



LABORATORY BULLETIN

2005-11-02

To: Transplant physicians, ID specialists, Laboratory Directors and Managers

Re: Changes and enhancements to infectious disease diagnosis and monitoring in transplant recipients (CMV, EBV and BKV)

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Nucleic acid amplification tests (NATs) for cytomegalovirus (CMV) Epstein-Barr virus (EBV) and BK virus (BKV) are emerging as the gold standard for monitoring solid organ transplant (SOT), hematopoietic stem cell transplant (HCT) and bone marrow transplant (BMT) recipients.

CMV diagnosis and monitoring

The CMV antigenaemia assay is poor in neutropenic patients as there are often insufficient cells for analysis. The subjective nature of this assay also makes the specificity difficult to maintain. Based on increasing requests for relevant NATs and following discussions with key stakeholders, **the locally available CMV PCR assay on plasma is to replace use of antigenaemia in the ProvLab in Calgary effective 14 November 2005.** Provision of this CMV plasma PCR assay for CMV will ensure standardized testing for transplant recipients who move around the province.

The CMV PCR assay to be used is sensitive, specific and correlates well with antigenaemia and other available viral load assays (1). The assay has been extensively validated. Monitoring of patients for surveillance and treatment will be based on evidence-based guidelines already developed for SOT (2) and adapted based on published guidelines for HCT and BMT recipients. Clinical indications and guidelines have been distributed separately and, through further discussion and follow up, will be reviewed frequently.

Specimen collection and submission for CMV PCR is the same as for the antigenaemia assay (one dedicated purple top EDTA tube submitted to ProvLab as soon as possible after collection). A specific requisition has been developed for this test (attached) to ensure specimens are identified and promptly handled, and to allow rapid confirmation of the key information required for processing.

CMV testing on plasma will be available locally (Calgary and Edmonton) with **testing routinely offered Monday – Friday**. A 24 hour turn-around is offered during regular week days. Results will generally be available the same day as submission provided the specimen is **received in the laboratory before 12 noon**. Testing during weekends / STAT holidays will need to be approved by the Microbiologist/Virologist on call (Calgary tel: 403 268 7210 or Edmonton tel: 780 407 7121) or tests will be held for the next regular work day.

The clinical cut-off of 25,000 copies/ml plasma used for pre-emptive therapy of SOT recipients may be too high for the BMT/HCT group if some high risk patients are included. Cut-off for instigation of therapy in BMT/HCT will be dependent on clinical risk. In the literature, suggested cut-off ranges from 100-1000 copies/ml (for T-cell depleted or other high-risk allogeneic recipients) to a higher cut-off used by some of more than 5,000 copies/ml. The assay to be used is sensitive down to 100-1000 copies/ml but quantification at the bottom end of the standard curve is not as accurate as for higher viral loads. Copy number below 500 copies/ml will not be provided but a positive result below this range (positive but <500 copies/ml) will be

given. Reports will be cumulative so that changes in viral load (the best measure of significant CMV activation) can be easily visualized. Changes of 3-5 fold in viral load have been shown to be biologically relevant and outside the assay variation in our, and other, studies.

EBV and BKV diagnosis and monitoring

EBV and BKV NATs have been available on a research basis in ProvLab for some time. Specific requisitions for ordering these tests are provided (attached) to ensure the specimens are easily identified and testing approval is not problematic. Clinical guidelines for testing are being developed and can be made available on request for those who have not been involved in their development. Testing for EBV and BKV is batched, and performed once-twice per week unless a specific urgent request is approved by the Microbiologist/Virologist on call.

If you have any queries or comments regarding the changes to testing and monitoring for CMV, EBV and BKV please contact one of us as below:

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References:

1) Pang, X. L., L. Chui, J. Fenton, B. LeBlanc, and J. K. Preiksaitis. 2003. Comparison of LightCycler-based PCR, COBAS amplicor CMV monitor, and pp65 antigenemia assays for quantitative measurement of cytomegalovirus viral load in peripheral blood specimens from patients after solid organ transplantation. J Clin Microbiol **41**:3167-3174.

2) Preiksaitis, J. K., D. C. Brennan, J. Fishman, and U. Allen. 2005. Canadian society of transplantation consensus workshop on cytomegalovirus management in solid organ transplantation final report. Am J Transplant **5**:218-227.



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