STEM CELLS TRANSPLANTATION

DEFINITION

- Stem cell transplantation is a procedure which involve

  - ü Eliminating an individual hemopoietic & immune system by radiation & chemotherapy

  - ü Replaced it with stem cell either from another individual or from the previously harvested portion of individual's own stem cells.

TYPES OF BMT

1. Allogeneic BMT the stem cells come from a *donor*- either related (usually an HLA-identical sibling) or from a closely HLA-matched volunteer unrelated donor (VUD).

2. *Autologous BMT* are harvested from the *patient* and stored in the vapour phase of liquid nitrogen until required.

STEM CELL SOURCES

- Autologous
- Allogeneic
  - Syngeneic (identical twin)
  - Related
  - Unrelated

STEM CELL TYPE

- Bone marrow
- Umbilical Cord blood
- PBSC (peripheral blood stem cells)

ALLOGENEIC TRANSPLANT INDICATIONS

Malignant Diseases

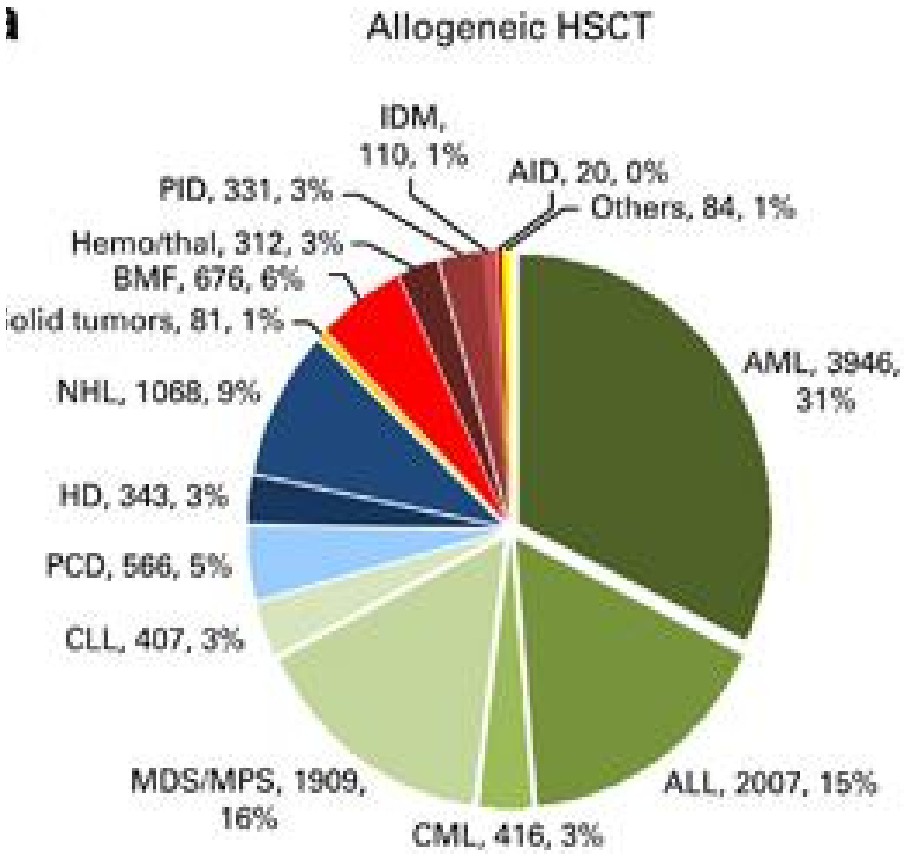
- High risk AML CR1 – Matched Sibling
- High Risk ALL CR1 (Ph+ ALL)
- Relapsed or Refractory AML or ALL
- CML resistant to imitanib, or accelerated or aplastic phase
- Multiple myeloma
- Juvenile myelomonocytic leukemia
- Myelodysplastic syndromes

