Bone Marrow Transplantation

Definition	Bone marrow transplantation was the original term used to "describe the collection & transplant. of haematopoietic stem cells (HSCs)," but w. the demonstration that peripheral blood and umbilical cord blood are also useful sources of stem cells – **HSC transplantation** has become the preferred generic term.

Properties of HSCs	• High regenerative capacity • Ability to home to the marrow space after IV injection • Feasible for cryopreservation

Types of HSC transplant	• Autologous • Allogenic (twin x genetically-different individual) ○ Pz. need to be HLA matched to reduce the risk of adverse events (esp. graft-versus-host disease aka GVHD.)

Indications	• Immunodeficiency disorders • Aplastic anaemia • Haemoglobinopathies • Acute leukaemia • Chronic leukaemia • Myelodysplasia • Lymphoma • Myeloma • Some solid tumours

Sources of HSC (About 1.5 to 5.0 x 10^8 cells are req. per transplant.)	• Posterior/Anterior Iliac Crests • Peripheral blood (req. administration of haematopoietic growth factors before collection. Haematopoietic growth factors incl. G-CSF, GM-CSF, etc.) ○ Donor are typically treated w. 4 or 5 days of haematopoietic growth factors, following which stem cells are collected in one or two pheresis sessions. • Umbilical cord blood

Transplant preparative regimen for recipients	• The Tx. regimen administered to Pz. immediately preceding transplantation is designed to eradicate the patient's underlying disease and, in the setting of allogenic transplantation, immunosuppress the Pz. adequately to prevent rejection.
	  ○ Aplastic anaemia
	  ▪ Use high-dose cyclophosphamide + antithymocyte globulin
	  ○ Thalassemia & Sickle-cell anaemia
	  ▪ High-dose busulfan ± cyclophosphamide
	  ○ Malignant diseases
	  ▪ Regimens typically incl. busulfan, cyclophosphamide, melphalan, carmustine, etoposide and total body irradiation (TBI) in various combinations.

Transplant procedure	• About 10 – 15 ml/kg of marrow is aspirated from the donors and placed in heparinized media or, alternatively, HSC may be collected from peripheral blood by lekapheresis. • The collected marrow undergoes further processing (removal of bone spicules, RBCs, removal of donor T-cells, etc.) • Stem cells for transplantation are usually infused through a large-bore central venous catheter.

Complications	• **Early direct chemoradiotoxicities**
	  ○ The preparative regimen may cause a spectrum of acute toxicities, but frequently results in nausea, vomiting and mild skin erythema.
	  ○ There may be oral mucositis, hepatotoxicity (may lead to ascites, jaundice, etc. May culminate in hepatorenal syndrome.)
	  ○ Regimens that incl. **high-dose cyclophosphamide** can cause haemorrhagic cystitis. Prevent w. bladder irrigation or MESNA (antidote.)
	
	• **Late direct chemoradiotoxicities**
	  ○ Late complications of the preparative regimen incl. decreased growth velocity in children and delayed dev. of secondary sex characteristics.
	  ○ Most men become azoospermic and most post-pubertal women will dev. ovarian failure.
	  ○ Thyroid dysfunction & cataracts are common in Pz. treated w. TBI.
	  ○ Aseptic necrosis of the femoral head is common in Pz. receiving GC therapy.
	
	• **GVHD**
	  ○ Is the result of allogenic T-cells that are transferred w. the donor's stem cell inoculum reacting w. antigenic targets on host cells.
	
	• **Graft Failure**
	  ○ While complete and sustained engraftment (functioning HSCs indicative of a successful transplant) is usually seen post-transplant, occasionally marrow function either does not return or, after a brief period of engraftment, is lost.