Hematopoietic Stem Cell Transplantation in Primary Immunodeficiency Diseases

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Disclosure Information

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-No financial interest or conflict of interest
Outline of the talk

• Overview of Primary immunodeficiency diseases and Hematopoietic stem cell transplantation
• CIBMTR Reporting Requirements
• Data points collected from CIBMTR forms
  – Pre-transplant data
  – Follow-up data
  – Disease data
• Keep an eye on...
• How can we help
Human Immune system

Immune system

Acquired

T-cell immunity
(cell-mediated immunity)

Whole T-cells released into:

Suppressor T-cells
Helper T-cells
Cytotoxic T-cells

Death of the body’s cells that are infected with a virus or otherwise damaged

B-cell immunity
(humoral immunity)

Antigen exposure

Lymphoblasts

Complement cascade
Clonal B-cells
Memory B-cells

Bloodbourne

Complement cascade
Alternative pathway

Phagocytes
1. Neutrophils
2. Macrophages
3. Basophils
4. Eosinophils
5. Natural killer cells

Death of dangerous organisms

Direct killing of bacteria

Physical barriers
1. Skin
2. Mucous membranes
3. Saliva
4. Flushing action of urine and tears
5. Stomach acid

Stops infection before it enters the body
Primary Immune deficiency Diseases

Primary immune deficiency diseases (PID) comprise a heterogeneous group of genetic disorders that affects distinct components of the innate and adaptive immune system such as neutrophils, macrophages, dendritic cells, natural killer cells, T and B lymphocytes and complement components.

- More than 200 distinct PID disorders have been identified and 276 gene have been associated with these diseases.
- Spectrum of these diseases can vary from mild presentation to lethal disorders. Lethality is due to increase susceptibility to infections and malignancies.
**Mode of Inheritance**

**X-Linked Inheritance: Scenario 1**

- **MOM**
  - Carrier (no symptoms)
  - Normal

- **DAD**
  - Normal

**Possible combinations:**

- Normal Girl
- Carrier Girl
- Normal Boy
- Affected Boy

*Only boys can be affected. Since girls will always inherit a normal copy of the gene from their fathers, they can become carriers.*

**X-Linked Inheritance: Scenario 2**

- **MOM**
  - Carrier (no symptoms)
  - Affected

- **DAD**
  - Normal

**Possible combinations:**

- Carrier Girl
- Affected Girl
- Normal Boy
- Affected Boy

*If both parents carry a copy of the defective gene, girls can be affected. The father will always pass the defective gene to each of his daughters.*

- ![X chromosome with normal copy of gene](image)
- ![Y chromosome (does not have any copies of gene)](image)
- ![X chromosome with defective copy of gene](image)
Mode of Inheritance

Autosomal Recessive Inheritance

MOM  DAD

Carrier (no symptoms)  Carrier (no symptoms)

Possible combinations:

Normal  Carrier  Carrier  Affected

Each child inherits one copy of the gene from each parent.

Chromosome with normal copy of gene
Chromosome with defective copy of gene
Autosomal Dominant Inheritance

- Affected father
- Unaffected mother
- Recessive gene
- Dominant gene
- Affected child
- Unaffected child
Many of the serious disorders of lympho-hematopoiesis have been cured with hematopoietic stem cell transplantation.
Landmark events in the field of HSCT and immune deficiency diseases

- **In 1968** first successful allogeneic bone marrow transplant in a patient with SCID from a histocompatible sibling donor became gold standard for HSCT.

- **In 1973** first unrelated donor marrow transplant was performed in a patient with SCID.

- **In 1980** first successful Haplo-identical marrow transplant was performed in SCID Patient.

- **In 1995** Gene therapy in ADA SCID.

