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Implicating the Need for Serological Testing of Borna Disease Virus and Dengue Virus During Blood Transfusion

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1. Introduction

Blood is a vital component for the living being to be alive. The composition of blood is plasma and blood cells. It helps in transport of gaseous, metabolic products, hormones, nutrients and enzymes. It helps to regulate the body temperature and body fluid electrolyte. Blood transfusion becomes a vital part during blood loss, due to severe anemic condition and during major surgeries. Despite their critical use, blood transfusion becomes risky these days by the transmission of viruses.

2. Basic information about viruses and blood transfusion

The viruses are known for its replication and functional activities inside the cells. They usually need a system to be 'alive'. Outside the cells or any living tissue, the viruses are dormant. Virus can be transmitted by various ways to human beings. The virus like hepatitis virus and its subtypes A, B, C, D, E and G, human immunodeficiency virus types 1 and 2 (HIV-1/2), human T-cell lymphotropic virus types I and II (HTLV-I/II), cytomegalovirus (CMV), Epstein-Barr virus (EBV), TT virus (TTV), human herpes virus type 6 (HHV-6), SEN virus (SEN-V), human parvovirus (HPV-B19) and West Nile Virus (WNV) has already been diagnosed and researched for its potential to cause disease via blood transfusion (Table 1). The viruses namely, Japanese encephalitis virus, WNV, Chikungunya virus, HIV, HHV, HTLV and rabies are even capable of entering into central nervous system through blood (Kristensson, 2011). However, some viruses are neither studied for their transmission through blood; because of little evidence to support their transmission and, even in some viruses the mode of transmission is not known. We would like to give more priority to Borna disease virus and Dengue virus, which has been less studied in terms of transmission and blood transfusion.

Virus	Mode of transfusion	Disease due to transmission
HBV, HCV, HIV-1/-2, HTLV-I/-II	Highly established	Yes
CMV, EBV, HAV, HPV-B19, HHV-6	Established	Only in immunocompromised state
Dengue, WNV	Rarely established	Not conclusive
HGV/GBV-C, TTV, SEN-V, HEV, HHV-8, BDV	Not well established	Not established

Table 1. Recognized mode of viral transmission and disease in human.

3. Borna disease virus

Borna disease, a fatal meningo-encephalitis was originally described in horses in Germany. The disease was named after the epidemic outbreak of equine deaths in the town Borna in Saxony, Germany in 1885 (Rott and Becht, 1995). In 1929, an infectious agent was said to the cause for Borna disease and, in 1990 the infectious agent was identified as virus (Cubitt and de la Torre, 1994). The virus was then named after the disease, Borna disease virus (BDV).

3.1 BDV genome

BDV is said to be the only non-segmented, negative sense RNA virus replicated in the nucleus and classified as a new family *Bornaviridae* under *Mononegavirales* (Briese et al., 1994; de la Torre, 2002; De La Torre et al., 1996; Ludwig et al., 1988; Ludwig et al., 1993). BDV has six open reading frames (ORF), namely nucleoprotein (N), phosphoprotein (P), matrix (M), L-polymerase (L), glycoprotein (G) and X protein (Briese et al., 1994; de la Torre, 1994). The BDV mRNA includes monocistronic, polycistronic and spliced transcripts with overlapping ORFs (Kobayashi et al., 2003). The structural proteins are nucleoprotein, matrix and glycoprotein and the functional proteins are L-polymerase, phosphoprotein and X protein. The G protein helps in entry of BDV into the host cells. The G protein is expressed as two products, 84 and 43kDa. The 84kDa protein is involved in attachment of the viral particles to the cell receptor and its cleavage product 43kDa is involved in pH-dependent fusion after internalization of the virion by endocytosis (Gonzalez-Dunia et al., 1998). The M protein observed as tetramers and octamers, helps in viral attachment to cellular membrane, essential for viral assembly and budding (Kraus et al., 2005; Stoyloff et al., 1997). The M protein is also an integral component of ribonucleoprotein complex (RNP) and, prerequisite for viral persistence in the neurons (Chase et al., 2007). The structural information on M protein, suggest that they involve in RNP formation, nucleocapsid targeting and viral

maturation (Neumann et al., 2009). The L protein is involved in replication and P protein is involved in transcription of the BDV genome (Schneider, 2005). Further, the P protein interacts with other structural and functional proteins of BDV genome (Schwemmle et al., 1998). The L protein is tightly regulated by N-P stoichiometric ratio (Schneider, 2005; Schneider et al., 2005; Walker et al., 2000; Walker and Lipkin, 2002). The X protein is 10kDA protein, interacts with P protein and, acts as a negative regulator of BDV polymerase and hinders viral replication (Poenisch et al., 2004; Poenisch et al., 2007; Schwardt et al., 2005).

3.2 Behavioural effects of BDV infection in animals

Behavioural alternations during viral infection are referred as 'sickness behaviour' that include alternation in body weight, taste preferences, temperature, food and water intake and sleep pattern (Kelley et al., 2003). The 'sickness behaviour' in BDV infected rats, shows body weight stunting and abnormal salt preferences (Hornig et al., 2001), high obese rate (Herden et al., 2000) and chronic emotional abnormalities (Pletnikov et al., 2002a; Pletnikov et al., 2002b, c).

3.3 Prevalence of BDV infection in psychiatric illness

The first isolation of BDV was from a patient with mood disorder (Bode et al., 1996). There have been totally six BDV isolates and the source of isolation was blood and brain tissues from patients with psychiatric illness. The six isolates of BDV are from blood samples of two bipolar disorder patients, one obsessive-compulsive disorder, one depression, one schizophrenic patient and one from brain tissue from a patient with schizophrenia in Japan (Bode and Ludwig, 2003). In this decade, many reports have been emphasizing BDV infection in psychiatric illness. The psychiatric illness includes depression, bipolar disorder, obsessive-compulsive disorder, severe mood disorder and non-psychotic bipolar disorder (Bode, 1995; Bode et al., 1997; Bode et al., 1996; Bode et al., 1992; Bode et al., 2001; Dietrich et al., 2000; Dietrich et al., 2005; Ohlmeier et al., 2007). The infection of BDV was analysed by western blot, ELISA, immunofluorescence assay, immunoprecipitation, circulating immune complexes (CIC) from the serum of the patients with psychiatric illness, affective disorder, schizophrenia and multiple sclerosis (Hornig et al., 2003). Apart from BDV antibodies, BDV RNA was found in peripheral blood cells of psychiatric patients (Miranda et al., 2006; Sauder et al., 1996). Bode et al., (2001) reported that BDV-CIC play a major role in detection of BDV activity in contrast to the state of illness. The high amount of CIC and plasma antigen correlates with the severity of depression. It was also found in the neurophysiologic studies that brain potential amplitude varies with BDV-CIC in obsessive-compulsive disorder (Dietrich et al., 2005).

3.4 Neurotrophism or trophism for BDV infection

Neurotrophism or trophism for BDV infection is not clearly understood. BDV was found to replicate in the neurons of limbic structures especially in the regions of hippocampus (Carbone et al., 1991a; Carbone et al., 1989). Hippocampus is rich in neurotrophic growth factors like nerve growth factor (NGF) (Nieto-Sampedro and Bovolenta, 1990) as well as in kinases (Olive and Hodge, 2000).

3.4.1 Nerve growth factor (NGF) as a neurotrophic factor

Hippocampus is said to be the preferred site for replication of BDV as it is rich in growth factors (Ojika and Appel, 1984). NGF affects the replication cycle of other viruses and associated with latent HSV infection; the absence or removal of NGF is associated with recrudescence of productive HSV replication (Clements and Kennedy, 1989; Wilcox and Johnson, 1988; Wilcox et al., 1990). Carbone et al., (1993) suggested that NGF to be the neurotrophic factor influencing the replication of BDV. It was found that astrocytic cell lines were able to produce more BDV protein and RNA and suggested that astrocytic cells secrete a factor or factors that enhance the production of BDV protein and BDV RNA. It has also been found that NGF treatment was also produced the same as in astrocytic cell lines (Carbone et al., 1993).

