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BLOOD & MARROW TRANSPLANT INFORMATION NETWORK

Infections after Transplant

Celebrating a Second Chance at Life Survivorship Symposium

April 17- 23, 2021




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Infections Following Hematopoietic Cell Transplantation

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ASBMT
American Society for Blood
and Marrow Transplantation

GUIDELINES

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

Biol Blood Marrow Transplant 15: 1143-1238 (2009) © 2009 American Society for Blood and Marrow Transplantation

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TRANSPLANTATION

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


Smita Bhatia,¹ Liton Francisco,¹ Andrea Carter,¹ Can-Lan Sun,¹ K. Scott Baker,² James G. Gurney,³ Philip B. McGlave,² Auayporn Nademanee,⁴ Margaret O'Donnell,⁴ Norma K. C. Ramsay,² Leslie L. Robison,⁵ David Snyder,⁴ Anthony Stein,⁴ Stephen J. Forman,⁴ and Daniel J. Weisdorf²

• 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.

BLOOD, 15 NOVEMBER 2007VOLUME 110, NUMBER 10



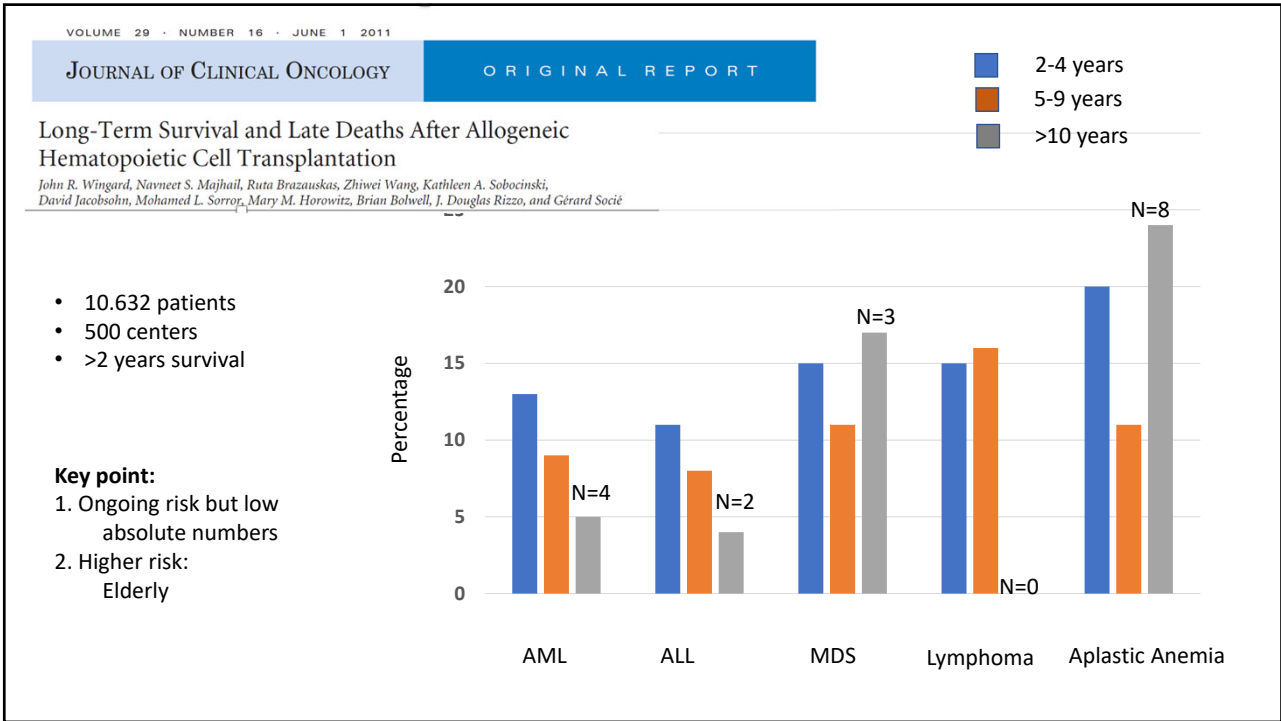
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What determines your risk for infection?