- **In 2012** PIDTC report more than 1,000 PID Children had received HSCT in USA.
PID Disorders Transplanted at CHLA
01/01/1983 - 01/13/16 n=175

- Bare Lymphocyte Syndrome
- CD40 Ligand Deficiency
- Chediak-Higashi Syndrome
- Chronic Granulomatous Disease
- Combined Immunodeficiency Disease
- Hereditary Lymphohistiocytic Hemophagocytosis
- Leukocyte Lymphoproliferative Syndrome
- Severe Combined Immunodeficiency Disease
- Wiskott-Aldrich
- X-linked Lymphoproliferative Syndrome
Bubble Boy Disease: SCID

- “Bubble Boy Disease” is severe combined immune deficiency Disease (baby born without immune system)

- Most of the time it is a genetic disorder, where either Mother carries the defective gene and disease express in male child, or both parents may carry the gene for the disease, and occasionally there may be spontaneous mutation in fetus and may cause the disease and affect male or female child

- Children get sick with in first 4-6 months of age

- Children die with in 1st year of life without definitive curative treatment

- Blood and marrow transplantation can construct the Normal Immune system in these patients
Combined T and B cell immune deficiency

1. T-/B+ SCID γc deficiency, JAK3 deficiency, interleukin 7 r deficiency, CD45 deficiency, CD3δ/CD3ε deficiency.
2. T-/B- SCID, RAG 1/2 deficiency, DCLRE1C deficiency, ADA deficiency, reticular dysgenesis
3. Omenn syndrome
4. DNA ligase type IV deficiency
5. Cernunnos deficiency
6. CD40 ligand deficiency
7. CD40 deficiency
8. Purine nucleoside phosphorylase (PNP) deficiency
9. CD3γ deficiency
10. CD8 deficiency
11. ZAP-70 deficiency
12. Ca++ channel deficiency
13. MHC class I deficiency
14. MHC class II deficiency
15. Winged helix deficiency
16. CD25 deficiency
17. STAT5b deficiency
18. Itk deficiency
19. DOCK8 deficiency
20. Activated
SCID: HPC Transplant outcome:
Pai et al. NEJM 2014
Chronic granulomatous disease (CGD) is a diverse group of hereditary diseases in which phagocytic cells are unable to form the reactive Oxygen Compounds most importantly superoxide radical due to defective phagocyte NADPH oxidase which kills ingested organisms.

- X-linked chronic granulomatous disease (CGD)
- Autosomal recessive cytochrome b-negative CGD
- Autosomal recessive cytochrome b-positive CGD type I
- Autosomal recessive cytochrome b-positive CGD type II
- Atypical granulomatous disease
Chronic granulomatous disease (CGD)

• **Symptoms**
  – Pneumonia, abscesses of the skin, tissues, and organs
  – Suppurative arthritis, osteomyelitis, superficial skin infections such as cellulitis or impetigo

• **Infections due to bacteria particularly those that are catalase-positive**

• **Infections due to fungi**
  – Aspergillus species. Aspergillus has a propensity to cause infection in people with CGD and of the Aspergillus species, Aspergillus fumigatus seems to be most common in CGD.
  – Candida species.
• 56 patients, aged 0-40 years median age: 13 years, using a reduced conditioning protocol.

• **42 of the 56 were considered high-risk patients not candidates for myeloablative HSCT.**

• 2-year overall survival of 96% and event-free survival of 91%.

• Incidence of severe acute GVHD grades III-IV was only 4% and chronic GVHD was 7%.

• Stable myeloid donor chimerism in 93% of surviving patients.

• Two adult patients were subsequently able to have children.
Wiskott -Aldrich Syndrome

• A rare X-linked immunodeficiency disorder has variable clinical phenotype which correlates with type of WASP gene mutation.

• The disease is associated with progressive combined immune deficiency, thrombocytopenia, small sized platelets, Eczema, and increased risk of autoimmune diseases and malignancy.
Wiskott-Aldrich Syndrome and HCT

- WAS is 2\textsuperscript{nd} most common PID treated with HSCT
- 1\textsuperscript{st} patient with WAS was transplanted in 1968
- Before 1990, only patients with WAS who had serious complications of disease and had matched sibling donors had HSCT.

- Disease correction required both myeloid and Lymphoid engraftment thus needs myeloablative conditioning regimen.

- Transplant corrects all aspects of this disease. Transplant from matched related/unrelated donor is standard of care.
Wiskott-Aldrich Syndrome and HCT

- CIBMTR results (Blood, 2001), 170 transplants performed between 1980-96 in multiple institutions worldwide. Overall 5 year survival.
  - Matched sibling donor transplant was 87%
  - Unrelated donor transplant for ≤5yr was 71%
  - Unrelated donor transplant for >5yr was 52%

- SCETIDE results at EBMT 2008, 166 Tx performed between 1968-2005 in 35 centers. 71% survival.

