Infections after Transplant

Celebrating a Second Chance at Life Survivorship Symposium

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Infections Following Hematopoietic Cell Transplantation

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Guidelines for Preventing Infectious Complications among Hematopoietic Cell Transplantation Recipients: A Global Perspective

Marcie Tomblyn, Tom Chiller, Hermann Einsele, Ronald Gress, Kent Sepkowitz, Jan Storek, John R. Wingard, Jo-Anne H. Young, Michael A. Boeckh


Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: report from the Bone Marrow Transplant Survivor Study


• HCT 1974-1998
• City of Hope and University of Minnesota

Late infection in the absence of cGVHD accounted for 11% of premature deaths, again emphasizing the need for recognizing and treating infections effectively and aggressively in this population that is at risk for prolonged periods of immune suppression.
What determines your risk for infection?

- Underlying disease
- Type of transplant
  - Preparative regimen
  - Source of graft: Umbilical cord, HLA-mismatched, T-cell depleted
  - Relatedness of donor to you: Autologous < Allogeneic
- Other conditions
  - Both prior to and following HCT (e.g. Diabetes, infections)
- Time since transplant
- Pulmonary disease
- GVHD: Prolonged immunosuppression

Key point:
1. Ongoing risk but low absolute numbers
2. Higher risk: Elderly

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ORIGINAL REPORT

Long-Term Survival and Late Deaths After Allogeneic Hematopoietic Cell Transplantation
John R. Wingard, Noreen S. Mighell, Ruta Brziouska, Zhong Xing, Kathleen A. Schierholz, David Jacobshagen, Mohamed L. Sayegh, Mary M. Horowitz, Brian Behnke, I. Douglas Ritz, and Gujarat Sidh

- 10,632 patients
- 500 centers
- >2 years survival

Key point:
1. Ongoing risk but low absolute numbers
2. Higher risk: Elderly

2-4 years
5-9 years
>10 years

AML  ALL  MDS  Lymphoma  Aplastic Anemia
N=4  N=2  N=3  N=0  N=8
N=0  N=2  N=3  N=8  N=0
Topics for Discussion

• My counts are normal, why do I still have to worry?
• Specific risks associated with common encounters in daily life
• What can I do to reduce risk?

Basic principles

• Infections are a part of life
• The most important issue is how your immune system resolves the infection
• Outcome is always better with early diagnosis
• Reconstitution of the immune system is frequently not a linear process
• It may take some time to learn how your immune system is evolving
My counts are normal, why do I still have to worry?

Immune reconstitution is complex

- There are three main features of a functional immune system:
  - Turning “on”
  - Precision (foreign versus self)
  - Turning “off”
- Many different branches of the immune system need to develop in order to reconstitute a functional response.
  - Not a linear process
  - Tissue specific
  - Pathogen-specific

Message:

Rebuilding a competent immune response to all classes of organisms takes time—

DAY +100

DAY +365
Graft Versus Host Disease: Very special situation

- GVHD itself causes impairment of immune function
- In order to reduce risk of infection:
  - Immune suppressant
  - Prophylactic antimicrobials
  - Health maintenance
  - Vigilance

- Antimicrobial therapy may be continued for the duration of immune suppressant therapies and/or years
- At risk for various organisms from all classes of organisms.

The evolution of functional immune reconstitution

- Too young to interpret and respond
- “Tantrum”: Over exuberant response that is frequently counter-productive
- “Tantrum”: trigger frequently unclear
Environmental pathogens/exposures

What do these activities have in common?
They pose a risk for invasive fungal infections and other soil organisms (eg, nocardia)
Inhalation of fungal spores is most common.

Risk of Infection from Home and Hobbies

- Avoid disrupting anything that will result in aerosolization, dust (e.g. tearing out walls, outdoor structures)
- Move out if necessary
- Wear mask – organic or inorganic material. May need:
  - Hepa filter
  - N95
Risk of Infection from Food

- **Raw or undercooked foods**
  - Seafood (oysters, *Vibrio; raw-fish sushi/sashimi*)
  - Meats (*toxoplasmosis, trichinosis*)
- **Unpasteurized foods**
  - Cheeses, drinks
- **Check for alerts** regarding food-related outbreaks
- **Wash fruits and vegetables**
  - Berries can be challenging
- **Do not smell** rotten or moldy food

Beyond the (stethe)scope

- Share the history of your residences/travel so that potential exposures can be thoroughly evaluated
  - Parasites
  - Tuberculosis
  - Endemic infections
- As we all have the bias of what we know, do not assume that your care team has fully assessed potential exposures
Pets and other members of the family

