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## **Haemovigilance and emerging infections in Blood Transfusion**

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Blood supply remains vulnerable to introduction of novel infectious blood borne agents. Haemovigilance is defined as a system of surveillance and alarm, ranging from the collection of blood products to the follow up of recipients, to gather and assess incidents resulting from the transfusion of the blood products. The main goal of haemovigilance is to prevent recurrence of incidents by identifying their causes. Blood Safety and Quality Regulations (BSQR) sets high standards of quality and safety in blood transfusion.

The instant traceability of infected or potentially infected individuals knowing test results, locations and movement over time and across borders is essential to containing the spread of highly contagious diseases.

West Nile virus (WNV) was discovered in 1937 in Uganda in Eastern Africa and was not found in the United States until the summer of 1999. Since then, over 30,000 individuals in the US have been positively diagnosed with illnesses attributable to the virus.

The vast majority of WNV infections are asymptomatic, about 20 percent of infections result in a flu-like illness called West Nile fever lasting from 3 to 6 days. The incubation period from infection to the onset of symptoms, when present is typically 2 to 14 days. Symptoms are generally mild and may include malaise, anorexia, nausea, vomiting, eye pain, headache, muscle pain, rash, and lymphadenopathy. Only about 1 in 150 people infected with WNV develop neuro-invasive West Nile disease, which may include meningitis, encephalitis, flaccid paralysis similar to that found in polio, and other neurologic manifestations.

Thus, PCR assays can detect WNV RNA in clinical samples as early as several days before symptom onset, prior to seroconversion. Although these assays have excellent analytical sensitivity, they lack

the clinical sensitivity of antibody tests and are typically not used alone for screening or diagnosis. By the time a patient presents with symptoms, viremia may be very low. Molecular assays may have some utility in patients with delayed or absent antibody response due to immunosuppression or other factors.

Hepatitis A to E viruses have immense and specific socioeconomic impact throughout the world. Viral hepatitis A and E are oro-faecal-transmitted diseases. They are particularly endemic in developing countries and are a public health issue for international travelers. Chronic hepatitis E is also becoming a concern for transplant patients. Viral hepatitis B, C and D are endemic in many parts of the world and transmitted by body fluid. They cause acute and chronic hepatitis with the potential to progress to cirrhosis and hepatocellular carcinoma.

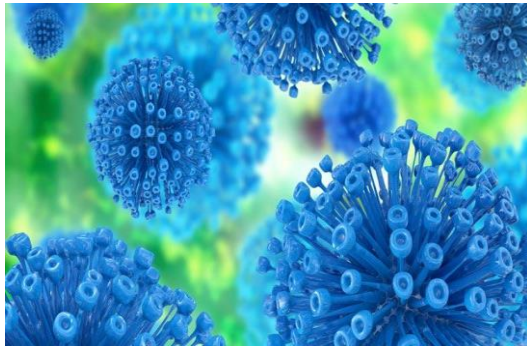
From a societal standpoint, control and prevention of viral hepatitis infections depend on public health policies and implementation. At the patient level, accurate and easily accessible diagnostic virologic tests, disease activity assessment, therapeutic response assays and genotypic analysis are essential for managing patients with chronic hepatitis.

Industry experts indicate the number of point-of-care devices being developed for the diagnosis of infectious diseases is increasing. Tests designed for infection control purposes may become more possible when developers better understand the limitations associated with their use.

Another pathogen emerging that is a potential threat to the U.S. blood supply is Dengue virus. This virus infects humans and is transmitted by mosquitos that have bitten infected animals or humans. This virus has enjoyed a resurgence in activity worldwide as mosquito populations have rebounded in the post-DDT era, and is prevalent in the Caribbean and many Latin American countries.

Continuous disease surveillance is also essential. It must be understood that strong surveillance systems for detecting conventional and emerging infectious diseases enhances our capacity to respond to the spread of diseases. The global Tuberculosis

epidemic and the Ebola outbreak in West Africa demonstrate the urgent need to explore new infection control technologies that can strengthen our defense against emerging pandemic threats from both bacterial and viral pathogens.



### **ZIKA VIRUS**

In 1947, the ZIKV was identified in Zika forest of Uganda and was named after the forest. The mode of transmission was by the Aedes mosquito. Dengue is the most common mosquito borne viral disease but soon Zika virus may soon be the most common mosquito borne viral disease as its geographical distribution is expanding.