- Great Ormond Street Hospital results (Blood, 2009) 17 patient transplanted with RIC1995-2007, all patients survived, 4/17 had mixed chimerism
Lesson learnt from these studies

• Diagnose these children with PID, before they get sick and encounter some serious infection, which might cause serious morbidity and mortality

• Definitive therapy earliest possible time to provide to provide best chance for the cure of the disease
As of November 1, 2015
States currently screening for SCID
N=34
• Arkansas, California, Colorado
• Connecticut, Delaware, Florida
• Hawaii, Illinois, Iowa, Maine
• Massachusetts, Michigan, Minnesota
• Mississippi, Montana, Nebraska
• New Hampshire, New Jersey,
• New Mexico, New York, Ohio
• Oklahoma, Oregon, Pennsylvania
• Rhode Island, South Carolina, Texas
• South Dakota, Utah, Virginia
• Washington, West Virginia
• Wisconsin, Wyoming
• District of Columbia, Navajo Nation

States and territories currently planning to begin screening in 2016:
N=9
• Alaska
• Georgia
• Idaho
• Kentucky
• Maryland
• North Carolina
• North Dakota
• Puerto Rico
• Tennessee
SCID Newborn Screening: Current Status of Implementation Map

- Screening
- Pilots and Planning in 2015 & 2016
- Not Screening
• On May 21, 2010, the Department of Health and Human Services (HHS) in California, announced the addition of Severe Combined Immunodeficiency (SCID) in New Born Screening panel
• We has adopted new born screening by testing dried blood spot for TREC
• In California in two years $1.5 \times 10^6$ infants were Screened for TREC (Average # of TREC 1030/3mm punch. In SCID<30 TREC)
• 50 infants had significant lymphopenia (low lymphocyte counts)
• 15 SCID were identified, 6 leaky SCID and 3 patients with Digeorge syndrome
• 93% are alive and well due to early interventions.
Essential steps for Blood Stem cell transplant from Allogeneic Donor

- Identification of the disease correctable with allo BMT
- **Identification of suitable HPC donor:**
  - 1. Matched related
  - 2. Matched unrelated
  - 3. Haploidentical related
- **Conditioning regimen:**
  - 1. Myeloablative
  - 2. Reduced intensity
  - 3. Immunosuppression alone
  - 4. No therapy
- **Graft source:**
  - Bone marrow, PBSC, Cord blood
  - T replete or T depleted grafts
- Post transplant immuno-suppression to prevent graft versus host disease and no immuno-suppression for T depleted graft
MAJOR HISTOCOMPATIBILITY SYSTEM

other genes

chromosome 6

HLA complex

Class II antigen
DP, DQ, DR

Class I antigen

0.5 cM

2 cM

3500 bp
SCHEMATIC REPRESENTATION OF INHERITANCE OF HLA REGION OF CHROMOSOME 6 WITHIN FAMILY

FATHER
A: 2-12-
B: -1-5

MOTHER
C: 5-2-
D: -3-7

PATIENT
A: 2-12-
B: 1-5
C: 1-5
D: -3-7

DONOR
A: 2-12-
B: 1-5
C: 1-5
D: -3-7
Availability of Donor

- For a patient with non genetic disease, there is 35% chance to have histocompatible donor with in sib ship
- For a patient with genetic disease there is <25% chance to have histocompatible sibling who is also healthy

- 60 to 75% must have alternative Stem cell donor

- Unrelated donor:
  - National Marrow Donor Program Ten Million volunteers
  - 193,474 cord Blood products
FOR JUST THE HLA-A,B,C AND DR LOCI-

~3 Billion different Genotypes
Likelihood of Finding a Matching Adult Donor by Race and Ethnicity
(Based on 7 of 8 matching)

- A patient’s likelihood of having a donor on the Be The Match Registry who is willing and able to help save a life is estimated to range from 66% to 93%, depending on race and ethnicity. Cord blood improves likelihood of finding an appropriate cell source. In 2012, 39 percent of minority patients who received a transplant used cord blood.

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients, depending on race and ethnicity</td>
<td>66-93%</td>
</tr>
<tr>
<td>African American or Black patients</td>
<td>66%</td>
</tr>
<tr>
<td>American Indian and Alaska Native</td>
<td>82%</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>73%</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>72%</td>
</tr>
<tr>
<td>White</td>
<td>93%</td>
</tr>
</tbody>
</table>

Source: NMDP Bioinformatics, 2010
Note: Percentages are based on matching an adult donor only. Cord blood further increases the chance of finding a match for some patients.

