Engraftment

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Scope

Aim:

• Provide a better understanding of the engraftment timeline and impacting factors

Objectives:

• Define haematological reconstitution
• What can affect engraftment?
• Recovery of immune function
• Failure of engraftment and rescue strategies
Haematological reconstitution

• Recovery of neutrophil and platelet counts after the nadir induced by conditioning therapy

• Sustained absolute neutrophil count (ANC) ≥ 0.5 x 10⁹/L
  – 1st of 3 consecutive days

• Unsupported platelet count ≥ 20 x 10⁹/L
  – 7 days after last platelet infusion

• Recovery of neutrophil and platelet counts after the nadir induced by conditioning therapy

• Time of engraftment = Number of days between HPC infusion and neutrophil or platelet recovery
Stem cell journey

- HPC transplant (intravenous infusion)
- Stem cells circulate via the blood stream
- “Home” to bone marrow niches within 24 hrs
- Proliferate & differentiate to generate mature blood cells
Stem cell homing (1)

Migrate from circulation to marrow cavity

- Roll along vessel wall
- Attach to endothelium via adhesion molecules and chemo attractants (like “grip ball”)
- Migrate through endothelial cells
- Lodge into BM niche which provides the environment for proliferation
Stem cell homing (2)

Annals of NY Acad Sci 2014: 301; 119-128
Engraftment

Mature blood cells migrate from the marrow niche into the blood vessels

https://basicmedicalkey.com/hemopoiesis/
Inter-site comparison - ANC

Neutrophil recovery after autologous HPC-A transplant

NSW
Median = 11 days

UK
Median = 12 days

BMT Network 2018

BMT 2017: 52; 992
Inter-site comparison - Plt

Platelet recovery after autologous HPC-A transplant

**NSW**
Median = 16 days

**UK**
Median = 24 days

*BMT Network 2018*

*BMT 2017: 52; 992*
Effect of donor & HPC source

Bone Marrow Transplantation
2013: 48; 691-697
Differential WBC recovery

Bone Marrow Transplantation 2009: 44; 457-462
Recovery of immune function

Donor type affects rate of immune function recovery
  - Autologous > Related allogeneic > Unrelated allogeneic

Innate (non-specific) immunity recovers within months
  - Monocytes > Granulocytes > NK cells

Adaptive (cellular & humoral) immunity takes at least 1-2 years
  - Expansion of infused donor T cells
  - Thymic T cell generation from donor HPC (needs functional thymus)
  - B cells recover by 6-9 months; function dependent on T cell help
  - Hence prolonged risk of infection
Graft failure

Primary
- Failure to attain sustained ANC $\geq 0.5 \times 10^9$/L, Plt $\geq 20 \times 10^9$/L, RBC transfusion independence
- Failure to achieve donor chimerism

Secondary
- Loss of graft / donor chimerism
- Usually within 6 months but can occur later
  - Higher risk in non-malignant disorders
  - Often precedes relapse in malignant disorders
Incidence of graft failure

- Autologous < 1%
- Allogeneic HLA matched sibling donor 1 – 2%

Risk factors:
- HLA or ABO group mismatch
- Donor: female, older age
- Non-malignant disorder, # blood transfusions
- Conditioning regimen
- HPC cell source, dose, quality & manipulation
- Post transplant myelosuppresive drugs
- Infection
Rescue strategies

- Growth factors, e.g. G-CSF
- Increase immunosuppression
- Donor lymphocyte infusions (DLI)
- Stem cell boost
- HPC transplant (same or different donor)
- Autologous HPC rescue (cryopreserved cells)
Summary

- **Engraftment:**
  - 1<sup>st</sup> of 3 consecutive days with blood ANC ≥ 0.5 x 10<sup>9</sup>/L
  - Platelet count ≥ 20 x 10<sup>9</sup>/L, 7 days after last platelet infusion

- Many factors influence engraftment rate

- Graft failure rate is low in autologous & MSD transplant

- Recovery of immune function takes months – years