Published in final edited form as:
Transpl Infect Dis. 2014 February ; 16(1): 90–97. doi:10.1111/tid.12165.

Early infections after autologous hematopoietic stem cell transplantation in children and adolescents: the St. Jude experience

A. Srinivasan[1,2], **L. McLaughlin**[3], **C. Wang**[4], **D.K. Srivastava**[4], **D.R. Shook**[1,2], **W. Leung**[1,2], and **R.T. Hayden**[5]

[1]Departments of Bone Marrow Transplantation and Cellular Therapy, St. Jude Children's Research Hospital, Memphis, Tennessee USA

[2]Department of Pediatrics, University of Tennessee Health Science Center, Memphis, Tennessee, USA

[3]Department of Medicine, Florida State University College of Medicine, Tallahassee, Florida, USA

[4]Biostatistics, St. Jude Children's Research Hospital, Memphis, Tennessee USA

[5]Pathology, St. Jude Children's Research Hospital, Memphis, Tennessee USA

Abstract

Introduction—Advances in autologous hematopoietic stem cell transplantation (HSCT) over the past 20 years may have had an impact on the morbidity and mortality associated with infections post transplant.

Patients and methods—We sought to retrospectively analyze the epidemiology of the first episode of bacterial, fungal, viral, or parasitic infections 0–30 days post transplant in a cohort of 320 children and adolescents who underwent autologous HSCT in a single institution, between 1990 and 2009 for solid tumors or lymphoma, and in 65 children transplanted for acute leukemia during the same period.

Results—Infections occurred in 66 (21%) patients with solid tumors or lymphoma. Bacterial infections occurred in 33 (10%) including bacteremia in 23 (7%), and viral infections in 34 (11%) patients. Gram-positive bacterial infections were more prevalent than gram-negative bacterial infections ($P = 0.03$). Infections caused by fungal or parasitic pathogens were uncommon. The decade when transplant was performed (1990–1999 vs. 2000–2009) had no impact on the incidence of bacterial ($P = 0.41$) or viral ($P = 0.47$) infection. Between 1990 and 1999, 60 (92%) children were transplanted for leukemia, and 5 (8%) in the 2000–2009 period ($P < 0.0001$). Infections occurred in 32 (49%) patients. Bacterial ($P = 0.004$), candidal ($P = 0.003$), and herpes

Correspondence to: Ashok Srinivasan, MD, Department of Bone Marrow Transplantation and Cellular Therapy, St. Jude Children's Research Hospital, 262 Danny Thomas Place, MS 1130, Memphis, TN 38105-2794 USA, Tel: (901) 595-4720, Fax: (901) 595-7944, ashok.srinivasan@stjude.org.

Author contributions: A.S. designed the study, analyzed and interpreted data, and wrote the paper; L.M. collected study material and analyzed the data; C.W., and D.K.S. performed statistical analysis; R.T.H., D.R.S., and W.L. provided study material and contributed to analysis and interpretation of data. All authors contributed to the revisions of the draft and approval of the final manuscript.

Conflict of interest disclosure: The authors declare no competing financial interests.

simplex viral ($P = 0.03$) infections were more common in patients transplanted for leukemia. In patients transplanted for leukemia, 3 deaths occurred attributed to infection, all before 2000.

Conclusion—Changes in epidemiology of infection are likely a result of decline in autologous transplantation for childhood leukemia in the recent era. Autologous transplantation for solid tumors or lymphoma was not associated with mortality from early infections at our institution.

Keywords

infections; children; autologous; stem cell transplantation

Autologous hematopoietic stem cell transplantation (HSCT) is a well established therapy for treatment of malignancies and immune disorders. Infections are an important cause of morbidity from the procedure. Changes in transplantation strategies and improvement in supportive care over the past 2 decades may have significantly altered the incidence and pattern of infections in these patients.