- 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*



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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?



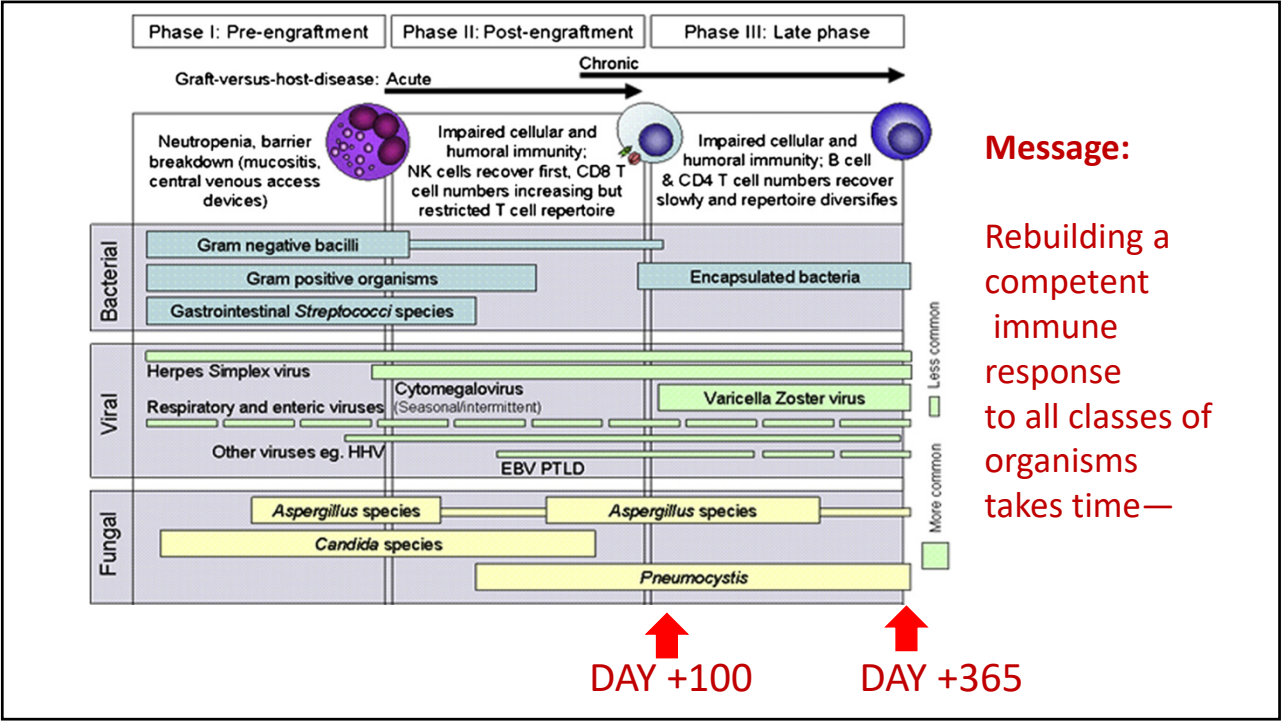
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Basic principles