Healing Benefit of Pets

- increased activity
- reduced serum cholesterol and triglycerides
- fewer cardiovascular events
- decreased depression and mental stress
- higher self esteem
Cats and kittens can transmit infections

**Scratch/Fleas**
- Cat scratch fever (*Bartonella*)
- Bird flu
- West Nile Virus

**Bite-related infections**
- Mixed bacteria (*Pasteurella*)

**Stool/litter and gardening**
- Toxoplasmosis (parasite)

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**Pasteurellosis and Bartonella**

- **Pasteurellosis** in humans:
  - Symptoms: swelling, cellulitis, and bloody drainage at the site of the wound.
  - Infection may progress to nearby joints, where it can cause further swelling, arthritis and abscesses.

- **Bartonella**:
  - Symptoms: fever, fatigue, headache, poor appetite, and an unusual streaked rash that resembles “stretch marks” from pregnancy.
  - Swollen glands are typical, especially around the head, neck and arms.
Toxoplasma gondii: Immunocompromised and pregnant women

Dogs can transmit infections

**Saliva/Bite**
- Capnocytophaga
- Methcillin-resistant Staph
- Aureus
- Mixed bacteria

**Stool**
- Salmonella
- Campylobacter
- Giardia
Dogs Bites/Saliva: Avoid

Saliva exposure of a minor wound OR Bites
- Scrub wound with soap and water
- Go to ED -- especially after a bite
- Intravenous antibiotics
- Rare
- Life threatening, fast-moving

Transmitted via stool
- Giardia
- Campylobacter
- Salmonella
- Norovirus?

Human Norovirus Books Dog Cruise, May Have Return Ticket
Birds, too...

Psittacosis (Chlamydia psittaci)
• Pet birds, chickens
• Designate others to clean cages/coops
• Clean cages outside
• Avoid kissing birds
• Avoid sick birds

It is not necessary to part with your pets
• Keep pets indoors
• Delegate the care of your pets to others
  • Feces: litter box, picking up waste
• Wash hands with soap and water after contact especially saliva
  • scrub if breaks in skin
• Go to Emergency Room if you have been bitten or scratched.
• Avoid contact with
  • Reptiles, ducklings, or chicks (salmonella)
  • Strays (do not adopt a new pet)
• Hunters: do not gut animals and avoid prolonged contact with earth matter; If fishing, avoid cleaning the fish.
Respiratory viruses: Early treatment
Influenza, respiratory syncytial (RSV), Metapneumovirus, Adenovirus, Parainfluenza

PNAS June 30, 2020 117 (26) 14857-14863; https://doi.org/10.1073/pnas.2009637117

Charting a Covid-19 Immune Response
By Katherine J. Wu and Jonathan Corum Oct. 5, 2020
COVID-19: Our protocol

• Give **monoclonal antibodies** ASAP
• **Low threshold for giving Remdesivir** – high risk patients even if not hypoxemic
• **Assess** carefully for secondary infection
• **Follow up** on a daily basis (Oxygen saturation, fever, symptoms)
• **Vaccination:** (Platelets >50K)
  • > D+30 in autologous patients
  • >D+60 in allogeneic, haplo, umbilical cord, and CAR-T if no GVHD

COVID-19: Our data

• 90 patients
• 60%: household member as source
• Median time of infection relative to transplant = 13 months
• Rituximab is a particular risk
• Longer course of infection (2-8 months)

• Mortality 15% (allogeneic >> autologous) which has declined precipitously since instituting monoclonal antibody therapy + remdesivir
### Bacterial infections

- **Conditions that increase risk**
  - Spleen:
    - surgical removal
    - decreased function
  - GVHD
  - Low neutrophil count
  - Low immunoglobulins
    - Hypogammaglobulinemia
    - Rituximab exposure

- **Vaccinations**
  - Pneumococcal infection
  - Hemophilus influenza (bacteria)
  - Meningococcal
  - Health maintenance/other organs:
    - Health of teeth
    - Skin
    - Gastrointestinal tract
    - Sinopulmonary

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### Oral care and regular dental appointments improve overall health

- Tooth and gum disease increase risk of serious infections
- Dental care team can identify a number of infections and other conditions that frequently are overlooked
- Conditions causing dry mouth – notably, GVHD – cause profound compromise of teeth leading to caries and tooth loss
Respiratory tract

• Do not vape or smoke
• Be aware of dirt/soil/environmental inhalation
• Wear industrial grade masks when using chemicals, paints, solvents
• Contact your team if you are prone to respiratory/sinus infections. You may need to be assessed for low immunoglobulin production
• Vaccination: for you and your household members