Serological analyses are also important for establishing whether long-term consequences, such as microcephaly and Guillain-Barré syndrome, are a result of a previous Zika virus infection. If the link to congenital malformations is confirmed, Zika virus serology could play an important future role in prenatal diagnostics. Pregnant women with serological evidence of an infection could be offered advanced prenatal monitoring. Serology may also be useful for screening sample donations at blood centers and blood banks in hospital settings. Travellers returning from affected regions to Zika-free countries are advised not to donate blood for 26 days. After this time, serological testing can verify the safety of donated blood products. A further, critical role for serological studies is to monitor the growing epidemiological reach of the Zika virus as new evidence suggested the virus may be transmitted through blood transfusion, sexual transmission, prenatal transmission, however, the risk remains low. As the virus is expected to continue to spread around the globe, knowledge about the regions it has reached is valuable for providing effective healthcare planning.

### **EBOLA VIRUS**

Ebola was first discovered in 1976 near the Ebola River in what is now the Democratic Republic of the

Congo. A 27-year-old Belgian microbiologist named Peter Piot and his colleagues were the first to scientifically identify the Ebola virus. Human infection is acquired by exposure to infected blood, body fluid or tissue of infected animal. The incubation period is varies between 2 to 21 days.

It can be difficult to distinguish Ebola from other infectious diseases, and current diagnostic tests are time-consuming and complex. They also create challenges related to sample storage and transportation, laboratory biosafety, and staff expertise in performing the assays. Having access to simple, rapid, and accurate viral testing in remote villages would be extremely useful for quelling this and future epidemics. With this goal in mind, Paul Pickering (Ubiquitome Limited, Auckland, New Zealand) is spearheading the project to develop the assay for use with the Ubiquitome Freedom4 device. This portable PCR machine processes 4 reactions (sample plus negative, positive, and extraction controls) in approximately 1 hour, and is easily controlled via an iPhone or laptop. The Freedom4 device eliminates the need for sample preservation and transportation to a laboratory-based testing facility, and can simply be brought to remote locations for use during time-sensitive, public health situations.

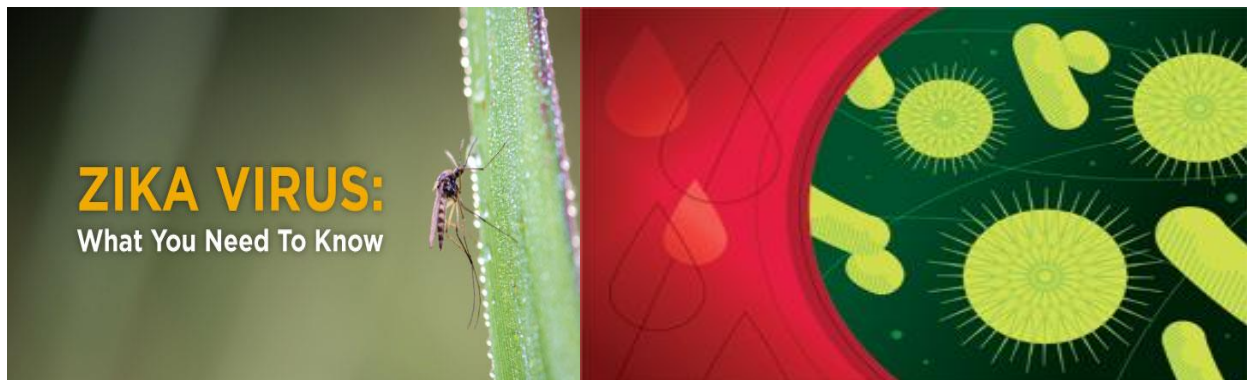
The Viral Haemorrhagic Fever Consortium, which is led by Tulane University and the diagnostic company Corgenix, has developed such a rapid test for Ebola. Called the ReEBOV Antigen Rapid Test Kit, this test uses a few drops of blood and the same technology used in at-home pregnancy tests to provide results in 15 minutes. In comparison, the current gold standard test for Ebola, qRT-PCR and can take up to a day to diagnose.