Few studies have evaluated the impact of these strategies on infections in both children and adults undergoing autologous HSCT, focusing on a large population, over a long period of time. Several small retrospective studies in adults have shown that gram-positive (GP) bacterial infections outnumber gram-negative (GN) bacterial infections, bacteremia is detected in up to one-fifth of patients, invasive fungal infections (IFI) are uncommon, and mortality from autologous transplants ranges from 2% to 4% (1–3). Studies in children are limited, with relatively small numbers of patients, and have focused on autologous transplants prior to 2000 (4, 5). We hypothesized that the institution of routine antiviral and antifungal prophylaxis after 2000 may have significantly altered the incidence and pattern of infections in these patients.

Patients and methods

This retrospective cohort consisted of 385 patients < 21 years of age, who underwent their first autologous HSCT over a 20-year period (January 1990 through December 2009) at St. Jude Children's Research Hospital (SJCRH). The study was approved by the SJCRH Institutional Review Board. The mean duration of follow-up for surviving patients was 8.73 (range 0.31–19.91) years.

Microbiologic methods

Microbiologic records were reviewed to identify patients with documented bacterial, fungal, or viral infections as diagnosed by culture (bacteria, fungi, viruses), fluorescent antibody testing (viruses and parasites), and polymerase chain reaction (viruses). Infection was defined as isolation or detection of an organism that was associated with symptoms or disease, and included viral pathogens detected on pre-emptive screening. Colonization detected in surveillance cultures and positive blood cultures caused by contamination were not considered as infections. Two consecutive positive cultures were required for inclusion of coagulase-negative staphylococci (CONS). Only the first episode of bacterial infection in a given patient, during the specified time period, was included in the univariate analyses. Bacterial infections included bacteremia and infections by *Clostridium difficile*. Only

infections occurring up to 30 days post transplant were included in the analyses, as the patient was transferred to the primary service after approximately 30 days in the absence of complications. The day of onset of infection was defined as the day when the first positive diagnostic sample was collected. Infection as the primary cause of death was used for analyses.

Peripheral blood samples were collected once weekly, on consecutively transplanted patients from January 2005 until September 2007 to prospectively screen for cytomegalovirus (CMV) by quantitative real-time polymerase chain reaction assays during the first 30 days post transplant, as previously described (6), using an ABI PRISM 7900HT Sequence Detection system (Applied Biosystems, Foster City, California USA). Screening for galactomannan was not performed. Only patients with proven fungal infections as defined by de Pauw et al. (7) were included.

Infection prophylaxis

Patients received prophylaxis against *Pneumocystis jirovecii* pneumonia with trimethoprim-sulfamethoxazole. Before the year 2000, patients at risk for herpes simplex virus (HSV) and varicella zoster virus (VZV) reactivation received acyclovir prophylaxis at the discretion of the supervising clinician. After January 2000, acyclovir prophylaxis was used routinely for 3 weeks post transplant in HSV-, VZV- or CMV-seropositive patients, and fluconazole was used routinely in all patients for antifungal prophylaxis up to 30 days post transplant.

Era of transplantation

The population was divided into 2 eras: 1990–1999 with 188 HSCT patients, and 2000–2009 with 197 HSCT patients. The year 2000 onward represented a boundary for preferential use of apheresis hematopoietic stem cell product (HPC-A) over bone marrow (HPC-M) and for routine use of antiviral and antifungal prophylaxis.

Transplantation methods

Transplant-related variables were abstracted from a prospectively collected database that included patient demographics, underlying diagnosis, remission status, product type, CMV status, and conditioning regimen.

A total of 141 (37%) patients received carboplatin-based conditioning in combination with etoposide (81; 21%) or etoposide + melphalan (60; 16%); 161 (42%) patients received cyclophosphamide-based conditioning with busulfan (70; 18%), topotecan (66; 17%), or etoposide (25; 7%); and 35 (9%) patients received busulfan and melphalan. The remaining 48 (12%) patients were treated with a combination of different agents. Three (0.8%) patients received total-body irradiation as part of their conditioning regimen.

