

Managing Infections after Transplant and CAR T-cell Therapy

Celebrating a Second Chance at Life
Survivorship Symposium

April 27 – May 3, 2024



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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



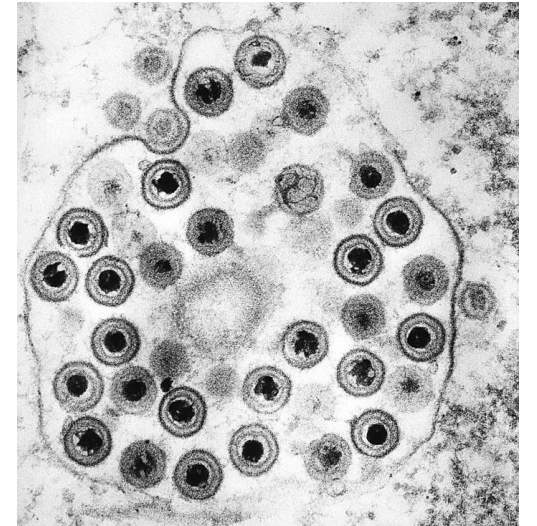
Disclaimer

- 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



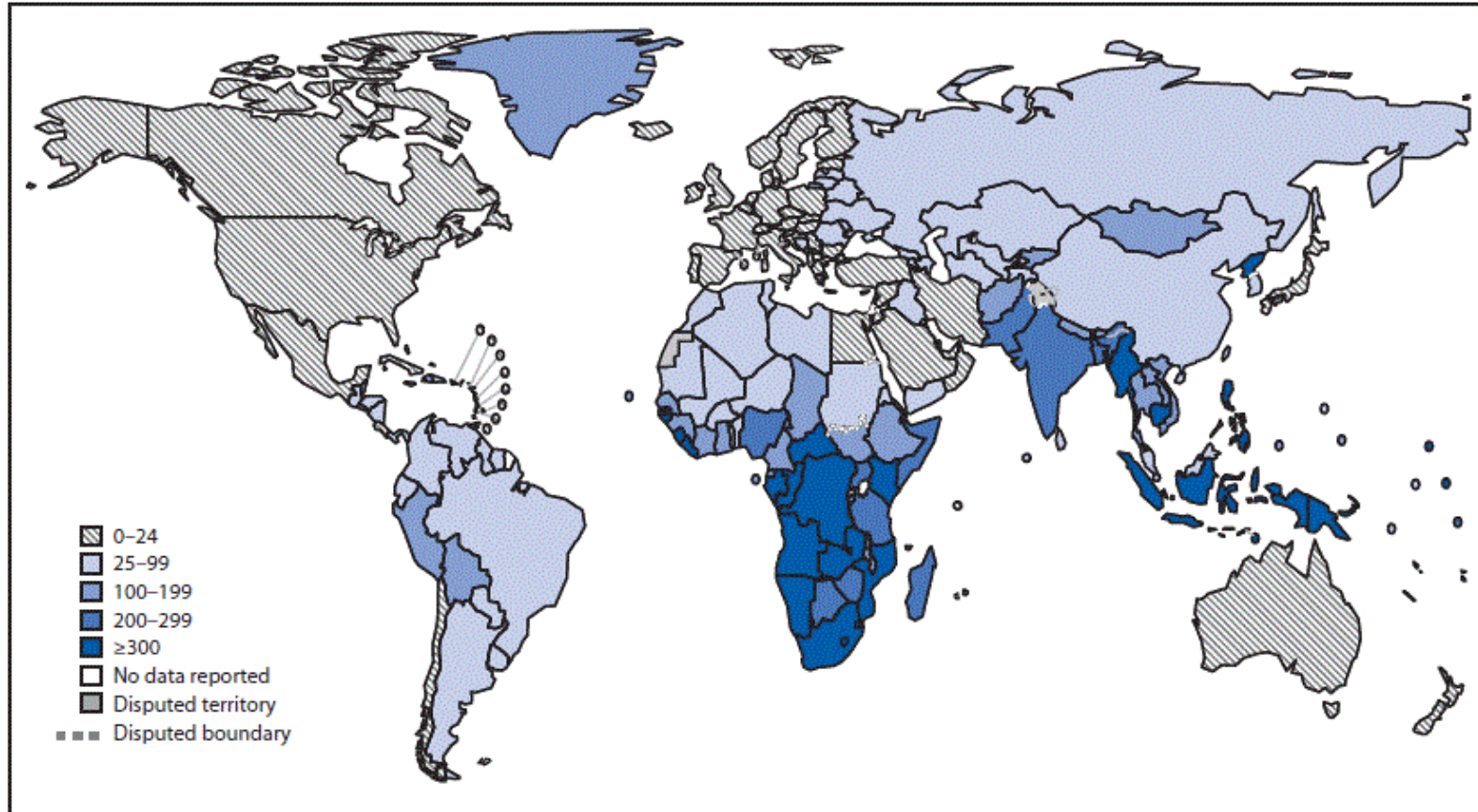
- Fungi

- 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

Defense mechanism	Infections seen when disrupted
Skin / mucus membranes	Bacteria from those surfaces Skin: Staph and strep bacteria Mouth: Step bacteria, Candida yeast Gut: Gram negative bacteria, Candida yeast
Neutrophils	Skin, mouth, and gut bacteria Candida yeast Molds
Lymphocytes B-cells (antibody producing cells)	Respiratory viruses, “encapsulated” bacteria (<i>Streptococcus pneumoniae</i>)
T-cells	Viruses, molds, parasites

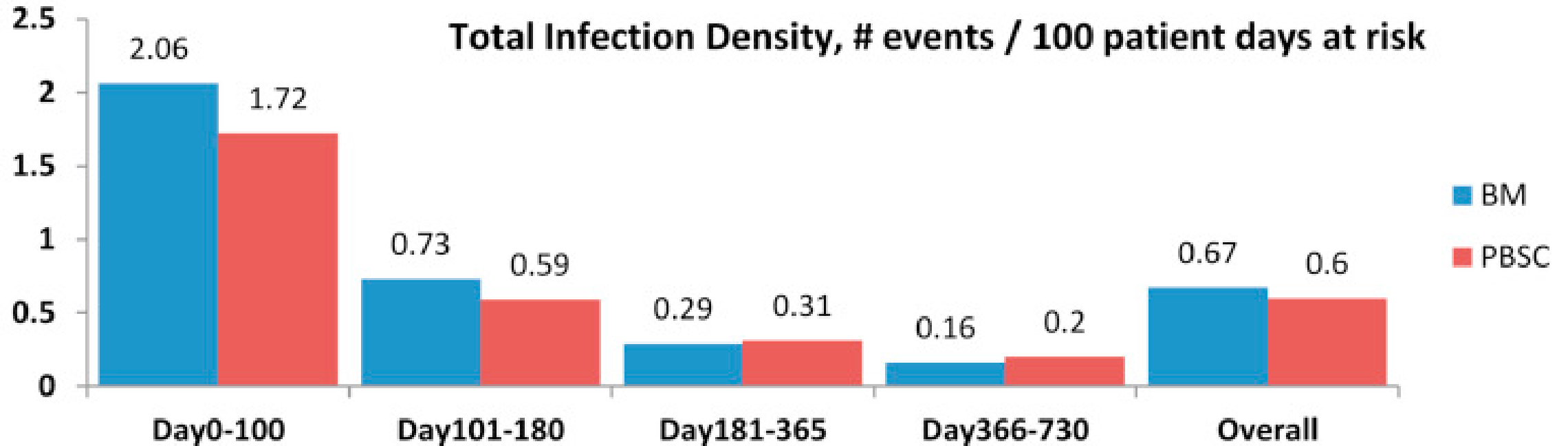
Periods of Infection Risk

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

- 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



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

Infection Monitoring / Prevention: Engraftment to Day 100

Infection	Main approaches	Additional comments
HSV / VZV	Acyclovir or valacyclovir	Very effective and well tolerated
CMV	Pre-emptive: regular monitoring of virus in blood, treatment started if detected Prophylactic: daily medication to prevent virus from activating	No clear “winner”
Pneumocystis (PJP or PCP)	Trimethoprim/sulfamethoxazole (Bactrim or Septra)	Alternatives: dapsone, atovaquone, pentamidine
Toxoplasmosis	Trimethoprim/sulfamethoxazole (Bactrim or Septra)	Usually only if evidence of past infection Alternatives: atovaquone, pyrimethamine plus clindamycin or sulfadiazine
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

Animal	Infection risk
Cats	Toxoplasmosis (feces) <i>Bartonella</i> (cat scratch disease)
Cats/dogs	Tick-borne illness
Reptiles	<i>Salmonella</i>
Poultry	<i>Salmonella</i> , <i>Campylobacter</i>
Fish	<i>Mycobacterium marinum</i>
Livestock	Q-fever, Brucellosis
Game	Tularemia
Birds	Psittacosis, Cryptococcus, Histoplasmosis
Exotic pets	Animal specific

