

# New Strategies in the Management of Herpesvirus Infections

Per Ljungman

*Head Department of Hematology, Huddinge University Hospital, Huddinge, Sweden*

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## **Abstract**

Herpesviruses have remained a major clinical problem in particular after allogeneic stem cell transplantation. During the last decade significant advances have been reached in management. These advances include development of new diagnostic techniques including measurement of viral load by quantitative detection of nucleic acid usually by PCR, use of preemptive antiviral strategies, better knowledge regarding the immune system's control of herpesvirus infections, and development of possible immune intervention strategies. The two herpesviruses for which these strategies have been employed are CMV and EBV. Antiviral prophylaxis as well as the strategy of preemptive therapy has reduced the CMV associated morbidity after allogeneic stem cell transplantation. However, both strategies result in over-treatment since more patients than necessary receive potentially toxic antiviral drugs. It has been shown that the CMV viral load and the increase in viral load both are significantly associated with the risk for CMV disease in allogeneic stem cell transplant patients. This allows for tailored antiviral therapy to those patients who have an increased risk for developing CMV disease. Another risk factor for CMV disease is the lack of developing a protective T-cell response. Patients at increased risk are those with graft-versus-host disease, having received a transplant from a mismatched or unrelated donor, or those patients who are seropositive but have received a graft from a CMV seronegative donor. These patients are prone to develop CMV disease late after transplant and therefore require prolonged or repeated antiviral therapy. Assessment of CMV specific immunity can be helpful and can today be performed by specific and sensitive techniques. A lot of work is currently ongoing to develop specific immune intervention strategies for example by T-cell infusions but this strategy remains to be proven clinically efficacious. EBV can cause fatal and rapidly progressive lymphoproliferative disease (PTLD) after stem cell transplantation. The risk factors are similar to those for CMV and EBV is also controlled by specific T-cells. Viral load measurements are being evaluated and several studies suggest that an increase in EBV viral load is predictive for PTLD. The usefulness of antiviral therapy is currently unknown. However, immune intervention has been studied both by the use of monoclonal antibodies (anti-CD20) against EBV infected B-cells and the prophylactic and therapeutic use of specific T-cell infusions. Thus, current development directions support that individualized rather than global preventive strategies against herpesviruses will be preferable in the future in allogeneic stem cell transplant patients. Further studies of the immune system as well as the viral replication biology will be essential to allow better and more effective use of these strategies.

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