All patients had marrow morphologically free of tumor at the time of collection of the HPC-A product or an unstimulated marrow harvest. Peripheral blood stem cell (PBSC) collection was performed after routine chemotherapy administration followed by granulocyte colony-stimulating factor 10 mcg/kg/day until apheresis was completed. Collection goal was ≥ 2×10^6 $CD34^+$ cells/kg for the HPC-A product, and $\geq1\times10^8$ total nucleated cells/kg for the

HPC-M product. All stem cell products were stored at –150°C in the vapor phase of liquid nitrogen using 10% dimethylsulfoxide and a controlled rate freeze program. Granulocyte colony-stimulating factor was given at 5 mcg/kg/day from either day +1 or day +5, depending on the protocol, until the absolute neutrophil count was ≥ 2000 cells/μL on 2 successive days. The day of engraftment was defined as the first of 3 consecutive days of achieving an absolute neutrophil count >500 cells/μL. Seventeen patients with solid tumors or lymphoma received a $CD34^+$ selected autologous bone marrow graft as described (8). Twelve patients with solid tumors or lymphoma received high-dose busulfan and melphalan followed by infusion of a CD133 selected autologous PBSC graft as described (9).

Statistical analysis

The association between infections (bacterial, viral) and the risk factors of interest was first evaluated using univariate logistic regression. Risk factors evaluated included age at transplant (0–2 vs. 2–10 vs. >10 years), gender, race, underlying diagnosis (solid tumors vs. lymphoma), stem cell product type (HPC-A vs. HPC-M), disease status before transplant (whether or not in complete remission), CMV serostatus (positive vs. negative), era of transplantation (1990–1999 vs. 2000–2009), and days to engraftment. The analyses for each type of infection were conducted independently. All factors that were significant at level $\alpha = 0.10$ in the univariate analyses were included in the multiple logistic regression models. CMV viremia was excluded from the univariate logistic analyses, as screening was done only in a subset of patients. The final model reports the results of all factors that remained significant at the 5% level.

Exact chi-square and Kruskal–Wallis tests were used to determine whether a significant difference in demographics existed between the 2 eras. Chi-square test was used to test whether there was a significant difference among GP vs. GN infections. All analyses were conducted in SAS version 9.2 (SAS Institute, Cary, North Carolina, USA) and StatXact (Cytel Corporation, Cambridge, Massachusetts, USA) Windows version 8.

Results

Patient characteristics

A total of 385 patients underwent an autologous HSCT between 1990 and 2009 at SJCRH, with 320 of the patients undergoing autologous HSCT for solid tumors or lymphoma. Demographics and patient characteristics are presented in Table 1. Of the 65 patients who underwent an autologous HSCT for leukemia, 60 (92%) were in 1990–1999, and 5 (8%) were in 2000–2009 ($P < 0.0001$). Of the 65 patients, 64 (98%) were diagnosed with acute myeloid leukemia (AML) and 1 with acute lymphoblastic leukemia. A comparison of demographic characteristics for patients with leukemia in the 2 eras was therefore not made.

Of the patients transplanted for solid tumors or lymphoma, significantly more patients were CMV positive ($P = 0.001$), received a HPC-A product ($P < 0.0001$), and engrafted within 28 days ($P < 0.0001$) in 2000–2009 than in 1990–1999. Patients with leukemia engrafted at a median time of 27 days compared to 12 days for patients with solid tumors or lymphoma ($P < 0.0001$).

Infections in patients transplanted for solid tumors or lymphoma

Infections were documented in 66 (21%) patients. Bacterial infections occurred in 33 (10%) patients. The median onset of bacterial infection was 5 days post transplant. GP were more prevalent than GN infections ($P = 0.03$; Table 2). No difference in GP/GN infections was seen between the 2 decades ($P = 0.45$). However GP infections were more prevalent than GN infections between 2000 and 2009 ($P = 0.02$). Patients with a diagnosis of lymphoma were not at higher risk for bacterial infections, compared with those with solid tumors ($P = 0.95$). Bacterial infections included bacteremia seen in 23 (7%) patients. GP bacteremia occurred in 12 patients, and GN bacteremia in 11 patients.

