Infection and Immune Reconstitution: The NEW Forms

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Why the changes?

• Infection data not previously collected on NMDP forms

• Neither IBMTR nor NMDP forms have collected information on immune reconstitution

Are these data elements relevant (or are we just making more work)?

• Infectious complications continue to contribute to significant transplant complications
  – Poster presentation shows that ~50% of TRM is related to infection regardless of intensity of conditioning
• Infection risk decreases as the immune system recovers
What does the literature tell us?

- Search stem cell transplant AND infection Limits: Publication Date from 2004 to 2006, English, Humans, Cancer
  - 524 hits
- Search stem cell transplant AND immune recovery Limits: Publication Date from 2004 to 2006, English, Humans, Cancer
  - 71 hits

What does the literature tell us?

- Infection data
  - Review of the first 250 found 80 potentially useful articles
  - Most are either single center or ‘evidence based’ guidelines
- Immune reconstitution data
  - 27 potentially useful with 9 being ‘Review’ articles

Immune Reconstitution
**Immune Recovery**

3 ‘parts’ of immune system

1. Neutrophils
   - determine as absolute neutrophil count and engraftment
2. Immunoglobulins (antibodies)
3. Lymphocytes
   - B lymphocytes (CD19+/20+)
   - T lymphocytes (CD3+, CD4+, CD8+)
   - NK cells (CD56+CD16+)

**Quantitative Immunoglobulins**

- Measure of the body's ability to make antibodies
- IgG, IgA, and IgM most common
  - May also measure IgE or IgG subclasses 1-4
- Values given as mg/dL, g/dL, or g/L
- Values altered by administration of IV IG (intravenous immunoglobulin)
  - often given in setting of infections or to prevent infectious complications

*NOTE: we do not ask for IgE or IgG subclasses*
**Supplemental IVIG**

56. Did the patient receive supplemental intravenous immunoglobulin (IVIG)?
   - [ ] yes
   - [ ] no

56a. New therapy regimen within one month of immunoglobulin therapy?
   - [ ] yes
   - [ ] no

Indication for use:
- [ ] yes
- [ ] no

56b. Dose: (g/kg) with no active infection
- [ ] prophylaxis for low IgG with no active infection
- [ ] prophylaxis for gamma globulin (IG)
- [ ] prophylaxis for cytomegalovirus (CMV) infection
- [ ] prophylaxis for herpes (virus or CMV infection)
- [ ] prophylaxis for respiratory syncytial virus (RSV) infection
- [ ] prophylaxis for infection with low IgG (all CMV or RSV)
- [ ] other indication: ____________________________

**Lymphocytes**

- B lymphocytes: make antibodies
  - CD19+, CD20+
- T lymphocytes: fight viral and fungal infections
  - CD3+, CD3+CD4+, CD3+CD8+
- NK cells: involved in early defense against infection
  - CD16+CD56+

**Lymphocyte Measurements**

- Quantitative
  - Flow cytometry analysis
    - Percentage of total number of lymphocytes (%)
    - Absolute count (x 10⁹/L, x 10⁶/L, x 10³/mm³)
      (% measured x absolute lymphocyte count)
  - TREC
    - T-cell Receptor Excision Circles

- Functional
  - Response to different challenges such as *Candida*
Lymphocyte Recovery

Do centers collect this data?

- Surveyed all transplant centers reporting to the CIBMTR
- More common to check immune status after allogeneic transplant
- Determined at various times post-transplant

Quantitative Immunoglobulins

- Autologous Transplant
  - IgG: 78%
  - IgA: 66%
  - IgM: 68%

- Allogeneic Transplant
  - IgG: 92%
  - IgA: 82%
  - IgM: 83%
Lymphocyte Recovery

- Autologous Transplant
  - CD3: 52%
  - CD4: 61%
  - CD8: 61%
  - CD20: 46%
  - CD56: 42%

- Allogeneic Transplant
  - CD3: 66%
  - CD4: 75%
  - CD8: 75%
  - CD20: 60%
  - CD56: 60%

So where is the data?

