POINTS TO CONSIDER

NON-TECHNICAL ABSTRACT

There has been much interest lately in the use of hemopoietic stem cell transplantation as therapy for autoimmune disease. The initial rationale for this approach comes from reports showing clinical improvement of autoimmune diseases in patients undergoing allogeneic transplantation for another reason. There are also several anecdotal reports of patients with autoimmune disorders who underwent autologous transplantation for another disorder and experienced remission of their auto-immune disorder although most have eventually relapsed. However, the majority of these patients received unmanipulated products.

The mechanism by which transplant mediates a beneficial effect may involve removal of the autoreactive T cell clone by the conditioning regimen and a resetting of the immune system derived from infused cells. With the availability of CD34 selection devices, investigators can positively select stem cells and then perform further T depletion procedures to ensure autoreactive cells are not reinfused. One concern with this strategy is that prolonged immunodeficiency may occur because regeneration is slow resulting in an increased risk of viral infection and malignant disease. A second issue is if the autoimmune disease recurs, whether more treatment of the patient or a different stem cell product would make the procedure more effective.

To address these questions we will mark the reinfused cells with the neomycin resistance gene. This will allow us to learn if T cells that come back which may cause relapse of multiple sclerosis come from the stem cell transplant or from cells left in the patient. It will also allow us to learn how quickly the immune system recovers from the stem cells in the transplant. This information will allow us to learn how to improve this therapy.