CONS and alpha-hemolytic streptococci (non-pneumococcal) were the most common GP organisms causing bacteremia in 6 and 3 patients each, respectively. Two patients had *Bacillus* species and 1 patient had *Staphylococcus aureus bacteremia. Klebsiella* species followed by *Escherchia coli* were the most common GN organisms causing bacteremia in 5 and 2 patients, respectively. One patient each had *Morganella, Proteus, Acenitobacter*, and *Enterobacter* species bacteremia, respectively. Only 2 patients had >1 bacterial infection. One patient had infection with *Morganella* species on day +4 and *C. difficile* infection on day +10 post transplant. Another patient had *C. difficile* infection on day +1 and *E. coli* infection on day +6 post transplant. Bacteremia led to hypotension requiring intensive care unit support in 4 (6%) patients. *C. difficile* infection was seen in 11 (3%) patients, and occurred at a median of 6.5 days post HCT. Symptoms resolved in all patients with metronidazole therapy, with no recurrences.

Candida albicans fungemia with tricuspid valve endocarditis was diagnosed in a patient with neuroblastoma who responded to antifungal therapy. *Aspergillus flavus* was isolated from the lung biopsy of another patient with neuroblastoma on day +7 post transplant; this patient had complete resolution of the infection after lobectomy and amphotericin B therapy. Both infections occurred before 2000. The median onset of fungal infection was 11 days post transplant. No patients had >1 fungal infection in the first 30 days post transplant.

Parasitic infections were uncommon, and detected only before 2000. Two patients had diarrhea and *Giardia* species infection 5 and 15 days post transplant, which responded to therapy.

A total of 34 (11%) patients had viral infections, with a median onset of 10 days post transplant. HSV was the most common cause of infection, seen in 17 (5%) patients. HSV was more common in 1990–1999 than in 2000–2009 ($P = 0.04$). Of the 50 patients who had surveillance screening for CMV, 6 (2%) patients with solid tumors or lymphoma had detectable viremia: 2 patients had <1000 copies/mL, 3 had 1000–1500 copies/mL, and 1 patient had 9000 copies/mL. Viremia resolved within 1 month post transplant. Patients with >1000 copies/mL received therapy with intravenous foscarnet. No patient developed CMV disease. All patients with respiratory virus infection had only upper respiratory tract involvement. No patients had >1 viral infection.

On multiple logistic regression analysis, the decade when transplant was performed (1990–1999 vs. 2000–2009) had no impact on the incidence of bacterial ($P = 0.41$) or viral ($P =$

0.47) infection. None of the other variables increased the risk for bacterial or viral infections. Fungal and parasitic infections were not included in logistic regression analysis, as they were few in number.

Of the 17 patients who had a $CD34^+$-selected bone marrow graft, 2 (12%) had infections, with CONS bacteremia and *Escherichia coli* lower urinary tract infection, respectively. Of the 12 patients who received a CD133-selected PBSC graft, 7 (58%) had infections, which included CONS bacteremia in 1 patient, GN bacteremia in 2 patients, CMV reactivation in 2 patients, *C. difficile* infection in 1 patient, and parainfluenza-3 upper respiratory tract infection in 1 patient.

Three isolates of alpha-hemolytic *Streptococcus* were all susceptible to cephalosporins, vancomycin, aminoglycosides, ciprofloxacin, and clindamycin, and resistant to trimethoprim-sulfamethoxazole and oxacillin. All gram-negative isolates were susceptible to cephalosporins, carbapenems, ciprofloxacin, and aminoglycosides, with no change in the 2 eras.

Infections in patients transplanted for leukemia

Infections were documented in 32 (49%) patients with leukemia. Bacterial infections occurred in 17 (26%) patients (Table 3). One patient had both a GP and a GN infection. GP were more prevalent than GN infections ($P < 0.0001$). Bacteremia was seen in 9 (14%) patients. The median onset of bacterial infections was not significantly different in patients with solid tumors or lymphoma, and in those with leukemia ($P = 0.75$). Patients with a diagnosis of leukemia had a higher risk of bacterial ($P = 0.004$, odd ratio 2.84, 95% confidence interval 1.45–5.55), *Candida* species ($P = 0.003$), and HSV ($P = 0.03$) infections compared to those with solid tumors or lymphoma.

Of the 385 patients in the cohort, 3 (0.7%) died primarily because of infections in the first 30 days post transplant. All were patients transplanted for AML in complete remission before transplant, and conditioned with busulfan and cyclophosphamide. Causes of death included sepsis from *C. albicans*, *Klebsiella pneumoniae*, and *Streptococcus mitis*, respectively. No patients with solid tumors or lymphoma died of infection in the first 30 days post transplant.

