Patient A received his transplant in July 2001. Cardiac biopsies showed no rejection on a stable immuno-suppressive regimen of mycophenolate, tacrolimus and prednisone. Renal status was stable with a creatinine of 1.4mg/dl and CMV prophylaxis with ganciclovir and valganciclovir was used. PCR prophylaxis with pentamidine was given. In mid October a BAL culture grew Aspergillus and Nocardia. Treatment was begun with tmp/smz, imipenem, and caspofungin plus lipid formulation amphotericin B. Ventilatory support and chest tube drainage were needed, and CT imaging showed cranial involvement. The patient died in December.

Patient B received his heart transplant in 1997. Surveillance heart biopsies showed no evidence of rejection and renal function was stable with a creatinine around 2mg/dl. PCR prophylaxis with tmp/smz was given for two years until July 1999. The patient developed persistent pleural effusions that reoccurred in spite of repeated drainage. Specimens from surgical decortication and evacuation of the effusions grew Nocardia that was treated with IV tmp/smz for one month. An MRI did not show any intracranial lesions. Outpatient treatment with oral tmp/smz was continued.

The third patient received his transplant in February 2001. Myocardial biopsies confirmed grade I and grade III rejection 2 months and 7 months post transplantation respectively. In the second instance a short-term increase in immunosuppression was given. The patient also received lamivudine and ganciclovir because the donor was hepatitis B core antibody positive and had positive CMV serology. Prophylaxis with tmp/smz three times weekly was begun in March. Renal function was stable. Subsequent to respiratory complaints a CT of the chest was obtained in October and showed a significant pulmonary lesion. Bronchoscopy specimens grew Nocardia and Aspergillus. Imaging of the head did not reveal any cranial involvement. IV treatment with caspofungin, imipenem and cefotaxime continued through the middle of December with improvement of the pulmonary lesions on repeat CT. The patient was discharged on outpatient oral therapy with tmp/smz and itraconazole.

This uncanny cluster of nocardia infections in heart transplant patients exhibits the importance of considering Nocardia as opportunistic pathogens in transplant patients even if tmp/smz prophylaxis has been given.

**Introduction:** Cytomegalovirus reactivation is common and carries serious morbidity and high mortality in patients undergoing allogeneic marrow transplantation, especially in recipients of marrow grafts from CMV-seropositive donors. The impact of early viral reactivation on response to antiviral treatment is uncertain.

**Methods:** Seven recipients of two and greater than two HLA-antigen mismatched, related marrow transplantation during 1999–2000 were evaluated prospectively for CMV viremia by real-time PCR technique (Speciality Laboratories, Santa Monica, CA) performed on post-transplantation day +1, and then weekly. All values are given in median+standard deviation.

**Results:** Five had refractory or recurrent acute myelogenous leukemia (AML), and two with acute lymphocytic leukemia (ALL). Four received 3 HLA-antigen mismatched marrow grafts from a related donor. Three had evidence of CMV in the peripheral blood on 12+5 days (age 17+11 years), whereas four (age 26+24 years) had evidence of reactivation on 30+4 days following BMT. In the sub-group with early reactivation (day 12+5), median CMV viral load was 258+91 copies/ml, and 1291+4220 copies/ml in the remaining four (P>0.5).

Four patients had clinical and virological failure to initial therapy with ganciclovir (5 mg/kg every 12 hours). Among these, two (2/3; 66.7%) patients had evidence of early CMV reactivation and the other two (2/4; 50%) had evidence of reactivation around post transplant day +30 (P>0.5).

**Conclusions:** Cytomegalovirus reactivation during the first two weeks of transplantation was associated with low-grade viremia. We did not observed a significant association with early CMV reactivation and failure to initial ganciclovir therapy in patients following high-risk allogeneic marrow transplantation.

**Mucosal lymphoid cells response to Escherichia coli vaccine in diabetic animals treated with pancreatic beta-cells**

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**Background and objective:** The present study was undertaken to evaluate the therapeutic effects of pancreatic beta-cells in diabetic animals immunized by Escherichii coli vaccine.

