


Care for kidney transplant patients: treatment and vaccination guidance

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Presentation Outline

- The post-transplant immunosuppressive regimen for kidney transplant recipients
- Application of generic medications
- Use of vaccines in kidney transplant recipients

Disclosure: no financial relationships to disclose

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The Post-Transplant Immunosuppressive Regimen

1. List the most common immunosuppressant medications utilized in the post-transplant regimen and explain the rationale for switching to agents less often used

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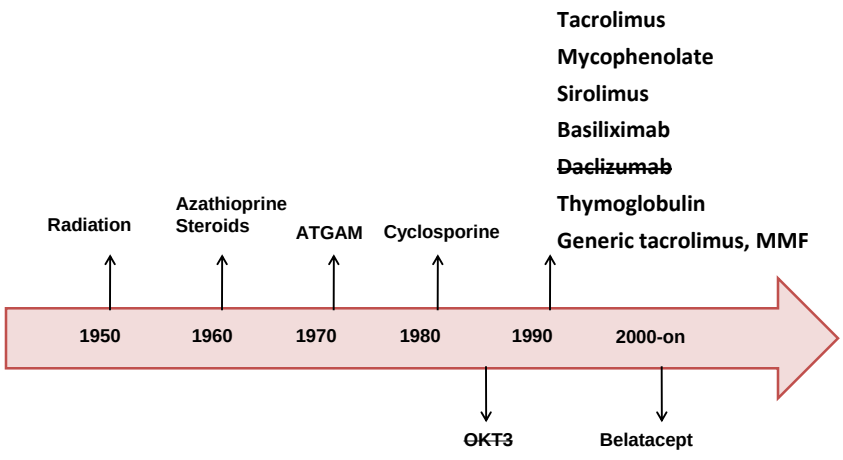
Timeline of immunosuppression



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The Menu of Immunosuppression

Polyclonal antibodies	•Equine anti-thymocyte globulin (ATGAM) •**Rabbit anti-thymocyte globulin (Thymoglobulin)**
Monoclonal antibodies	•Basiliximab (Simulect)
Calcineurin inhibitors	•Cyclosporine: Neoral (modified) •Sandimmune (non-modified) •**Tacrolimus**
Anti-proliferatives	•Azathioprine (Imuran) and generics •**Mycophenolate mofetil (Cellcept)** •EC-mycophenolate sodium (myfortic) •Sirolimus (rapamune) •Everolimus (Zostress)
Steroids	•**Methylprednisolone (Solu-medrol)** •**Prednisone (Deltasone) and generics**

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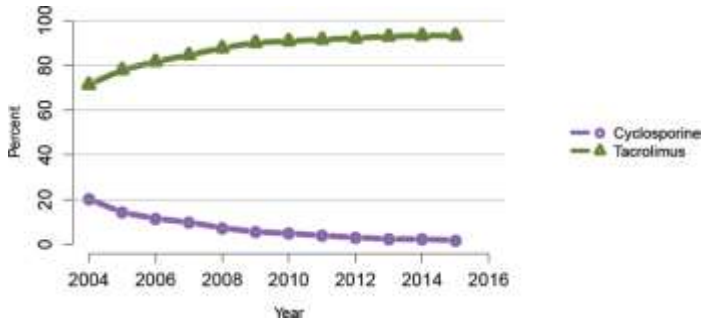
Calcineurin Inhibitors



- First line CNI: tacrolimus (2A)
- CNI (tacrolimus (2D) or cyclosporine (2B)) should be started before or at the time of transplantation, rather than delayed until the onset of graft function

OPTN/SRTR Annual Data Report. 2015 American Journal of Transplantation 2017; 17 (S1): 1–564
Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (S3): 6-13

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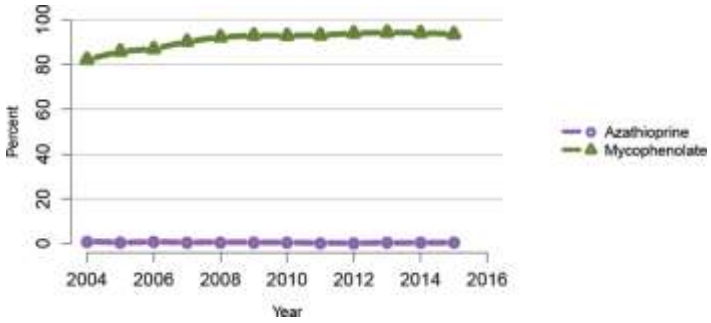
Anti-metabolites



