIV infection post transfusion occurring from false reporting of high risk behavior by the donor during the questionnaire procedure[26]. Although HIV infection by blood donation is extremely low in the United States, still the transfusion should be considered along with other possible sources of HIV infection when observed in a patient who has no other HIV risk factors. In addition the number of HIV transfusion associated infections may be underreported due to various reasons[26]: 1) Recipient death attributed to the underlying condition or some other cause before detection of HIV infection from the receipt of infected blood or blood components, 2) Poor recall by infected persons regarding receipt of blood or blood components before their HIV diagnosis, 3) Inability to confirm or rule out transfusion as the source of infection because no HIV-infected donors were identified, 4) Under recognition of HIV infections among recipients of potentially infected blood or blood components who recover and might never have been subsequently tested for HIV infection, or 5) Misclassification of a transfusion-transmitted HIV infection in a person who also had other risk factors more frequently associated with HIV transmission (e.g., male-to-male sexual contact or injection drug use) to which that infection was attributed.

BLOOD DONATION AND SEXUAL TRANSMITTED DISEASE

Females having HIV infection have been shown to have a great prevalence of cervical human papillomavirus (HPV) infection and cervical cancer[27]. Both HIV and HPV are sexually transmitted, the HIV-associated immunosuppression is believed to contribute to reactivation of preexisting HPV infection and incur a predisposition of patients to high grade squamous intraepithelial lesions[28]. It has been known that DNA of HPV can be found in peripheral blood mononuclear cells (PBMCs)[29] as well as sera or plasma[30, 31]. Continuing in this study the investigators found in a subpopulation of eight patients, seven patients acquired HIV from transfusion, finding that the HPV genome was detected in PBMC of all individuals thus substantiating the assertion that PBMCs could act as HPV carriers and could spread this virus through blood and consequently blood harvested for medical application[29].

Human herpes virus-8 (HHV-8) is the pathological agent associated with the development of AIDS-related, iatrogenic, and endemic Kaposi's sarcoma[30, 31]. Evidence supports the contention that HHV-8 may be transmitted through sexual contact[32], saliva[33], and blood transfusion[34, 35]. In the United States, where the seroprevalence of HHV-8 is low (<10%), HHV-8 is spread by the sexual route, at least among homosexual men[32]. In addition, HHV-8 infection has been observed in patients who received non-leukocyte-reduced blood[34]. Infectious viruses or viral DNA has been identified from blood donors in the United States as well as Africa[36, 37]. In addition, HHV-8 infection has been observed in patients receiving blood transfusions in Uganda, thereby indicating blood-borne transmission of HHV-8[38, 39].

Altogether it is essential that risk assessment for HHV-8 and the potential for transmission by blood transfusion is pursued[35].

Syphilis has become a major health problem for public health worldwide[40, 41, 42], and there is increasing evidence that this disease is widespread in Africa[43]. A significant route of syphilis infection is by blood transfusion[44]. Other studies performed in numerous African nations show an indication of a high incidence of blood-borne pathogens, including syphilis, found among health blood donors[45]. The overall assertion of these studies is the vital need for the continued screening of blood donors for antibodies revealing syphilis infection.

A 3.5-year study, covering a period from October 2002 to April 2006 was conducted at the blood transfusion centre of Maharaja Agrasen Medical College, Agroha (Hisar) Haryana. A grand total of 5849 donors were tested, and showed that the seroprevalence of HIV was 0.3% in the donors. However the seroprevalence of HBV, HCV and syphilis was 1.7%, 1.0%, and 0.9%, respectively, in the total number of donors. The seroprevalence of hepatitis and syphilis was found more in replacement donors as compared to the total number of voluntary donors. The overall low seropositive findings among donors is attributed to the

pre-donation counseling in donor selection[46].

Infection with hepatitis G virus-HGV, (a virus of the Flaviviridae family and a RNA virus) is primarily by blood borne vector and accounts for up to 0.3% of acute viral hepatitis within the United States. HGV is found in up to 15% in West African children, and up to 2% of blood donors will test positive in many countries. HGV is transmitted by the same routes as HCV (hepatitis C virus)[47] and co-infection by these two virus is common. The majority of individuals infected with HGV by blood transfusion route do not develop serious chronic hepatitis. However transfusion-transmissible infectious agents such as human immunodeficiency virus, hepatitis B virus, hepatitis C virus, and syphilis are considered among the greatest threats to blood safety for the recipient[47]. A study conducted among blood donors at Gondar University Teaching Hospital, in Northwest Ethiopia, covering the period between January 2003 and December 2007, from a total of 6361 consecutive blood donors showed an overall seroprevalence of HIV, HBV, HCV and syphilis as 3.8%, 4.7%, 0.7%, and 1.3% respectively[47]. Among those with multiple infections, the most common combinations were HIV-syphilis 19 (38%) and HIV-HBV 17 (34%). The seropositive rate of HIV was significantly increased among female blood donors, first time donors, housewives, merchants, soldiers, drivers and construction workers[47].

