Vaccinations in Transplant Candidates

Marianna Leung, PharmD
Clinical Pharmacy Specialist
St. Paul's Hospital
Vancouver, BC
Renal Pharmacist Network Education Day

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2 Disclosures

None to declare

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3 Objectives

- Review appropriate vaccinations in transplant candidates
- Discuss the optimal timing of vaccinations in pre-transplant
- Review the challenges with inadequate pre-transplant vaccination

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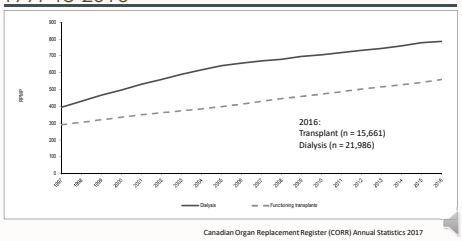
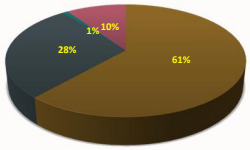
Prevalence Rates for Patients on Dialysis or Transplant in Canada, 1997 to 2016



Canadian Organ Replacement Register (CORR) Annual Statistics 2017

Kidney Transplants by Donor Type, 2016



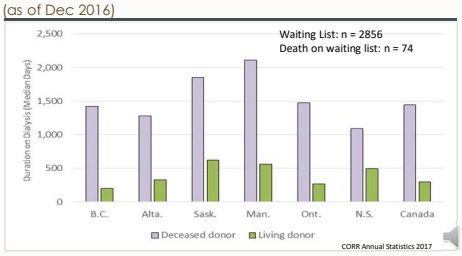
n =1280

- Kidney only, first graft, deceased donor
- Kidney only, first graft, living donor
- Kidney combination, first graft, deceased donor*
- Re-transplants

CORR Annual Statistics 2017

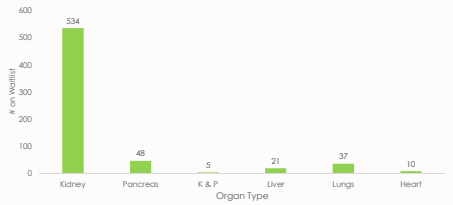
Duration on Dialysis Prior to Transplant

(as of Dec 2016)



CORR Annual Statistics 2017

7 Solid Organ Transplant (SOT) Waitlist – BC data



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Why vaccinate pre-transplant?

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9 General Principles of Immunization in SOT Recipients

- Vaccine-preventable diseases cause major morbidity and mortality in SOT recipients
- Immunosuppressants suppress T-cell and B-cell immunity
  - Vaccinations less effective
  - Cannot administer live vaccines
- Timing of immunizations is important
- ? effect of vaccination on allo-immunity leading to rejection risk

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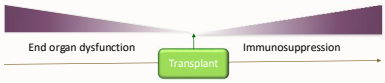
Clin Ther 2017;39:1581-98

10 When to vaccinate?



- Altered immune response along the continuum
- In general, pre-transplant has best immune responses
  - Healthy > end stage renal disease > post-transplant
  - Pre-transplant antibodies (Ab) predicts post-transplant Ab
- Degree & duration of immunity reduced in SOT

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http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/immunization/immunization-of-special-populations

11 Timing around Immunosuppression is Critical!

- Inactivated: Avoid within 2 weeks
- Live: Avoid within 6 weeks (BC Transplant)

After immunosuppression:

- Wait at least 3 months after immunosuppression
- Wait at least 6 months after rituximab/ATG

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BCT Guidelines: BCCDC

12 Immunosuppression Pre-transplant

- Corticosteroids at doses > 20mg prednisone/day for > 2 wks (wait as least 1 mo)
- Azathioprine > 3mg/kg/day
- 6-mercaptopurine > 1.5mg/kg/day
- Methotrexate >0.4mg/kg/wk
- TNF-α
- Rituximab (wait 6 mos)
- Antirejection meds
- Active chemotherapy (wait 6 mos)

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BCCDC Immunosuppressive Therapy