Discussion

This study retrospectively evaluated the infectious complications of autologous HSCT performed over a 20-year period in a cohort of 385 patients, mostly children and adolescents (84%), with a few infants (9%) and young adults 18 to <21 years of age (7%). The underlying diagnosis was a solid tumor in 62% and lymphoma in 21% patients. Patients with a diagnosis of acute leukemia (17%) were mostly transplanted between 1990 and 1999.

GP infections were more prevalent than GN bacterial infections, consistent with a study in adults with predominantly solid tumors (10) and with another study in adults with solid tumor, lymphoma, and multiple myeloma (11). Bacteremia occurred in 7% of our patients. This rate is lower than the 13% (1) to 21% (11) incidence of bacteremia in adult patients transplanted for breast cancer (1), or solid tumor, lymphoma, and multiple myeloma (11),

within 1 month post transplant. No differences in the incidence, type, and clinical course of infection based on underlying disease were seen in the latter study (11).

The incidence of bacteremia after autologous HSCT in our series is similar to the 8% incidence of bacteremia seen 0–30 days post transplant in a cohort of 759 children who underwent allogeneic transplantation at SJCRH during the same period (12), emphasizing the role of neutropenia, mucositis, and gastrointestinal toxicity as important risk factors, independent of HSCT source. CONS and alpha-hemolytic streptococci were the most common GP organisms, and *Klebsiella* species and *E. coli* were the most common GN organisms causing bacteremia in both autologous and allogeneic patients at our institution.

Adults transplanted for acute leukemia had a higher probability of infection with a longer median time to engraftment (13). Higher bacterial infection rates were seen in patients with leukemia who had significantly delayed engraftment compared with patients with solid tumors or lymphoma in our study. Although age <18 years has been identified as a risk factor for streptococcal bacteremia (14), its incidence was only 2% in our series, compared with 17.5% in adult patients with predominantly solid tumors or lymphoma undergoing autologous HCT (15). *Streptococcus viridans* was isolated a median of 6 (range 2–8) days post transplant (15). The high incidence in adults may have been a result of the use of prophylactic fluoroquinolones, to which streptococci are usually resistant. None of our patients received prophylactic antibiotics. This may partly explain the lack of changing bacterial resistance over the years. The incidence of *C. difficile* infection in our study was 3% compared with 10% in adults transplanted for breast cancer (1), and 6% in adults transplanted predominantly for leukemia (16).

The incidence of *Candida* and proven aspergillosis infections in the period 1990–1999 was 1%, similar to the 1% (1) to 2% (11) incidence reported in adults. No cases of IFI occurred from 2000–2009, in the era of standard antifungal prophylaxis. Furthermore, patients transplanted for leukemia had significantly more *Candida* species infections compared with patients transplanted for solid tumors or lymphoma. Since few patients were transplanted for leukemia after 2000, this may have contributed significantly to the lack of IFI after this period.

Only 3 deaths were attributed to infection. All occurred before the year 2000 in patients transplanted for acute leukemia. No mortality from infection was observed in patients transplanted for solid tumors or lymphoma. The rarity of transplantation for childhood leukemia in the recent era contributed significantly to the absent mortality from infection in this period.

Antiviral prophylaxis with acyclovir reduced HSV disease, although it remained the most frequently occurring viral infection in the first month post transplant. VZV reactivation was observed in 1% of children, far lower than the incidence in adults. Older age has been noted to be a risk factor for herpes zoster in children (17). T-cell receptor rearrangement excision circles (TRECs) were shown to be significantly higher in patients <19 years of age as compared with older patients (18). Routine CMV surveillance for autologous transplants

was discontinued after a low incidence of clinically significant viremia. However, high-risk symptomatic patients may benefit from CMV monitoring in the autologous setting (19).

Rate of respiratory virus infection was 2% among this cohort, much higher than the 0.4% observed in a prospective study by Ljungman et al. (20) of respiratory virus infections among 1154 predominantly adult autologous HCT recipients, over a period of 30 months. Children are more prone than adults to develop respiratory virus infections, and shed virus for longer periods of time.