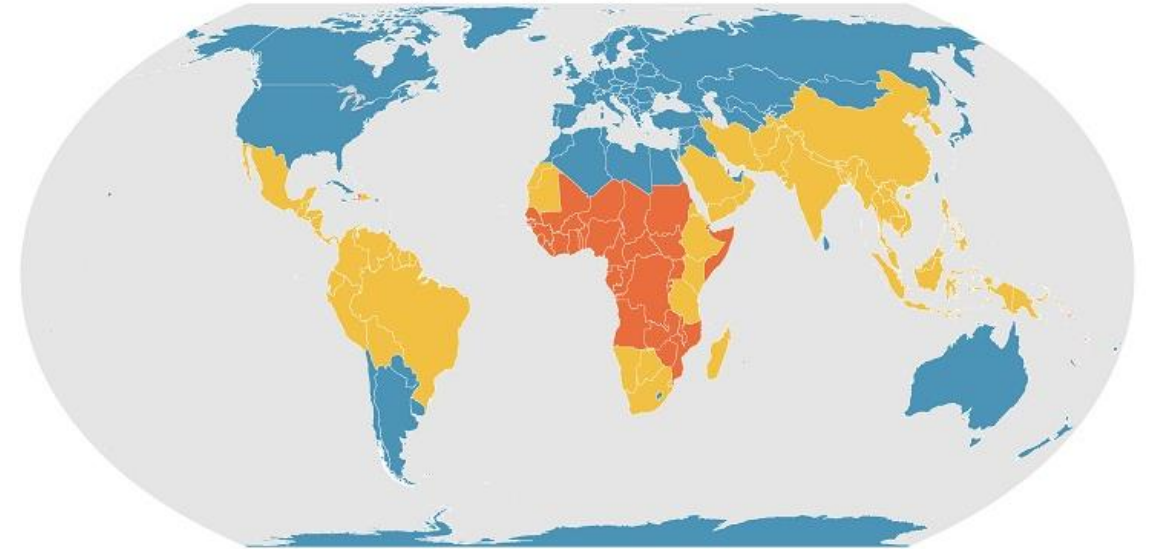
Miscellaneous Exposures

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



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

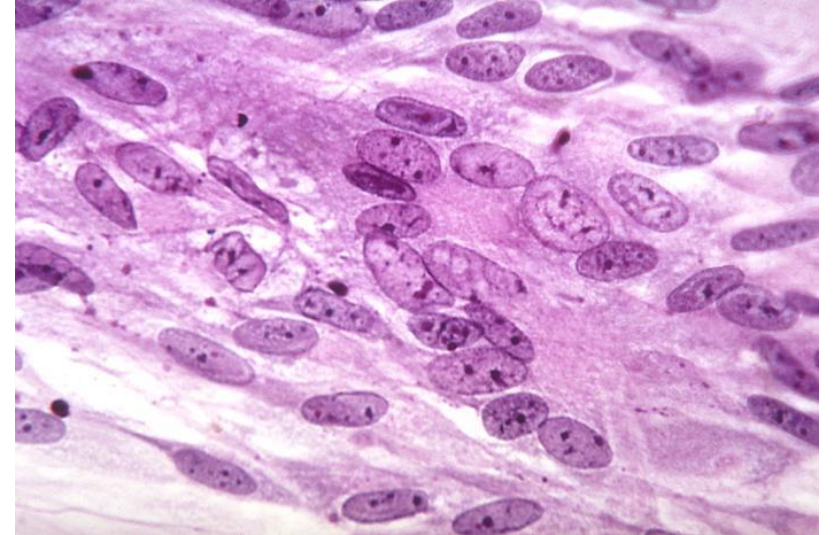
Vaccination



- 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

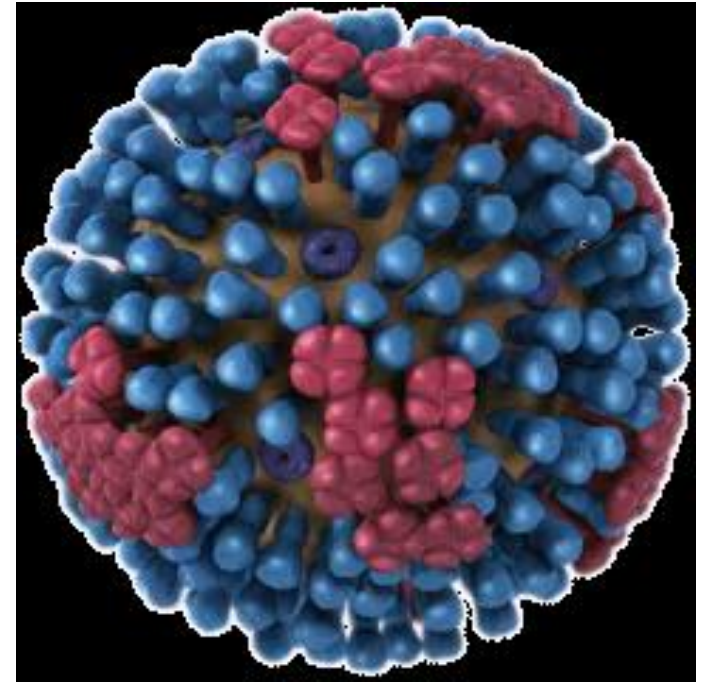
Shingles Vaccination