13 Live vs Inactive Vaccines

Live

- Mumps Measles Rubella (MMR)
- Varicella Zoster vaccine (VZV)
- Live attenuated influenza vaccine (LAIV)
- Yellow fever
- Bacille Calmette-Guerin (BCG)
- Smallpox
- Oral polio
- Oral typhoid

Inactive

- Tetanus diphtheria/acellular pertussis (Td/Tdap)
- Hepatitis A vaccine (HAV)
- Hepatitis B vaccine (HBV
- Influenza A/B/H1N1 (TIV)
- Meningococcal vaccine (MCV)
- Pneumococcal vaccines
- Rabies vaccine
- Inactivated polio vaccine (IPV)
- Typhoid polysaccharide vaccine

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14 Safety of vaccines

Vaccine	Pre-Transplant?	Post-Transplant?
Dukoral	✓	✓
HAV	✓	✓
HBV	✓	✓
HPV	✓	✓
MMR	✓	✗
Pneumococcal	✓	✓
Rabies	✓	✓
Tdap	✓	✓
Typhoid IM	✓	✓
VZV	✓	✗
Yellow Fever	✓	✗

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Can we screen pre-transplant?

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16 Serology Pre-transplant Work-up

- Hepatitis A
- Hepatitis B
- Measles, Mumps, Rubella (MMR)
- Varicella

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17 Serology Results

Hepatitis B Virus

Hepatitis B Virus Surface Ab	This test was performed at Burnaby Reference Laboratory - 3680 Gilmore Way, Burnaby, V5G 4W8 208 Post-vaccine HBsAb levels of at least 10 are protective. Patients with lower levels are considered immune if they have previously had a protective HBsAb level.	(IU)/L	09/Mar/2017 16:01
Hepatitis B Virus Surface Ag	Non-Reactive No evidence of active Hepatitis B infection.		09/Mar/2017 16:01

Measles Virus Ab IgG

Measles Virus Ab IgG	715	m[IU]/mL	19/Aug/2016 10:54
Measles Virus Ab IgG	Reactive. INTERPRETATION: Immune to Measles from vaccination or past infection.		19/Aug/2016 10:54

Mumps Virus Ab IgG

Mumps Virus Ab IgG	324	(Titre)	19/Aug/2016 10:55
Mumps Virus Ab IgG	Equivocal. INTERPRETATION: Antibody to Mumps may be present but below level of definitive detection.		19/Aug/2016 10:55

Rubella Virus Ab IgG	41.7 Reactive. Immune to Rubella from vaccination or past infection.	[IU]/mL	17/Aug/2016 17:39

Varicella Zoster Virus Ab IgG

Varicella Zoster Virus Ab IgG	306	m[IU]/mL	18/Aug/2016 13:32
Varicella Zoster Virus Ab IgG	Reactive. INTERPRETATION: Immune to VZV.		18/Aug/2016 13:32

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18 Request for Vaccination

Please fax a copy of the completed immunization record to:
St. Paul's Hospital Kidney Pre-Transplant office: Fax 604 806 8902

Vaccinations Required	Date Administered or notes
Please adminster vaccines checked off, if not already completed	
☑ Td / Tdap	
☑ Polio	
☑ Hepatitis B	
☐ Meningococcal Quadrivalent Conjugate	
☑ Pneumococcal	
☐ Haemophilus Influenza B	
☑ Influenza	
☑ *MMR (*Live vaccine – do not give if immune suppressed, please verify medications with patient prior to administration)	
☑ *Varicella (*Live vaccine – do not give if immune suppressed, please verify medications with patient prior to administration)	
☑	

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Measles Mumps Rubella (MMR)

20 Case 1

- ID: 37 yo male (born in England 1978)
- Referral:
  - Planning a trip to Disneyland in Mar 2015
  - Measles outbreak linked to theme park in Feb 2015
- PMH:
  - Renal transplant Oct 2013
  - ESRD secondary to IgA nephropathy
- Serology: Measles Ab IgG 167 mIU/mL (equivocal)

21 Case 2

- ID: 38 yo male
- Referral:
  - Went to GP's office for a check-up
  - Notified by Public Health a couple of days later to get measles vaccination due to an index case found at the same time of his visit
- PMH:
  - Renal transplant Feb 2009
  - ESRD secondary to lupus nephritis
- No serology on file