Patients who received $CD34^{+}$-selected bone marrow grafts did not have a higher incidence of infection, similar to the experience in adults after autologous HSCT for solid tumors (10). The risk of infections with CD133-selected PBSC grafts will need to be explored with larger numbers of patients.

Ours is the largest retrospective study, to our knowledge, on the epidemiology of infections in children who underwent autologous HSCT over the last 20 years (1990–2009). A retrospective study of 185 children who underwent autologous HSCT between 1990 and 1998 (4) showed a higher incidence of GN (20; 11%) vs. GP (17; 9%) infections, and of candidiasis (8; 4%). Another retrospective study in 75 children who underwent autologous HSCT between 1986 and 1996 identified 6 (8%) cases of proven IFI, including 2 cases each of *Candida* and *Aspergillus* species (5). These studies included smaller numbers of patients; approximately 15% were diagnosed with leukemia, and highlight the incidence of IFI in children before 2000, when routine antifungal prophylaxis was not widely prevalent. GP infections appear to have become more common than GN infections, in the recent era.

Our study had several limitations. The patient population that was studied was heterogeneous, analyses were retrospective, and prophylaxis differed across the 2 decades. Only microbiologically documented infections were included. Fungal and parasitic infections were few in number and could not be analyzed. Only infections 0–30 days post transplant were studied.

While bacteremias were as prevalent in the autologous and allogeneic transplant settings in our institution, no significant change in the epidemiology of bacterial infections was noted in patients with solid tumors or lymphoma who underwent an autologous transplant. GP were more common than GN bacterial infections. No proven IFI were seen in the recent era. This finding may have implications for empiric antifungal therapy. Antiviral prophylaxis reduced HSV infections in this population. Infection-related mortality was absent in the recent era, with the rarity of autologous HSCT for pediatric AML. Autologous transplantation for solid tumors or lymphoma was not associated with mortality caused by infections at our institution.

Acknowledgments

Thanks: The authors thank Mark Mestemacher (Clinical Laboratory), Pamela Young (Cancer Center Administration), and Nancy L. Hooper (Bone Marrow Transplantation and Cellular Therapy, clinical research office) at SJCRH, Memphis, TN, for assistance in data collection.

Support: This work was supported by National Cancer Institute Cancer Center CORE Support Grant P30 CA 21765 and by the American Lebanese Syrian Associated Charities. L.M. was supported in part by 5R25CA02394 from the National Cancer Institute.

