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Anti-viral immunity and measures to control disease pathogenesisin the hematopoietic stem cell transplant setting

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Allogeneic hematopoietic stem cell transplantation (HSCT) is a curative modality for children with certain hematologic malignancies and non-malignant disorders. Viral infections post-transplant contribute significantly to the morbidity and mortality from this procedure.Serious viral infections are fatal in 15-20% of cases. Cytomegalovirus (CMV), adenovirus (ADV), Epstein-Barr virus (EBV), respiratory viruses, human herpes viruses, and BK virus account for the majority of viral infections. Screening for CMV and ADV viremia, and pre-emptive therapy has significantly reduced the incidence of CMV and ADV disease. Newer drugs for adenovirus such as brincidofovirmay be less toxic,andmore efficacious compared to cidofovir. EBV-specific cytotoxic T-lymphocytes are an attractive adjunct to monoclonal anti-B-cell antibody therapy. Therapeutic option forparainfluenza virus with a drug cleaving the sialic acid viral receptor on respiratory epithelial cells is in a clinical trial. Manipulation of the graft withselective depletion of naïve T-cells to prevent graft-versus-host disease (GVHD), and infusion of NK cells post-transplant may allow for early immune reconstitution and improved anti-viral immunity in the haplo-identical transplant setting. However T-cell depletion is associated with increased relapse. An alternative to ex-vivo T-cell depletion is to administer donor T-cells that incorporate a suicide gene that can be activated in the event of GVHD. Treatment with allogeneic virus-specific cytotoxic T-lymphocytes can effectively reconstitute antiviral immunity against CMV, EBV and ADV. Newer antiviral drugs and cellular therapy promise an exciting future to control viral disease in the HSCT setting.

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