B-cell Reconstitution and IgG Infusion for SCID

August 31st, 2022
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- Attendees will not have access to their microphone or webcam throughout the event.
- To see the full slides, you can adjust the settings on the speaker view panel on the top of the Zoom screen and select "side-by-side" in the dropdown option.
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B cell reconstitution and IgG replacement

SCID Compass Lunch & Learn

Manish Butte, MD/PhD, UCLA Health
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SCID

How we started

How it’s going
Immune system development from bone marrow stem cells

How blood cells are made

Bone marrow

Haematopoietic stem cells

Myeloid progenitor cells

Erythrocytes

Lymphoid progenitor cell

Platelets

Eosinophil

Basophil

Neutrophil

Monocyte

T-cell

B-cell

Immunodeficiency UK
Immune system with SCID

How blood cells are made

- Bone marrow
- Haematopoietic stem cells
- Platelets
- Myeloid progenitor cells
- Eosinophil
- Basophil
- Neutrophil
- Erythrocytes
- Monocyte
- Lymphoid progenitor cell
- T-cell
- B-cell

Immunodeficiency UK
IMMUNE SYSTEM RESET
IN CASE OF EMERGENCY
BREAK GLASS
What is blood and marrow transplant (BMT)?

Diseased stem cells

Replacement of diseased stem cells

Healthy stem cells
Immune expectations after transplant

SCID: no T cells

Kim Caesar/ Nature Publishing Group
After transplant reconstitution timeline

- **Day - n**: Conditioning period
  - Pancytopenia, Infection, Organ toxicity
- **Day 0**: Stem cell infusion
- **Day 14**: Neutropenia
- **Day 28**: Engraftment
- **Day 100**: Immune reconstitution
- **Day 180**: NK cells, T cells
- **Day 300**: Cell expansion

- **B cells**
B cells make antibodies

CellCartoons.net
B cells mature to plasma cells

Take that flu virus!!!

Plasma Cell
Shooting Antibodies
B cell reconstitution after transplant

- Overshoot of B cells is common (partially from graft itself)
- Memory B cells are low for 2 years
- Vaccine responses are often very low for 1-2 years
What are the factors that influence B cell reconstitution after SCID BMT?

• Genetic cause of SCID? Yes
• Conditioning regimen? Yes (71% with, 15% without)

• Can you have functioning B cells without conditioning? Yes but unlikely
• Is busulfan needed to get B cell reconstitution? Jury is still out, likely yes busulfan helps a lot

Haddad E et al, JACI April 2013
The different types of immunoglobulins
<table>
<thead>
<tr>
<th></th>
<th>IgA</th>
<th>IgD</th>
<th>IgE</th>
<th>IgG</th>
<th>IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% total Ig in serum</strong></td>
<td>10-20</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>70-85</td>
<td>10</td>
</tr>
<tr>
<td><strong>Where found in body</strong></td>
<td>Found in bodily secretions.</td>
<td>Found on B-cell surface</td>
<td>Attach to basophils and mast cells.</td>
<td>Blood &amp; extracellular fluid</td>
<td>Blood &amp; extracellular fluid</td>
</tr>
<tr>
<td><strong>Functions</strong></td>
<td>Protect external openings</td>
<td>Unknown; maybe antigen detection</td>
<td>Allergic response and defend infection by large parasite</td>
<td>Long term Ab that protect the body</td>
<td>Appear earlier in the infection and offer valuable defense during critical stage of the infection</td>
</tr>
</tbody>
</table>

Creative Biolabs
IgG Replacement Facts

• Products are meant to replace only the IgG component of the immune system protection (not IgA or IgM)

• Generally, IgG antibodies protect you from recurrent infections of the ears, sinuses, and lungs
  • IgG supplementation contains many kinds of antibodies to viruses as well, but this tends not to be the main *impact* of replacement
How it's made

• IgG is a blood product; it utilizes up to 1000 different donors to make a pool of antibodies
  • Donors must be screened and their first donation is held; they return for a second screening 3-6 months later, and then donations can be released.

• Ultrafiltration process is different between companies, but the products are generally very similar
  • Some patients need one specific type of product, but most patients do well on any of the products
Dosing

• Based initially on the weight of the patient (usually around 500 mg for every kg of weight)

• Adjusted based on how well the patient is protected from infections
  • Are they having issues with ear, sinus, lung infections?
  • Are they having symptoms which are towards the end of their window, just before their next treatment?
Intravenous Immunoglobulin (IVIg)

- In-the-vein therapy
  - Needs IV placement each month (may use indwelling catheters in the beginning)
  - Sometimes premedication is given, though not always necessary; topical anesthesia can be used
  - Hydration prior to infusion is important to reduce side effects
  - Usually given every 3-4 weeks, depending on needs
    - Can take 3-4 hours for infusion appointment- bring distractions!
Intravenous Immunoglobulin (IVIg)
Subcutaneous Immunoglobulin (SCIg)

• Under-the-skin therapy
  • Can be done at home with needle placement by a caregiver (can keep medicine refrigerated at home)
  • Sometimes premedication is given, though not always necessary; topical anesthesia can be used
  • Usually given every 1-2 weeks, depending on needs
    • Lasts 30 minutes to 2 hours, depending on dosing and product
  • Can adjust locations, number of sites
  • Need to be able to schedule yourself consistently
Subcutaneous Immunoglobulin (SC Ig)
Following Up

- Labs: Blood counts, chemistry, IgG level every 6-12 months (may be more frequent with your team)
- Review any infections
  - Adjust dosing if needed
- Review IgG side-effects
  - headaches, fatigue, local reactivity, time to resolve skin swelling, etc.
- Remember:
  - You cannot test for antibodies to vaccines or for infections while on IgG replacement, as this will reflect what is in the therapy
  - Sometimes you can have false-positive antibody testing to thyroid or anti-nuclear antibodies (ANA), which are common in the population
Side Effects

• **IVIg:**
  - headache, which occurs at a frequency of 8%–15%
  - Infrequent: fatigue, aches, fever/chills, and nausea/diarrhea

• **SCl Ig**
  - Headache at rates of 1.4%–4%
  - Fatigue, etc, is at a much lower rate
  - Local adverse events such as discomfort and pain, erythema, swelling/edema, and pruritis
    - Often can be modified by needle and location adjustments
Vaccines while on IgG replacement

• **Check with your team first**

• In general, once cleared to restart non-live vaccines, yearly influenza is also recommended for all patients on IgG replacement

• Live vaccines should be specifically recommended by your care team
  
  • Caregivers should be vaccinated, in general, to protect our patients; In cases where caregivers are receiving live vaccines, they should check with the team first
To Sum Up...

- Supplementation is important until the B cells can return to making antibodies again.
- There is flexibility in how you receive IgG replacement which can keep you safe and still be compatible with your daily activities.
- The goal is to eventually be able to stop needing IgG infusions once the immune system is replenished 😊
ANTIBODIES
AFFINITY WAR

THE BULK

IgG Man

CAPTAIN IMMUNOGLOBULIN

BLACK ANTIGEN

By: Dzung Nguyen, Dzu-Doodles
THANK YOU!

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Q&A SESSION:
YOUR QUESTIONS ANSWERED
Have more Questions?

primaryimmune.org/ask-idf
800-296-4433
SCID Compass Lunch & Learn: ADA SCID Gene Therapy Update with Donald Kohn, MD

September 14th, 2022
2:00-3:00 PM ET

REGISTER

www.scidcompass.org/events