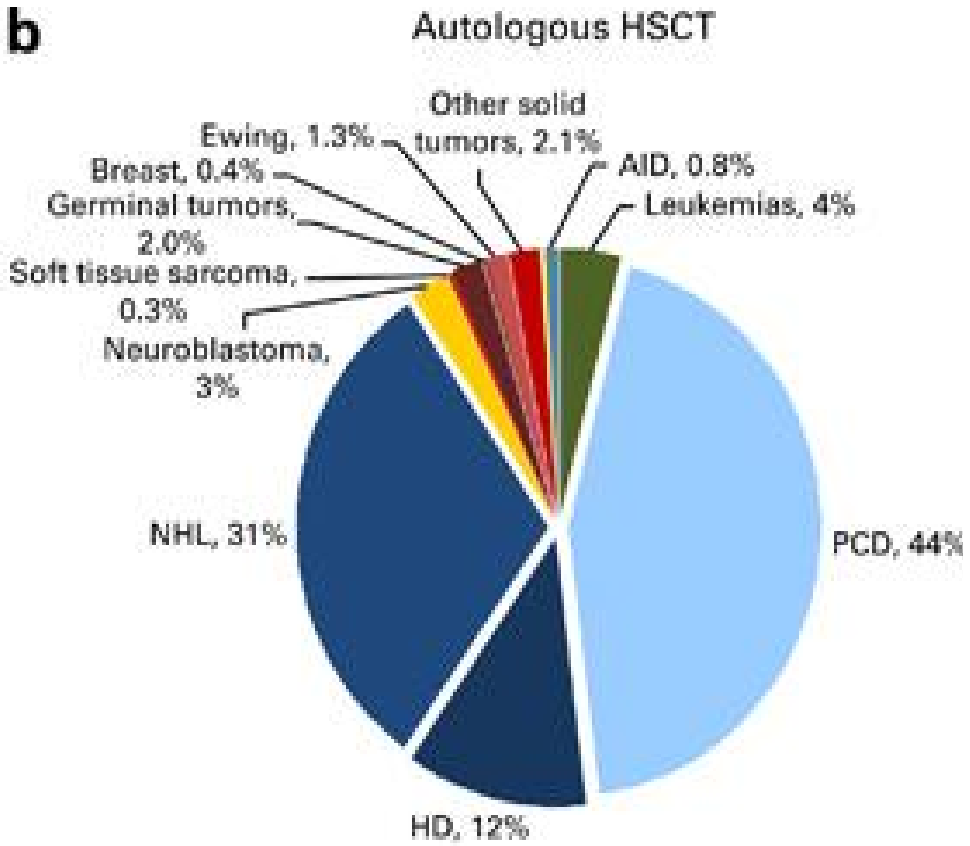
ALLOTRANSPLANT FOR NON-MALIGNANT DISEASES

- *Inherited metabolic disorders*: osteopetrosis
- *Inherited immune disorders*: Severe combined immunodeficiency
- *Inherited red cell disorders*: Pure red cell aplasia, sickle cell disease, beta-thalassemia, and others
- *Marrow failure:* Severe aplastic anemia, myelofibrosis, Fanconi anemia, and others

INDICATION OF AUTOLOGOUS BMT

- Relapsed Non-Hodgkin lymphoma & Hodgkin disease
- Multiple myeloma
- Stage IV Neuroblastoma
- Relapsed Ewing Sarcoma
- Medulloblastoma, germ cell tumors
- Autoimmune disorders





THE BMT PROCESS

- The transplant process generally is divided into :

1. Conditioning
2. Stem cell infusion
3. Neutropenic phase
4. Engraftment phase
5. Postengraftment phase

CONDITIONING

- The period typically lasts 7-10 days.
- The purpose is to deliver chemotherapy and/or radiation to
  - Eliminate malignancy,
  - Prevent rejection of new stem cells, and
  - Create space for the new cells.

- The most common conditioning regimens include total body irradiation (TBI) and cyclophosphamide or busulfan and cyclophosphamide.

STEM CELL INFUSION

- Stem cell infusion usually is performed over about an hour.
- Before infusion, the patient is premedicated with acetaminophen and diphenhydramine to prevent reaction.

NEUTROPENIC PHASE

- During this period (2-4 wk), the patient essentially has no effective immune system. Healing is poor, and the patient is susceptible to infection.
- Supportive care and empiric antibiotic therapy are the mainstays of successful passage through this phase