For 10-45% of patients, there are no matched sibling or unrelated donor options. Option for those patients: Haploidentical donor transplants.
Gene Therapy

• Primary immune deficiencies (PID) were amongst the first group of diseases to be effectively treated with gene therapy and this field has rapidly expanded over the past two decades with innovative new technologies being rapidly incorporated into clinical practice.

• Correction of autologous hematopoietic stem cells (HSC) using viral vectors to deliver the appropriate transgene has changed the management landscape for these groups of patients.

• The successful outcome of a number of clinical trials is bringing gene therapy towards a first line treatment option for selected conditions.

• Younger, non infected patients have better outcome
Primary Immune deficiency Disorders
Transplant Consortium (PIDTC)

- **PIDTC established in 2009**
- The first grant cycle dates: Sep 1, 2009 - Aug 31, 2014
- Participating sites: \( n = 33 \)
- 13 primary sites and 20 sites under the PBMTC umbrella.

- The second grant cycle dates: Sep 1, 2014 - Aug 31, 2019
- Participating sites: \( n = 45 \)
- 33 original sites + 9 additional sites which are under the PBMTC umbrella + 3 European sites.
- Currently 45 PIDTC sites and expect to have 47 total for this second grant cycle.

- **CIBMTR provides data on transplant patients to the PIDTC**
PIDTC Studies

- PIDTC 6901: A Prospective Natural History Study of Diagnosis, Treatment and Outcomes of Children with SCID Disorders. Thirty centers are participating and about 160 patients have been enrolled on this study.

- PIDTC 6902: A Retrospective and Cross-Sectional Analysis of Patients Treated for SCID Since January 1, 1968.

- PIDTC 6903: Analysis of Patients Treated for Chronic Granulomatous Disease Since January 1, 1995.


- PIDTC 6905: A randomized trial of very low- and low-dose busulfan for infants with severe combined immunodeficiency (SCID): A Phase II study by PIDTC and PBMTC*
CIBMTR Reporting Requirements (contd..)

- Pre-HCT Data points are collected from:
  - Form 2400 (Pre-TED)
  - Form 2000 (Baseline)
  - Form 2005 (Confirmation of HLA typing)
  - Form 2006 (Infusion form)
  - Form 2031 (Immune Deficiencies Pre-HSCT Data)

- Post-HCT Data points are collected from:
  - Form 2100, Form 2200 and Form 2300
  - Form 2131
  - Form 2900
Data Points Collected from CIBMTR Pre-HCT forms (2005/2006)

- HLA typing - Form 2005
  - Donor and Recipient typing
- Product information - Form 2006
  - Pre-collection therapy
  - Product processing/manipulation
  - Product analysis
  - Donor relation
Data Points Collected from CIBMTR Pre-HCT forms (2400/2000)

• Recipients Demographics
  – Gender, Ethnicity, Race, blood type and Rh factor
• Coexisting diseases
  – Hemorrhage, chromosome abnormality....
• Preparative Regimen
  – ATG, Busulfan, corticosteroids, Melphalan....
Data Points Collected from CIBMTR Post-HCT forms (Form 2100/2200/2300)

- Some of the important Data points are:
  - Chimerism studies (Form 2100/2200)
  - acute/chronic GVHD
  - Infection
  - Organ function
  - Subsequent transplant/DCI
CIBMTR Data forms

• **Immune deficiency disease**
  – Pre HSCT data form 2031 R3.0 (190 Questions data points)
  – Post HSCT data form 2131 R3.0 (170 Questions/data points)

• **Chronic granulomatous disease**
  – Pre HSCT data form 2055 R2.0 (172 Questions/data points)
  – Post HSCT data form 2155 R2.0 (232 Questions/data points)

• **Wiskott Aldrich Syndrome**
  – Pre HSCT data form 2033 R2.0 (140 Questions/data points)
  – Post HSCT data form 2133 R2.0 (174 Questions/data points)
Data Points Collected from CIBMTR Pre-HCT forms (Form 2031)

• Some of the important Data points are:
  - Clinical status
  - Failure to thrive
  - GVHD due to maternal engraftment
  - Immunoglobulin Analysis
  - Lymphocyte Analysis
  - Infection
Some of the important Data points are:

