Managing Infections after Transplant and CAR T-cell Therapy

Celebrating a Second Chance at Life
Survivorship Symposium

April 27 – May 3, 2024

Erik Dubberke MD, MSPH
Professor of Medicine Co-Founder, Transplant Infectious Disease Service,
Washington University School of Medicine
Disclosures

• Research: Theriva Biologics
Learning Objectives

- Risk for developing infections after transplant and CAR T-cell therapy
- Recommended tests and procedures to monitor / prevent infections
- Lifestyle changes to minimize risk for infection
- When patients should be revaccinated
  - COVID, Flu, Shingles, RSV
Disclaimer

• This talk: general principles
• Often more than one approach OK
• Rapidly evolving field
  • Recommendations change
• Each transplant center will have their general approach
  • All infectious disease epidemiology is local
  • May be modified based on your specific needs
Some General Infection Concepts

• Opportunistic infection
  • Infection that occurs much more commonly or only in people whose immune system does not work properly

• Virus
  • Unable to make copies on its own
  • “Hijacks” living cells to make copies of itself
  • Treatments available for some, but many have no proven treatments
Some General Infection Concepts cont’d

• Bacteria
  • Can make own copies
  • Lives on our skin and in our intestines
  • Present in soil and water
  • Most have effective treatments, but resistance becoming more common

• Fungi
  • Can make own copies
  • Candida yeast lives on our skin and in our intestines
  • Molds live in the environment / decaying organic matter
  • Proven treatments for the most common causes of infection
Pre-Transplant Considerations

• Exposures
  • Occupation / hobbies
  • Travel
    • Past, recent, planned
  • Diet
  • Animal exposures
    • Pets, livestock, wild

• Current infections

Yearly incidence of tuberculosis per 100,000 population in 2017

https://www.cdc.gov/mmwr/volumes/68/wr/mm6811a3.htm
Pre-Transplant Screening Tests for Infection

• Viruses
  • Cytomegalovirus (CMV)
    • Mono-like illness
  • Varicella Zoster Virus (VZV)
    • Chicken pox / shingles
  • Herpes simplex virus (HSV)
    • Cold sores
  • Epstein-Barr Virus (EBV)*
    • Mono
  • Human immunodeficiency virus (HIV)
  • Hepatitis B virus (HBV)
  • Hepatitis C virus (HCV)
  • Respiratory viruses

• Bacteria
  • Syphilis
  • Resistant bacteria*
  • Tuberculosis (TB)*

• Parasites
  • Toxoplasmosis
  • Strongyloides*
  • Trypanosoma cruzi*

*Risk factor based
Risk for Infection

- Underling condition and past treatments
- Transplant conditioning regimen
- Type of transplant
  - Autologous (your donor cells) and CAR T-cell lower risk than allogeneic (someone else’s donor cells)
- For allogeneic, source of donor cells
  - Highest Risk cord blood -> mismatched -> haplo -> matched Lowest Risk
  - Graft versus host disease (GVHD)
## Immune Defenses

<table>
<thead>
<tr>
<th>Defense mechanism</th>
<th>Infections seen when disrupted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin / mucus membranes</td>
<td>Bacteria from those surfaces&lt;br&gt;Skin: Staph and strep bacteria&lt;br&gt;Mouth: Step bacteria, Candida yeast&lt;br&gt;Gut: Gram negative bacteria, Candida yeast</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>Skin, mouth, and gut bacteria&lt;br&gt;Candida yeast&lt;br&gt;Molds</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>Respiratory viruses, “encapsulated” bacteria&lt;br&gt;(<em>Streptococcus pneumoniae</em>)</td>
</tr>
<tr>
<td>B-cells (antibody producing cells)</td>
<td></td>
</tr>
<tr>
<td>T-cells</td>
<td>Viruses, molds, parasites</td>
</tr>
</tbody>
</table>
### Periods of Infection Risk

<table>
<thead>
<tr>
<th></th>
<th>Before Engraftment</th>
<th>Engraftment to day 100</th>
<th>After day 100</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factor</strong></td>
<td>Low neutrophils</td>
<td>Low lymphocytes</td>
<td>GVHD*</td>
</tr>
<tr>
<td></td>
<td>Mucositis</td>
<td>Graft vs. host disease (GVHD)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Central venous catheter</td>
<td>Central venous catheter</td>
<td></td>
</tr>
<tr>
<td><strong>Infections</strong></td>
<td>Bacteria (skin and gut)</td>
<td>Bacteria (skin)</td>
<td>Minimal GVHD*:</td>
</tr>
<tr>
<td></td>
<td>Candida yeast</td>
<td>CMV</td>
<td>Encapsulated bacteria</td>
</tr>
<tr>
<td></td>
<td>Mold</td>
<td>VZV</td>
<td>Severe GVHD*:</td>
</tr>
<tr>
<td></td>
<td>HSV (herpes simplex virus)</td>
<td>Adenovirus (children)</td>
<td>bacteria, viruses and molds</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pneumocystis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Toxoplasmosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Molds</td>
<td></td>
</tr>
</tbody>
</table>