3.4.2 Protein Kinase C (PKC) as a trophic factor

The P protein is involved in replication and also acts as a transcription factor. It has the nuclear localization signal that helps in transportation of P, L and X proteins into the nucleus (Schneider, 2005; Shoya et al., 1998; Walker et al., 2000; Walker and Lipkin, 2002). P protein is directly involved in glial cell dysfunction by reducing Brain Derived Growth Factor (BDNF) and serotonin receptor expression that results in neuropathological and neurophysiological abnormalities (Kamitani et al., 2003). The P protein is activated by phosphorylation. The kinases responsible for phosphorylation of P protein are Protein Kinase C (PKC)ε and Casein Kinase II. The major phosphorylation is through PKCε and the minor is from Casein Kinase II (Schwemmle et al., 1997). PKCε is present in higher concentrations in neuronal than in glial nuclei and are located inside the nucleus and at the nuclear envelope in brain cell nuclei (Rosenberger et al., 1995). It is found higher in the limbic structures (Olive and Hodge, 2000). BDV blocks neuronal presynaptic activity by inhibiting PKC signalling (Volmer et al., 2006), which was proved by P mutant phenotype where BDV is not able to interfere with neuronal signalling (Prat et al., 2009). The recent report indicate that PKC mediated signalling is necessary for viral spread (Schmid et al., 2010), which further proves that PKC is as tropic factor for BDV replication in hippocampal neurons.

3.5 Molecular basis of human mental disorder in virus-induced neurobehavioral disorder

Brain damage is usually observed in neurotrophic virus infection. The mechanism of virus induced neural damage occurs by direct and indirect pathways. The direct pathway involves viral replication in the nucleus leading to direct cell lysis or apoptosis. This was more commonly observed in infections with HSV, rabies virus, reovirus and alphavirus (Griffin and Hardwick, 1999). In case of BDV infection in rat models, the virus can cause neuronal cell dysfunctions in the absence of immune mediated cell destruction leading to neurological disorder (Tomonaga et al., 2002). The indirect pathway involves the modulation of host response to the viral infection. In BDV infection, the modulation occurs by the infiltrating immune cells such as CD4-positive, CD8-positive T-cells, macrophages and B cells. CD8-positive T cells represent the effector cell population exhibiting antigen specificity for the nucleoprotein (Stitz et al., 2002). Administration with anti-CD8+ results in reduction of neuronal degeneration and inhibits inflammation (Bilzer and Stitz, 1994).

Proinflammatory cytokines also play an important role in BDV infection, which alter the behaviour (Konsman et al., 2002).

3.5.1 Role of proinflammatory cytokines

Proinflammatory cytokines like IL-1α, IL-1β, IL-6 and TNF-α have a role in major depressive disorder (Licinio and Wong, 1999). The involvement of proinflammatory cytokines in experimental animals shows that the alteration in biological and behavioural abnormalities, as an analogue found in depressive patients (Konsman et al., 2002). The behavioural change mediated by cytokine seems to be regulated by multiple pathways. IL-1 is mainly involved in anxiety and sickness behaviour (Montkowski et al., 1997; Tomonaga, 2004). Likewise, in BDV infected patients, there was an increase of IL-6 was observed (personal communication). Experiments with animal model infected with BDV clearly show that there is an increase in the cytokines IL-1α, IL-6 and TNF-α (Sauder and de la Torre, 1999; Shankar et al., 1992). This may be one of the pathways of BDV in inducing psychiatric behavioural and cognitive deficits.

3.5.2 Role of serotonin system

Virus infection can directly or indirectly alter the serotonin system. Proinflammatory cytokines can also alter the expression of serotonin system (Dunn, 2000). Alteration of 5-HT (hydroxyl-tryptophan) systems leads to several mental and behavioural problems that include aggression, violence, sexual dysfunction, sleep and eating disorder in humans (Manji et al., 2001) and in rat models, reduction of 5-HT increases aggression (Nelson and Chiavegatto, 2001). In transgenic mice expressing P protein, the serotonin receptors in the hippocampus are reduced as well as these mice exhibit neurobehavioral abnormalities as in BDV infected animals (Kamitani et al., 2003). The transgenic mice also exhibit insulin-like growth factor 3 in their astrocytes, suggesting the increased vulnerability of purkinje cells in the brain (Honda et al., 2011).

3.6 Role of amantadine in BDV-infected psychiatric illness

Amantadine has been reported as an effective drug in reducing BDV replication in vitro and in vivo (Bode et al., 1997; Dietrich et al., 2000; Ferszt et al., 1999). Amantadine sulphate was used as an antiviral therapy in patients with bipolar disorder and found to be remarkable (Bode et al., 1997). All human BDV isolates are sensitive to amantadine treatment in vitro (Bode and Ludwig, 2003). Since the molecular mechanism of amantadine is unknown, here we discuss a putative mechanism based on the current understanding.

3.6.1 Amantadine in BDV infection

Astrocytes play an essential role in the homeostasis of CNS microenvironment for the proper neuronal function, where the alteration of astrocytic function leads to neuronal pathology (Benveniste, 1992, 1997). The function of astrocytes in BDV infection has been intensively studied in various aspects; the ability to uptake glucose, protein synthesis, cell viability and rate of proliferation (Billaud et al., 2000), accumulation of macrophage migratory inhibitory factor in astrocytes (Bacher et al., 2002), the expression of tissue factor, a primary cellular initiation of the coagulation protein cascades, resulting in protease thrombin by astrocytes (Gonzalez-Dunia et al., 1996), astrocytes as an antigen-presenting

and target cells for virus specific CD4 lymphocytes (Richt and Stitz, 1992) and cytokine expression as a result of BDV infection resulting in neuropathology (Sauder and de la Torre, 1999; Shankar et al., 1992).

BDV infection has been reported in psychiatric illness by the presence of BDV RNA, antigen, circulating immune complex (CIC) in blood and post-mortem brain in psychiatric patients (Bode et al., 1997; Bode et al., 1995; Miranda et al., 2006; Sauder et al., 1996; Terayama et al., 2003). Amantadine is said to improve psychiatric illness such as mania and depression in bipolar disease and depressive patients (Dietrich et al., 2000; Moryl et al., 1993; Ohlmeier et al., 2007; Ohlmeier et al., 2008). Further amantadine was shown to have no role against BDV infection (Cubitt and de la Torre, 1997; Hallensleben et al., 1997; Stitz et al., 1998). Amantadine inhibits replication of BDV in cells and also prevents the infection of the naïve cells (Bode et al., 1997; Bode et al., 2001). Amantadine may not be an antiviral agent that improves psychiatric illness in BDV infected patients. Here we hypothesize the role of amantadine in improvement of psychiatric illness in patients infected with BDV.

3.6.1.1 Amantadine as a kinase inhibitor

In BDV infection, Raf/MEK/ERK signalling cascade is activated due to the infection (Planz et al., 2001) and also BDNF induced ERK1/2 phosphorylation is blocked (Hans et al., 2004). Thus BDV involves in signalling cascade that results in abnormal signalling or reduction of synaptogenesis. The MEK-specific inhibitor U0126 (1,4-diamino-2,3-dicyano-1,4-bis[2-aminophenylthio] butadiene) blocks the spread of BDV to the neighbouring cells, thereby infectious viral particle are concentrated in the nucleus. In the absence of the MEK-inhibitor, BDV regains the ability to spread in the cell culture and BDV infectious particles have been recovered from the infected cells, after the removal of MEK inhibitor. This showed that MEK inhibitor results in alteration of cellular or viral mediated process, subsequently the spreading from cell to cell, but does not interfere with the infectivity once the virus is released by cell disruption (Planz et al., 2001). Similarly amantadine was shown to prevent spreading to the naïve cells (Bode et al., 1997; Bode et al., 2001).

In influenza virus infected human bronchial epithelial cells, amantadine exhibits inhibitory effect on p38 mitogen activated protein (MAP) kinase and c-Jun-NH_2-terminal kinase (JNK) activity (Asai et al., 2001). Likewise, amantadine may act as a kinase inhibitor to relieve from mania or depression in BDV-infected psychiatric patients. Thus amantadine might acts as a kinase inhibitor allowing cellular changes in astrocytes.