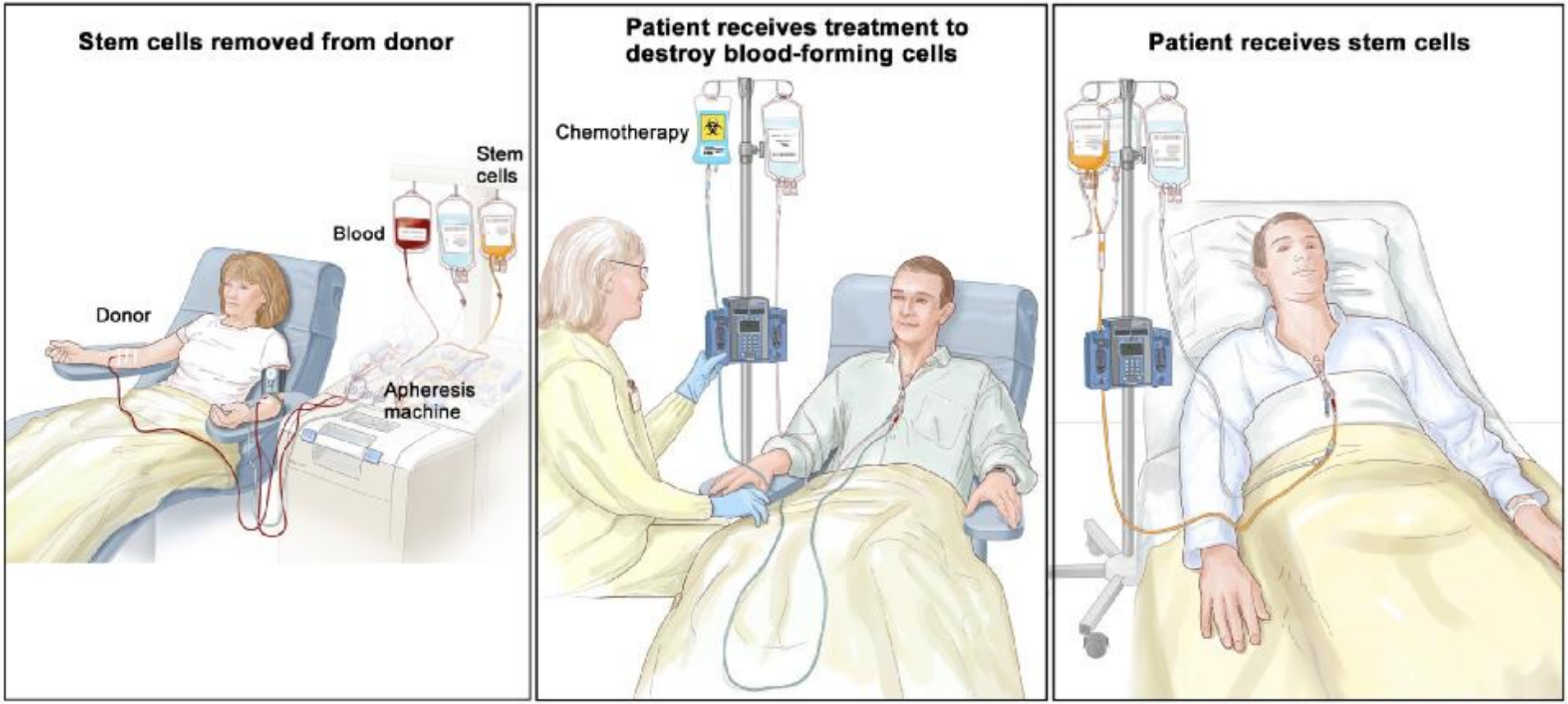
ENGRAFTMENT PHASE

- The injected donor cells, engraft and produce enough erythrocytes, granulocytes and platelets for the patient's needs after 3-4 weeks.
- During this period, the healing process begins with resolution of mucositis and infections often begin to clear.

- An advantage of receiving allogeneic donor stem cells is that the donor's immunological system can recognize residual malignant recipient cells and destroy them.

POST ENGRAFTMENT PHASE

This period lasts for months to years. Hallmarks of this phase include the gradual development of tolerance, weaning off of immunosuppression, management of chronic GVHD, and documentation of immune reconstitution.



COMPLICATIONS

- The risks and outcomes of transplantation depend upon several patient- and disease-related factors.
- In general, 25% die from procedure-related complications.

COMPLICATION

- Mucositis
- Infection , Bleeding
- Cataract formation
- Pneumonitis
- Infertility
- Venoocclusive disease of the liver
- Organ Toxicity (lung, heart, kidney)

- Secondary malignant disease
- Hemorrhagic Cystitis
- Chronic and acute graft-versus-host disease
  - ü If donor cells see the host cells as foreign, the donor cells will attack the host.
  - ü Skin, gut, and liver most likely to be affected.
  - ü Acute < 100 days after the transplant
  - ü Chronic > 100 days