Previous studies have found that a substantial percentage of the blood donors harbor HIV, HBV, HCV, and syphilis infections however hepatitis C virus is the agent responsible for most blood borne non-A and non-B hepatitis cases[47].

Only continuous improvement and implementation of donor selection, sensitive screening tests, and effective inactivation methodologies will ensure the elimination, or reduction of the risk of acquiring TTIs[48]. Unsafe transfusion practices can also put millions of people at risk of transfusion-transmissible infections[49]. In a study among blood donors in Kathmandu, Nepal it was found that there existed a seroprevalence of HIV, HBV (HBsAg), HCV and syphilis observed at a rate to be 0.12%, 0.47%, 0.64%, and 0.48%, respectively. TTIs were dominant among the male blood donors compared to the female blood donors and higher HCV seroprevalence was found among males compared to females[49].

In a study conducted in the United States covering 1995 to 2000, it was estimated that, over the 6 years, approximately 1200 cases of early syphilis were detected nationally through donation screening, of with 58% of the case subjects were volunteer donors[50]. However, 81% of volunteer donors and 64% of paid donors reported no risk factors for syphilis[50]. In 2000, 69 cases of early syphilis were identified through donation screening in 16 states[50]. In the 6 states that reported 53 of these cases, 31 case subjects (58%) were volunteer donors and 22 (42%) were paid donors[50].

In 2009, a study conducted by the Center for Disease Control and Prevention (CDC) in 40 states and 5 dependent areas of the United States, presented results for transmission category in the diagnoses of HIV infection among adults and adolescent males, to be 74.2% was by male to male sexual contact, with the

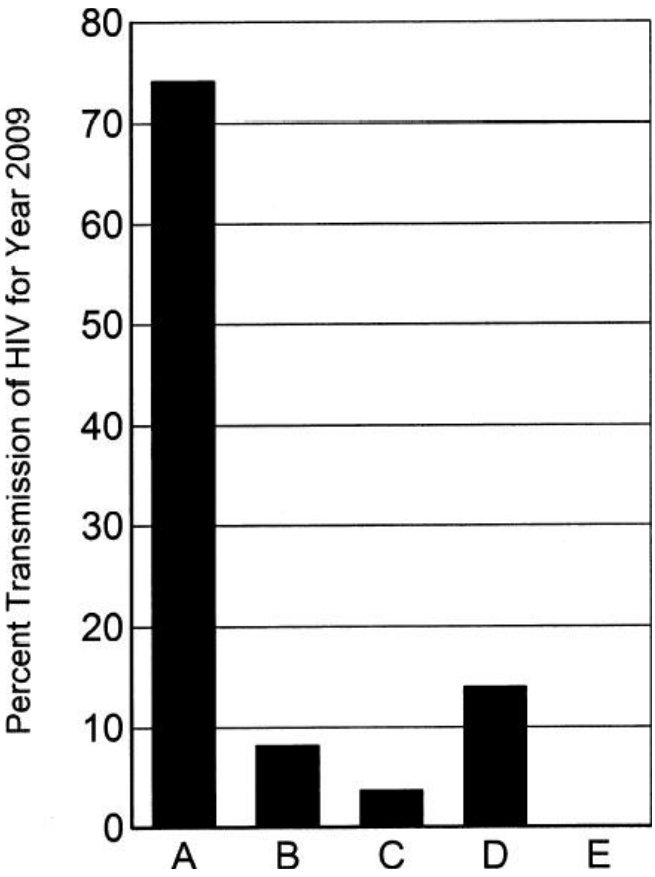

Figure 3 : Percent transmission of HIV for year 2009 by event. Mode of transmission: (A) Male to male sexual contact; (B) Drug injection; (C) Male to male sexual contact and drug injection; (D) Heterosexual sexual contact; and (E) Transfusion, hemophilia, perinatal.

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remaining transmitted by means including injection drug use, male to male sexual contact and injection drug use, heterosexual contact, and miscellaneous (see Figure 3).