Mad cow disease, known as variant Creutzfeldt-Jakob disease (vCJD) in humans, is a fatal degenerative neurologic condition believed to be caused by prions, which are recently identified infectious agents consisting only of protein with no nucleic acid genome. CJD, identified in 1920, is the prototype human TSE, according to the World Health Organization. Hereditary CJD accounts for between 5% and 15% of cases, and a sporadic form accounts for between 85% and 90% of cases, WHO says. A small percentage of cases results from the accidental transmission of the infectious agent by way of contaminated surgical equipment, dura mater or corneal transplants, or through treatment with natural human growth hormone derived from cadaveric pituitary glands. CJD occurs worldwide with an incidence of about one case per million people annually, according to the CJD Foundation. The mechanisms for these diseases were unknown until Stanley Prusiner, MD, of the University of California San Francisco, proposed the prion theory in 1982 to explain a disease of sheep and goats called Scrapie. Similar diseases are known to affect other mammals. Skepticism and derision followed Dr. Prusiner's hypothesis. Colleagues made vicious

personal attacks in the press. Ridicule has turned to respect over the last 20 years, and significant evidence supports the prion theory, even though some researchers still dispute it. Prusiner won the 1997 Noble Prize in Medicine for "his discovery of prions a new biological principle of infection."

#### **Lassa fever or Lassa haemorrhagic fever (LHF)**

LHF is an acute viral haemorrhagic fever caused by the Lassa virus and first described in 1969 in the town of Lassa, in Borno State, Nigeria. Lassa virus is a member of the Arenaviridae virus family. Similar to Ebola,—clinical cases of Lassa fever had been known for over a decade, but had not been connected with a viral pathogen. While most humans are infected either from contact with an infected rat or inhalation of air contaminated with rat excretions, like other haemorrhagic fevers, Lassa fever can be transmitted directly from one human to another. It can be contracted through direct contact with infected human blood excretions and secretions, including through sexual contact. No evidence of airborne transmission person-to-person is seen. Transmission through breast milk has also been observed.



#### **Lessons Learned from the Ebola Outbreak**

According to Wilson, the U.S. has learned that the lack of available POCTs for specialized crisis scenarios such as the unexpected introduction of Ebola to a major metropolitan hospital (the Dallas crisis, for example) means delays in recognition of a potentially serious, life- and infrastructure-threatening pathogen.

"It's important to note that we all must follow guidelines when attempting to process a suspect Ebola patient," Wilson said. "The ability to rule-in or rule-out a situation dangerous not only to the patient, but healthcare staff, the medical infrastructure, and the community itself is critical."

Wilson believes the Ebola scare was a lesson from the pages of biodefense. "While such events are exceedingly rare, they are associated with consequences for the involved healthcare system and its community," he observed.

Khayriyyah Mohd Hanafiah and his fellow investigators determined the future will bring "an increasing need to develop cost-effective POCTs that address biomarkers that are well established in laboratory settings but are not currently amenable to point-of-care, such as molecular tests for drug resistance in TB and viral load in HIV and viral hepatitis."

Industry experts indicate the number of point-of-care devices being developed for the diagnosis of

infectious diseases is increasing. Tests designed for infection control purposes may become more possible when developers better understand the limitations associated with their use.

With modern high-throughput DNA sequencing, new viruses are identified much more rapidly than even a decade ago, but developing an effective test still takes time once a novel pathogen is identified.

### **Pathogen Reduction Technology**

The ideal scenario to prevent new and rare threats to the blood supply would be to develop a treatment that could inactivate pathogens that had escaped detection. These treatments exist for plasma, the liquid part of blood, but are too harsh to be applied to platelets or red blood cells as they would damage the product. Several companies have developed technologies to eliminate pathogens from blood products, and two are licensed for treatment of platelets in Europe, Intercept<sup>®</sup> produced by Cerus Corporation and Mirasol<sup>®</sup> produced by Terumo BCT. Both systems rely on ultraviolet (UV) light to activate amotosalen or riboflavin to damage nucleic acids in pathogens and kill them. These systems can reduce the level of viruses, bacteria and parasites (such as malaria) by one thousand- to one million-fold.

Although these systems are effective in treating platelets, they have not yet been approved to treat blood products containing red blood cells. The haemoglobin in red blood cells absorbs UV light, decreasing the ability of the light to reach pathogens to kill them.

### **Further reading**

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