Laboratory Bulletin

Date: June 4, 2018
To: Infectious Disease physicians, Transplant Programs, Laboratory managers
From: Provincial Laboratory for Public Health (ProvLab)
Re: Implementation of quantitative PCR for Human Herpesviruses 6 A and B (HHV-6 A and HHV-6 B) starting June 7, 2018

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Key Message:

- HHV-6 A and B, latent viruses with near universal prevalence, can be significant opportunistic pathogens.
- In immunodeficient patients, these viruses can cause diseases such as encephalitis, hepatitis or failure to engraft a bone marrow transplant.
- The diagnosis of HHV-6 disease can be facilitated by quantitative PCR on plasma or CSF.
- Quantitative HHV-6 PCR will be available at ProvLab starting June 7, 2018, by request to the Virologist on Call (VOC)

Background:

- HHV-6 belongs to the *Herpesviridae* family and possesses a wide tissue tropism. There are two variants of HHV-6, HHV-6 A and HHV-6 B, which some authors consider to be distinct species of viruses, in spite of their close genetic homology. Following primary infection, which is a nearly universal occurrence by age two, the virus establishes latency in T lymphocytes. Primary infection is typically asymptomatic, but may present with fever and possibly rhinorrhea and cough. Roseola (aka roseola infantum, exanthema subitum, 6th disease) is also a classical presentation. There has been several reported cases of association of febrile seizures in children and HHV6 detection by PCR on a CSF sample.
- HHV-6 periodically reactivates from latency, and is frequently shed in the saliva. HHV-6 B is the most pathogenic, whereas HHV-6 A is more neurotropic and is also more likely to be resistant to ganciclovir. HHV-6 can cause several opportunistic diseases among immunodeficient patients, including encephalitis, hepatitis, colitis, and in bone marrow transplant recipients, failure to engraft.
- The diagnosis of HHV-6 opportunistic infection can be facilitated by PCR detection of viral DNA in clinical samples, although the near universal presence of latent viruses in some T-cells complicates the diagnosis, which remains in part a diagnosis of exclusion. The diagnosis may be helped by testing for the viral DNA in plasma rather than whole blood, thereby avoiding cell associated latent viral genomes; but in many circumstances, such as failure to engraft, tissues (eg bone marrow aspirates) must be tested.
- Quantitative HHV-6 PCR can help to distinguish between latent and acute infection, to identify replication at only low level, and to monitor the disease evolution and response to antiviral therapy. Alone among human herpes viruses, HHV-6 is present in a small fraction of the human population as an integrated genome in a chromosome, acquired vertically and as such present in all cells. Whereas the definitive proof of this condition requires in situ hybridization of the chromosomes, high suspicion can be triggered by the demonstration of a very high viral load from cell-containing samples (whole blood, tissue biopsy) maintained over long period of time.

Availability of testing:

- ProvLab has now validated and implemented the Altona Real Star assay for HHV-6. The assay distinguishes between HHV-6 A and B, and is quantitative.
  Testing will be restricted to immunodeficient patients with compatible illness after consultation with the Virologist on Call.

Specimen submission:

- For testing on plasma, submit one blood in EDTA sample.
- For testing on CSF, submit at least 0.2 mL of CSF in a sterile container without additives.

Inquiries and feedback may be directed to:

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This bulletin has been reviewed and approved by:

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