22 Measles

- High morbidity and mortality
  - Pneumonia, encephalitis, Subacute sclerosing panencephalitis
- Measles immunity
  - Born before 1970, OR
  - Lab confirmed infection or immunity (titer ≥ 150 mIU/mL), OR
  - Documentation of 2 vaccines if 2-17 yo OR
  - Documentation of 1 vaccine if ≥ 18 yo and born after 1970

National Advisory Committee on Immunization. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci.html

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23 MMR

- Live attenuated vaccine (LAV)
- NACI recommends 2 doses @
  - 12-15 mos of age
  - 18 mos to 4-6 yrs of age
- Prior to mid-1990's, only 1 dose was given
  - Patient may need 2nd dose
- If high risk, need 2 doses or lab-confirmed immunity
  - At least 4 weeks apart

https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-12-measles-vaccine.html#p4c11a1

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24 MMR - Pre-transplant

- Confirm serology for MMR
- Vaccinate if receiving minimal immunosuppression
- Vaccinate at least 4 wks prior to transplant
- Seronegative adults should receive 1 dose of MMR with serologic testing post-vaccination
- If seroconversion does not occur, the dose can be repeated once if time permits

https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-12-measles-vaccine.html#p4c11a1

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Varicella

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26 Varicella Zoster Vaccine

- LAV with Oka strain
- NACI recommends 2 doses 6 weeks apart if seronegative and ≥ 13 yo
- Pre-transplant
  - Confirm serology for Varicella Zoster Virus (VZV) IgG
  - Vaccinate if receiving minimal immunosuppression
  - Vaccinate at least 4 wks prior to transplant
  - Seronegative adults should receive 1 dose with serologic testing post-vaccination
  - If seroconversion does not occur, the dose can be repeated once if time permits

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https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-24-varicella-chickenpox-vaccine.html

27 Case 3

- ID: 77 yo retired pharmacist
- CC: progressive ataxia & confusion with a vesicular rash around his left eye and a non-reactive pupil
- PMH:
  - Kidney transplant 10 mos ago
  - T2DM
  - HTN
  - TIA
- Lumbar puncture: +ve CSF for varicella zoster virus (VZV)
- DX: VZV encephalitis

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28 Case 3 (cont'd)

- Serology work-up pre-transplant: VZV IgG +ve
- Had chickenpox as a child
- Never received herpes zoster vaccine pre-transplant

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29 Herpes Zoster (HZ)

- Caused by reactivation of VZV
- Occurs in up to 20% of transplant recipients
- HZ vaccine is recommended for VZV IgG +ve transplant candidates ≥ 50 yo but not funded in some provinces
- Immunogenicity of vaccination pre-transplant in preventing post-transplant HZ disease is unknown
- Wait at least 1 year from a prior episode of shingles before being vaccinated

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Curr Infect Dis 2014;27:329-35

30 Herpes Zoster Vaccines

Zostavax®

- LAV ~14x PFU of Oka strain
- Single dose
- Recommended for SOT **candidates**; not funded
- Vaccinate at least 4 wks pre-transplant
- **Contraindicated** in SOT **recipients**
- Cost ~$175

Shingrix ®

- Inactivated – glycoprotein E, a surface protein on the virus + 2 adjuvants
- 2 doses at months 0 and 2-6
- Preliminary data in kidney transplant recipients: immunogenic and similar rejection rates
- $250 for 2 doses

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CST information on new inactivated shingles vaccine Jan 2018| IDWeek Abstract 2017

31 Hepatitis A Vaccine

- Recommended in seronegative individuals
  - liver transplant candidates
  - high risk of exposure (e.g. travel, occupational or lifestyle risk)
- Inactivated
- Seroconversion rate post-transplant ~25%

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Clin Ther 2017;39:1581-98

32 Hepatitis B Vaccine

- Routine vaccine schedule recommended based on serology and as early in the course of disease as possible
- If seronegative (anti-HBs titer < 10)
  - 3 dose series: 0, 1, 6 mos
  - Accelerated: 0,1, 2, 12 mos
  - Rpt 2nd series if anti-HBs < 10, then booster