3.6.1.2 Amantadine and IL 6

Astrocytes are one of the primary resident cells of the central nervous system with the production of cytokines. BDV-infections, neurons die both from direct viral lysis and immunopathological responses, while BDV-infected astrocytes appear to increase (Carbone et al., 1991a; Carbone et al., 1991b; Carbone et al., 1989). In rats, after intranasal infection with BDV, the proinflammatory cytokines mRNA namely interleukin (IL)-6, IL-1α and TNF-α were found to increase (Shankar et al., 1992). Similar results have been observed by Sauder and de la Torre (Sauder and de la Torre, 1999), in rats infected with BDV, the proinflammatory cytokines like IL-6, TNF-α, IL-1α, IL-1β found to be increased in the hippocampus and cerebellum in the infected rats that shows distinct behavioural and neurodevelopmental abnormalities. It is obvious that infection results in the expression of cytokines by the astrocytes.

IL-6 expression can be induced by the proinflammatory cytokines, IL-1β and TNF-α via protein kinase C (PKC) in astrocytes (Di Santo et al., 1996; Norris et al., 1994). IL-6 can also be a destructive agent during dysregulation in CNS, where over-expression leads to neuropathological conditions that include neurodegeneration, breakdown of blood-brain barrier, angiogenesis and increased expression of complement proteins (Campbell et al., 1993). The proinflammatory cytokines such as IL-6, TNF-α, IL-1α, IL-1β is known to contribute in neuropsychiatric syndromes, especially in major depression (Licinio and Wong, 1999; Tomonaga, 2004).

In BDV-infected psychiatric patients with bipolar mania or depression, after treatment with amantadine, there is a reduction in IL-6 and in BDV-CIC (personal communication). So the reduction in proinflammatory cytokine IL-6 shows that amantadine has some effects in treating BDV-infected patients. It suggests that treatment with amantadine regulates reduction of IL-6 and CIC in BDV infected patients.

In conclusion, amantadine may reduce the spread of BDV by acting as a kinase inhibitor and thereby reduce the severity by inhibiting the spreading of BDV to the neighbouring cells and also results in reduction of IL-6 by alteration of cellular mechanism in signalling pathways. Thus, amantadine can be used clinically in treating BDV-infected psychiatric patients.

3.7 Blood transfusion and BDV

Blood transfusion and BDV is least studied, because of the lack of evidence for transmission in humans and; also as a causative agent for neuropsychiatric illness in humans. In few studies, BDV has been suggested as a contributing source for neuropsychiatric illness (Chen et al., 1999), but BDV and or its viral component has been reported to present in blood of psychiatric patients (Bode et al., 1997; Bode et al., 1996; Heinrich and Adamaszek, 2010; Kitani et al., 1996; Sauder et al., 1996). In animal models, the transfusion/transfer of lymphocytes from brain of BDV-infected to immuno-compromised rats results in clinical symptoms and neuropathology of Borna disease in the recipients (Batra et al., 2003). Thus, the need for blood test for BDV has been suggested to be included during blood donation and transfusion (Alwin Prem Anand, 2010). If the viral component and/or the lymphocyte are sufficient to cause the clinical symptoms and neuropathology in recipients, blood transfusion might result in the same. Though, it is really a question whether BDV is the causative agent of neuropsychiatric illness in human. But preferably BDV infection in human beings might worsen the symptoms of any neuropsychiatric illness, if present.

4. Dengue viral disease

Dengue is the most important arthropod-borne viral infection of humans, which affects millions of people, particularly in urban and semi-urban areas. Worldwide, an estimated 2.5 billion people are at risk of infection (Gubler, 2002), with more than 100 million new infections each year. This includes 500,000 hospitalizations cases for dengue hemorrhagic fever, predominantly among children (Dussart et al., 2006). The annual average number of dengue fever/dengue hemorrhagic fever (DF/DHF) cases reported to the WHO has increased significantly in recent years. For the period 2000–2004, the annual average was 925,896 cases; almost double the figure of 479,848 cases that was reported in the period 1990–1999. Travelers' from endemic areas serve as vehicles for further spread. Dengue

epidemics can have a significant economic and health toll. In endemic countries in Asia and the Americas, the burden of dengue is approximately 1,300 disability-adjusted life years per million populations, which is similar to the disease burden of other childhood and tropical diseases including tuberculosis in these regions (Gubler and Meltzer, 1999).

4.1 Dengue virus genome structure and function

Dengue viruses (DENV) belong to the genus flavivirus within the Flaviviridae family. The virus evolved in non-human primates from a common ancestor and entered the urban cycle some 500–1,000 years ago. The virus has a positive strand RNA whose genome is approximately 11kb in length. It has four antigenically distinct serotypes (Dengue virus 1-4). The RNA has a single open reading frame that encoding three structural proteins, nucleocapsid/core protein (C), membrane protein (M) and envelope protein (E) and; seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5) (Chambers et al., 1990). The envelope (E) and membrane proteins (M) are inserted in the lipid membrane. The glycoprotein E contains most of the antigenic determinants of the virus and essential for viral attachment and entry, while membrane protein (M) is synthesized as the precursor protein (prM), which acts as a chaperone during maturation of the viral particle. The nucleocapsid consists of capsid protein (C).

4.2 Dengue infection

Though dengue infection occurs as a mild febrile, self limiting illness i.e., Dengue fever (DF), its severe form causes Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) are important public health problem because of its disease burden and high mortality rate (more than 5% in case of DHF/DSS) (Wilder-Smith et al., 2009). Infection by one serotype induces a lifelong immunity to the particular serotype and transient immunity to other serotypes, while concurrent infection by other serotype induces DHF/DSS.

4.2.1 Stages of DENV infection

In the skin, dengue viruses infect immature dendritic cells through the non-specific receptor dendritic cell specific ICAM3 grabbing non-integrin (DC-SIGN) (Wu et al., 2000). Infected dendritic cells mature and migrate to local or regional lymph nodes where they present viral antigens to T cells, initiating the cellular and humoral immune responses (Green et al., 1999). DENV also shown to replicate well in liver parenchymal cells, lymph node macrophages, liver, spleen, as well as in peripheral blood monocytes. DENVs produce several clinical syndromes, which depend up on age and immunological status of the individual. During initial stages, most infections are sub clinical (especially in children) or with mild undifferentiated febrile syndrome. In adults, primary infections with each of the four DENV serotypes, particularly with DENV-1 and -3, often results in DF. Some outbreaks of primary DENV-2 infections have been predominantly subclinical. During secondary dengue infections the pathophysiology of the disease changes dramatically. Sequential infections in which infection with DENV-1 is followed by infection with DENV-2 or DENV-3, or infection with DENV-3 is followed by infection with DENV-2 results in acute vascular permeability called as DSS (Alvarez et al., 2006). The severity of DSS is age-dependent and most severe in young children, which is due to the integrity of the capillaries (Gamble et al., 2000).

4.2.2 Genetic pre-disposition and host factors in DENV infection

Dengue infections can be life-threatening when they occur in individuals with asthma, diabetes and other chronic diseases (Lee et al., 2006). Host factors that increase the risk of severe dengue disease include sex, several human leukocyte antigen class I alleles, promoter variant of the DC-SIGN receptor gene, single-nucleotide polymorphism in the tumour necrosis factor gene and AB blood group. Host factors that reduce the risk of severe disease during a second dengue infection includes race, malnutrition, and polymorphisms in the Fcγ receptor and vitamin D receptor genes (Martina et al., 2009).

4.3 Pathogenesis of DENV infection

In adults secondary dengue infections either produces the classical DSS or severe disease complicated by hemorrhages. Most notably, in island outbreaks the severity of secondary dengue infections has been observed to increase from month-to-month (Guzman et al., 2000); and longer the interval between the first and second infection the more severe is the accompanying syndromes (Chareonsirisuthigul et al., 2007).

4.3.1 Antibody Dependent Enhancement (ADE)

Macrophages and monocytes participate in antibody dependent enhancement (ADE). Immune complexes formed between DENV antigens and non-neutralizing antibodies due to previous heterotypic dengue infections or from low concentrations of dengue antibodies of maternal origin in infant sera cross-react with Fc receptors of mononuclear phagocytes. The co-circulation of four DENV serotypes in a given population might augment the ADE phenomenon (Martina et al., 2009). One working hypothesis of dengue pathogenesis that is consistent with the available evidence is that severe disease in infants with primary infections and in older individuals with secondary infections is the result of ADE of infection of mononuclear phagocytes. Infection by an antibody–virus complex suppresses innate immune responses, increasing intracellular infection and generating inflammatory cytokines and chemokines that, collectively, result in enhanced disease.