Gastrointestinal/Genitourinary

• Avoid firm stools or straining with bowel movements (diverticulosis)
• Consult with specialists regarding any symptoms
• Optimizing organ function and minimizing trauma will reduce infection risk; eg:
  o vaginal dryness
  o urinary retention
  o hemorrhoids or rectal fissures
Skin and nails

- **Use sunscreen:** Reduce skin cancer
- **Avoid skin trauma:** moisturize
- **Seek attention for deeper wounds or potentially contaminated source**
  - Confirm tetanus status after cleaning aggressively with soap and water
  - slow healing wound
- **Fungal nail disease**
  - Manicures/pedicures – avoid soaking in large baths, use personal tools
  - Topical antifungal: if not clearing, use topical even if on systemic antifungal medication. *New: efinaconazole (Jublia)*

Vaccinations

**Guidelines for Vaccination of Adult Bone Marrow Transplant (BMT) Candidates and Recipients**

**A. VACCINATION SCHEDULE FOR BMT PATIENTS**

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Vaccine Abbreviation</th>
<th>Months post-transplant</th>
<th>Minimum interval between doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>IIV (inactivated influenza vaccine)</td>
<td>Annually starting at 6 months</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal Group A</td>
<td>PCV13/PPSV23a</td>
<td>#1 #2 #3 #4</td>
<td>b</td>
</tr>
<tr>
<td>Haemophilus</td>
<td>Hib</td>
<td>#1 #2 #3</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Diptheria/tetanus/perussis</td>
<td>DTaP (or Tdap x1, then Td x2)</td>
<td>#1 #2 #3</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>HepA-HepB</td>
<td>#1 #2</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Papillomavirus</td>
<td>9vHPV (if ≤ 45 years old)</td>
<td>#1 #2</td>
<td>e</td>
</tr>
<tr>
<td>Measles, mumps, rubella</td>
<td>MMR¹</td>
<td>#1 #2</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Varicella</td>
<td>VAR¹ (if VZV IgG negative)</td>
<td>#1 #2</td>
<td></td>
</tr>
</tbody>
</table>
Vaccinating others in the household

- **Vaccinating others in your household and/or “bubble” offers perhaps the best protection**
- **Children** should even receive the following live virus vaccines:
  - MMR (measles, mumps, and rubella)
  - Varicella (chickenpox) may pose a very small risk of transmission but acyclovir should decrease risk
- Adults that receive other live virus vaccines for travel (e.g. yellow fever, vaccinia) should discuss precautions with their physician

Herpesviruses

- **Risk reduces with time.** GVHD increases risk
  - Much was made of late CMV but this is likely important only in people with GVHD or less than optimal engraftment on immunosuppression
- **Monitoring is not typically necessary** if you are well, but should be considered if you have certain illnesses
- **Two key treatments:**
  - Varicella zoster (shingles) vaccine
  - Acyclovir prophylaxis: Varicella and HSV
Health maintenance

Keeping up with routine health maintenance and minimizing tissue injury will decrease infection

- Routine dental examinations every 6-12 months
- Avoid smoking, vaping
- Skin and nail care
- Gynecologic evaluations
- Regular activity
- Normalize diet unless otherwise directed
- Stress reduction

What can I do to reduce my risk of infection?

- Mitigate exposures:
  - Keep animals indoors, avoid oral/fecal contact
  - Standard approach to food safety:
    - Avoid undercooked, unpasteurized food
    - Avoid tissue injury (eg smoking/vaping, chemical exposures
- Vaccines
- **Take any prophylactic antimicrobials prescribed**
  - but if you are not able to, notify your care team so the risk of certain infection can be calculated.
Reduce the risk of infection

- Partner with your care team
  - If you do not feel well – even if you do not have a fever – report your symptoms and share your concerns
- Seek help early for any conditions especially:
  - wounds especially with animal exposure
  - respiratory infections
- If you are diagnosed with an infection
  - work with your care providers and notify your transplant team
- If you are getting recurrent infections
  - further evaluation may be warranted, especially regarding complications such as GVHD or low immunoglobulin production

What should I avoid if my immune system is weak?

- Others who are ill, especially school-aged children
- Crowded areas
- Construction sites, buildings or wear HEPA-filtered mask
- Wood burning fireplaces
- Air humidifiers
- Well-water, swimming in lakes, hot tubs
Don’t stop enjoying life!

• “Balanced caution”
• Your body as a Ferrari
• Handwashing

There’s a gap in your CV...
What were you doing in 2020?
I was washing my hands...
Questions?

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