

Reconstitution

• Engraftment (graft take)

- Migration of infused donor HSC to recipient's bone marrow followed by production of the precursors of all hematological lineages.
 - Occurs normally 2-3 weeks after transplantation
 - Severity of conditioning, GVHD prophylaxis and a low degree of histocompatibility may cause slow engraftment
 - Slow engraftment may be at the origin of infectious complications (neutropenia!)
- The first day that the number of granulocytes > 0.5 G/L is defined as the day of engraftment

• Red cells, platelets and cells of innate immunity

Normalization after about 1 month (the granulocytes and monocytes will provide protection against bacterial infections)

• Regeneration of T cell immunity

Δ Recovery of normal T cell numbers ≠ recovery of normal T cell immunity !!

--> T cell immunity consists in the diversity for antigen specificity of the T cell repertoire.

T cell repertoire constituted during first years of life is mostly destroyed through the conditioning.

Two pathways to reconstitute the T cell pool:

- expansion of mature T cells transplanted with the graft --> fast , low diversity of T cell repertoire, holes in the repertoire (missing specificities against various antigens)
- emergence of new naive T cells from the thymus --> slow/very slow in elderly, diverse repertoire

• Regeneration of B cell immunity

Normal numbers of B cells are reached after about 6 months, however B cell immunity that depends on T cell help may remain impeded

→1-2 years to recover T and B cell immunity in adults (diminished thymic function), prolonged risk of viral (and fungal) infections.

• Chimerism

Mixed chimerism: persistence and further reappearance of recipient HSC after transplantation

Complete chimerism: all cells produced by HSC are of donor origin

Mixed chimerism is usually a sign of recurring disease (relapse). However, after reduced intensity conditioning some recipient stem cell may survive and continue to produce blood cells of recipient origin. This may also occur when the graft has been depleted of T cell that normally would contribute to the destruction of recipient HSC.

Recipient & Transplantation

- Hematopoiesis
- Type of transplant
- Indications
- Decision to treat
- Conditioning
- Transplantation

Donor & Compatibility

- Criteria
 - HLA typing
- Search
- Stem cell source

Transplantation barriers

- Structures recognized
 - MHC
 - mHC
- Allorecognition
 - T cells
 - B cells
 - NK cells

Immunosuppression

- Immunosuppressive drugs
- T cell depletion

Complications

- Graft rejection
- GVHD
- Infections
- Side effects
- Relapse

LEARNING OBJECTIVES

- Reconstitution of the immune system after chemotherapy