4.3.2 Cytokines and soluble mediators

The infection of human monocytes and mature dendritic cells results in suppression of the interferon system and increases virus replication. Type I interferon-associated genes are less activated severe dengue disease. Increased number of infected cells presenting targets for CD4+ and CD8+ T cells, results in large quantities of interleukin IL-10, IL-2, interferon (IFN)-γ and TNF which lonely or synergistically, contributes to endothelial damage and altered homeostasis (Bosch et al., 2002; Talavera et al., 2004). Sub viral particles and virions released from infected cells also damages endothelial cells. Uptake of the non-structural protein NS1 by hepatocytes promotes viral infection of the liver. During DHF, the complement cascade is also activated and the levels of the complement activation products C3a and C5a correlate with the severity of illness (Malasit, 1987). Soluble and membrane-associated NS1 have been demonstrated to activate human complement. The levels of plasma NS1 correlated with disease severity, suggesting links between the virus, complement activation and the development of DHF/DSS (Navarro-Sanchez et al., 2005).

Alternative hypothesis for dengue pathogenesis points out the role of secondary T-cell responses. Researches point that the stimulation of T-cell memory results in the production of heterotypic CD4 and CD8 cells, which are less powerful in killing but release considerable amount of pro-inflammatory cytokines that contribute to disease severity. Cross-reactivity between antibodies produced against NS with human platelets, and endothelial cells, damages these cells. In patients with DF, IFN production and activated natural killer cells can limit disease severity (Mongkolsapaya et al., 2003; Zivna et al., 2002).

4.4 DENV transmission by non-vector modes

Other mosquito-borne flavivirus, such as West Nile virus, is transmitted efficiently in breast milk, blood transfusion, organ transplantation, stem cell transplantation, intra-uterine exposure and needle stick injuries (Hong et al., 2003; Iwamoto et al., 2003). The main transmission route for DENV is by vector mosquito. It is also transmitted by needle stick injuries, bone marrow transplantation and intrapartum vertical transmissions (Rodriguez Rodriguez et al., 2009). Recent reports have demonstrated dengue viremia in blood donors from Honduras, Brazil, Australia and Puerto Rico, which are endemic areas for dengue infection. Transmission of dengue infection has been reported from donor to recipient in one case of living donor renal transplant (Tan et al., 2005). The clinical presentation and course of illness was similar to that of an immuno-competent patient, except for prolonged course of illness (19 days) and duration of thrombocytopenia. Transmission during a bone marrow transplant was reported in one instance during a dengue epidemic in Puerto Rico in 1994 (Rigau-Perez et al., 2001).

4.4.1 Individual reported cases of transfusion mediated transmission

There are only two reported instances of transmission through blood transfusion. The first involved a patient in Hong Kong who developed fever 3 days after a blood transfusion, associated with moderate neutropenia, severe thrombocytopenia and hypotension responsive to fluid therapy. The donor was asymptomatic at the time of donation but developed mild symptoms of DF 1 day after blood donation. Stored sample from the donor tested positive for dengue virus by RT-PCR (Chuang et al., 2008). The second involved the transmission of dengue from an asymptomatic blood donor from Singapore who developed an acute febrile illness the day after donating blood. Investigation confirmed dengue infection in the recipients of the three blood products from his donation. Two recipients had DF with some evidence of capillary leakage, whereas the platelet recipient had asymptomatic seroconversion and all patients recovered. A stored serum sample from the donation tested positive for DEN-2 by RT-PCR (Tambyah et al., 2008).

4.4.2 Population based study on DENV transmission through transfusion

Various studies have shown the presence of asymptomatic or subclinical infection, which can range from 0.77 to 87% depending on the population studied (Ooi et al., 2006). It is estimated that for every one symptomatic case, there can be 6.7 cases that are asymptomatic (Chen and Wilson, 2005). A study found silent transmission of dengue commonly in 15 to 40 year age group. Among 329 healthy volunteers in a province in Thailand with high rate of dengue infection, 29 (8.8%) had a serum sample positive for dengue IgM, of which two

samples tested positive for viral RNA (Poblap et al., 2006). Cluster sampling studies around index cases in Indonesia detected eight asymptomatic dengue infections of 785 volunteers over a 2-year period, of which two demonstrated viraemia by RT-PCR (Beckett et al., 2005). Virus was isolated in 215 of 3189 (6.7%) persons in a study evaluating the dynamics of transmission of dengue virus in a dengue epidemic area of Colombia, most of who were asymptomatic (Mendez et al., 2006). Two recent studies reported viraemia in blood donations collected from four countries experiencing high dengue transmission rates. In the first study, twelve (0.07%) of 16,521 blood donations collected in Puerto Rico tested positive using the dengue-specific nucleic acid amplification test (NAT). Testing using RT-PCR was positive in four samples and live virus was recovered from three of the PCR-positive samples (Mohammed et al., 2008). In the second study, samples from asymptomatic blood donors in Honduras, Brazil and Australia were obtained during periods of clinical dengue outbreaks and screened using the dengue-specific TMA assay. Nine (0.30%) of 2994 Honduran samples were tested positive, of which 8 were confirmed by RT-PCR and 4 samples yielded infectious viruses. Three (0.06%) of 4858 Brazilian samples tested positive, of which 2 were RTPCR positive (Linnen et al., 2008).

Technically, it is possible for DENV to be transmitted through blood transfusions because the disease courses with a transient viremia after infection and can be asymptomatic or have only mild symptoms. DENV was identified as one of three high-priority infectious agents with actual or potential risk of transfusion transmission in the United States or Canada. The rate of asymptomatic DENV infection in blood donors has been determined retrospectively in Puerto Rico and several other countries where dengue is endemic using molecular diagnostic. Infection rates have been shown to vary with disease incidence in the community, including the seasonal variation of dengue. In Puerto Rico, nearly 1 in 1000 blood donations were positive for DENV nucleic acid by during the 2005 dengue season (Mohammed et al., 2008) versus 1 in 600 positive during the 2007 outbreak (Tomashek and Margolis, 2011). The prevalence of DENV nucleic acid in blood donations in Puerto Rico in 2005 was similar to that estimated for WNV in areas experiencing outbreaks in the United States in 2002 before universal screening was implemented in 2003.

4.5 Challenges in identifying DENV as a risk in blood transfusion

Lack of knowledge in endemic areas - researchers and clinicians may not know/ consider blood transfusion as a source of infection.

Inconclusive data of dengue cases - may have been transfusion transmitted but has not been confirmed due to unavailability of complete information and serological tests.

Presence of high rate of existing antibodies - among transfusion recipients and donors especially in endemic areas will hinder to calculate the actual risk of dengue after transfusion.

4.6 Serological testing for DENV

At present, the only approach to prevent transfusion of DENV-positive blood would be screening with sensitive nucleic acid amplification tests to detect asymptomatic DENV infections in otherwise healthy donors and asymptomatic viremia in the 24 to 48 hours before donors becoming ill with dengue. Exclusion of donors in endemic areas during the high-incidence dengue season or during an outbreak is not feasible since the entire

population is at risk of DENV infection, the need for blood components is typically high during outbreaks, and outbreaks can be long lasting.

The small number of reports of transfusion transmission could be because of the fact that it is difficult to differentiate between non-mosquito transmission and mosquito mediated transmission. Future studies are needed to establish rates of transfusion-transmitted DENV by viremic donations and their clinical consequences in recipients (Chen and Wilson, 2005). These evaluations should determine the most cost and prevention-effective approaches to prevent transfusion-transmitted dengue infections.

5. Conclusion

Hence, both BDV and DENV are less studied in transfusion medicine. It might be due to the incomplete evidence of transmission in BDV and, non-availability of better testing module for DV. In both the cases, the severity of causing serious damage to health is pretty high. The evidence for causing neuropsychiatric illness in BDV has not been proven or there is lack of evidence in it, but it may worsen the situation of a patient who is suffering from any prior neuropsychiatric illness. Ignoring the need for testing of the presence of these viruses in blood transfusion might result in serious health issues at global level. So in order to prevent potential risk of BDV and DENV infection through transfusion medicine, precautionary measures should be taken to diagnose and prevent BDV and DENV infection during blood transfusion.