Mycophenolate suggested as the first-line antiproliferative agent (2B)

OPTN/SRTR Annual Data Report. 2015 American Journal of Transplantation 2017; 17 (S1): 1–564
Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (S3): 6-13

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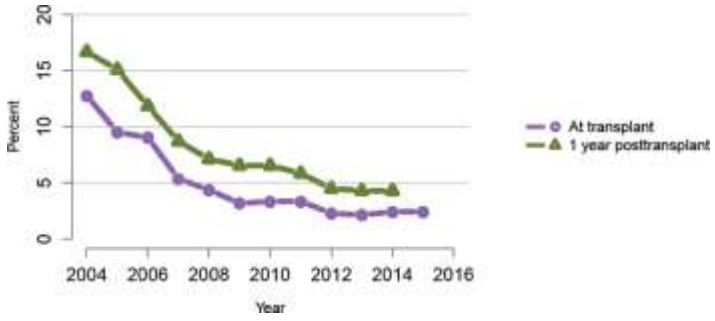
Mammalian Target of Rapamycin Inhibitors (mTORi)



Do not start until graft function is established and surgical wounds are healed (1B)

OPTN/SRTR Annual Data Report. 2015 American Journal of Transplantation 2017; 17 (S1): 1–564
Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (S3): 6-13

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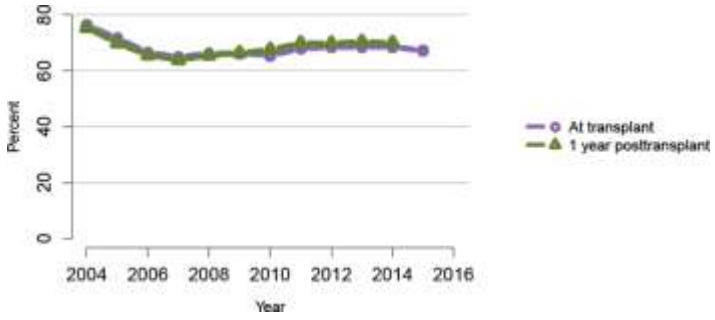
Corticosteroids



In patients who are at low immunological risk of rejection and who receive induction therapy, corticosteroids could be discontinued during the first week after transplantation (2B)

OPTN/SRTR Annual Data Report. 2015 American Journal of Transplantation 2017; 17 (S1): 1–564
Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (S3): 6-13

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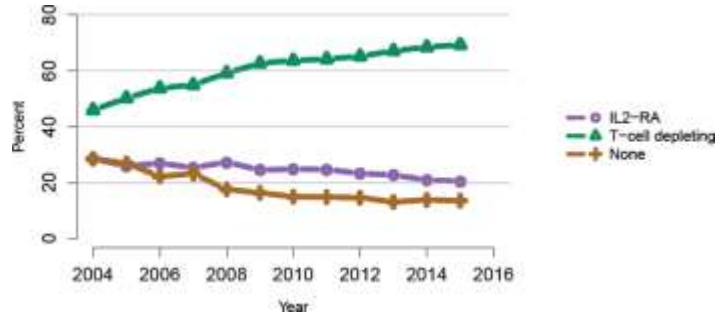
Induction therapy



- First line induction therapy: Basiliximab (IL2-RA) (1B)
- High immunologic risk: Thymoglobulin (T-cell depleting) (2B)

OPTN/SRTR Annual Data Report. 2015 American Journal of Transplantation 2017; 17 (S1): 1–564
Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (S3): 6-13

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Toxicity Profiles of Immunosuppressive Medications

Adverse effect	Steroids	CsA	Tac	mTORi	MMF	AZA
New-onset diabetes mellitus	↑	↑	↑↑	↑		
Dyslipidemias	↑	↑		↑↑		
Hypertension	↑↑	↑↑	↑			
Osteopenia	↑↑	↑	(↑)			
Anemia and leucopenia				↑	↑	↑
Delayed wound healing				↑		
Diarrhea, nausea/vomiting			↑		↑↑	
Proteinuria				↑↑		
Decreased GFR		↑	↑			

Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (3): S6-S13

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Summary of Immunosuppression

- Tacrolimus and mycophenolate represent the mainstay of immunosuppression used today
- Side effects and tolerability may lead to selection of less commonly used immunosuppressants

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Generic Immunosuppressants

2. Explain the role of the pharmacist when counseling patients prescribed generic immunosuppressants

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Background

- Between 2008 and 2010, FDA approved several generic formulations
  - Tacrolimus
  - Mycophenolate mofetil
- Can generic medications (tacrolimus) be safely as substitutes for innovative product?

