

## **SCIDs: Curative Role of Allogeneic Hematopoietic Stem Cell Transplant**

**Satellite Conference and Live Webcast  
Tuesday, August 23, 2016  
2:00 – 3:30 p.m. Central Time**

**Produced by the Alabama Department of Public Health  
Video Communications and Distance Learning Division**

## **Faculty**

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## **Disclosures**

- **Jazz Pharmaceuticals**
  - Scientific advisory board
- **GLG**
  - Medical consultant

## **Typical Presentation for SCIDs (in the early days)**

- 4 month old male with respiratory distress
- Chronic URI / Otitis
- RSV pneumonia at 2 weeks of age
- Feeding difficulties, formula intolerance, diarrhea

## **Typical Presentation for SCIDs (in the early days)**

- Birth and family history unremarkable
- PE with marked FTT, eczema, wheezing
- Labs
  - “Normal” CBC (except total absolute lymphocyte count = 400)
  - Low serum IgG, IgM, IgA
  - >90 % B cells, absent T cells
  - Bronchoscopy revealed PCP

## **Severe Combined Immune Deficiency per Pediatric Immune Deficiency Transplant Consortium**

- Classic SCID criteria
  - 1) Absent or very low T cell count (<300 / ul, normal is >1000)

### Severe Combined Immune Deficiency

2) No or very low T cell function (<10% of lower limit of normal) as measured by response to mitogen PHA

OR

T cells of maternal origin

### Common features of Primary Immunodeficiency

- Failure to thrive
  - Weight, height < 5%
- Diarrhea
- Neurological deficits
  - Loss of milestones
  - Developmental delays

### Common features of Primary Immunodeficiency

- Skin and nail abnormalities
  - Eczema, atopia
  - Candidiasis
  - Thrush, diaper dermatitis



### Clinical Features of Primary Immunodeficiency

- Infections
  - Recurrent
    - What is normal?
      - <10 in first year of life
  - Severe or invasive
  - Viral URI
    - RSV, parainfluenza

### Clinical Features of Primary Immunodeficiency

- Unusual / opportunistic
  - Fungus, i.e. aspergillus
  - Atypical bacteria
    - Mycobacterium
    - Histoplasmosis
    - Pneumocystis carinii

### Laboratory Data

- Lymphopenia (low ALC)
  - Absent T cells, +/- B cells
- T cell function absent
  - Poor mitogen responses or recall to immunization
- Low / absent serum immunoglobulin
  - IgG level may be maternal!!!

### History of BMT and SCIDs

- Prior to 1968, every child born with SCIDs died
- First successful allogeneic BMT ever performed was for SCID in Minnesota in 1968

### History of BMT and SCIDs

- 5 month old male with “sex linked lymphopenic hypogammaglobulinemia”
- Brother died from SCIDs
- Received MLC compatible bone marrow from sister
- Graft vs host disease
- Alive today

### SCIDS- “Bubble boy” disease

David Phillip Vetter September 21, 1971 – February 22, 1984

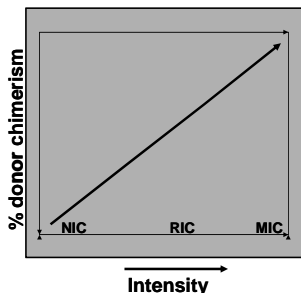


- X linked SCIDS
- Diagnosed by family history
- Confined to bubble at advise of MD at Baylor
- Extreme depression and behavior issues due to isolation
- Underwent BMT at age 13 and died of 3 months later

### Transplant Phases and Complications

- Preparative Therapy
  - days -10 to 0
  - Nausea from chemo
- Pre / early engraftment
  - Days 0-30
  - Organ toxicity of chemo
  - Mucositis
  - Infections due to low WBC
- Post engraftment
  - 1-12 month
  - Graft vs host disease
  - Viral reactivation

### Transplant Phases and Complications



- Myeloablative conditioning (MIC)
  - Counts drop out completely
- Reduced intensity conditioning (RIC)
  - Counts drop but less toxicity
- Non myeloablative conditioning (NIC)
  - Counts may not drop, goal to achieve partial chimerism

### Supportive Care Anticipatory Guidelines for SCIDs

- No live viral vaccines
  - Rotavirus or varicella can disseminate in immune compromised host
- Avoid contact with sick persons and young children

