

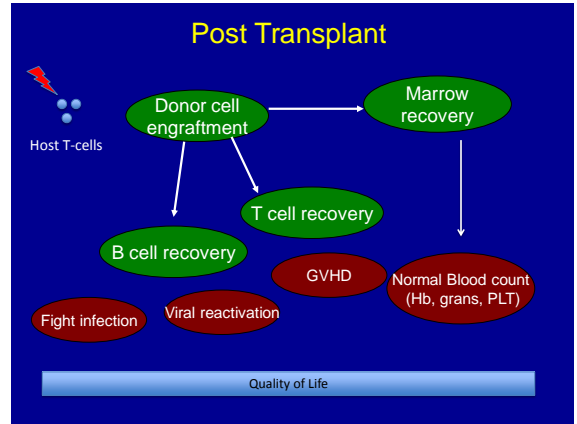
Bone Marrow Transplant for SAA: Managing Post BMT – Health and Support

Richard W. Childs, M.D.
 Clinical Director NHLBI
 Chief, Laboratory of Transplantation Immunotherapy
 Senior Investigator, Hematology Branch,
 National Heart, Lung, and Blood Institute

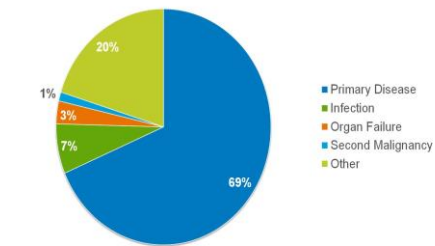
Enkhtsetseg Purev, MD, PhD
 Assistant Professor
 University of Colorado Anschutz Medical Center

Aplastic Anemia & MDS International Foundation

November 14, 2015



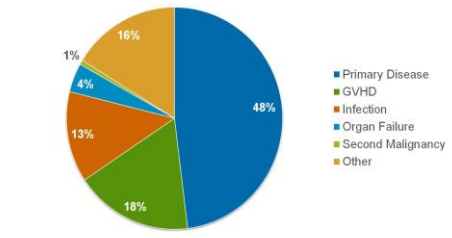
Causes of Death after Autologous Transplants done in 2011-2012



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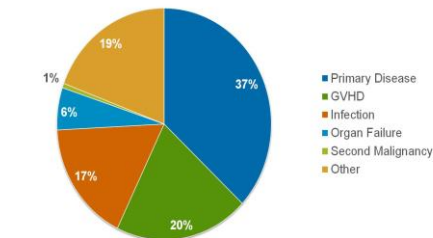
Causes of Death after HLA Match Sibling Transplants done in 2011-2012



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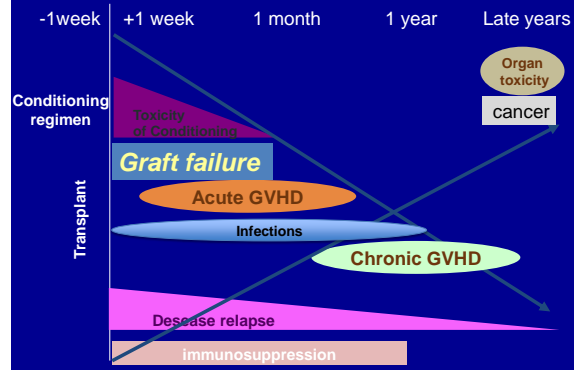
Causes of Death after Unrelated Donor Transplants done in 2011-2012



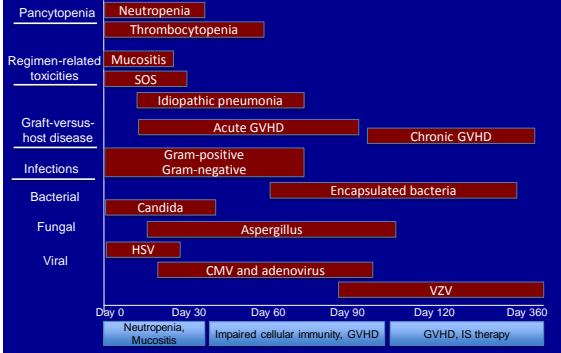
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Problems and limitations of SCT



Approximate Timing of Possible Toxicities After Allo HSCT



Antimicrobial Prophylaxis

- Antibacterial: Levofloxacin 500 mg daily until neutrophil recovery
- Antifungal: Voriconazole 200 mg twice a day or fluconazole 200mg daily
- Antitoxoplasma: Bactrim DS 1 tab three times a week
- Antiviral: Valacyclovir 500 mg daily

