Stem Cell Transplantation

Types	• **Allogenic**: Healthy donor marrow replaces recipient's marrow • **Autologous**: Patient's own bone marrow is harvest prior to conditioning and transplanted back
Timeline	• **Day -4 to -21**: conditioning (varies by protocol) • **Day 0**: stem cell infusion; actual infusion is similar to a transfusion given over several hours with premedication. • **Day 10 to 14**: generally WBC nadir with symptoms (mucositis) • **Day +24 to +48**: Engraftment, varies by protocol but generally ANC >500 x3 days. Generally sooner if autologous
Diseases Commonly Treated w/ SCT	• SCT can be used for both malignant and non-malignant conditions • **Autologous**: resistant cancers (lymphoma, neuroblastoma, brain tumors, Wilm's tumor) when toxic doses of chemotherapy are needed • **Allogenic**: Potentially curative for leukemias, hemoglobinopathies, some metabolic conditions (adrenoleukodystrophy, mucolipidoses), bone marrow failure syndromes (Fanconi anemia, aplastic anemia), severe primary immunodeficiences • Graft-versus-leukemia (donor lymphocyte vs leukemia) is primary mechanism of cure for leukemias
Autologous Transplants	• Primary aim is to deliver very high doses of chemotherapy, that would otherwise not be tolerated and to then "rescue" the patient w/ an infusion of their own stem cells • Generally not used for diseases present in the bone marrow as hard to eliminate cells • Generally better tolerated than allogeneic transplants • No risk for GVHD
Sources of Stem Cells for Allogenic Transplants	• Peripheral stem cell mobilization: GCSF is given, followed by pheresis • Bone marrow harvest: Multiple bone marrow aspirations are generally taken from pelvis • Umbilical cord blood: Cord blood has relatively high proportion of hematopoietic stem cells
HLA Typing	

Donor type	GVHD risk	GVL effect	Other
Identical twins	+	+/-	
Matched sibling donors	++	+++	Generally best outcomes
Partially matched alternative relative	++	+++	
Haploidentical	+++	+++	Parent/sibling with one identical chromosome 6; highest risk transplants
Matched unrelated donor (marrow/ peripheral blood)	+++/++	+++/+++	Generally the next choice after a matched sibling. Via BM registries. Ethnicity, gender, CMV status can matter.
Umbilical cord blood	+	++	Higher risk of infection, can be one or two donors (inc risk of GVHD with more donors)
Legend: no (-), low (+), medium (++), or high (+++)			

Stem Cell Transplantation

HLA Typing	• 'High resolution' typing is sent on the patient, any siblings and often parents. HLA genes are found on chromosome 6 and a set is inherited from each parent. • Typing includes HLA-A, HLA-B, HLA-C, HLA-DR, HLA-DP, HLA-DQ • In general, a donor/recipient should match at 9/10 or 10/10 loci (8/10 allowable for cord blood given decreased risk of GVHD) • Generally, a mismatch in HLA-A, HLA-B, HLA-C (Type I genes) increases graft rejection; a mismatch in HLA-DR, HLA-DP, HLA-DQ (Type II genes) increases GVHD risk.
Conditioning Regimens	Vary widely based on disease and co-morbidities • Myeloablative ▪ Most intense; requiring stem cell rescue and high chance of side effects ▪ Often uses Total Body Irradiation (TBI) and cyclophosphamide or busulfan and cyclophosphamide ▪ Use of ATG (anti-thymocyte globulin) is associated with a dec risk of GVHD • Reduced intensity conditioning ▪ Intermediate conditioning between myeloablative and non-myeloablative • Non-myeloablative ▪ Target recipient lymphocytes without aim of myeloablation
Chimerism	• After transplant, chimerism is measured at set intervals on bone marrow samples to see what percentage of marrow is donor or recipent's original marrow • If the donor percentage appears to be dropping, salvage donor lymphocyte infusions can be tried
Common Complications & Management	**Mucositis** • Occurs in most patients who receive myeloablative conditioning • Patients may require TPN given inability for PO intake **Veno-occlusive Disease** (aka Hepatic Sinusoidal Obstructive syndrome) • Occurs in ~14% of patients at 1-3 weeks post-transplant with mortality of up to 80% • Pathophysiology of hepatic endothelial damage leading to hepatic and renal injury • Clinically: weight gain with ascites, hepatomegaly and direct hyperbilirubinemia • Prophylactic vitamin E and ursodiol given to almost all patients • Treatment is defibrotide and supportive with careful fluid management, drainage of ascites/ pleural effusions. **Graft vs Host Disease**: transplanted immune cells recognize the recipient as foreign and react **Acute** • **Timeline**: from engraftment up to day +100. Severity graded I-IV • **Skin**: rash, graded based on area and severity. Ranges from mild maculopapular rash to generalized erythroderma • **GI**: most commonly with diarrhea+/- abdominal pain. Graded based on volume of diarrhea (or severe other symptoms) • **Liver**: mostly commonly presenting with rising bilirubin. Graded based on bilirubin level • Prevention regimen varies but generally involves prophylaxis cyclosporine (over several months) and methotrexate (several doses prior to engraftment). Patients at higher risk may get prophylactic steroids and lower risk may get mycophenolate mofetil in place of MTX. Balance between preventing GVHD and promoting GVL/preventing infection. • **Treatment**: Mild skin GVHD can respond to topical steroids. Otherwise, increased systemic immunosuppression with systemic steroids +/- other agents **Chronic** • Develops after 100 days • Can be mucocutaneous, or involve liver, lungs, muscles, GI tract or have hematologic manifestations • Severe chronic GVHD has a high mortality • Treatment usually involves systemic steroids +/- other agents. Patients with refractory disease may receive extra-corporeal pheresis

Stem Cell Transplantation continued on next page →