References

1. Barton TD, Collis T, Stadtmauer E, Schuster MG. Infectious complications the year after autologous bone marrow transplantation or peripheral stem cell transplantation for treatment of breast cancer. Clin Infect Dis. 2001; 32:391–395. [PubMed: 11170946]
2. Auner HW, Zebisch A, Ofner P, Sill H, Linkesch W, Krause R. Evaluation of potential risk factors for early infectious complications after autologous peripheral blood stem cell transplantation in patients with lymphoproliferative diseases. Ann Hematol. 2005; 84:532–537. [PubMed: 15809882]
3. Pagano L, Caira M, Nosari A, et al. Fungal infections in recipients of hematopoietic stem cell transplants: results of the SEIFEM B-2004 study--Sorveglianza Epidemiologica Infezioni Fungine Nelle Emopatie Maligne. Clin Infect Dis. 2007; 45(9):1161–1170. [PubMed: 17918077]
4. Benjamin DK Jr, Miller WC, Bayliff S, Martel L, Alexander KA, Martin PL. Infections diagnosed in the first year after pediatric stem cell transplantation. Pediatr Infect Dis J. 2002; 21(3):227–234. [PubMed: 12005087]
5. Hovi L, Saarinen-Pihkala UM, Vettenranta K, Saxen H. Invasive fungal infections in pediatric bone marrow transplant recipients: single center experience of 10 years. Bone Marrow Transplant. 2000; 26:999–1004. [PubMed: 11100280]
6. Gu Z, Belzer SW, Gibson CS, Bankowski MJ, Hayden RT. Multiplexed, real-time PCR for quantitative detection of human adenovirus. J Clin Microb. 2003; 41(10):4636–4641.
7. DePauw B, Walsh TJ, Donnelly JP, et al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clin Infect Dis. 2008; 46(12):1813–1821. http://www.ncbi.nlm.nih.gov/pubmed/18462102. [PubMed: 18462102]
8. Kasow KA, Sims-Poston L, Eldridge P, et al. CD34+ hematopoietic progenitor cell selection of bone marrow grafts for autologous transplantation in pediatric patients. Biol Blood Marrow Transplant. 2007; 13:608–614. [PubMed: 17448921]
9. Leung W, Handgretinger R, Iyengar R, et al. Inhibitory KIR-HLA receptor-ligand mismatch in autologous haematopoietic stem cell transplantation for solid tumor and lymphoma. Br J Cancer. 2007; 97:539–542. [PubMed: 17667923]
10. Frere P, Pereira M, Fillet G, Beguin Y. Infections after CD-34 selected or unmanipulated autologous hematopoietic stem cell transplantation. Eur J Hematology. 2006; 76:102–108.
11. Reich G, Mapara MY, Reichardt P, Dorken B, Maschmeyer G. Infectious complications after high-dose chemotherapy and autologous stem cell transplantation: comparison between patients with lymphoma or multiple myeloma and patients with solid tumors. Bone Marrow Transplant. 2001; 27:525–529. [PubMed: 11313687]
12. Srinivasan A, Chong W, Srivastava DK, et al. Timeline, epidemiology and risk factors for bacterial, fungal and viral infections in children and adolescents after allogeneic hematopoietic transplantation. Biol Blood Marrow Transplant. 2013; 19:94–101. [PubMed: 22922523]
13. Gil L, Styczynski J, Komarnicki M. Infectious complication in 314 patients after high-dose therapy and autologous hematopoietic stem cell transplantation: risk factors analysis and outcome. Infection. 2007; 35(6):421–427. [PubMed: 17926001]
14. Mascret B, Maraninchi D, Gastaut JA, et al. Risk factors for streptococcal septicemia after marrow transplantation. Lancet. 1984; 1(8387):1185–1186. [PubMed: 6144912]
15. Bilgrami S, Feingold JM, Dorsky D, et al. *Streptococcus viridans* bacteremia following autologous peripheral blood stem cell transplantation. Bone Marrow Transplant. 1998; 21:591–595. [PubMed: 9543063]
16. Alonso CD, Treadway SB, Hanna DB, et al. Epidemiology and outcomes of *Clostridium difficile* infections in hematopoietic stem cell transplant recipients. Clin Infect Dis. 2012; 54(8):1053–1063. [PubMed: 22412059]

17. Berman JN, Wang M, Berry W, Neuberg DS, Guinan EC. Herpes zoster infection in the post-hematopoietic stem cell transplant pediatric population may be preceded by transaminitis: an institutional experience. Bone Marrow Transplant. 2006; 37:73–80. [PubMed: 16247423]

18. Lewin SR, Heller G, Zhang L, et al. Direct evidence for new T-cell generation by patients after either T-cell depleted or unmodified allogeneic hematopoietic stem cell transplantations. Blood. 2002; 100(6):2235–2242. [PubMed: 12200390]

19. Bilgrami S, Aslanzadeh J, Feingold JM, et al. Cytomegalovirus viremia, viruria and disease after autologous peripheral blood stem cell transplantation: no need for surveillance. Bone Marrow Transplant. 1999; 24:69–73. [PubMed: 10435738]

20. Ljungman P, Ward KN, Crooks BNA, et al. Respiratory virus infections after stem cell transplantation: a prospective study from the Infectious Diseases Working Party of the European Group for Blood and Marrow Transplantation. Bone Marrow Transplant. 2001; 28:479–484. [PubMed: 11593321]

Table 1

Demographics and characteristics of pediatric patients with solid tumors and lymphoma who underwent an autologous HSCT at SJCRH between 1990 and 2009