6. References

Alvarez, M., Rodriguez-Roche, R., Bernardo, L., Vazquez, S., Morier, L., Gonzalez, D., Castro, O., Kouri, G., Halstead, S.B., Guzman, M.G., 2006. Dengue hemorrhagic Fever caused by sequential dengue 1-3 virus infections over a long time interval: Havana epidemic, 2001-2002. Am J Trop Med Hyg 75, 1113-1117.

Alwin Prem Anand, A., 2010. Is blood transfusion safe? BDV and neuropsychiatric illness. Acta Neuropsychiatrica 22, 208-208.

Asai, Y., Hashimoto, S., Kujime, K., Gon, Y., Mizumura, K., Shimizu, K., Horie, T., 2001. Amantadine inhibits RANTES production by influenzavirus-infected human bronchial epithelial cells. Br J Pharmacol 132, 918-924.

Bacher, M., Weihe, E., Dietzschold, B., Meinhardt, A., Vedder, H., Gemsa, D., Bette, M., 2002. Borna disease virus-induced accumulation of macrophage migration inhibitory factor in rat brain astrocytes is associated with inhibition of macrophage infiltration. Glia 37, 291-306.

Batra, A., Planz, O., Bilzer, T., Stitz, L., 2003. Precursors of Borna disease virus-specific T cells in secondary lymphatic tissue of experimentally infected rats. J Neurovirol 9, 325-335.

Beckett, C.G., Kosasih, H., Faisal, I., Nurhayati, Tan, R., Widjaja, S., Listiyaningsih, E., Ma'roef, C., Wuryadi, S., Bangs, M.J., Samsi, T.K., Yuwono, D., Hayes, C.G., Porter, K.R., 2005. Early detection of dengue infections using cluster sampling around index cases. Am J Trop Med Hyg 72, 777-782.

Benveniste, E.N., 1992. Cytokines: influence on glial cell gene expression and function. Chem Immunol 52, 106-153.

Benveniste, E.N., 1997. Cytokines: influence on glial cell gene expression and function. Chem Immunol 69, 31-75.

Billaud, J.N., Ly, C., Phillips, T.R., de la Torre, J.C., 2000. Borna disease virus persistence causes inhibition of glutamate uptake by feline primary cortical astrocytes. J Virol 74, 10438-10446.

Bilzer, T., Stitz, L., 1994. Immune-mediated brain atrophy. CD8+ T cells contribute to tissue destruction during borna disease. J Immunol 153, 818-823.

Bode, L., 1995. Human infections with Borna disease virus and potential pathogenic implications. Curr Top Microbiol Immunol 190, 103-130.

Bode, L., Dietrich, D.E., Stoyloff, R., Emrich, H.M., Ludwig, H., 1997. Amantadine and human Borna disease virus in vitro and in vivo in an infected patient with bipolar depression. Lancet 349, 178-179.

Bode, L., Durrwald, R., Rantam, F.A., Ferszt, R., Ludwig, H., 1996. First isolates of infectious human Borna disease virus from patients with mood disorders. Mol Psychiatry 1, 200-212.

Bode, L., Komaroff, A.L., Ludwig, H., 1992. No serologic evidence of borna disease virus in patients with chronic fatigue syndrome. Clin Infect Dis 15, 1049.

Bode, L., Ludwig, H., 2003. Borna disease virus infection, a human mental-health risk. Clin Microbiol Rev 16, 534-545.

Bode, L., Reckwald, P., Severus, W.E., Stoyloff, R., Ferszt, R., Dietrich, D.E., Ludwig, H., 2001. Borna disease virus-specific circulating immune complexes, antigenemia, and free antibodies--the key marker triplet determining infection and prevailing in severe mood disorders. Mol Psychiatry 6, 481-491.

Bode, L., Zimmermann, W., Ferszt, R., Steinbach, F., Ludwig, H., 1995. Borna disease virus genome transcribed and expressed in psychiatric patients. Nat Med 1, 232-236.

Bosch, I., Xhaja, K., Estevez, L., Raines, G., Melichar, H., Warke, R.V., Fournier, M.V., Ennis, F.A., Rothman, A.L., 2002. Increased production of interleukin-8 in primary human monocytes and in human epithelial and endothelial cell lines after dengue virus challenge. Journal of virology 76, 5588-5597.

Briese, T., Schneemann, A., Lewis, A.J., Park, Y.S., Kim, S., Ludwig, H., Lipkin, W.I., 1994. Genomic organization of Borna disease virus. Proc Natl Acad Sci U S A 91, 4362-4366.

Campbell, I.L., Abraham, C.R., Masliah, E., Kemper, P., Inglis, J.D., Oldstone, M.B., Mucke, L., 1993. Neurologic disease induced in transgenic mice by cerebral overexpression of interleukin 6. Proc Natl Acad Sci U S A 90, 10061-10065.

Carbone, K.M., Moench, T.R., Lipkin, W.I., 1991a. Borna disease virus replicates in astrocytes, Schwann cells and ependymal cells in persistently infected rats: location of viral genomic and messenger RNAs by in situ hybridization. J Neuropathol Exp Neurol 50, 205-214.

Carbone, K.M., Park, S.W., Rubin, S.A., Waltrip, R.W., 2nd, Vogelsang, G.B., 1991b. Borna disease: association with a maturation defect in the cellular immune response. J Virol 65, 6154-6164.

Carbone, K.M., Rubin, S.A., Sierra-Honigmann, A.M., Lederman, H.M., 1993. Characterization of a glial cell line persistently infected with borna disease virus (BDV): influence of neurotrophic factors on BDV protein and RNA expression. J Virol 67, 1453-1460.

Carbone, K.M., Trapp, B.D., Griffin, J.W., Duchala, C.S., Narayan, O., 1989. Astrocytes and Schwann cells are virus-host cells in the nervous system of rats with Borna disease. J Neuropathol Exp Neurol 48, 631-644.

Chambers, T.J., Hahn, C.S., Galler, R., Rice, C.M., 1990. Flavivirus genome organization, expression, and replication. Annu Rev Microbiol 44, 649-688.

Chareonsirisuthigul, T., Kalayanarooj, S., Ubol, S., 2007. Dengue virus (DENV) antibody-dependent enhancement of infection upregulates the production of anti-inflammatory cytokines, but suppresses anti-DENV free radical and pro-inflammatory cytokine production, in THP-1 cells. The Journal of general virology 88, 365-375.

Chase, G., Mayer, D., Hildebrand, A., Frank, R., Hayashi, Y., Tomonaga, K., Schwemmle, M., 2007. Borna disease virus matrix protein is an integral component of the viral ribonucleoprotein complex that does not interfere with polymerase activity. J Virol 81, 743-749.

Chen, C.H., Chiu, Y.L., Shaw, C.K., Tsai, M.T., Hwang, A.L., Hsiao, K.J., 1999. Detection of Borna disease virus RNA from peripheral blood cells in schizophrenic patients and mental health workers. Mol Psychiatry 4, 566-571.

Chen, L.H., Wilson, M.E., 2005. Nosocomial dengue by mucocutaneous transmission. Emerging infectious diseases 11, 775.

Chuang, V.W., Wong, T.Y., Leung, Y.H., Ma, E.S., Law, Y.L., Tsang, O.T., Chan, K.M., Tsang, I.H., Que, T.L., Yung, R.W., Liu, S.H., 2008. Review of dengue fever cases in Hong Kong during 1998 to 2005. Hong Kong Med J 14, 170-177.

Clements, G.B., Kennedy, P.G., 1989. Modulation of herpes simplex virus (HSV) infection of cultured neuronal cells by nerve growth factor and antibody to HSV. Brain 112 (Pt 5), 1277-1294.

Cubitt, B., de la Torre, J.C., 1994. Borna disease virus (BDV), a nonsegmented RNA virus, replicates in the nuclei of infected cells where infectious BDV ribonucleoproteins are present. J Virol 68, 1371-1381.

Cubitt, B., de la Torre, J.C., 1997. Amantadine does not have antiviral activity against Borna disease virus. Arch Virol 142, 2035-2042.

de la Torre, J.C., 1994. Molecular biology of borna disease virus: prototype of a new group of animal viruses. J Virol 68, 7669-7675.

de la Torre, J.C., 2002. Molecular biology of Borna disease virus and persistence. Front Biosci 7, d569-579.