CMV Pneumonitis

Incidence

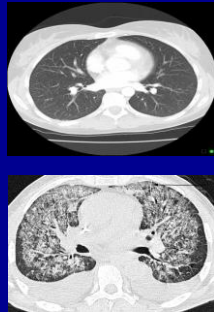
- 10-15%
- 90% cases before Day 100
- Fatality 80-90%

Risk

- Seropositive recipient seronegative donor
- Cord->MUD>MRD
- Conditioning (Alemtuzumab)

Treatment

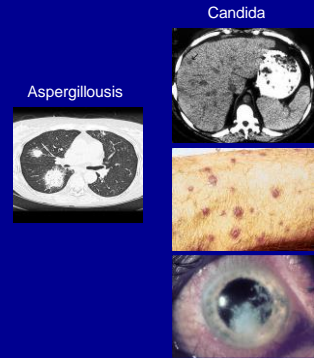
- Gancyclovir, foscarnet, IVIG, preventive letermovir



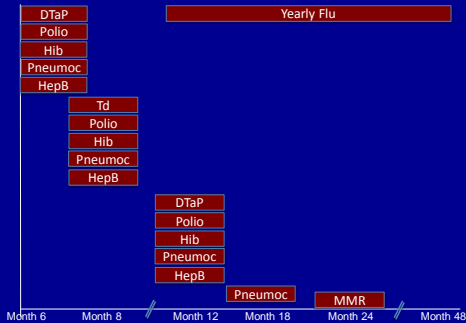
Fungal Infection

Treatment

- Voriconazole
- Lipid Amphotericin
- Isavuconazole
- Echinocandins
- COmbination

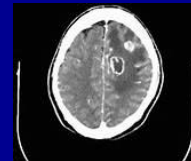


Immunization

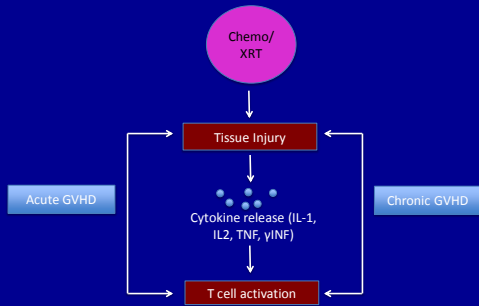


Toxoplasma

23 yo M day 78 post sib matched transplant presented with low grade, intermittent fever, and mild headache



Graft-vs-Host Disease (Donor immune Cells attacking patient tissues)



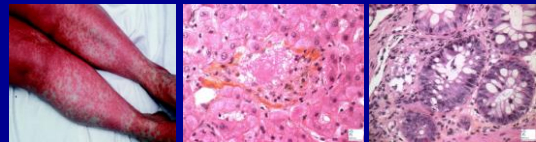
Acute GVHD

- From time of engraftment to day 100
- Incidence: 10-50% of sibling matched transplant
- Organs involved:
 - GI track: nausea, vomiting, diarrhea
 - Liver: jaundice, elevated enzymes, elevated bilirubin
 - Skin: maculopapular rash

Risk Factors for Acute GVHD

- HLA mismatch
- Older age
- Source of stem cells cord<MRD<MUD
- Preparative regimen
- Type of GVHD prophylaxis
- Gender of the donor
- NIMA, NIPA

Acute GVHD



Skin aGVHD

Liver aGVHD

Gut aGVHD

Chronic GVHD

- Occurs >Day 100
- Incidence: 30% of MRD, 75% MUD
- Organs involved (similar to autoimmune disorders):
 - Skin, lung, fascia, eyes, scalp, joints, mouth, liver
 - Presents as sicca syndrome, dermatomyositis, scleroderma, carpal tunnel syndrome, BOS

Risk Factors for Chronic GVHD

- HLA mismatch
- Prior acute GVHD
- Older age
- Source of stem cells: bone marrow<peripheral blood

Skin GVHD



Oral Chronic GVHD



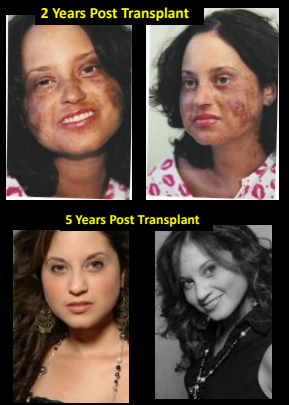
Bronchiolitis Obliterans



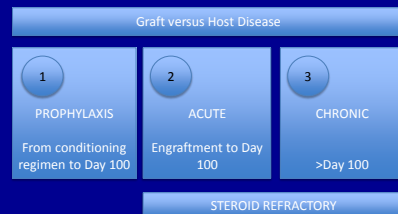
Improvement in GVHD of the Skin with Time