### Supportive Care Anticipatory Guidelines for SCIDs

- Culture for pathogens, including viral
  - Nasal swab for VRP
  - Blood for CMV, Toxo, Adeno,
  - Consider bronchoscopy
- Avoid breast feeding (CMV transmission)

### Supportive Care Anticipatory Guidelines for SCIDs

- Transfuse only with irradiated, leukodepleted blood products
  - Prevent transmission of CMV and Graft vs host disease
- House in protected environment on BMT unit

### Supportive Care Anticipatory Guidelines for SCIDs

- Initiate Bactrim immediately
  - PCP is primary cause of death of SCIDs patients
- Intravenous immunoglobulin
- Liberal use of broad spectrum antibiotics

### HSCT Transplant Workup

- Early referral to transplant center optimal
- Arrange tissue typing for donor identification
  - Blood sent to the tissue typing lab
  - Family members, sibs typed
  - Search the National Marrow Donor Program data base

### HSCT Transplant Workup

- Pre - transplant testing
  - Organ function assessment
  - Serologies (maternal)
  - Infection workup
  - Social work and neuropsych team to help with financial assistance, coping, and family issues

### Factors Affecting Transplant Outcome in SCIDs

- Age of patient
  - Transplants done early, within the first few months of life, associated with best outcome
  - Reason NBS is so important!

### **Factors Affecting Transplant Outcome in SCIDs**

- Infections
  - Lack of opportunistic or severe infection or ventilator support associated with best outcome
- SCID phenotype
  - Omenns, Reticular dysgenesis worst

### **Factors Affecting Transplant Outcome in SCIDs**

- HLA match and donor source
  - Matched sibling best
  - Haplo vs cord vs MUD ~ similar outcome
- Pre - transplant care

### **Should We Be Considering Cord Blood as Donor Source in SCID?**

- Over 20,000 cord blood transplants performed to date
- Donor pool is expanding
  - Over 590,000 potential donor cords frozen
- Several advantages of cord blood transplant versus bone marrow

### **Cord Blood Advantages**

- No need for perfect HLA match (6 / 6)
  - Easier to find match for minorities
- Rapid turn-around time
  - Cord blood search and delivery = 1 week
  - Bone marrow search, donor work up, confirmation of tissue typing, harvest, delivery = 2 months (avg)

### **Cord Blood Advantages**

- Less risk to donor
  - Cord blood donation is non-invasive, painless and risk - free for the mother and infant
  - Bone marrow donation requires a general anesthesia to harvest bone marrow

### **Cord Blood Disadvantages**

- Higher incidence of post transplant viral infections
- Increase in autoimmune cytopenia post transplant
- No availability of same donor for stem cell boost
- Donor history incomplete

## Current Controversies in SCIDs and BMT

- What is the best donor in the absence of a matched related donor
  - Matched unrelated donor-delays in getting marrow collected
  - Haplo-identical donor- T cell depletion, delays in immune reconstitution
  - Cord blood donor- delay in immune recovery due to small number of T cells in graft

## Current Controversies

- Should we be doing chemo / immuno ablation preparative therapy
  - Those that get chemo are more likely to fully engraft and be weaned off IVIG
  - Chemo has long term side effects, including sterility

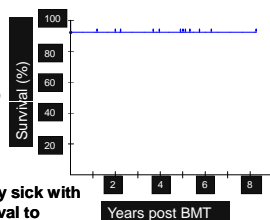
## Children's of Alabama BMT for Typical SCIDs

### • Donor type

- MUD donors (7)
- Haplo donors (3)
- Cord Blood donor (2)
- MRD (1)

### • One death

- Patient was extremely sick with PCP and RSV on arrival to hospital, on ventilator within 3 days. Received a cord blood transplant while on ventilator



## Children's of Alabama BMT for Atypical SCIDs

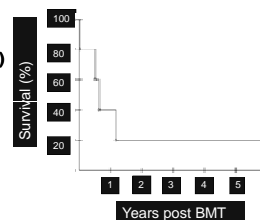
### • Donor type

- MUD donors (2)
- Cord Blood donor (2)
- MRD (1)

### • Disease types

- IPEX
- Omenns (2)
- NEMO
- Leaky SCIDs

- All received some conditioning



## Summary

- Diagnosing SCIDs by NBS is feasible and will save lives!
- Early referral of a SCIDs patient to an experienced center is crucial
- BMT for SCIDs should be done early for optimal results
- New approaches to standardizing transplant for SCIDs patients is on the horizon