De La Torre, J.C., Gonzalez-Dunia, D., Cubitt, B., Mallory, M., Mueller-Lantzsch, N., Grasser, F.A., Hansen, L.A., Masliah, E., 1996. Detection of borna disease virus antigen and RNA in human autopsy brain samples from neuropsychiatric patients. Virology 223, 272-282.

Di Santo, E., Alonzi, T., Fattori, E., Poli, V., Ciliberto, G., Sironi, M., Gnocchi, P., Ricciardi-Castagnoli, P., Ghezzi, P., 1996. Overexpression of interleukin-6 in the central nervous system of transgenic mice increases central but not systemic proinflammatory cytokine production. Brain Res 740, 239-244.

Dietrich, D.E., Bode, L., Spannhuth, C.W., Lau, T., Huber, T.J., Brodhun, B., Ludwig, H., Emrich, H.M., 2000. Amantadine in depressive patients with Borna disease virus (BDV) infection: an open trial. Bipolar Disord 2, 65-70.

Dietrich, D.E., Zhang, Y., Bode, L., Munte, T.F., Hauser, U., Schmorl, P., Richter-Witte, C., Godecke-Koch, T., Feutl, S., Schramm, J., Ludwig, H., Johannes, S., Emrich, H.M., 2005. Brain potential amplitude varies as a function of Borna disease virus-specific immune complexes in obsessive-compulsive disorder. Mol Psychiatry 10, 515, 519-520.

Dunn, A.J., 2000. Cytokine activation of the HPA axis. Ann N Y Acad Sci 917, 608-617.

Dussart, P., Labeau, B., Lagathu, G., Louis, P., Nunes, M.R., Rodrigues, S.G., Storck-Herrmann, C., Cesaire, R., Morvan, J., Flamand, M., Baril, L., 2006. Evaluation of an enzyme immunoassay for detection of dengue virus NS1 antigen in human serum. Clin Vaccine Immunol 13, 1185-1189.

Ferszt, R., Kuhl, K.P., Bode, L., Severus, E.W., Winzer, B., Berghofer, A., Beelitz, G., Brodhun, B., Muller-Oerlinghausen, B., Ludwig, H., 1999. Amantadine revisited: an open trial of amantadinesulfate treatment in chronically depressed patients with Borna disease virus infection. Pharmacopsychiatry 32, 142-147.

Gamble, J., Bethell, D., Day, N.P., Loc, P.P., Phu, N.H., Gartside, I.B., Farrar, J.F., White, N.J., 2000. Age-related changes in microvascular permeability: a significant factor in the susceptibility of children to shock? Clin Sci (Lond) 98, 211-216.

Gonzalez-Dunia, D., Cubitt, B., de la Torre, J.C., 1998. Mechanism of Borna disease virus entry into cells. J Virol 72, 783-788.

Gonzalez-Dunia, D., Eddleston, M., Mackman, N., Carbone, K., de la Torre, J.C., 1996. Expression of tissue factor is increased in astrocytes within the central nervous system during persistent infection with borna disease virus. J Virol 70, 5812-5820.

Green, S., Vaughn, D.W., Kalayanarooj, S., Nimmannitya, S., Suntayakorn, S., Nisalak, A., Lew, R., Innis, B.L., Kurane, I., Rothman, A.L., Ennis, F.A., 1999. Early immune activation in acute dengue illness is related to development of plasma leakage and disease severity. The Journal of infectious diseases 179, 755-762.

Griffin, D.E., Hardwick, J.M., 1999. Perspective: virus infections and the death of neurons. Trends Microbiol 7, 155-160.

Gubler, D.J., 2002. The global emergence/resurgence of arboviral diseases as public health problems. Arch Med Res 33, 330-342.

Gubler, D.J., Meltzer, M., 1999. Impact of dengue/dengue hemorrhagic fever on the developing world. Adv Virus Res 53, 35-70.

Hallensleben, W., Zocher, M., Staeheli, P., 1997. Borna disease virus is not sensitive to amantadine. Arch Virol 142, 2043-2048.

Hans, A., Bajramovic, J.J., Syan, S., Perret, E., Dunia, I., Brahic, M., Gonzalez-Dunia, D., 2004. Persistent, noncytolytic infection of neurons by Borna disease virus interferes with ERK 1/2 signaling and abrogates BDNF-induced synaptogenesis. FASEB J 18, 863-865.

Heinrich, A., Adamaszek, M., 2010. Anti-Borna disease virus antibody responses in psychiatric patients: long-term follow up. Psychiatry Clin Neurosci 64, 255-261.

Herden, C., Herzog, S., Richt, J.A., Nesseler, A., Christ, M., Failing, K., Frese, K., 2000. Distribution of Borna disease virus in the brain of rats infected with an obesity-inducing virus strain. Brain Pathol 10, 39-48.

Honda, T., Fujino, K., Okuzaki, D., Ohtaki, N., Matsumoto, Y., Horie, M., Daito, T., Itoh, M., Tomonaga, K., 2011. Upregulation of insulin-like growth factor binding protein 3 in

astrocytes of transgenic mice that express borna disease virus phosphoprotein. J Virol 85, 4567-4571.

Hong, D.S., Jacobson, K.L., Raad, II, de Lima, M., Anderlini, P., Fuller, G.N., Ippoliti, C., Cool, R.M., Leeds, N.E., Narvios, A., Han, X.Y., Padula, A., Champlin, R.E., Hosing, C., 2003. West Nile encephalitis in 2 hematopoietic stem cell transplant recipients: case series and literature review. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 37, 1044-1049.

Hornig, M., Briese, T., Lipkin, W.I., 2003. Borna disease virus. J Neurovirol 9, 259-273.

Hornig, M., Solbrig, M., Horscroft, N., Weissenbock, H., Lipkin, W.I., 2001. Borna disease virus infection of adult and neonatal rats: models for neuropsychiatric disease. Curr Top Microbiol Immunol 253, 157-177.

Iwamoto, M., Jernigan, D.B., Guasch, A., Trepka, M.J., Blackmore, C.G., Hellinger, W.C., Pham, S.M., Zaki, S., Lanciotti, R.S., Lance-Parker, S.E., DiazGranados, C.A., Winquist, A.G., Perlino, C.A., Wiersma, S., Hillyer, K.L., Goodman, J.L., Marfin, A.A., Chamberland, M.E., Petersen, L.R., 2003. Transmission of West Nile virus from an organ donor to four transplant recipients. The New England journal of medicine 348, 2196-2203.

Kamitani, W., Ono, E., Yoshino, S., Kobayashi, T., Taharaguchi, S., Lee, B.J., Yamashita, M., Okamoto, M., Taniyama, H., Tomonaga, K., Ikuta, K., 2003. Glial expression of Borna disease virus phosphoprotein induces behavioral and neurological abnormalities in transgenic mice. Proc Natl Acad Sci U S A 100, 8969-8974.

Kelley, K.W., Bluthe, R.M., Dantzer, R., Zhou, J.H., Shen, W.H., Johnson, R.W., Broussard, S.R., 2003. Cytokine-induced sickness behavior. Brain Behav Immun 17 Suppl 1, S112-118.

Kitani, T., Kuratsune, H., Fuke, I., Nakamura, Y., Nakaya, T., Asahi, S., Tobiume, M., Yamaguti, K., Machii, T., Inagi, R., Yamanishi, K., Ikuta, K., 1996. Possible correlation between Borna disease virus infection and Japanese patients with chronic fatigue syndrome. Microbiol Immunol 40, 459-462.

Kobayashi, T., Zhang, G., Lee, B.J., Baba, S., Yamashita, M., Kamitani, W., Yanai, H., Tomonaga, K., Ikuta, K., 2003. Modulation of Borna disease virus phosphoprotein nuclear localization by the viral protein X encoded in the overlapping open reading frame. J Virol 77, 8099-8107.

Konsman, J.P., Parnet, P., Dantzer, R., 2002. Cytokine-induced sickness behaviour: mechanisms and implications. Trends Neurosci 25, 154-159.