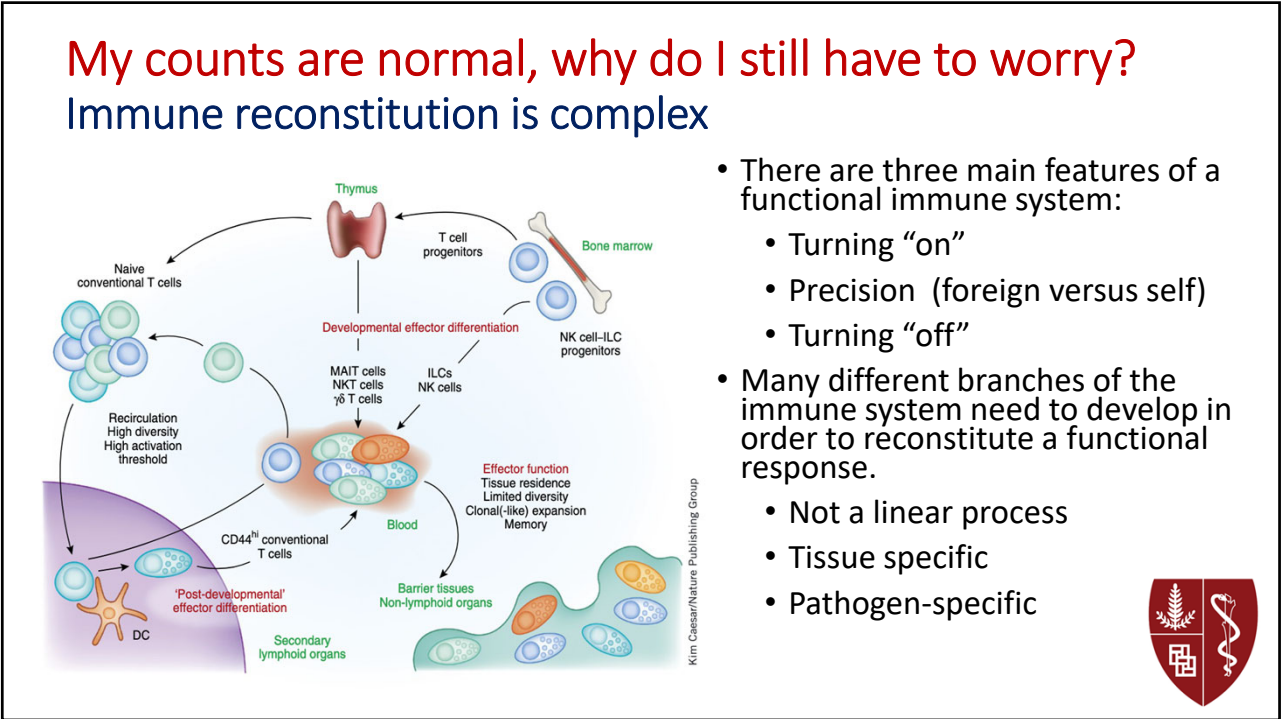
- Infections are a part of life
- The most important issue is how your immune system resolves the infection
- Outcome is always better with early diagnosis
- Reconstitution of the immune system is frequently not a linear process
- It may take some time to learn how your immune system is evolving



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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

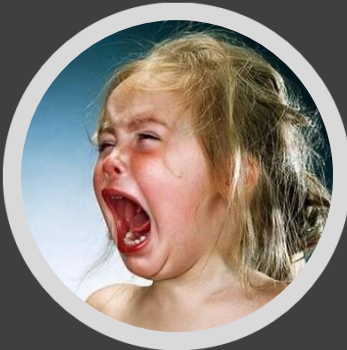
- Antimicrobial therapy may be continued for the duration of immune suppressant therapies and/or years
- At risk for various organisms from all classes of organisms.

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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



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Environmental pathogens/exposures



