Brief Overview of Hematopoietic Cell Transplantation (HCT)

**Autologous HCT**

1. Typically used as consolidation--more successful if disease burden is less
   a. Improve response to initial therapy for multiple myeloma
   b. Salvage relapses of aggressive lymphomas following first-line therapy
   c. Occasionally used for refractory solid tumors (testicular, Ewings sarcoma, etc.)
   d. Not favored for acute leukemias

2. Two phases for the patient:
   a. Stem cell collection
      i. Mobilization of stem cells into the peripheral blood with chemotherapy (e.g., cyclophosphamide, etoposide) and/or filgrastim (G-CSF)
      ii. Stem cells collected via apheresis, then cryopreserved
   b. High-dose conditioning therapy and stem cell rescue
      i. Chemotherapy +/- radiation to a hematologically lethal dose
      ii. Thaw and re-infuse stem cells after this treatment
      iii. Blood counts recover after about 2 weeks

3. Major principle:
   a. Doses of standard chemotherapy used are often limited by hematologic toxicity
   b. Use stem cell reinfusion to overcome these limitations (hence, "rescue")

4. Goal:
   a. Aggressive lymphoma: cure
   b. Indolent lymphoma or myeloma: prolonged remissions

5. Limitations:
   a. Need adequate venous access for apheresis
   b. Organ toxicity and infections

**Allogeneic HCT**

1. Typically used as consolidation--much more successful if patient is in remission

2. In addition to replacing recipient’s hematopoietic cells, donor’s immune system offers "graft versus tumor" effect

3. Offered for a range of conditions
   a. First remission for select intermediate- and most unfavorable-risk AML patients
   b. Relapse after standard therapy (i.e., second remission) for acute leukemia
   c. Occasionally used in highly-selected lymphoid malignancies (e.g., CLL, myeloma)
   d. Only known curative therapy for MDS and myeloproliferative neoplasms
   e. Some role in inherited or acquired non-malignant hematologic disorders (e.g., sickle cell disease, immunodeficiency syndromes, aplastic anemia, etc.)

4. Two methods:
   a. Myeloablative (a.k.a. "full"): 
i. High-dose chemotherapy +/- radiation followed by stem cell infusion
ii. Counts recover after about 3 weeks
iii. Generally used in patients less than 50-55 years old
b. Non-myeloablative (a.k.a. reduced-intensity, "mini"):
   i. Low-dose chemotherapy + radiation followed by stem cell infusion
   ii. Counts recover after about 3 weeks
   iii. Can be done in patients as old as 75 and in patients with prior myeloablative
treatment (usually a prior auto transplant)

5. Unique complications
   a. Graft versus host disease: immune-mediated attack of donor cells against host tissue
      (skin, gut, liver in particular)
   b. Immunosuppression: opportunistic infections, secondary malignancies

6. Determining stem-cell donor
   a. Patient’s HLA type must be determined; ABO blood type is not critical
   b. Siblings (if available) then typed--these are preferred donors
      i. HLA haplotypes inherited by Mendelian genetics (1 from each parent)
      ii. Each sibling has 1 in 4 chance of being a match
   c. If siblings not available or not matched, then go to unrelated donor
      i. Likelihood of finding donor depends on number of donors with shared HLA
         haplotypes--often predictable by ethnicity
      ii. Certain ethnicities are under-represented
   d. If matched unrelated donor not available, alternative sources available
      i. Mismatched sibling or unrelated donor
      ii. Umbilical cord blood
      iii. HLA haploidentical donor (usually parents or children)

7. Goal: Cure

8. Limitations:
   a. Finding suitable stem cell source
   b. Achieving adequate disease control prior to procedure
   c. Age and medical comorbidities can make this prohibitively risky, though "mini"
      transplants are expanding the utility of this approach
   d. Balance between risk, including treatment-related death, vs. potential benefit

Suggested Additional Reading
1. National Marrow Donor Program (NMDP) website, section for Physicians:
   http://marrow.org/Physicians/Physicians.aspx
4. Many topics on UpToDate.