- 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



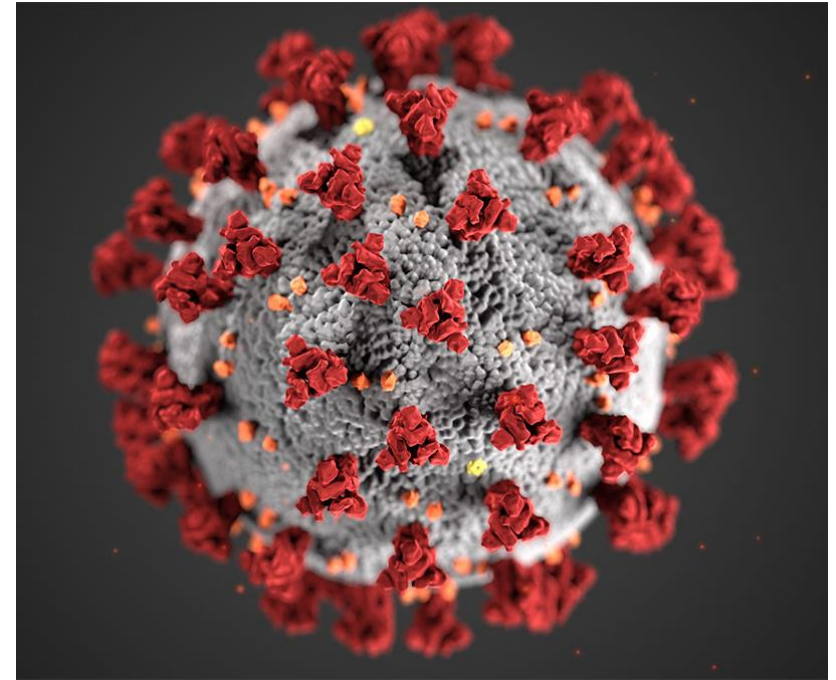
Influenza Vaccination

- 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



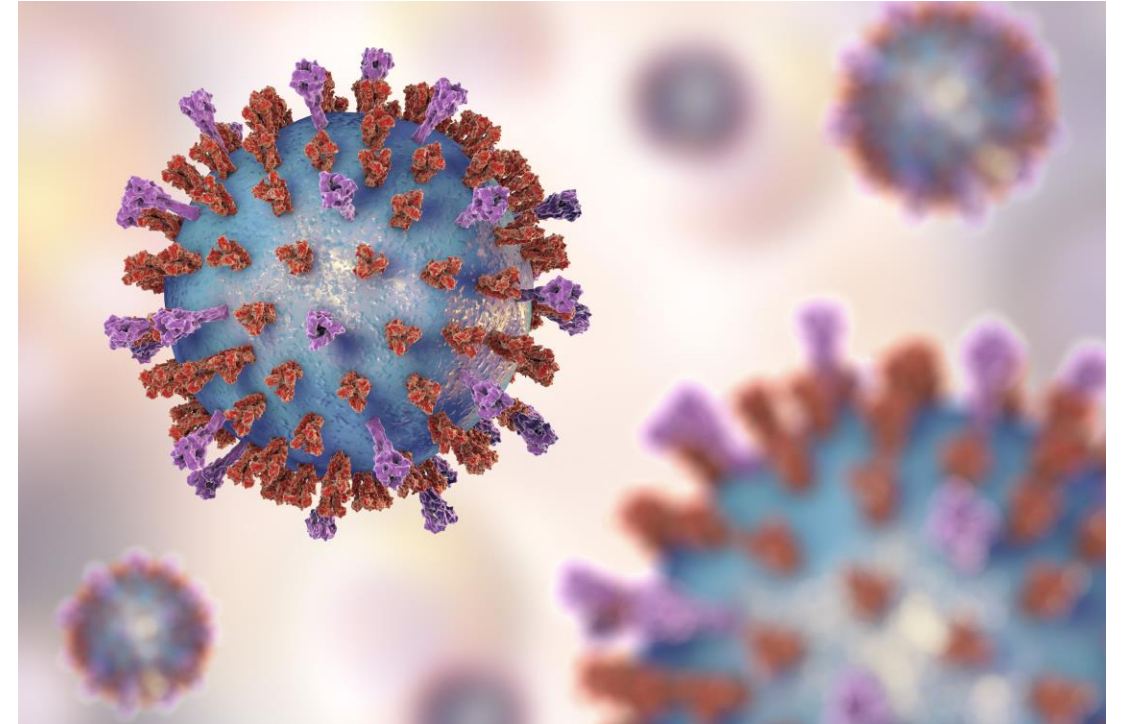
COVID-19 Vaccination

- 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?



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