Analysis by the Food and Drug Administration of the United States (Department of Health & Human Services year 2011) asserted that the collection of blood from persons having an increased risk of HIV infection also presents an added risk for transfusion directed blood products that were accidentally given to a patient in error either before testing is completed or following a positive test. It is ascertained that such medical errors occur rarely, however because there are over 20 million transfusions provided every year within the USA, these instances can occur. Scientific models have shown there would be a small but definite increased risk to people who receive blood transfusions if policies concerning male to male sex policies were altered with the consequence that preventable transfusion transmission of HIV could occur. Men who have had sex with men (MSM) are the largest single group of blood donors who are found HIV positive by blood donor testing. MSM also have an increased risk of having other infections that can be transmitted to others by blood transfusion. Infection with the HBV is approximately 5 to 6 times more common and Hepatitis C virus infections are about 2 times more common in men who have sex with other men than in the general population. Other studies covered this issue of blood donation screening involving male to male sexual activity[51, 52].

Individuals who are men that have sex with men comprise an estimated 2% of the population of the United States greater than 12 years of age and are 59% of persons to be diagnosed with HIV as of 2009[53]. Aging lesbian, gay, and bisexual adults (ages 50-70) document that they have higher rates of several serious chronic physical and mental health conditions compared to similar heterosexual adults[54]. Previous studies have shown that HCV incidence had increased among HIV-infected MSM from the mid-1990s in Europe[55]. The seroconversions of HIV and syphilis in a cohort study of MSM in Beijing, China were considered very serious, that the associated factors for seroconversions were rectal douching after homosexual anal intercourse commensurate with meeting male sex partners in parks, public washrooms or bathhouses[56]. An investigation concerning an outbreak of hepatitis A that evolved in Northern Ireland between October 2008 and July 2009, and against a backdrop of a large concurrent hepatitis A outbreaks in various parts of Europe inclusive of thirty-eight cases defined as outbreak cases; 36 were males with a median age of 29 years and of the 28 males whose sexual orientation was known, 26 were men who have sex with men[57]. Sexual health of gay, bisexual, and other MSM within the United States is not improving despite substantial advances[58]. Instead of improving, HIV and sexually transmitted infections remain disproportionately high among MSM and have been increasing for almost two decades[58]. Sexual transmitted infections (STI) transmission among HIV-positive men have contributed substantially to increasing trends in STIs seen among MSM in Western Europe and since 1996[59]. These findings highlight the need for safer sex messages highlighting the implications of STI coinfection[59].

EPIDEMIOLOGY IN NORTH AMERICA

Annually within the United States there are estimated 56,000 new cases of HIV infections (with approximately 1.1 million individuals living with HIV)[60]. In 2008 of all individuals diagnosed with HIV in the U.S., 32% were also diagnosed with AIDS within 12 months of identification of the infection[60]. Of these diagnosed infections, 72% of the individuals received medical care with 4 months of diagnosis[60].

Within 1 year of the initial report which was made in 1981, of a deadly new disease that occurred predominantly in previously healthy persons and manifested by *Pneumocystis carinii* pneumonia with Kaposi's sarcoma, the disease had a name: acquired immune deficiency syndrome (AIDS). Within 2 years, the causative agent had been identified: human immunodeficiency virus (HIV)[61]. HIV infection is notifiable in all 50 states and the District of Columbia (DC) within the U.S.; with AIDS is now notifiable as stage 3 HIV infection[61]. It was determined that in 2008 within the U.S. there were 236,400 HIV cases whose infection were undiagnosed[61]. This reality accents the profound need for filtering methods of donation including questionnaire and accurate post donation assay tests for detection of infected units of blood products.

Other investigators have shown that the decrease

in transfusion transmitted HIV and HCV rates, when combined with the previously documented lower rates of infection in first-time donors compared with the general population, suggests the continued benefit of behavioral risk factor screening[62]. A study accomplished in Canada showed that with exception for hepatitis B virus, the transmissible-disease rates by transfusion of the other evaluated viruses decreased over the study period (1990 to 2000), however with less of a decrease for HTLV[63].

EMERGENT BLOOD TRANSFUSION AGENTS

Infectious agents, including viruses, bacteria, and parasites, can be transmitted by human blood products[64]. The variety of blood-borne infectious agents which are transmitted through transfusion of infected blood, donated by apparently healthy and asymptomatic blood donors, are problematic for safe and dependable supplies. The diverse infectious agents which include hepatitis B virus, hepatitis C virus, hepatitis A, hepatitis G, human immunodeficiency viruses (HIV-1/2), human T-cell lymphotropic viruses (HTLV-I/II), Cytomegalovirus, Parvovirus B19, West Nile Virus, Dengue virus, trypanosomiasis, malaria, Chikungunya, and variant CJD[64, 65], are dangerous and require meticulous effort to detect and eliminate. The emergence of a new form of the Creutzfeldt-Jakob disease (nvCJD) introduces a new series of questions about the safety of blood products[66].