Characteristic	1990–1999 *n*=128	2000–2009 *n*=192	1990–2009 *n*=320	*P*-value
Mean age in years	9.0	8.3	8.6	0.80
0–<2	9 (7)	16 (8)	25 (8)	
2– <10	68 (53)	108 (56)	176 (55)	
>10	51 (40)	68 (35)	119 (37)	
Males	85 (66)	115 (60)	200 (63)	0.29
Race				0.41
White	102 (80)	145 (76)	247 (77)	
AA	23 (18)	37 (19)	60 (19)	
Others	3 (2)	10 (5)	13 (4)	
Diagnosis				0.69
Solid tumor	98 (77)	143 (74)	241 (75)	
NB	62 (48)	88 (46)	150 (47)	
EWS	3 (2)	19 (10)	22 (7)	
RMS	6 (5)	1 (1)	7 (2)	
Others	27 (21)	34 (18)	61 (1)	
Pineoblastoma	0 (0)	1 (1)	1 (<1)	
Lymphoma	30 (23)	49 (26)	79 (25)	
HD	12 (9)	35 (18)	47 (15)	
NHL	18 (14)	14 (7)	32 (10)	
Disease status				1.00
Remission	50 (39)	74 (39)	124 (39)	
Non-remission[1]	78 (61)	118 (61)	196 (61)	
Product type				<0.0001
HPC-A	30 (23)	133 (69)	163 (51)	
HPC-M	98 (77)	59 (31)	157 (49)	
CMV status				0.001
Positive	50 (39)	115 (60)	165 (52)	
Negative	72 (56)	77 (40)	149 (47)	
NA	6 (5)	0 (0)	6 (2)	
Time to engraftment[2]				<0.0001
Within 28 days	101 (79)	185 (96)	286 (89)	
After 28 days	24 (19)	7 (4)	31 (10)	

Data are no. (%) of patients, unless otherwise indicated

[1] Includes patients with very good partial response, partial response to chemotherapy, stable, and progressive disease.

[2] Three patients failed to engraft 1990–1999.

HSCT, hematopoietic stem cell transplantation; SJCRH, St. Jude Children's Research Hospital; AA, African-American; NB, neuroblastoma; EWS, Ewing's sarcoma; RMS, rhabdomyosarcoma; HD, Hodgkin's disease; NHL, non-Hodgkin's lymphoma; HPC-A/M, human progenitor cells-apheresis/-marrow; CMV, cytomegalovirus; NA, not available.

Table 2

Infections in patients with solid tumors (ST)/lymphoma and leukemia post autologous hematopoietic stem cell transplantation

	ST/Lymphoma		Leukemia	
Infection	**1990–1999 *n*=128**	**2000–2009 *n*=192**	**1990–2009 *n*=320**	**1990–2009 *n*=65**
Bacterial infections[1,2]				
GP infections	7 (5)	17 (9)	24 (8)	15 (23)
GN infections	5 (4)	6 (3)	11 (3)	3 (5)
Bacteremia	7 (5)	16 (8)	23 (7)	8 (12)
Clostridium difficile	5 (4)	6 (3)	11 (3)	9 (14)
Fungal infections				
Candida	1 (1)	0 (0)	1 (<1)	4 (6)
Aspergillosis	1 (1)	0 (0)	1 (<1)	1 (2)
Viral infections[3]				
HSV	10 (8)	7 (4)	17 (5)	9 (14)
HHV-6	0 (0)	2 (1)	2 (1)	0 (0)
VZV	1 (1)	1 (1)	2 (1)	3 (5)
PIV	2 (2)	2 (1)	4 (1)	0 (0)
RSV	0 (0)	3 (2)	3 (1)	1 (2)
Influenza	0 (0)	0 (0)	0 (0)	1 (2)
Parasitic infections				
Parasites	2 (2)	0 (0)	2 (1)	1 (2)

Data are no. (%) of patients, unless otherwise indicated.

[1] Gram-positive (GP) and gram-negative (GN) infections included bacteremia. GP infections included *C. difficile* infections.

[2] Two solid tumor/lymphoma patients had both GP and GN infections, and were counted twice, once for each infection.

[3] Cytomegalovirus (CMV) viremia was excluded from this table, as screening was done only in a subset of patients.

HSV, herpes simplex virus; HHV-6, human herpesvirus-6; VZV, varicella zoster virus; PIV, parainfluenza virus; RSV, respiratory syncytial virus.