Neutrophil Recovery: The First Step in Posttransplant Recovery

No conflicts of interest to disclose

Blood is Made in the Bone Marrow

Goals of Blood and Marrow Transplantation

- Replace blood stem cells destroyed by disease or drugs used to treat disease
- Destroy malignancy
  - High-dose chemotherapy/ radiation (which also destroys blood stem cells)
  - Immune effects of donor cells

Blood and Marrow Transplantation

Transplantation of Stem Cells Allows Us to Increase the Dose Intensity of our Treatments

Patient as donor: Autologous Collect & freeze cells

Support until recovery

Stem cells to restore marrow & immune defense

Radiation/ Chemotherapy to kill the cancer

Support until recovery

Stem cells to restore marrow & immune defense

Marrow suppression

Need growth factors

Need Stem cells

Non-hematologic toxicity

Blood

Bone marrow

White cells
- Lymphocyte
- T Lymphocyte
- Neutrophils
- Red cells
- Platelets

Blood Stem Cell

CFU-GEMM

Pre-B

BP/E

Mega

BFU-E CFU-E
Healthy Donor: Allogeneic Graft

Conditioning may or may not kill cancer cells

Stem cells to restore marrow & immune defense, destroy cancer cells

Support until recovery

Competing Risks

Support until recovery

Blood is Made in the Bone Marrow

Bone marrow

Blood

White cells
- B Lymphocyte
- T Lymphocyte
- Neutrophils

Red cells
- Platelets

CFU-GEMM

BFU-E CFU-E

Pre-B

Mega

Myeloblast

Eosinophils

Appearance of bands and segs is the earliest dependable sign of marrow regeneration – key milestone in posttransplant recovery

Complications of Prolonged Neutropenia

- Infection
- Infection
- Infection
- Risk of infection increases dramatically when:
  - Neutrophils are < 500/mm³
  - Neutropenia persists for >10 days

Also, when occurs after conditioning, usually accompanied by lack of recovery of all other blood cells

Maturation of Neutrophils
Absolute Neutrophil Count

What
• Number of bands+segs per mm³
• (% bands + % segs) x WBC/mm³

When
• First of three consecutive measurements >500/mm³
• AFTER an initial decline

POST-TED

INITIAL ANC RECOVERY
Was ≥0.5 x 10⁹/L achieved for 3 consecutive labs?
**☐ ☐ Yes, first date of 3 labs: □□□□ M M D D
**☐ ☐ No, last assessment: □□□□ M M D D
**☐ ☐ Never below □□□□ Previously reported □□□□ Unknown

Did graft failure occur? ☐ ☐ Yes ☐ ☐ No

Form 2100

Is (was) there evidence of hematopoietic recovery following the initial HSCT? (check only one)
1 Yes, ANC ≥ 500/mm³ achieved and sustained for 3 lab values with no subsequent decline (date)
2 Yes, ANC ≥ 500/mm³ for 3 lab values with subsequent decline in ANC to < 500/mm³ for ≥ 3 days (dates)
3 No, ANC ≥ 500/mm³ was not achieved and there was no evidence of recurrent disease in the bone marrow
4 No, ANC ≥500/mm³ was not achieved and there was documented persistent disease in the bone marrow post-HSCT
5 ANC never dropped below 500/mm³ at any time after the start of the preparative regimen

What Declines Are We interested In?
• Declines that compromise patient well-being and/or require intervention
• Not the "wigging" around the 500 level that can occur in the early posttransplant period
• Consider the inherent error of the test

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What Does “Never” Below Mean?
• Not in the early posttransplant period when engraftment usually occurs (first 28 days)
• Not until you do something to make them go below (e.g., additional chemotherapy)

Duration of Neutropenia
• Affected by both rate and depth of decline and rate of recovery
• Reduced intensity regimens may lead to slow or small decreases in cell counts – no or short period of neutropenia

Neutrophil Recovery Varies by Graft Type and Conditioning Regimens

Neutrophil Recovery ≠ Engraftment
• Engraftment implies presence of donor cells
• Must be proved by chimerism studies

Myeloablative Regimens
Very low intensity regimens: gradual transition from host to donor without cytopenia

What Affects Recovery Rate?
- Donor type: Auto > HLA-id > HLA ≠
- Graft type: PB > BM > CB
- Cell dose: High > Low
- Conditioning regimen: More intense > less intense
- GVHD prophylaxis: MTX ↓
- Infection: may suppress counts

What About Graft Failure and Autologous Recovery
- Graft Failure – persistent ANC <500/mm³
  - Does not include the “wiggling” sometimes seen in early posttransplant period
  - Includes failure to ever get to 500 and decline to <500 after initial recovery
  - Does not necessarily mean graft rejection (which implies that the recipient cells have immunologically rejected the donor cells)
  - Autologous recovery – requires proving the cells are host cells

What Affects Graft Failure Risk?
- Disease: Malignant < Non-malignant
- Donor type: Auto <<< HLA-id < HLA ≠
- Cell dose: High < Low
- Conditioning regimen: More intense < less intense
- Infection: particularly viral infection
- Some drugs

WHAT IS A BOOST?
- Additional cells given to facilitate hematopoietic recovery
- No additional conditioning
- Generally uses cells previously stored
- Autologous – does not require second transplant form
- Allogeneic – does require a second transplant form
- Reasons are operational not biologic