- Seasonal / community infections
  - Mirror seasonality
  - Risk higher than general populations
  - Closer to transplant / CAR-T cell, greater the risk

*GVHD seen after allogeneic (other people’s stem cells) transplant
Timing of Infection

Total Infection Density, # events / 100 patient days at risk

BM – bone marrow
PBSC – peripheral blood stem cells
Infection Monitoring / Prevention: Before Engraftment

• Catheter / skin care:
  • prevent infections from catheter

• Antibacterials (not always used)

• Antifungals (not always used)

• Antivirals: prevent HSV (herpes simplex virus)

• Blood cultures for fevers and starting antibiotics

• Special ventilation in hospital rooms: prevent mold infections

Visitors

• Do not visit if sick
• Stay up to date with vaccinations
<table>
<thead>
<tr>
<th>Infection</th>
<th>Main approaches</th>
<th>Additional comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV / VZV</td>
<td>Acyclovir or valacyclovir</td>
<td>Very effective and well tolerated</td>
</tr>
<tr>
<td>CMV</td>
<td>Pre-emptive: regular monitory of virus in blood, treatment started if detected Prophylactic: daily medication to prevent virus from activating</td>
<td>No clear “winner”</td>
</tr>
<tr>
<td>Pneumocystis (PJP or PCP)</td>
<td>Trimethoprim/sulfamethoxazole (Bactrim or Septra)</td>
<td>Alternatives: dapsone, atovaquone, pentamidine</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>Trimethoprim/sulfamethoxazole (Bactrim or Septra)</td>
<td>Usually only if evidence of past infection Alternatives: atovaquone, pyrimethamine plus clindamycin or sulfadiazine</td>
</tr>
</tbody>
</table>
| Molds              | Will vary based on center, medications/GVHD, and insurance approval; “azole” antifungal | }
Infection Monitoring / Prevention: After Day 100

- Graft vs. Host Disease (GVHD) requiring treatment
  - Same as Engraftment to day 100
- Minimal / no GVHD
  - Infection risk at lowest point
  - Still at increased risk for infection compared to non-immunocompromised people
  - Vaccinations
  - Prevention of *Streptococcus pneumoniae*
Food Safety

- OK to eat well cooked food stored properly
  - 4 steps: Clean, separate, cook, chill
- If not prepared at home, ask
  - Check health department rating
- Use thermometer to check internal temperature
  - Beef, veal, pork, lamb chops/steaks/roasts and fish: 145°F
  - Ground beef, veal, pork, lamb; egg dishes: 160°F
  - Chicken, turkey, duck; cured meats; left-overs: 165°F
- Ok to eat washed fruits and vegetables
  - Wash before peeling / cutting
Food Avoidance

- Undercooked meats
- Deli counter at grocery store
  - Deli/cured meats (unless cooked to 165°F)
  - Cheese sliced at the deli
  - Prepared salads (pasta, potato, chicken, etc)
- Unpasteurized dairy ("raw milk" products)
- Soft cheeses
- Food with mold (example: blue cheese)
- Multi-serve condiments / foods people dip their food in (unless only for you)
- Fresh fruits / vegetables you did not wash / multi-use (example: salad bar)
- Raw sprouts (even if washed)
- Cold brewed teas
Animal Safety

- Avoid new pets for 6-12 months
  - Juvenile / stray: more infections
  - Bites / scratches
  - Vaccinations
  - Flea / tick preventative
- Do not:
  - Clean cages / tanks
  - Handle feces / droppings
  - Touch reptiles / poultry / livestock / game / exotic pets
- Wear gloves and wash hands if unable to avoid
  - And wear N-95 mask if dust / aerosol generated

<table>
<thead>
<tr>
<th>Animal</th>
<th>Infection risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cats</td>
<td>Toxoplasmosis (feces)</td>
</tr>
<tr>
<td></td>
<td><em>Bartonella</em> (cat scratch disease)</td>
</tr>
<tr>
<td>Cats/dogs</td>
<td>Tick-borne illness</td>
</tr>
<tr>
<td>Reptiles</td>
<td><em>Salmonella</em></td>
</tr>
<tr>
<td>Poultry</td>
<td><em>Salmonella, Campylobacter</em></td>
</tr>
<tr>
<td>Fish</td>
<td><em>Mycobacterium marinum</em></td>
</tr>
<tr>
<td>Livestock</td>
<td>Q-fever, Brucellosis</td>
</tr>
<tr>
<td>Game</td>
<td>Tularemia</td>
</tr>
<tr>
<td>Birds</td>
<td>Psittacosis, Cryptococcus, Histoplasmosis</td>
</tr>
<tr>
<td>Exotic pets</td>
<td>Animal specific</td>
</tr>
</tbody>
</table>
## Miscellaneous Exposures