- Serum Immunoglobulin levels
- Lymphocyte analysis T cell, B cells, NK Cells
- Immune functions Mitogen and Antigen responses
- Infection
# Form 2031 R3.0: Immune Deficiencies Pre-HSCT Data

**Center:**

<table>
<thead>
<tr>
<th>Field</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>28  Absolute lymphocyte count</td>
<td></td>
</tr>
<tr>
<td>29  CD3 (T cells) not tested</td>
<td></td>
</tr>
<tr>
<td>30  CD4 (T helper cells) not tested</td>
<td></td>
</tr>
<tr>
<td>31  CD8 (cytotoxic T cells) not tested</td>
<td></td>
</tr>
<tr>
<td>32  CD20 (B lymphocyte cells) not tested</td>
<td></td>
</tr>
<tr>
<td>33  CD56 (natural killer (NK) cells) not tested</td>
<td></td>
</tr>
<tr>
<td>34  CD4+/CD45RA+ (memory T cells) not tested</td>
<td></td>
</tr>
<tr>
<td>35  CD4+/CD45RO+ (memory T cells) not tested</td>
<td></td>
</tr>
</tbody>
</table>

**Antibody Response**

<table>
<thead>
<tr>
<th>Antibody Response</th>
<th>Absent</th>
<th>Low</th>
<th>Normal</th>
<th>Not Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>36  Date antibody responses were assessed: (date closest to diagnosis, before any IVIG)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37  Bacitracin x-174 or other neomycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>38  Diphtheria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>39  Isohemagglutinin anti-A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40  Isohemagglutinin anti-B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>41  Protein conjugated HIB or pneumococcal vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42  Tetanus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>43  Unconjugated pneumococcal polysaccharide</td>
<td>Number of in</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Lymphocyte Function**

<table>
<thead>
<tr>
<th>Lymphocyte Function</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>44  Date lymphocyte function was assessed:</td>
<td></td>
</tr>
<tr>
<td>45  ABS-CD3</td>
<td></td>
</tr>
<tr>
<td>46  Candida antigen</td>
<td></td>
</tr>
<tr>
<td>47  Concanavalin A (ConA)</td>
<td></td>
</tr>
<tr>
<td>48  Phytohemagglutinin (PHA)</td>
<td></td>
</tr>
</tbody>
</table>

**CRID:**
## Form 2131 R3.0: Immune Deficiencies Post-HSCT Data

### Lymphocyte Analysis

Specify the most recent lymphocyte assessment measured since the date of the last report.

18. Were lymphocyte analyses performed?
   - [ ] yes
   - [ ] no

19. Date of most recent testing performed: __ __ __ __ __ __ __ __

20. Absolute lymphocyte count: ___________________________ cells/ul (cells/mm³)

21. [ ] CD3 not tested

   CD3 (T cells) % of total lymphocytes ______________________ %

   CD3 (T cells) value ___________________________ x 10⁹/L (x 10⁹/mm³)

   [ ] x 10⁹/L

22. [ ] CD4 (T helper cells) not tested

   CD4 (T helper cells) % of total lymphocytes ______________________ %

   CD4 (T helper cells) value ___________________________ x 10⁹/L (x 10⁹/mm³)

   [ ] x 10⁹/L

23. [ ] CD8 (cytotoxic T cells) not tested

   CD8 (cytotoxic T cells) % of total lymphocytes ______________________ %

   CD8 (cytotoxic T cells) value ___________________________ x 10⁹/L (x 10⁹/mm³)

   [ ] x 10⁹/L

24. [ ] CD20 (B lymphocyte cells) not tested

   CD20 (B lymphocyte cells) % of total lymphocytes ______________________ %

   CD20 (B lymphocyte cells) value ___________________________ x 10⁹/L (x 10⁹/mm³)

   [ ] x 10⁹/L

25. [ ] CD56 (natural killer (NK) cells) not tested

   CD56 (natural killer (NK) cells) % of total lymphocytes ______________________ %

   CD56 (natural killer (NK) cells) value ___________________________ x 10⁹/L (x 10⁹/mm³)

   [ ] x 10⁹/L

26. [ ] CD4+/CD45RA+ (memory T cells) not tested

   CD4+/CD45RA+ (naive T cells) % of total lymphocytes ______________________ %

   CD4+/CD45RA+ (naive T cells) value ___________________________ x 10⁹/L (x 10⁹/mm³)

   [ ] x 10⁹/L

27. [ ] CD4+/CD45RO+ (memory T cells) not tested

   CD4+/CD45RO+ (memory T cells) % of total lymphocytes ______________________ %

   CD4+/CD45RO+ (memory T cells) value ___________________________ x 10⁹/L (x 10⁹/mm³)

   [ ] x 10⁹/L
Form 2131 R3.0: Immune Deficiencies Post-HSCT Data

Specify the most recent quantitative immunoglobulins measured since the date of the last report.