Donor ignorance or confusion of disease symptoms makes problematic risk identification through questionnaires concerning inquiry of health history. Unusual cases of sexually transmitted disease may make ineffective the identification of disease conditions, for example the incidence of anorectal syphilis has been mistaken for Crohn's disease[67].

Human herpesvirus 8 (HHV-8), or Kaposi sarcoma–associated herpesvirus, is associated with malignant disorders such as Kaposi sarcoma, primary effusion lymphoma, and multicentric Castleman disease[68]. Although HHV-8 does not necessarily cause life-threatening infection in healthy persons, it causes more severe infection in those who are immunocompromised, such as organ recipients and HIV-infected persons. Identification of infectious virus in lymphocytes from a healthy blood donors and evidence that HHV-8 might be transmitted by blood has raised concern about the safety of the blood supply[68]. Human herpes virus 6 (HHV-6) is found worldwide and is found in the saliva of the majority of adults (>90%). It replicates in B and T lymphocytes and can set up a latent infection in T cells which can later be activated when the cells are stimulated to divide[69]. HHV-6 has been associated with a number of neurological disorders, including encephalitis and seizures. It has been postulated to play a role in multiple sclerosis and chronic fatigue immunodeficiency syndrome. The presence of HHV-6 in B and T lymphocytes raises concern for the safety of the blood supply and transmission through defiled blood units.

West Nile virus (WNV) is a virus of the family Flaviviridae and is a significant problem in blood donation safety. West Nile Virus is most commonly spread by mosquito bites and is a flavivirus that is common in West Asia, Africa, and the Middle East. West Nile Virus appeared in the United States in 1999 along with reports that the virus can be transmitted by blood and organ exposures. West Nile virus has been shown to be transmitted through granulocytes (a category of white blood cells characterized by the presence of granules in their cytoplasm) transfusion[70]. West Nile Virus appeared in the United States in 1999 along with reports that the virus can be transmitted by blood and organ exposures. From June 2003 through 2008, the American Red Cross determined that 821 of donors in the U.S. were subsequently confirmed to have West Nile virus infections in blood[71]. Nucleic acid amplification testing led to the identification of 519 donors who were positive for West Nile virus RNA and the removal of more than 1000 potentially infectious related components from the blood supply of the Red Cross[72].

Screening of the blood supply has not been implemented consistently in developing countries[73]. An estimated 5% to 10% of all HIV transmissions in these countries remains attributable to blood transfusions[73]. This situation is further aggravated by problems recruiting and retaining safe donors, a lack of essential laboratory services for blood banking and screening, the nonavailability of rapid tests, inadequate supervision of personnel, and widespread need for blood transfusions for malaria-related severe anemia[73]. For sub-Saharan

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Africa, transfusions alone would be responsible for 28,595 HBV infections, 16,625 HCV infections, and 6650 HIV infections every year, however sensitivity analysis suggests that the true risks may be even higher[74]. Studies confirm the blood donor recruitment and coverage of screening for transfusion-transmitted infections, especially HCV, must be improved in the Caribbean countries[75].

HEPATITIS E, HTLV, ERYTHROVIRUS B19, XMRV, AND LEISHMANIASIS

Hepatitis E virus (HEV) infection commonly occurs through fecal-oral transmission, placement of infected object in mouth[76], and through plasma donation, but was effectively detected via reverse transcription-polymerase chain reaction in a study in India finding that 1.5% of 200 voluntary blood donors were infected[77]. In this same study, none of the HEV RNA-positive blood donors showed symptoms at the time of donation[76]. In a study conducted in 1999 in Spain showed 2.8% and 6.3% of 863 blood donors and 63 haemodialysis patients, respectively, had HEV infection[76].