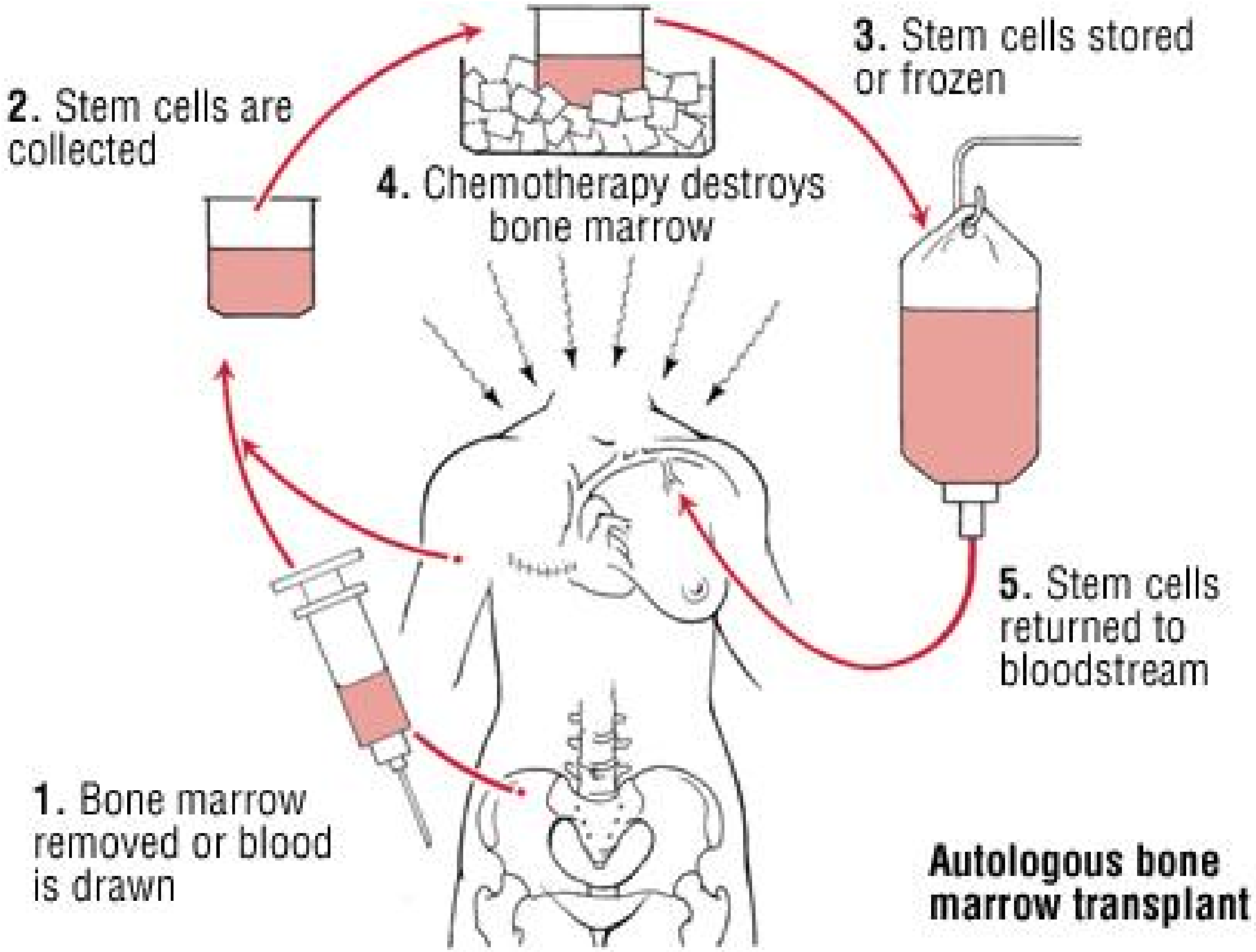
REDUCED-INTENSITY BMT

- This concept has been developed in an attempt to reduce the mortality of allografting. This approach is less toxic and allows BMT to be offered to an older group of patients.

- Rather than use very intensive conditioning which causes morbidity from organ damage, relatively low doses of drugs are used simply to immunosuppress the recipient and allow donor stem cells to engraft.

AUTOLOGOUS BMT

- The patient's own stem cells from blood or marrow are first harvested and frozen.
- After conditioning therapy, the autologous stem cells are reinfused in order to rescue the patient from the marrow damage and aplasia caused by chemotherapy.



- Autologous BMT may be used for disorders which do not primarily involve the hematopoietic tissues, or in patients in whom very good remissions have been achieved.

- There is no risk of GVHD and no immunosuppression is required.
- Thus autologous BMT carries a lower mortality rate than allogeneic BMT at around 5%, but there is a higher rate of recurrence of malignancy.