Kraus, I., Bogner, E., Lilie, H., Eickmann, M., Garten, W., 2005. Oligomerization and assembly of the matrix protein of Borna disease virus. FEBS Lett 579, 2686-2692.

Kristensson, K., 2011. Microbes' roadmap to neurons. Nat Rev Neurosci 12, 345-357.

Lee, M.S., Hwang, K.P., Chen, T.C., Lu, P.L., Chen, T.P., 2006. Clinical characteristics of dengue and dengue hemorrhagic fever in a medical center of southern Taiwan during the 2002 epidemic. J Microbiol Immunol Infect 39, 121-129.

Licinio, J., Wong, M.L., 1999. The role of inflammatory mediators in the biology of major depression: central nervous system cytokines modulate the biological substrate of depressive symptoms, regulate stress-responsive systems, and contribute to neurotoxicity and neuroprotection. Mol Psychiatry 4, 317-327.

Linnen, J.M., Vinelli, E., Sabino, E.C., Tobler, L.H., Hyland, C., Lee, T.H., Kolk, D.P., Broulik, A.S., Collins, C.S., Lanciotti, R.S., Busch, M.P., 2008. Dengue viremia in blood donors from Honduras, Brazil, and Australia. Transfusion 48, 1355-1362.

Ludwig, H., Bode, L., Gosztonyi, G., 1988. Borna disease: a persistent virus infection of the central nervous system. Prog Med Virol 35, 107-151.

Ludwig, H., Furuya, K., Bode, L., Klein, N., Durrwald, R., Lee, D.S., 1993. Biology and neurobiology of Borna disease viruses (BDV), defined by antibodies, neutralizability and their pathogenic potential. Arch Virol Suppl 7, 111-133.

Malasit, P., 1987. Complement and dengue haemorrhagic fever/shock syndrome. Southeast Asian J Trop Med Public Health 18, 316-320.

Manji, H.K., Drevets, W.C., Charney, D.S., 2001. The cellular neurobiology of depression. Nat Med 7, 541-547.

Martina, B.E., Koraka, P., Osterhaus, A.D., 2009. Dengue virus pathogenesis: an integrated view. Clinical microbiology reviews 22, 564-581.

Miranda, H.C., Nunes, S.O., Calvo, E.S., Suzart, S., Itano, E.N., Watanabe, M.A., 2006. Detection of Borna disease virus p24 RNA in peripheral blood cells from Brazilian mood and psychotic disorder patients. J Affect Disord 90, 43-47.

Mohammed, H., Linnen, J.M., Munoz-Jordan, J.L., Tomashek, K., Foster, G., Broulik, A.S., Petersen, L., Stramer, S.L., 2008. Dengue virus in blood donations, Puerto Rico, 2005. Transfusion 48, 1348-1354.

Mongkolsapaya, J., Dejnirattisai, W., Xu, X.N., Vasanawathana, S., Tangthawornchaikul, N., Chairunsri, A., Sawasdivorn, S., Duangchinda, T., Dong, T., Rowland-Jones, S., Yenchitsomanus, P.T., McMichael, A., Malasit, P., Screaton, G., 2003. Original antigenic sin and apoptosis in the pathogenesis of dengue hemorrhagic fever. Nature medicine 9, 921-927.

Montkowski, A., Landgraf, R., Yassouridis, A., Holsboer, F., Schobitz, B., 1997. Central administration of IL-1 reduces anxiety and induces sickness behaviour in rats. Pharmacol Biochem Behav 58, 329-336.

Moryl, E., Danysz, W., Quack, G., 1993. Potential antidepressive properties of amantadine, memantine and bifemelane. Pharmacol Toxicol 72, 394-397.

Navarro-Sanchez, E., Despres, P., Cedillo-Barron, L., 2005. Innate immune responses to dengue virus. Arch Med Res 36, 425-435.

Nelson, R.J., Chiavegatto, S., 2001. Molecular basis of aggression. Trends Neurosci 24, 713-719.

Neumann, P., Lieber, D., Meyer, S., Dautel, P., Kerth, A., Kraus, I., Garten, W., Stubbs, M.T., 2009. Crystal structure of the Borna disease virus matrix protein (BDV-M) reveals ssRNA binding properties. Proc Natl Acad Sci U S A 106, 3710-3715.

Nieto-Sampedro, M., Bovolenta, P., 1990. Growth factors and growth factor receptors in the hippocampus. Role in plasticity and response to injury. Prog Brain Res 83, 341-355.

Norris, J.G., Tang, L.P., Sparacio, S.M., Benveniste, E.N., 1994. Signal transduction pathways mediating astrocyte IL-6 induction by IL-1 beta and tumor necrosis factor-alpha. J Immunol 152, 841-850.

Ohlmeier, M.D., Sieg, S., Emrich, H.M., Dietrich, D.E., 2007. Amantadine in acute bipolar mania. Aust N Z J Psychiatry 41, 194.

Ohlmeier, M.D., Zhang, Y., Bode, L., Sieg, S., Feutl, S., Ludwig, H., Emrich, H.M., Dietrich, D.E., 2008. Amantadine reduces mania in borna disease virus-infected non-psychotic bipolar patients. Pharmacopsychiatry 41, 202-203.

Ojika, K., Appel, S.H., 1984. Neurotrophic effects of hippocampal extracts on medial septal nucleus in vitro. Proc Natl Acad Sci U S A 81, 2567-2571.

Olive, M.F., Hodge, C.W., 2000. Co-localization of PKCepsilon with various GABA(A) receptor subunits in the mouse limbic system. Neuroreport 11, 683-687.

Ooi, E.E., Goh, K.T., Gubler, D.J., 2006. Dengue prevention and 35 years of vector control in Singapore. Emerging infectious diseases 12, 887-893.

Planz, O., Pleschka, S., Ludwig, S., 2001. MEK-specific inhibitor U0126 blocks spread of Borna disease virus in cultured cells. J Virol 75, 4871-4877.

Pletnikov, M.V., Moran, T.H., Carbone, K.M., 2002a. Borna disease virus infection of the neonatal rat: developmental brain injury model of autism spectrum disorders. Front Biosci 7, d593-607.

Pletnikov, M.V., Rubin, S.A., Vogel, M.W., Moran, T.H., Carbone, K.M., 2002b. Effects of genetic background on neonatal Borna disease virus infection-induced neurodevelopmental damage. I. Brain pathology and behavioral deficits. Brain Res 944, 97-107.

Pletnikov, M.V., Rubin, S.A., Vogel, M.W., Moran, T.H., Carbone, K.M., 2002c. Effects of genetic background on neonatal Borna disease virus infection-induced neurodevelopmental damage. II. Neurochemical alterations and responses to pharmacological treatments. Brain Res 944, 108-123.

Poblap, T., Nitatpattana, N., Chaimarin, A., Barbazan, P., Chauvancy, G., Yoksan, S., Gonzalez, J.P., 2006. Silent transmission of virus during a Dengue epidemic, Nakhon Pathom Province, Thailand 2001. Southeast Asian J Trop Med Public Health 37, 899-903.

Poenisch, M., Unterstab, G., Wolff, T., Staeheli, P., Schneider, U., 2004. The X protein of Borna disease virus regulates viral polymerase activity through interaction with the P protein. J Gen Virol 85, 1895-1898.

Poenisch, M., Wille, S., Ackermann, A., Staeheli, P., Schneider, U., 2007. The X protein of borna disease virus serves essential functions in the viral multiplication cycle. J Virol 81, 7297-7299.

Prat, C.M., Schmid, S., Farrugia, F., Cenac, N., Le Masson, G., Schwemmle, M., Gonzalez-Dunia, D., 2009. Mutation of the protein kinase C site in borna disease virus phosphoprotein abrogates viral interference with neuronal signaling and restores normal synaptic activity. PLoS Pathog 5, e1000425.

Richt, J.A., Stitz, L., 1992. Borna disease virus-infected astrocytes function in vitro as antigen-presenting and target cells for virus-specific CD4-bearing lymphocytes. Arch Virol 124, 95-109.

Rigau-Perez, J.G., Vorndam, A.V., Clark, G.G., 2001. The dengue and dengue hemorrhagic fever epidemic in Puerto Rico, 1994-1995. Am J Trop Med Hyg 64, 67-74.