As recently as 2011 a study in England demonstrated that HEV infection had an attack rate of 2.8% within donors[78]. In addition, a study conducted in Southwest England found that HEV IgG incidence was found in 16% of blood donors[79]. In Japan 2008, a single case of Hepatitis E transmitted by blood from a donor infected with HEV through zoonotic food-borne route was identified, raising concerns of prevalence in industrialized nations[80]. Additionally, a previous study in Japan (2004) suggested that a small but significant percentage of blood donors were potentially able to cause transfusion-associated hepatitis E[81]. An investigation conducted in Brazil found that 2.3% of 996 volunteer donors were seroprevalent for HEV infection and was able to trace a geographical region of origin to the city of Londrina, South Brazil[82]. Anti-HEV IgG was detected in 27 of 550 donors, a presence of 4.9%, in a study conducted in southwest Switzerland[83]. Serum samples collected from 95 unpaid blood donors and 96 haemodialysis patients in a 1998 Egyptian study found that 45.2% of blood donors and 39.6% of haemodialysis patients had prevalence of anti-HEV IgG[84]. Erythrovirus B19 (or parvovirus B19), an isocahedral non-enveloped virus that is ubiquitous infectious agent in industrialised countries has a wide range of disease manifestations from asymptomatic (the majority of victims) to severe, including persistent infection. The risk of erythrovirus B19 transmission by blood products is increased if a high virus titer exists in the infected donor, the pooling of many donations, and by its resistance to inactivation methods such as heat and solvent-detergent treatments[85]. To reduce the risk of B19 donor mediated transmission there are two mechanisms to consider: (1) reducing the viral load in the manufacture plasma pool by discarding B19-DNA-positive donations; and (2) developing new strong virus inactivation methods. However the physico-resistant properties of B19 make it a particularly troublesome entity for infecting blood products[86]. Utilizing real-time polymerase chain reaction for screening of parvovirus B19 DNA a detection level for viral load ranging from1.0 x 10(3) to 1.0 x 10(6) genome equivalents per 1 ml was accomplished in a study conducted within the Russian Federation[87]. Whereas in the United States, also utilizing real-time B19 DNA polymerase chain reaction, detection sensitivity of B19 DNA titers of at least 20 IU per mL was achieved, having a median DNA concentration of 105 IU per mL and an interquartile range of 42 to 481 IU per mL (the highest value was 1869 IU per mL)[88].

HTLV-I and HTLV-II are single-stranded RNA retroviruses of the C type found in humans in which infections occur worldwide[89]. The main source of transfusion-associated HTLV transmission is by cellular blood products, however fresh frozen plasma, cryoprecipitates, or coagulation factor concentrates do not appear to be a vector of infection (other routes of infection include needle/syringe sharing, sexual contact, and breast feeding)[89]. The HTLV provirus can survive in stored red blood cell concentrates up to 14 days[89]. Enzyme immunoassays (EIAs) are used primarily for blood donor screening in the United States (highly sensitive, efficient, and can be accomplished in 2 to 3 hours), however agglutination assays and the more cumbersome indirect immunofluorescence tests are widely used in Japan[89].

There have been conflicting findings reported by different laboratories concerning the significance of

Xenotropic murine leukemia virus (or XMRV), a gamma retrovirus, to blood donation risk[90]. Investigators have failed to detect XMRV in blood donors in studies conducted in China[90], the United States[91], and Africa[92]. The early phase of studies presented in 2011 showed inconclusive evidence as to the significance of XMRV prevalence in the blood supply[93].

Transfusion associated proliferation of Leishmaniasis is increasing continually[94], with this increase appearing to be associated with individuals who are also HIV positive. The transmission of Leishmaniasis by transfusion requires that the parasites be present in the peripheral blood of the donor, and survive the processing and storage process within the blood bank, before infection of the recipient[94]. Leishmaniasis is now found in over 90 countries and where it is endemic the population of infected individuals will be much higher and when the screening process for donors is less rigorous, then transfusion-associated Leishmaniasis is more common[94]. However, the too-expensive screening for Leishmaniasis contributes to the spread via blood donation[94].

CONCLUSIONS

Blood transfusions are a vital practice for healthcare practice and facilities. Donor selection is of the utmost importance so that transfusion-transmissible infections are avoided. World wide there are up to 4 million blood donations which are not evaluated for HIV or hepatitis B virus (HBV), with few being tested for hepatitis C virus. Blood donated that is contaminated with CMV can cause serious problems in neonates and immunocompromised patients. Transfusion associated proliferation of Leishmaniasis is increasing continually, with this increase appearing to be associated with individuals who are also HIV positive.

The risk of HIV infection following needle stick event increases as volume of blood increases, and accordingly with increased titer of HIV within the source blood. Syphilis has become a major health problem for public health worldwide and there is increasing evidence that this disease is widespread in Africa. A significant route of syphilis infection is by blood transfusion. The collection of blood from persons having an increased risk of HIV infection also presents an added risk for transfusion directed blood products that were accidentally given to a patient in error either before testing is completed or following a positive test.

Strict selection of blood donors and comprehensive screening of donors' blood using standard methods are highly recommended to ensure the safety of blood for recipient. Only continuous improvement and implementation of donor selection, sensitive screening tests, and effective inactivation methodologies will ensure the elimination, or reduction of the risk of acquiring TTIs.

ACKNOWLEDGEMENTS

This study was supported by the College of Arts and Science, University of Nebraska, Durham Science Center, Omaha, Nebraska 68182 USA.

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