For questions 8–13, also report immunoglobulins in the Form 2100 – 100 Days Post-HSCT Data beginning at question 55, or in the Form 2200 — Six Months to Two Years Post-HSCT Data beginning at question 26.

For questions 16–17, also report IVIG in the Form 2100 – 100 Days Post-HSCT Data beginning at question 61, or in the Form 2200 — Six Months to Two Years Post-HSCT Data beginning at question 32.

8 □ IgG not tested

IgG: ____________ mg/dL g/dL g/L

9 Date tested: ____________

10 □ IgM not tested

IgM: ____________ mg/dL g/dL g/L

11 Date tested: ____________

12 □ IgA not tested

IgA: ____________ mg/dL g/dL g/L

13 Date tested: ____________

14 □ IgE not tested

IgE: ____________ IU/mL

15 Date tested: ____________

16 Did the recipient receive supplemental intravenous immunoglobulins (IVIG) since the date of the last report?

  ○ yes  ○ no  ○ Unknown

17 Was therapy ongoing within one month of immunoglobulin testing?

  ○ yes  ○ no

28 Date antibody responses were assessed: _______ _______ _______ _______

29 Bacteriophage phi X-174 or other neoantigen

  ○ Absent  ○ Low  ○ Normal  ○ Not Tested

30 Diptheria

  ○ Absent  ○ Low  ○ Normal  ○ Not Tested

31 Isohemagglutinin anti-A

  ○ Absent  ○ Low  ○ Normal  ○ Not Tested

32 Isohemagglutinin anti-B

  ○ Absent  ○ Low  ○ Normal  ○ Not Tested

33 Protein conjugated HIB or pneumococcal vaccine

  ○ Absent  ○ Low  ○ Normal  ○ Not Tested

34 Tetanus

  ○ Absent  ○ Low  ○ Normal  ○ Not Tested

35 Unconjugated pneumococcal polysaccharide:

  Number of serotypes producing a protective level

36 Conjugated pneumococcal polysaccharide:

  Number of serotypes producing a protective level
Lymphocyte Analysis

- Absolute lymphocyte count is very important when also reporting %s.
  - Reported on Flow Cytometry or CBC results
- Reporting % vs value and unit
- Some suggestions for completing the form:
  - CD20: acceptable to report CD19
  - CD56: acceptable to report CD16
  - Report the memory and naïve T cells

Center contact for updating forms
Keep an eye on.....

• Chimerism Studies
  – Must be performed and reported at 100 days, 6 month, 1 year and 2 year time-points
  – Specifying the cell lineage is important
    • T-cells, B-cells or Myeloid cells
  – Center Contact for updating forms
Need Help........

- Do not Hesitate to call on people around to get clarification on Data
- When in Doubt........
  - Contact your PIDTC PI
  - Contact Swati Kulkarni @ skulkarni@mcw.edu
Because of some transplant related morbidity mortality, the therapy is being offered only to the patients with the **highest risk of the disease**.

The questions...who to transplant, when to transplant, how to transplant, from whom to transplant are still not answered clearly.

Therefore looking at every single patient transplanted in detail, is critical to understand the disease, its course, the best ways to treat the disease and improve the outcome of the procedure and Quality of life for these patients.
In Conclusion

• Primary Immunodeficiency diseases are rare and heterogeneous group of genetic disorders.

• For many diseases genetic abnormalities and mode of inheritance has been identified

• The spectrum of presentation of these diseases varies from very mild symptoms to serious and potentially lethal illness.

• Such diseases identified early in life can be potentially cured with Stem Cell Transplant and Gene Therapy

• By gathering complete and accurate information about these patients and learning from it, the medical community can offer better and more appropriate therapy in the management of these patients
Thank you
Questions/Comments