COVID-19: What Transplant Patients Need to Know in 2022

Celebrating a Second Chance at Life Survivorship Symposium

April 30 - May 6, 2022

John Wingard MD
UF Health Cancer Center

COVID 19: What Transplant Survivors Need to Know
John R Wingard, MD
University of Florida

May 2, 2022
“I’ve lost count of how many patients I’ve lost to COVID-19. I’ve probably lost way more patients to COVID-19 than I have to actual cancer in the last two years.”

- A hematologist in Colorado

**Caution!**

- HCT = hematopoietic cell transplant; aka, bone marrow or peripheral blood transplant, stem cell transplant
- COVID-19 = illness; SARS-CoV-2 = virus causing the COVID-19 illness
- This is a very rapidly changing field of knowledge
  - Some of the reports are in news releases, not peer-reviewed publications
  - Some of the reports are preliminary
  - Insights and recommendations are changing at a rapid pace
Learning Objectives

• How does COVID-19 differ from other viruses, like the annual flu
• Do HCT* recipients have a higher risk of developing a COVID-19 infection
• Do HCT recipients have a higher risk of developing a severe case of COVID-19 and/or death
• What precautions can a HCT recipient take to minimize the risk of a severe COVID-19 infection?
  • Who should be vaccinated and when?
  • Is one vaccine better for HCT recipients than another?
• What are the currently available treatments for COVID-19 and what’s in the pipeline

*HCT = hematopoietic cell transplant; aka, bone marrow or peripheral blood transplant, stem cell transplant
COVID-19 = illness; SARS-CoV-2 = virus causing the COVID-19 illness

How does COVID-19 differ from other viruses, like the annual flu?

• The “flu” is not always the flu (influenza)
• There are nearly two dozen different respiratory viruses
  • Coronavirus is one of them
  • They infect animals as well as humans
• Genetic variations in the viruses occur naturally in all viruses
• Coronaviruses have been with us for a very long time
  • Most cause only mild illness
  • SARS-CoV-2 is one type of coronavirus
How does COVID-19 differ from other viruses, cont’d

• SARS-CoV-2 virus causes COVID-19 infection
  • This is not the first variant to cause serious illness
    • SARS, MERS
• What makes SARS-CoV-2 nasty:
  • risk for deadly harm
  • highly contagious

How does COVID-19 differ from other viruses?

- Influenza virus
  - Upper airways
  - Lower airways
  - Air sacs

- COVID-19
  - Nasal passages
  - Indirect effects on taste
    • Airways
    • Lungs
Global Impact

Influenza

COVID-19

<table>
<thead>
<tr>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>458 million</td>
<td>6 million reported</td>
</tr>
<tr>
<td>Daily deaths</td>
<td>3,547</td>
</tr>
</tbody>
</table>

As of March 19, 2022:

Impact of COVID-19 on U.S.

Influenza

COVID-19

<table>
<thead>
<tr>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>81.3 million</td>
<td>997,227</td>
</tr>
</tbody>
</table>

As of March 19, 2022

Flerlage, Nature Reviews Microbiology, 4/2021
Risk factors - Influenza

Risk factors - COVID-19

Flerlage, Nature Reviews Microbiology, 4/2021
Most respiratory infections are seasonal

![Graph showing seasonal activity of influenza A, influenza B, and endemic coronaviruses by epidemiological week.]

Note: Peak activity (100%) is defined as maximum percent positive tests for each virus.

Figure 3: The 10-year average activity of influenza A, influenza B and endemic coronaviruses by epidemiological week.

In contrast, pandemic COVID-19 comes at us in waves

COVID-19 Infections, State of Florida, as of October 2021

![Graph showing weekly new reported cases, tests, hospitalized, and deaths in Florida.]

John Wingard MD
Do HCT recipients have a higher risk of developing a COVID-19 infection?

Probably not

Do HCT recipients have a higher risk of developing a severe case of COVID-19 and/or death?

- Yes
- Death rate from COVID-19 in patients with blood cancers: 17%,
- Death rate from COVID-19 in general population in (U.S.): 1.2%
- Death rate from COVID-19 in HCT recipients
  - during first year: 22%
  - after first year: lower, but still higher than in general population
  - Autotransplants: higher than in general population
- Risk factors:
  - Recent HCT
  - use of immunosuppressive therapy
  - ?GVHD

ASH Research Collaborative COVID-19 Registry (Hicks, ASH annual meeting 2021, Abstr 3040; Johns Hopkins University (1/21/21))
What precautions can an HCT recipient take to minimize the risk of a severe COVID-19 infection?

How can we prevent exposure?
Swiss Cheese Respiratory Virus Pandemic Defense

New York Times, 2020
Fast facts about the COVID-19 vaccines

- 3 approved vaccines in the US
  - Two are messenger RNA vaccines (Pfizer, Moderna)
  - One is an adenovirus (chimpanzee), that has been engineered (J and J vaccine)
- None of these are live vaccines
- All have side effects, which generally are mild
- All have enormous safety records in large and rigorous trials
  - J and J: rare clotting disorder

How do the mRNA vaccines work?