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Pneumococcus

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34 Pneumococcal Vaccines

- Pneumococcal disease has 13x greater relative risk in SOT than general population
- 2 vaccines:
  - Conjugate (PCV-13)
    - Diphtheria protein added to stimulate T-cells and memory B cells
    - Serotype 6A not found in PPSV-23
  - Polysaccharide (PPSV-23)
    - Stimulates B cells to produce Ab
    - Booster dose at 5 yrs

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Curr Infect Dis 2014;27:329-35

35 Pneumococcal Vaccines

- Prime-boost strategy in immunocompromised:
  - PCV followed by PPSV after 8 wks
  - Data limited in SOT: boosting not found to occur in SOT
- PCV-13 only covered in HSCT and HIV patients in BC
- Sequence/timing is important:
  - PCV-13 followed by PPSV-23 at 8 wks
  - PPSV-23 followed by PCV-13 at 1 yr
  - Reflects hyporesponsiveness of PPS antigens

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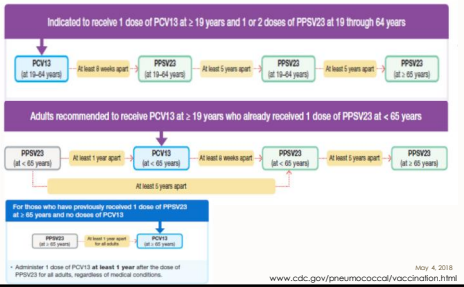
Curr Infect Dis 2014;27:329-35

36 Timing



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www.cdc.gov/pneumococcal/vaccination.html

37 Influenza

- Influenza vaccination is found to be efficacious and safe in renal transplant recipients
  - Seroprotection rate 79-93% (less in other studies)
  - No benefit to booster dose
  - No increased rejection
- 2 vaccines:

Inactivated Influenza vaccine (IIV)

- More common
- Usually trivalent +/- adjuvants
- Recommended in both SOT candidates & recipients

Live attenuated Influenza vaccine (LAIV)

- Administered intranasally
- **Contraindicated** in SOT **recipients**
- Free for children 2-17 yo only in BC

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Am J Transplant 2008;8:332-7

38 Human Papillomavirus (HPV)

- Causes significant morbidity and mortality in SOT
  - Increased risk of anogenital cancers, skin cancer, warts
- Eligible and funded:
  - Women born ≥ 1994
  - High risk individuals 9-26 yo (HIV +ve, transgender, MSM, no fixed address)
  - High risk males 9-18 yo (care of Ministry, custody)
- Eligible and not free:
  - Women ≤ 45 yo, males 9-26 yo, MSM ≥ 27 yo
- Cervarix® (HPV2) and Gardasil®9 (HPV9)
  - Inactivated; 2 doses @ 6 mos apart

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39 Recommendations for SOT Candidates

Vaccine	For Whom?	Dose	Comments
HAV	Seronegative for anti-HAV	2 doses at 0 & 6 mos	Liver transplant; high risk individuals
HBV	Seronegative for anti-HBV	3 doses at 0, 1, 6 mos	40mcg/dose for dialysis pts; booster PRN anti-HBS <10
HPV	High risk individuals, 9-26 yo Women born ≥ 1994	2 doses	
Influenza	All	1 dose	Give pre-influenza season
MMR	seronegative	1-2 doses	> 4 wks from anticipated transplant & not on IMS
PCV-13	All	1 lifetime dose	Follow PPSV-23 by 1 yr
PPV-23	All	2 doses 5 yrs apart	Follow PCV-13 by 8 wks
Tdap	✓	1 dose	Particular healthcare workers
Varicella	Seronegative for VZV	1-2 doses (check serology after 1st dose)	> 4 wks from anticipated transplant & not on IMS
VZV	≥ 50 yo		

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40 Summary

- Updating vaccine status is a critical part of pre- & post-transplant care
- Timing of immunizations if critical
  - Healthy > end stage renal disease > post-transplant
  - Avoid inactivated vaccine 2 wks pre-transplant
  - Avoid live vaccine at least 4 wks pre-transplant
  - Avoid vaccination 3-6 mos post-transplant
- Check serology and keep vaccinations up-to-date

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