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Generics: Definitions and Regulations

- **Pharmaceutical equivalence**: same active ingredient, identical strength, dosage form, and route
- **Bioequivalence**: must reach the systemic circulation at an equivalent rate extent
- **Labeling**
- **Good manufacturing practice regulations**

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Concerns with Generic Regulations

- Clinical data not required
- Time to C_{max} or trough concentration (C_0) are not assessed or compared
- AB generics are not tested to see if they are bioequivalent to each other

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Tacrolimus: Available Generics

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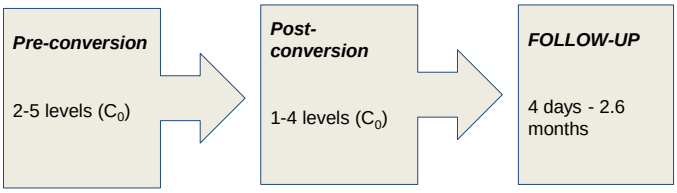
Conversion from Brand to Generic



Pre-conversion C_0 levels	Post-conversion C_0 levels
1.1 - 14.3	1.1 -10.3

Overall: < than 5% change

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Venkataramanan R et al. Am J Transplant 2010;10(S4): abstract 1741

Impact of Changing to Generic Formulation

Trough level (C_0)	Patients (n)
Increase > 20%	5
Any increase	16
Decrease > 20%	9
Any decrease	16

- 78% significant variation
- 43% change greater than 20%

No increase in signs or confirmed diagnosis of acute rejection

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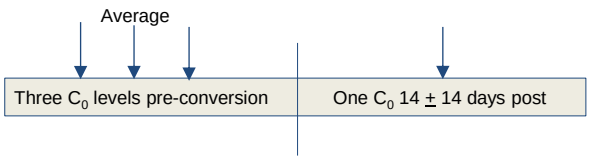
Venkataramanan R et al. Am J Transplant 2010;10(S4): abstract 1741

Multi-Center Experience

1:1 dose conversion (brand: generic)



Patients (n = 102)
57 ± 51 months post-transplant
Stable tacrolimus dose for at least 4 weeks

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Transplantation. 2011 Sep 27;92(6):653-7.

Generic Dose Requirements & Cost

Savings		
	($) per mo.	**($) per avg. life of the graft (8.7 years)**
AWP	77	8,105
Co-pay	19	2,000

Dosage titrations occurred in 29%

Transplantation. 2011; 92(6):653-7

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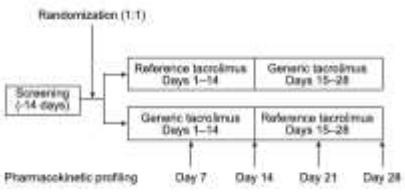
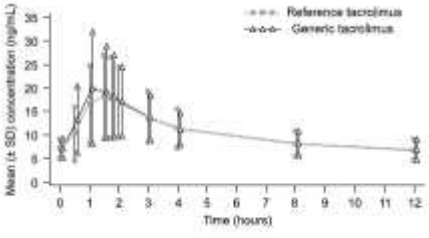
American Journal of Transplantation 2012; 12: 2825–2831
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2012.04174.x

Brief Communication

A Randomized Pharmacokinetic Study of Generic Tacrolimus Versus Reference Tacrolimus in Kidney Transplant Recipients





American Journal of Transplantation 2012; 12: 2825–2831

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Summary

- ❑ Conversion is permissible without any impact on transplant outcomes
- ❑ Some will require dose titration

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Recommendations for Use of Generics

- Initial dose conversion 1:1
- Notify the transplant center of switch
- Increase oversight during switch
- Therapeutic drug monitoring
  - Increase frequency of monitoring
  - Return to normal monitoring schedule:
    - steady state
    - stable levels

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Immunization of Kidney Transplant Recipients