1. Vaccine fuses with a cell
2. mRNA goes into cell
3. Cell machinery makes spike proteins, which combine to form spike
4. Spike is displayed on the outside of the cell

Can the vaccine integrate into my DNA?
No!
How good are the COVID-19 vaccines?

- **In the general population**, the mRNA vaccines provide >90% protection against serious illness
  - There are some breakthrough infections, but they tend to be asymptomatic or mild illness
  - BTW: this level of protection is better than provided by many of the influenza vaccines over the years
  - BTW: these vaccines are more effective than a number of other vaccines approved in other countries, notably in China
  - Vaccines offer added protection for individuals with prior natural infection
  - The J and J vaccine has a lower rate of protection than the mRNA vaccines
  - The vaccines may provide different amounts of protection against different variants
    - For now, this is not a big issue: the mRNA vaccines offer good protection against omicron
  - Over time, immunity wanes

How good are the COVID-19 vaccines for HCT recipients?

- For cancer patients, unfortunately, COVID-19 vaccines **responses are much lower**
  - One study showed 25% failed to mount antibody response after the second dose of an mRNA vaccine (Greenberger, Cancer Cell 39: 1031)
    - Especially those with B cell lymphoma, and CLL
    - Drugs such as ibrutinib and rituximab can block antibody responses
  - Small studies showed that 43% who failed to respond after 2 doses responded to a 3rd (Greenberger, ASH annual meeting, 2021, abstr 185)
  - For HCT recipients: several studies in patients who were vaccinated more than one year after transplant showed reasonably good antibody responses
  - The reported data for early vaccination response is very small, but the data available suggests very low response rates
**REVISED COVID-19 Vaccination Schedule for People Who Are Moderately or Severely Immunocompromised**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Vaccination Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pfizer-BioNTech</strong></td>
<td></td>
</tr>
<tr>
<td>(ages 5 years and older)</td>
<td>1st dose</td>
</tr>
<tr>
<td></td>
<td>2nd dose</td>
</tr>
<tr>
<td></td>
<td>3rd dose</td>
</tr>
<tr>
<td></td>
<td>Booster dose*</td>
</tr>
<tr>
<td></td>
<td>(at least 3 months after 3rd dose)</td>
</tr>
<tr>
<td><strong>Moderna</strong></td>
<td></td>
</tr>
<tr>
<td>(ages 18 years and older)</td>
<td>1st dose</td>
</tr>
<tr>
<td></td>
<td>2nd dose</td>
</tr>
<tr>
<td></td>
<td>3rd dose</td>
</tr>
<tr>
<td></td>
<td>Booster dose*</td>
</tr>
<tr>
<td></td>
<td>(at least 3 months after 3rd dose)</td>
</tr>
<tr>
<td><strong>Janssen</strong></td>
<td></td>
</tr>
<tr>
<td>(ages 18 years and older)</td>
<td>1st dose</td>
</tr>
<tr>
<td></td>
<td>Additional dose†</td>
</tr>
<tr>
<td></td>
<td>Booster dose*</td>
</tr>
<tr>
<td></td>
<td>(at least 2 months after additional dose)</td>
</tr>
</tbody>
</table>

*Any COVID-19 vaccine can be used for the booster dose in people ages 18 years and older, though mRNA vaccines are preferred. For people ages 12–17 years, only Pfizer-BioNTech can be used. People ages 5–11 years should not receive a booster dose.

†Only Pfizer-BioNTech or Moderna COVID-19 Vaccine should be used

---

**Clarification of Existing Recommendation for mRNA COVID-19 Vaccine Primary Series**

- People who are moderately or severely immunocompromised should receive:
  - 3-dose primary series
  - 1 booster dose

---

John Wingard MD
Schedule for People Who Received a Janssen COVID-19 Vaccine Primary Series

**Primary dose**
- **Guidance before Feb. 2022**
  - At least 2 months
  - Dose 1
  - Dose 2

**Booster dose**
- **Revised guidance As of Feb, 2022**
  - At least 28 days
  - Dose 1
  - Dose 2
  - Dose 3

---

Updates for People Who Are Moderately or Severely Immunocompromised

- Shorter booster interval after an mRNA COVID-19 vaccine primary series
- An additional dose after a Janssen COVID-19 Vaccine primary series
- Revaccination for certain sub-groups **HCT patients**
- Case-by-case clinical decision making

CDC, updated February, 2022
Revised Guidance for a 3-Month Booster Interval After an mRNA COVID-19 Vaccine Primary Series

**Guidance before Feb. 2022**

People who are moderately or severely immunocompromised should receive a booster dose at least 5 months after the last (third) dose of an mRNA COVID-19 vaccine.