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Primary concern</th>
<th>Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dirt / dust / construction</td>
<td>Molds</td>
<td>N-95 mask (check if safe to use)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gloves</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Washing hands</td>
</tr>
<tr>
<td>Outdoors</td>
<td>Tick-borne illness</td>
<td>DEET, long pants/sleeves, tick checks</td>
</tr>
<tr>
<td>Hiking</td>
<td>Bacterial infections</td>
<td>Avoid swimming until told safe</td>
</tr>
<tr>
<td>Swimming</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crowds</td>
<td>Respiratory viruses</td>
<td>Avoidance; vaccination, masks</td>
</tr>
<tr>
<td>Drinking water</td>
<td>Bacterial and parasitic infections</td>
<td>Municipal water generally safe. Test well water as recommended and/or boil.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Developing countries: bottled water for drinking and brushing teeth, no ice.</td>
</tr>
</tbody>
</table>
International Travel

• Ask your transplant center if it is OK to travel
  • Autologous (your stem cells)/ CAR T-cell: avoid 3-6 months
  • Allogeneic (someone else’s stem cells): avoid 6-12 months
• Start investigating travel risk right away
  • CDC website: [https://wwwnc.cdc.gov/travel/](https://wwwnc.cdc.gov/travel/)
• Travel / infectious diseases clinic
  • Any travel to developing countries
    • May need vaccinations / exemptions and/or medications
    • If any concerns / outbreaks in developed country

![Malaria transmission map](map.png)

- Malaria transmission not known to occur
- Malaria transmission occurs in some places
- Malaria transmission occurs throughout
Vaccination

- Start 6-12 months after transplant
  - Live vaccines should be avoided for 2 years
    - Measles, mumps, rubella (MMR)
    - Chicken pox (VariVax)
- Full vaccine series, even if past vaccination
- Immune response / protection lower than general population
  - Still decreases risk of bad outcomes
- Household contacts / visitors should be vaccinated
  - Decrease risk of getting infected
  - Decrease risk of spread if infected
  - Avoid live vaccines if possible
Shingles Vaccination

- One of the most common infections after day 100
  - After prophylaxis is typically stopped (acyclovir or valacyclovir)
  - Same virus as chicken pox virus: VZV
- First vaccine available
  - Zostavax: live-viral vaccine
    - Cannot give to transplant recipients for at least 2 years
    - Cannot give while on prophylaxis
- Shingrix now available
  - Viral proteins
    - Recommended for immunocompromised people ≥18 years old
    - Past history of chicken pox or chicken pox vaccination
    - OK to give while still on prophylaxis
Influenza Vaccination

• Updated every year because influenza evolves
  • 4 influenza strains
  • Provides ~6 months of protection

• Types available:
  • Inactivated virus: grown in eggs
  • Cell-culture grown viral proteins: safe if egg allergy
  • Live virus (Flumist): AVOID

• Even “bad match” protects against bad outcomes

• Cannot get flu from influenza vaccine
COVID-19 Vaccination

• Updated based on variant evolution
  • Provides ~6 months of protection
  • Get boosters as recommended: still learning
• Protects against bad outcomes
• mRNA: Modern, Pfizer-BioNTech
• Viral protein: Novavax
RSV Vaccination

• Approved for use in people ≥60 years old and pregnant women
  • No official recommendations for non-pregnant people <60 years old

• Viral protein

• Single dose currently recommended
  • Effectiveness declines by year 2
Summary

- Transplant and CAR T-cell recipients go through predictable stages of infection risk
  - Based on how immune system is being affected
- Specific tests / treatments used to monitor / prevent specific infections
- Safe living after transplant may involve lifestyle modifications
  - Crowd avoidance / masking, washing hands
  - Food safety
  - Animal safety
  - Activities / travel
  - Family / friends
Summary cont’d

• Vaccination is recommended
  • Repeat full vaccination series
  • Shingles vaccine now recommended: Shingrix
  • Influenza: every year
  • COVID-19 and RSV: get as recommended, continuing to learn
Questions?

Erik Dubberke MD, MSPH
Professor of Medicine Co-Founder,
Transplant Infectious Disease Service,
Washington University School of Medicine
Let Us Know How We Can Help You

Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

Phone: 888-597-7674 or 847-433-3313

Find us on:

Facebook, facebook.com/bmtinfonet

X, twitter.com/BMTInfoNet