Rodriguez Rodriguez, D., Garza Rodriguez, M., Chavarria, A.M., Ramos-Jimenez, J., Rivera, M.A., Tamez, R.C., Farfan-Ale, J., Rivas-Estilla, A.M., 2009. Dengue virus antibodies in blood donors from an endemic area. Transfus Med 19, 125-131.

Rosenberger, U., Shakibaei, M., Buchner, K., 1995. Localization of non-conventional protein kinase C isoforms in bovine brain cell nuclei. Biochem J 305 (Pt 1), 269-275.

Rott, R., Becht, H., 1995. Natural and experimental Borna disease in animals. Curr Top Microbiol Immunol 190, 17-30.

Sauder, C., de la Torre, J.C., 1999. Cytokine expression in the rat central nervous system following perinatal Borna disease virus infection. J Neuroimmunol 96, 29-45.

Sauder, C., Muller, A., Cubitt, B., Mayer, J., Steinmetz, J., Trabert, W., Ziegler, B., Wanke, K., Mueller-Lantzsch, N., de la Torre, J.C., Grasser, F.A., 1996. Detection of Borna disease virus (BDV) antibodies and BDV RNA in psychiatric patients: evidence for high sequence conservation of human blood-derived BDV RNA. J Virol 70, 7713-7724.

Schmid, S., Metz, P., Prat, C.M., Gonzalez-Dunia, D., Schwemmle, M., 2010. Protein kinase C-dependent phosphorylation of Borna disease virus P protein is required for efficient viral spread. Arch Virol 155, 789-793.

Schneider, U., 2005. Novel insights into the regulation of the viral polymerase complex of neurotropic Borna disease virus. Virus Res 111, 148-160.

Schneider, U., Schwemmle, M., Staeheli, P., 2005. Genome trimming: a unique strategy for replication control employed by Borna disease virus. Proc Natl Acad Sci U S A 102, 3441-3446.

Schwardt, M., Mayer, D., Frank, R., Schneider, U., Eickmann, M., Planz, O., Wolff, T., Schwemmle, M., 2005. The negative regulator of Borna disease virus polymerase is a non-structural protein. J Gen Virol 86, 3163-3169.

Schwemmle, M., De, B., Shi, L., Banerjee, A., Lipkin, W.I., 1997. Borna disease virus P-protein is phosphorylated by protein kinase Cepsilon and casein kinase II. J Biol Chem 272, 21818-21823.

Schwemmle, M., Salvatore, M., Shi, L., Richt, J., Lee, C.H., Lipkin, W.I., 1998. Interactions of the borna disease virus P, N, and X proteins and their functional implications. J Biol Chem 273, 9007-9012.

Shankar, V., Kao, M., Hamir, A.N., Sheng, H., Koprowski, H., Dietzschold, B., 1992. Kinetics of virus spread and changes in levels of several cytokine mRNAs in the brain after intranasal infection of rats with Borna disease virus. J Virol 66, 992-998.

Shoya, Y., Kobayashi, T., Koda, T., Ikuta, K., Kakinuma, M., Kishi, M., 1998. Two proline-rich nuclear localization signals in the amino- and carboxyl-terminal regions of the Borna disease virus phosphoprotein. J Virol 72, 9755-9762.

Stitz, L., Bilzer, T., Planz, O., 2002. The immunopathogenesis of Borna disease virus infection. Front Biosci 7, d541-555.

Stitz, L., Planz, O., Bilzer, T., 1998. Lack of antiviral effect of amantadine in Borna disease virus infection. Med Microbiol Immunol 186, 195-200.

Stoyloff, R., Strecker, A., Bode, L., Franke, P., Ludwig, H., Hucho, F., 1997. The glycosylated matrix protein of Borna disease virus is a tetrameric membrane-bound viral component essential for infection. Eur J Biochem 246, 252-257.

Talavera, D., Castillo, A.M., Dominguez, M.C., Gutierrez, A.E., Meza, I., 2004. IL8 release, tight junction and cytoskeleton dynamic reorganization conducive to permeability increase are induced by dengue virus infection of microvascular endothelial monolayers. The Journal of general virology 85, 1801-1813.

Tambyah, P.A., Koay, E.S., Poon, M.L., Lin, R.V., Ong, B.K., 2008. Dengue hemorrhagic fever transmitted by blood transfusion. The New England journal of medicine 359, 1526-1527.

Tan, F.L., Loh, D.L., Prabhakaran, K., Tambyah, P.A., Yap, H.K., 2005. Dengue haemorrhagic fever after living donor renal transplantation. Nephrol Dial Transplant 20, 447-448.

Terayama, H., Nishino, Y., Kishi, M., Ikuta, K., Itoh, M., Iwahashi, K., 2003. Detection of anti-Borna Disease Virus (BDV) antibodies from patients with schizophrenia and mood disorders in Japan. Psychiatry Res 120, 201-206.

Tomashek, K.M., Margolis, H.S., 2011. Dengue: a potential transfusion-transmitted disease. Transfusion 51, 1654-1660.

Tomonaga, K., 2004. Virus-induced neurobehavioral disorders: mechanisms and implications. Trends Mol Med 10, 71-77.

Tomonaga, K., Kobayashi, T., Ikuta, K., 2002. Molecular and cellular biology of Borna disease virus infection. Microbes Infect 4, 491-500.

Volmer, R., Monnet, C., Gonzalez-Dunia, D., 2006. Borna disease virus blocks potentiation of presynaptic activity through inhibition of protein kinase C signaling. PLoS Pathog 2, e19.

Walker, M.P., Jordan, I., Briese, T., Fischer, N., Lipkin, W.I., 2000. Expression and characterization of the Borna disease virus polymerase. J Virol 74, 4425-4428.

Walker, M.P., Lipkin, W.I., 2002. Characterization of the nuclear localization signal of the borna disease virus polymerase. J Virol 76, 8460-8467.

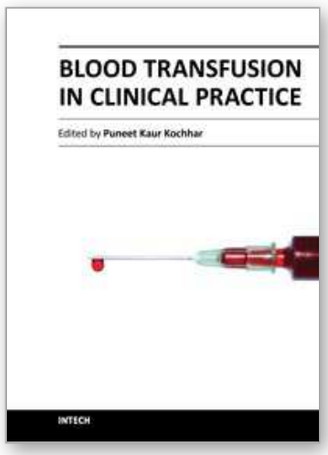
Wilcox, C.L., Johnson, E.M., Jr., 1988. Characterization of nerve growth factor-dependent herpes simplex virus latency in neurons in vitro. J Virol 62, 393-399.

Wilcox, C.L., Smith, R.L., Freed, C.R., Johnson, E.M., Jr., 1990. Nerve growth factor-dependence of herpes simplex virus latency in peripheral sympathetic and sensory neurons in vitro. J Neurosci 10, 1268-1275.

Wilder-Smith, A., Chen, L.H., Massad, E., Wilson, M.E., 2009. Threat of dengue to blood safety in dengue-endemic countries. Emerging infectious diseases 15, 8-11.

Wu, S.J., Grouard-Vogel, G., Sun, W., Mascola, J.R., Brachtel, E., Putvatana, R., Louder, M.K., Filgueira, L., Marovich, M.A., Wong, H.K., Blauvelt, A., Murphy, G.S., Robb, M.L., Innes, B.L., Birx, D.L., Hayes, C.G., Frankel, S.S., 2000. Human skin Langerhans cells are targets of dengue virus infection. Nature medicine 6, 816-820.

Zivna, I., Green, S., Vaughn, D.W., Kalayanarooj, S., Stephens, H.A., Chandanayingyong, D., Nisalak, A., Ennis, F.A., Rothman, A.L., 2002. T cell responses to an HLA-B*07-restricted epitope on the dengue NS3 protein correlate with disease severity. Journal of immunology 168, 5959-5965.



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Blood Transfusion in Clinical Practice focuses on the application of blood transfusion in different clinical settings. The text has been divided into five sections. The first section includes a chapter describing the basic principles of ABO blood group system in blood transfusion. The second section discusses the use of transfusion in various clinical settings including orthopedics, obstetrics, cardiac surgery, etc. The third section covers transfusion transmitted infections, while section four describes alternative strategies to allogenic blood transfusion. The last section speculates over immunomodulatory effects of blood transfusion.

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