**Revised guidance As of Feb, 2022**

People who are moderately or severely immunocompromised should receive a booster dose at least 3 months after the last (third) dose of an mRNA COVID-19 vaccine.

Rationale for 3-Month Booster Interval After an mRNA COVID-19 Vaccine Primary Series

- Concern about initial immune response and loss of protection over time, particularly during period of high community transmission.
- Small studies in people with immune compromise demonstrate immunogenicity of a 4th dose when administered “1-3 months after the 3rd dose.
- Multiple studies in the general population demonstrate immunogenicity of a booster as early as 3 months following a 2-dose primary series.
- Multiple countries have implemented booster doses as early as 3 months in the general population following a 2-dose primary series.
Revaccination for Certain Sub-Groups

- **Prior guidance**: Limited to recipients of hematopoietic cell transplant (HCT) and chimeric antigen receptor (CAR)-T cell therapy.

- **Revised guidance**: Recipients of HCT, CAR-T-cell or other B-cell depleting therapies who received doses of COVID-19 vaccine **prior to or during treatment** should be revaccinated for doses received before or during treatment.

- Based on clinical judgement, revaccination may also be considered once immune competence is regained for people who received COVID-19 vaccines doses during chemotherapy or radiation treatment.

Case-by-Case Decision Making Based on Clinical Judgement

- On a case-by-case basis, providers who care for moderately or severely immunocompromised patients may administer mRNA COVID-19 vaccines outside of the FDA and CDC dosing intervals based on clinical judgement when the benefits of vaccination are deemed to outweigh the potential and unknown risks.
Several considerations to ponder about the COVID-19 vaccine

- The response to the vaccine peaks 10-14 days after the vaccine
- A COVID-19 monoclonal antibody present in the blood at time of vaccine probably neutralizes the vaccine
- These considerations suggest:
  - Wait for some time after a COVID-19 monoclonal antibody or infection before vaccination
  - Try to avoid drugs that suppress immune responses or the cells that produce immune responses after the vaccine

hematology.org/covid-19/ash-astct-covid-19-vaccination-for-hct-and-car-t-cell-recipients
Is there something to do if your immunity is so suppressed that you are not likely to respond to the vaccine?

Tixagevimab co-packaged with cilgavimab (Evusheld)

- COVID-19 Monoclonal antibody, approved for pre-exposure prophylaxis
- Good activity against omicron variant
- Tested in patients with moderate to severe immunodeficiency
- found to cut the risk of developing symptomatic Covid-19 by 77%, with protection lasting for at least six months after a single dose, given as two injection
- This is for patients who would be expected to have poor or suboptimal vaccine responses
- Short supplies required rationing initially, supply has increased
- [https://www.fda.gov/media/154702/download](https://www.fda.gov/media/154702/download)
- Wait for at least 2 weeks after COVID-19 vaccine
What Treatments are available?

How COVID-19 treatments could work

- **Antivirals**
  - Virus particles multiply inside the body
  - Antiretroviral drug prevents virus from multiplying

- **Anti-inflammatories**
  - Immune system dangerously overreacts to virus
  - Anti-inflammatory drug calms immune response

- **Antibody treatments**
  - Antibody specific to coronavirus binds to it and makes it harmless

Which treatments work?

- Some therapies work for some variants, but are not so good against omicron
- Some have been studied only in moderate to severe infections
  - Low oxygen level is a key indicator of severity; get a pulse oximeter
- Early start of therapy is crucial
  - Some are IV
  - Some new drugs are oral
    - in short supply
    - have potentially serious drug interactions

John Wingard MD
Which treatments work? cont’d

- Nirmatrelvir plus ritonavir (Paxlovid) (Pfizer) is very promising

  - For those with

    - at least one risk factor for progression to severe disease and
    - not vaccinated and
    - treated within 5 days after onset

    - hospitalization or death dropped from 6.31% to 0.77%, a relative risk reduction of 88% Hammond NEJM 2.6.22

- Be careful of drug interactions

I just got infected by COVID, how do I decide what is the best treatment for me?

You don’t: It’s complicated! And it changes week by week. Contact your transplant team.
Sources of authoritative COVID-19 information

- Centers for Disease Control (CDC)
- Food and Drug Administration (FDA)
- National Institutes of Health (NIH)
- American Society for Hematology (ASH)
- American Society for Transplantation and Cellular Therapy (ASTCT)
- Your transplant team

https://files.covid19treatmentguidelines.nih.gov/guidelines/section/section_111.pdf

Questions?

Celebrating a Second Chance at Life Survivorship Symposium 2022

John Wingard MD

bmtinfonet.org ✪ help@bmtinfonet.org ✪ 847-433-3313
Let Us Know How BMT InfoNet Can Help YOU!

Visit our website: bmtinfonet.org
Email us: help@bmtinfonet.org
Give us call: 888-597-7674

We're here to help every step of the way!