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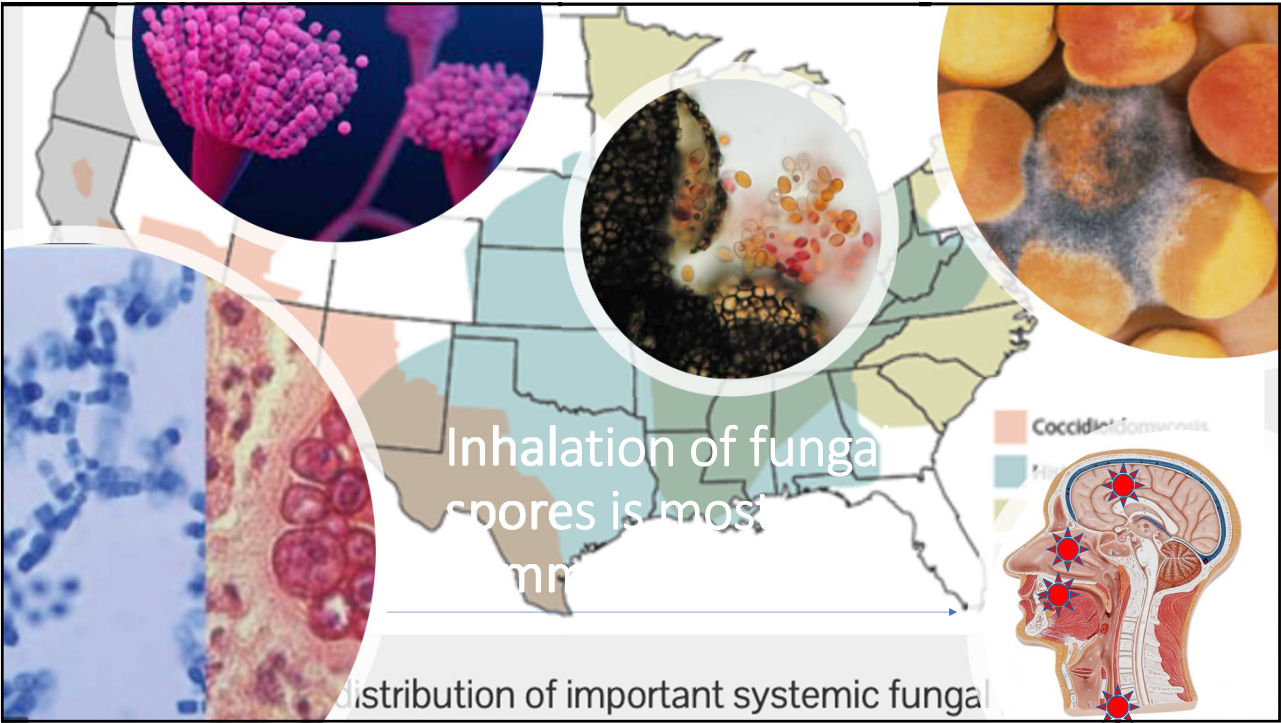
Mowing the Lawn is Bad for your Health
Posted on April 27, 2020 by Nikki Featheringham

What do these activities have in common?

They pose a risk for invasive fungal infections and other soil organisms (eg, nocardia)



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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



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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



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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

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Pets and other members of the family



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Healing Benefit of Pets

- increased activity
- reduced serum cholesterol and triglycerides
- fewer cardiovascular events
- decreased depression and mental stress
- higher self esteem



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Cats and kittens can transmit infections

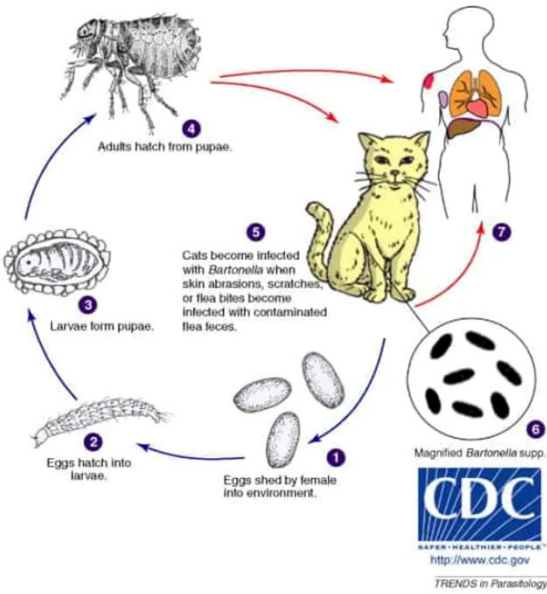


- Scratch/Fleas**
- Cat scratch fever (*Bartonella*)
 - Bird flu
 - West Nile Virus
- Bite-related infections**
- Mixed bacteria (*Pasturella*)
- Stool/litter and gardening**
- Toxoplasmosis (parasite)

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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.