**Study design/ materials and methods:** Ten days after streptozocin injection (60 mg/kg), diabetic rats received intraperitoneal injection of pancreatic beta-cells (5.7×10⁷ cells/rat). Twelve days later both the diabetic and healthy animals were immunized by oral route with enteroinvasive E. coli (0136 serotype) acetone-killed vaccine. Twenty-one days after beta-cells transplantation lamina propria and Peyer’s patches lymphoid T cells were obtained from the intestine.
Main results: Intraperitoneal implantation of purified beta-cells improved the diabetic state within 8–10 days. The metabolic parameters were stable within 4–5 weeks after islet transplantation in fifteen of twenty-one recipients (71.4%). Stimulation with PHA at 21 days post beta-cells grafts produced a marked increase in βThymidine incorporation in lamina propria and Peyer’s patches lymphoid T cells.

Conclusions: (1) These results demonstrated normalization of metabolic and immunologic parameters in diabetic rats which received associated therapy (pancreatic beta-cells and E. coli vaccine) and (2) beta-cells stimulated the immune response to Escherichia coli vaccine.

Infectious outcomes after alternative donor stem cell transplantation: a retrospective cohort comparison

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Allogeneic stem cell transplantation from donors other than HLA-matched siblings results in a high risk of post-transplant infections because of the risk of graft-versus-host disease (GVHD) with an unmanipulated graft, or delayed immune reconstitution following T cell-depletion (TCD). We compared infectious outcomes in the first yr post-transplant (tx) in 28 consecutive recipients of stringently TCD blood hematopoietic progenitor cell (HPC) grafts from haploidentical family donors (HD), and 28 consecutive recipients of unmanipulated grafts from matched or 1 Ag mismatched unrelated donors (URD). Included are pts (excluding CML-CP1) transplanted at our center between 6/98 and 12/01 after myeloablative conditioning. HD pts received pre-tx ATG, and no scheduled post-tx immunosuppression. URD pts received tacrolimus and methotrexate for GVHD and no scheduled post-tx immunosuppression. HD pts were in relapse at the time of transplant. Acute and/or chronic extensive GVHD occurred in 80% of evaluable HD pts vs 15% of HD pts (p<0.001). Bacteremias were the most common infections, occurring at similar frequencies in the two groups. Polymicrobial bacteremias occurred exclusively in URD patients (n=7; p=0.009). Proven/probable invasive fungal infections (IFI) occurred in 23% of HD pts, and 12% of URD pts (p=NS). Frequency and timing of CMV reactivation (by PCR), late CMV reactivation (>d 100), and CMV disease were similar in the two groups. EBV-associated PTLD was unique to HD pts (n=3), and drug-resistant HSV disease was also more common after HD tx. Infection related deaths (censored at 1 yr) in HD pts included bacterial sepsis (3), Aspergillosis (3), paramilfluenza pneumonia (2), PCP (1), other pneumonia (1), amebic encephalitis (1), toxoplasmosis (1), EBV-PTLD (1), and acalculous cholecystitis (1). Infectious deaths in URD pts resulted from IFI (3), bacterial sepsis (2), CMV pneumonia (1), aspiration pneumonia (1), and acalculous cholecystitis (1).

Infections are the most common cause of death in these pts. The trend toward higher risk of infectious death following TCD HD vs unmanipulated URD transplants was not statistically significant, although the spectrum of infections was different. Strategies aimed at enhancing immune reconstitution without stimulating GVHD are needed to reduce the risks of infection and relapse after stringently TCD alternative donor transplantation.

Fungal Infections

Invasive Aspergillosis in chronic lung disease

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The spectrum of Aspergillus induced human pulmonary afflictions vary greatly from apparently harmless colonization to a fulminant and rapidly fatal disease. Invasive aspergillosis (IA) is a disease that occurs primarily in severely immunocompromised patients, clinical diagnosis in whom is often difficult and missed, adding to the severity of the outcome.

Aims and objectives: To study the occurrence of IA in cases of chronic bronchopulmonary disorders with locally and/or systemically immunocompromised conditions and correlate the role of clinical and radiological parameters of these patients with a battery of laboratory investigations in the early diagnosis and management.

Materials and methods: Thirty-four patients of chronic bronchopulmonary disorders with suspected aspergillosis and underlying immunocompromised state were studied. Thorough clinical, hematological and radiological examinations were carried out. Sputum, bronchial aspirate/ BAL and serum samples were collected. Microscopy and culture for Aspergillus spp in addition to detection of specific anti-A. fumigatus IgG and IgE by ELISA and skin sensitivity tests against Aspergillus spp were performed.

Results: Out of 34 cases studied, 7 were diagnosed as IA: 2 as highly probable and 5 as probable cases. IA was found to be most common in <20 and >60 years of age.