- Quantitative Immunoglobulins
  - >85% performed in the center’s hospital lab
  - Will likely be reported in hospital lab system

- Lymphocytes
  - >75% measured via flow cytometry
  - Nearly all centers report both percentage and absolute numbers
  - ~75% performed in the center’s hospital lab

Infection
Pre-transplant Infections

- 'Clinically significant' = required treatment
  - Only interested in prior fungal infections
  - List even if in distant past or suspected
- Viral serologies
  - Critical for determining outcomes in particularly high risk patients

Prior Fungal Infections

- Critical for determining outcomes in particularly high risk patients

Prior Viral Exposures

Testing for serological evidence of prior viral exposure / infection
**Prophylactic Medications**

- Antimicrobial drugs given to **prevent** infection
  - generally start either at onset of conditioning regimen or on day of transplant
- Expect to find
  - Antiviral (ex. Acyclovir)
  - Antifungal (ex. Fluconazole)
  - Antibacterial (ex. Levaquin)
  - Anti-PCP (ex. Bactrim or Pentamidine)
Infection Reporting-NEW

What changes and why?

- List consecutive infections
  - Does not require you to determine 'type' of infection
  - Provides multiple lines so less need to copy the page
  - Document organism identified or suspected
    - Should avoid 'other organism, specify'
- Do not list fever without suspected infection

Clarifications

- If the same organism is identified multiple times within a 7 day period, only list the first date of infection unless found in multiple sites
  - Ex: CMV
    - 1/15/06 Antigenemia positive = blood (site 1)
    - 1/18/06 bronchoscopy performed and lavage fluid positive for CMV = lower respiratory tract (site 33)
    - 1/20/06 Antigenemia positive: do not need to list again
### Common Sites: Old

<table>
<thead>
<tr>
<th>Codes for Common Sites of Infection (Continued)</th>
<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.</td>
<td>Mediastinum</td>
<td>Mediastinal abscess</td>
</tr>
<tr>
<td>21.</td>
<td>Peritoneum</td>
<td>Peritoneal abscess</td>
</tr>
<tr>
<td>22.</td>
<td>Pancreas</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>23.</td>
<td>Spleen</td>
<td>Spleen abscess</td>
</tr>
<tr>
<td>24.</td>
<td>Bladder</td>
<td>Bladder stone</td>
</tr>
<tr>
<td>25.</td>
<td>Rectum</td>
<td>Rectal abscess</td>
</tr>
<tr>
<td>26.</td>
<td>Vulva</td>
<td>Vulvar abscess</td>
</tr>
</tbody>
</table>

### Common Sites: New

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<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>17.</td>
<td>Large intestine</td>
<td>Colon cancer</td>
</tr>
<tr>
<td>18.</td>
<td>Rectum</td>
<td>Rectal polyp</td>
</tr>
<tr>
<td>19.</td>
<td>Appendix</td>
<td>Appendix torsion</td>
</tr>
<tr>
<td>20.</td>
<td>Liver</td>
<td>Hepatic abscess</td>
</tr>
<tr>
<td>21.</td>
<td>Spleen</td>
<td>Spleen laceration</td>
</tr>
<tr>
<td>22.</td>
<td>Pancreas</td>
<td>Pancreatic pseudocyst</td>
</tr>
<tr>
<td>23.</td>
<td>Gallbladder</td>
<td>Cholecystitis</td>
</tr>
<tr>
<td>24.</td>
<td>Bladder</td>
<td>Bladder tumor</td>
</tr>
<tr>
<td>25.</td>
<td>Urethra</td>
<td>Urethral stricture</td>
</tr>
</tbody>
</table>

Please report the exact specific site of infection.
Changes and Clarifications

- Sites of infection
  - Merged CNS into one category to include brain, spinal cord, meninges, and CSF

- Lower respiratory tract
  - Includes brocho-alveolar (BAL) lavage fluid

Improvements in transplant depend upon accurate data on every patient transplanted

YOU ARE VITAL TO OUR PATIENTS AND THEIR PHYSICIANS!

QUESTIONS?