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Toxoplasma gondii: Immunocompromised and pregnant women



The diagram illustrates the life cycle of Toxoplasma gondii. It shows the parasite's development in the intestines of a cat, its shedding in feces, and its subsequent infection of a host (represented by a human figure). The parasite is shown in various stages of development, including oocysts and trophozoites. To the right of the diagram are two photographs: a small white kitten sitting on a surface and a tabby cat sitting in a blue litter box.

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Dogs can transmit infections

Saliva/Bite

- Capnocytophaga
- Methcillin-resistant Staph
- Aureus
- Mixed bacteria

Stool

- Salmonella
- Campylobacter
- Giardia

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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

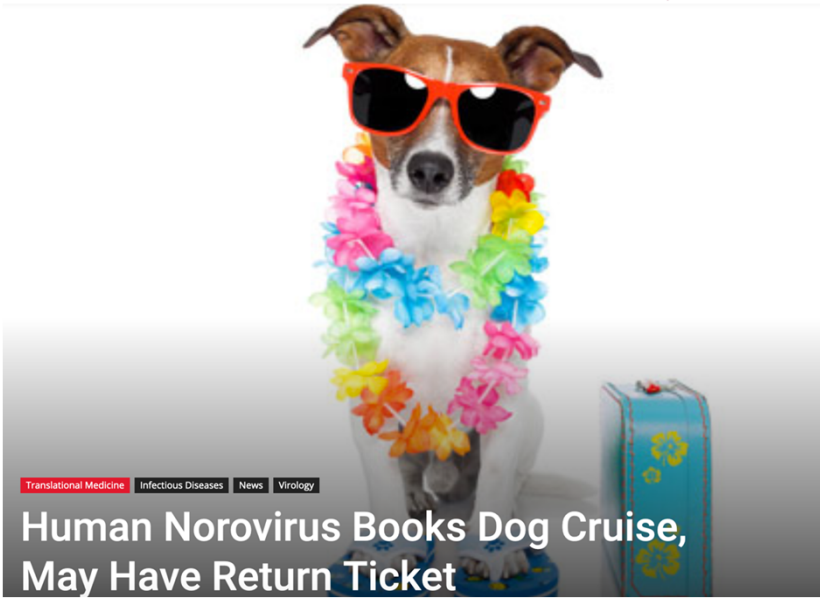
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Transmitted via stool

- Giardia
- Campylobacter
- Salmonella
- Norovirus ?

GEN Genetic Engineering
& Biotechnology News

Mary Ann Liebert, Inc. a publisher



Translational Medicine Infectious Diseases News Virology

Human Norovirus Books Dog Cruise,
May Have Return Ticket

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Birds, too...

Psittacosis (Chlamydia psittaci)

- Pet birds, chickens
- Designate others to clean cages/coops
- Clean cages outside
- Avoid kissing birds
- Avoid sick birds

AMERICAN CHRONICLES JUNE 1, 2009 ISSUE

IT'S SPREADING

Outbreaks, media scares, and the parrot panic of 1930.



By Jill Lepore



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It is not necessary to part with your pets



Todd, 28-year transplant survivor

- 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.

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Respiratory viruses: Early treatment

Influenza, respiratory syncytial (RSV), Metapneumonvirus, Adenovirus, Parainfluenza

The diagram illustrates the transmission of respiratory viruses. It shows a person on the left coughing or sneezing, releasing aerosols. These aerosols can be inhaled by another person (airborne transmission) or settle on a surface (contact transmission). The diagram also shows a person on the right inhaling aerosols. A legend indicates: Viral shedding from coughing/sneezing (dark blue arrow), Settling for person/object contamination (teal arrow), Dispersion in air (light blue arrow), and Deep and continuous respiratory deposition by nasal breathing (light blue arrow). The diagram is labeled 'Airborne transmission', 'Aerosols', 'Atomization', 'Droplets', and 'Contact transmission'. It is a slide from a presentation, indicated by '4 of 5' and a close button.