GVHD



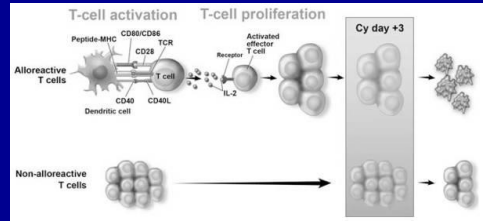
Immunosuppressive Agent to Treat GVHD



Immunosuppressive Agent to Treat GVHD

	Methotrexate	Corticosteroids	Cyclosporine	Tacrolimus	Sirolimus	Mycophenolate	Alemtuzumab	Anti-thymocyte globulin	Daclizumab	Basiliximab	Denileukin Difitox	Infliximab	Etanercept	Budesonide	Rituximab	Peritostatin	Imatinib	Interleukin-2	Extracorporeal Photopheresis (ECP)
PROPHYLAXIS	✓	✓	✓	✓	✓	✓	✓	✓											
ACUTE		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CHRONIC		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
STERIOD REFRACTORY		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Cost	1	1	1	1	10	10	100	100	100	100	1000	1000	100	10	10	1000	100	10	1000

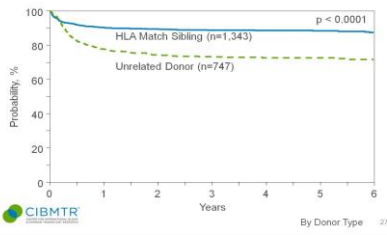
Post Transplant Cyclophosphamide



Luznil et al Immunol Res 2010

Long Term Survival

Survival after Allogeneic Transplants for Severe Aplastic Anemia, < 20 Years, 2002-2012



Long Term Survivors Report

- More likely to lose jobs
- Less likely to get married
- Have difficulty in obtaining health and life insurance
- More likely to have insomnia, anxiety, and depressed

Bhatia et al Blood 2007

Long Term Survivors: Secondary Cancer

- MDS/AML
 - 10% after autotransplant at 5 years post transplant, rare after allo
- EBV lymphoma (PTLD)
 - ~2% with ATG in preparative regimen
- Solid Tumor (squamous cell)
 - 3.8-15% at 15 years

Long Term Survivors: Organ Damage

- **Liver**
 - Hepatitis B, C, Iron overload
- **Cardiovascular**
 - Cardiomyopathy, CAD, HTN
 - Increase with anthracyclines, mediastinal radiation, cyclophosphamide
- **Endocrine**
 - Higher incidence of DM, lower height, adrenal insufficiency
 - Thyroid dysfunction
 - Osteoporosis
 - Avascular necrosis
- **Infertility**
- **Pulmonary**
 - Restrictive (radiation, bleomycine, melphalan, BCNU); obstructive (GVHD-BOS)
- **Eyes**
 - Sicca
 - Cataract

Major Improvements in Transplant Outcomes Over the Past 2 Decades

Historical Problem

- Conditioning regimens too toxic
- Older patients ineligible due to prohibitive risk of mortality
- Death from invasive fungal process and CMV frequent
- Lack of donors precludes the use of the procedure

Solution

- Development of safer conditioning regimens (IV busulfan)/use of lung shielding
- Development of reduced intensity conditioning regimens
- Advent of voriconazole, PCR to detect early CMV reactivation with use of empiric gancyclovir
- Growth of unrelated registry size, increasing use unrelated donors and mismatched unrelated cord transplants and haploidentical donors

Conclusions

- Long term survival post transplant continue to improve
- Secondary malignancy and organ damage can occur many years after the transplant
- Long term follow up is essential
- Screening
- Social support
- Early diagnosis
- Early intervention if needed



NHLBI Childs Lab

Richard Childs
George Aue
Lisa Cook
Catalina Ramos
Elena Cho
Ladan Foroughi
Rob Reger
Rob Reger

NIH CC

3 NE nursing staff
1 NW nursing staff
CC SW Dept
3SW ICU staff
CC SW Dept
David Lang- Pediatrics
NIAID ID consult service
Roger Kurlander

NIH Dept Tran Med

Hahn Khuu
David Stroncek
Susan Leitman
Jolynn Procter
Naoza Collins
Sharon Adams
Willy Flegel

NHLBI

Xin Tian
Patricia Prince

SAIC

Jennifer Wilder