Cytomegalovirus (CMV) infection is still a major concern following allogeneic hematopoietic transplantation because CMV pneumonia is fatal in 70% of patients, even when treated with a combination of antiviral therapies and CMV hyperimmune immunoglobulin. Allogeneic cord blood transplantation, especially from unrelated donors, has progressively gained favor as treatment for patients with both malignant and non-malignant disorders. As compared to allogeneic bone marrow transplantation (BMT) and peripheral blood stem cell transplantation (PBSCBT), advantages of unrelated cord blood transplantation (UCBT) include ease and safety of cell collection, low risk of transmitting viral infections, prompt availability of stem cells, and reduced incidence and severity of graft-versus-host disease (GVHD). The reduction of GVHD after UCBT is likely due to the naïve state of cord blood lymphocytes and the low cytotoxic capacity of cord blood T cells. However, such immunological immaturity after UCBT can place a patient at risk of early infectious complications, accounting for most transplant-related deaths, especially in adults. We have observed that patients undergoing UCBT appear to be at increased risk of CMV infection.

Ninety-one consecutive adult patients who were CMV-seropositive and received non-T-cell-depleted allogeneic transplants at the Kanazawa University Hospital between April 1999 and April 2004 were eligible for inclusion in this study to evaluate CMV reactivation in transplant recipients. Written informed consent was obtained from all patients. Six patients died of regimen-related toxicities before engraftment and one developed primary graft rejection followed by autologous hematopoietic recovery. The remaining 84 patients had successful initial engraftment and were included in the analysis. The patients’ characteristics are given in Table 1.

CMV antigenemia assays were carried out as previously described. In brief, heparinized blood samples were fractionated by dextran sedimentation. Slides were prepared in duplicate after cytocentrifugation; 1.5×10^5 leukocytes were fixed with formaldehyde and stained with HRP-C7 monoclonal antibodies that specifically bind the pp65 antigen of CMV (Teijin, Tokyo, Japan). The degree of CMV antigenemia was expressed as the number of CMV antigen-positive cells per 5×10^5 leukocytes. For the evaluation of CMV antigenemia, 5×10^5 leukocytes were...
always analyzed, because the detection limit was one CMV antigen-positive cell per $5 \times 10^4$ leukocytes in this assay. CMV antigenemia was defined as ≥1 antigen-positive cell. For the diagnosis of CMV disease, such as pneumonia, gastroenteritis, retinitis, and hepatitis, the CMV antigenemia had to be accompanied by clinical symptoms, signs, and histologic confirmation. Late CMV antigenemia was defined as that occurring after day 100. Ganciclovir or foscarnet was used as pre-emptive therapy to prevent CMV disease. The decision to use pre-emptive therapy was based entirely on a positive antigenemia test (≥3 antigen-positive cells/$5 \times 10^4$ leukocytes). Ganciclovir was administered as an intravenous infusion at the dose of 5 mg/kg/b.i.d. Neutropenic patients (absolute neutrophil count, less than 750/$\mu$L) were given foscarnet instead of ganciclovir; the induction dose of foscarnet was 60 mg/kg intravenously every 12 hours, followed by maintenance doses of 90 mg/kg once daily. Treatment was stopped if two consecutive CMV antigenemia assays were negative. Granulocyte colony-stimulating factor was administered when the absolute neutrophil count was <500/$\mu$L. Previous reports demonstrated the high sensitivity of the HRP-C7 assay and validated the analyzed cell count and the cut-off we relied on in our study.

All UCBT recipients developed CMV antigenemia whereas 44% of the recipients of related matched donor grafts, 70% of the recipients of unrelated matched donor grafts, and 67% of those receiving mismatched related donor transplants did so (Table 2). CMV-associated disease occurred in three patients (4%), gastroenteritis in two and interstitial pneumonia in one. Of these three patients only one patient, who developed interstitial pneumonia after UCBT, died of CMV disease. Forty-one patients (80%) received antiviral therapy; ganciclovir was used in 20 patients, foscarnet in 5, and the combination of both in 16. In the remaining 10 patients, CMV antigenemia remained below the detection level and disappeared without antiviral therapy. Although our data still require confirmation in a larger study.
prospective study, the impact of UCBT on the development of CMV antigenemia might be considered when designing future transplant strategies, at least until more effective methods for prophylaxis of CMV reactivation become available.

References