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

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The New York Times

PLAY THE CROSSWORD

The Coronavirus Outbreak >

LIVE Latest Updates

Maps and Cases

Risk in Santa Clara County

Vaccine Rollout

Guidelines After Vaccination

The graph shows the timeline of a Covid-19 infection. The x-axis represents time, starting from 'exposure' (marked with a red dot). Three curves are plotted: 'innate immune response' (blue curve, peaks early and then declines), 'viral load' (orange curve, peaks after the innate response and then declines), and 'adaptive immune response' (purple curve, peaks after the viral load and then declines). The graph is titled 'Charting a Covid-19 Immune Response'.

Charting a Covid-19 Immune Response

By Katherine J. Wu and Jonathan Corum Oct. 5, 2020

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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



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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



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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



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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



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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:
 - vaginal dryness
 - urinary retention
 - hemorrhoids or rectal fissures



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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)*



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Vaccinations



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

A. VACCINATION SCHEDULE FOR BMT PATIENTS

Vaccine Type	Vaccine Abbreviation	Months post-transplant							Minimum interval between doses
		6	12	13	14	18	24	25	
Influenza	IIV (inactivated influenza vaccine)	Annually starting at 6 months							
Pneumococcal	PCV13/PPSV23^a	#1	#2	#3	#4				^b
Meningococcal Group A	MenACWY (Menveo)	#1	#2	#3					8 weeks
Haemophilus	Hib	#1	#2	#3					4 weeks
Diphtheria/tetanus/pertussis	DTaP (or Tdap x1, then Td x2)	#1	#2	#3					4 weeks
Hepatitis	HepA-HepB	#1	#2		#3 ^c				^d
Papillomavirivurus	9vHPV (if ≤ 45 years old)	#1	#2		#3				^e
Measles, mumps, rubella	MMR^f						#1	#2	4 weeks
Varicella	VAR^f (if VZV IgG negative)						#1	#2	4 weeks

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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



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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



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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



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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.



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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



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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




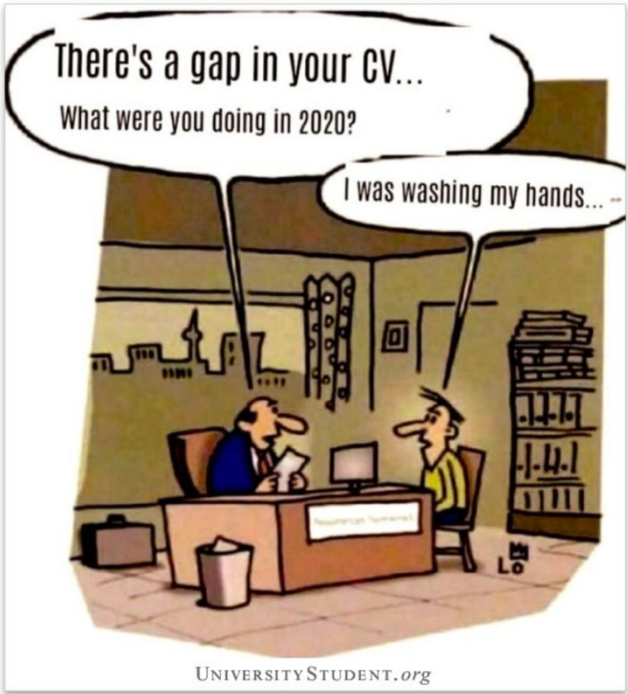
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Don't stop enjoying life!

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



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Questions?

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