SUMMARY

Bone marrow transplantation has been shown to provide a means for curative correction of a number of lethal congenital and acquired disorders of the hematopoietic and lymphoid systems .

Marrow transplantation is the therapy of choice for patients with severe aplastic anaemia at the time of diagnosis and severe combined immunodeficiency . Marrow transplantation has emerged as a highly promising approach to the treatment of high risk forms of leukemia, particularly when applied to patients in remission early in the course of their disease. It has been evaluated in the treatment of chronic myelogenous leukemia, non Hodjkin's lymphomas, neuroblastoma and other solid tumours and in a number of immunodeficiencies and inborn errors of metabolism .

Depending on the genetic relationship between the donor and recipient, there are three types of transplants performed in clinical bone marrow transplantation. Syngeneic refers to transplants between genetically identical members of the same species, such as identical twins , allogenic refers to transplants in which the donor and

recipient are genetically dissimilar members of the same species, usually siblings, and autologous refers to those transplants where patients are transplanted with their own previously harvested marrow . The majority of bone marrow transplants at present are allogenic .

Except in patients undergoing syngeneic transplants and in those with severe combined immunodeficiency, immunosuppression is required to permit engraftment of donor marrow . Patients with aplastic anaemia who have not been transfused before transplantation are given cyclophosphamide alone but those who have been transfused are given cyclophosphamide and total lymphoid irradiation or cyclophosphamide and addition of viable donor buffy coat cells .

Patients with neoplasms require total body irradiation or addition of high dose chemotherapy to eradicate existing disease,and to create space within host marrow to allow the transplanted stem cells to proliferate . Because most tumour cells repair radiation-induced D N A damage poorly as compared to most normalcells, fractionating TBI permits the

administration of higher total doses .

Bone marrow donors are selected by human leukocyte antigen (HLA) typing . Histocompatibility between donor and recipient is established by demonstrating HLA-A, B, C, and DR identity and mutual nonreactivity in mixed lymphocyte culture . At present, transplants are carried out mostly between histocompatible siblings. Practically, this translates into finding matches for only about 35 to 40 percent of potential transplant candidates.

After appropriate patient and donor selection , the recipient may undergo a pretransplant evaluation of the status of the underlying disease and the function of various organ systems that may be adversely affected during and after transplantation . Any existing infection is treated vigorously. Many patients receive trimethoprim - sulfamethoxazole for 10 to 14 days prior to their transplants to prevent pneumocystis carinii pneumonia.

In patients with aplastic anaemia, transfusions of blood products should be limited before transplantation since they induce sensitization and increase the

likelihood of graft rejection . The marrow donor or other family members should not serve as pretransplant blood component donors.

Following infusion of the marrow inoculum, management of the recipient is similar to the case of any patient with prolonged pancytopenia following intensive anticancer treatment . The risk of exogenous infection is minimized by housing patients in strict reverse isolation and decontamination in a laminar air flow rooms Because of the risk of infection from the patients own bacterial flora, the patients may be given oral non-absorbable antibiotics and fed a sterile diet . Microbicidal agents are used to bathe the patients, and antibacterial and antifungal creams may be applied to skin folds and orifices . Transfusions of platelets and red blood cells are necessary until the donor bone marrow becomes fully functional and hematologic reconstitution is achieved within 4 to 6 weeks following infusion .

One of the major problems encountered in bone marrow transplantation is the graft rejection especially in multiply transfused patients with aplastic anaemia,

the incidence of graft rejection is thus quite minimal in untransfused patients with aplastic anaemia . Sensitization is less likely to occur in patients with leukemia who receive transfusion support because of the chronic immunosuppression induced by their antileukemic chemotherapy . The high rejection rate has been markedly reduced by augmenting the pretransplant immunosuppressive regimens with low doses of TBI , total lymphoid irradiation, procarbazine, antithymocyte globulin (ATG),or additional donor peripheral blood buffy coat cells.

GVHD remains one of the major obstacles to successful allogenic BMT . Because of difficulty in treating it once it has occurred, attention has been directed toward prevention several approaches have been investigated in attempts to decrease its incidence, these include using methotrexate early after transplantation and on a prolonged schedule or methotrexate, antithymocyte globulin,and prednisone or immunosuppression with cyclosporin A . There are two types of Graft versus host didisease . The acute GVHD and the chronic GVHD . Acute GVHD develops within the first 100 days post transplant, and occurs in 30 to 70 percent of all patients.

The chronic form of GVHD begins 6 to 18 months after transplantation and occurs in 15 to 40 per cent of the long term survivors of HLA matched transplant. It may follow acute GVHD or occur de novo .

Because of the myeloablative and immunosuppressive therapy used prior to BMT and the prolonged period of immunodeficiency that follows it, infections frequently complicate bone marrow transplantation and account for a substantial number of the fatalities among transplant recipients.

During the immediate post transplant period , patients are neutropenic and lymphopenic and may develop septicemia and localized bacterial or fungal infections, or reactivate latent herpes simplex or herpes zoster infections . Interstitial pneumonia develops in 35 to 40 per cent of all allogenic marrow transplants and continues to be a major obstacle to the long-term survival of many transplant recipients.

Recurrence of leukemia following marrow grafting continues to be a major complication, particularly in patients with Acute lymphoblastic leukemia (ALL).

The risk of leukemic relapse have been reduced, mainly in patients who had acute GVHD and in whom chronic GVHD developed subsequently, and exert an antileukemic effect.