3. Explain current guidelines and recommendations for the vaccination of kidney transplant recipients
4. List the types of vaccines that are contraindicated, discuss the rationale, and explain how to counsel patients and caregivers on the appropriate use of vaccines
5. Describe the differences in the treatment of influenza in the immunosuppressed kidney transplant patient vs. a non-immunocompromised patient
6. Provide counseling to patients and caregivers on the use of vaccines

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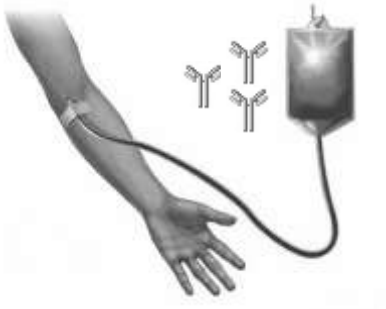
Immunity

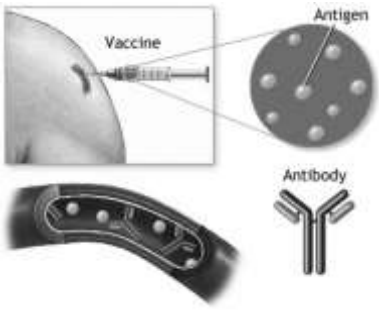
Passive immunity

- Intravenous immunoglobulin



Adaptive immunity

- Vaccination (live or inactive)



Clinical pearl: blood products (IVIG) interfere with the response to live vaccines; delay these vaccines for 3 months after receiving blood products

Adapted from: http://keckmedicine.adam.com/content.aspx?productId=617&pid=1&gid=002024
http://www.fragmenthealth.com/galery/blood_transfusion.jpg

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Comparison: Passive vs. Adaptive

Passive

- Short duration
  - A few weeks
- Effective immediately
- Receipt of non-self antibodies

Adaptive

- Long duration
  - Lifelong
- Delayed effectiveness
  - May take weeks
- Self production of antibodies

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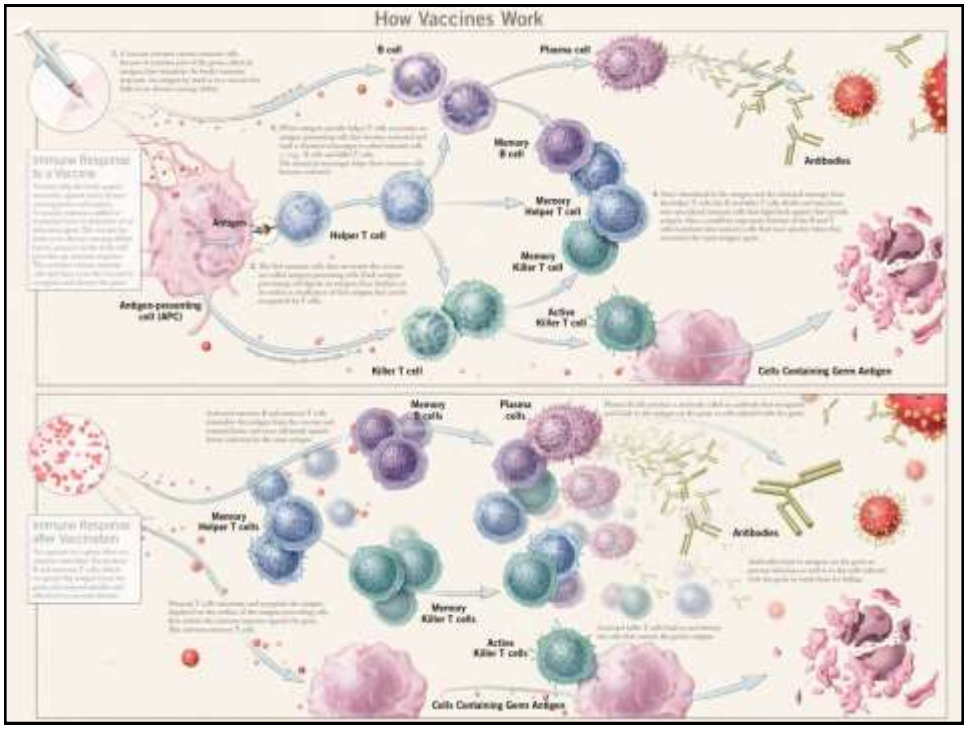
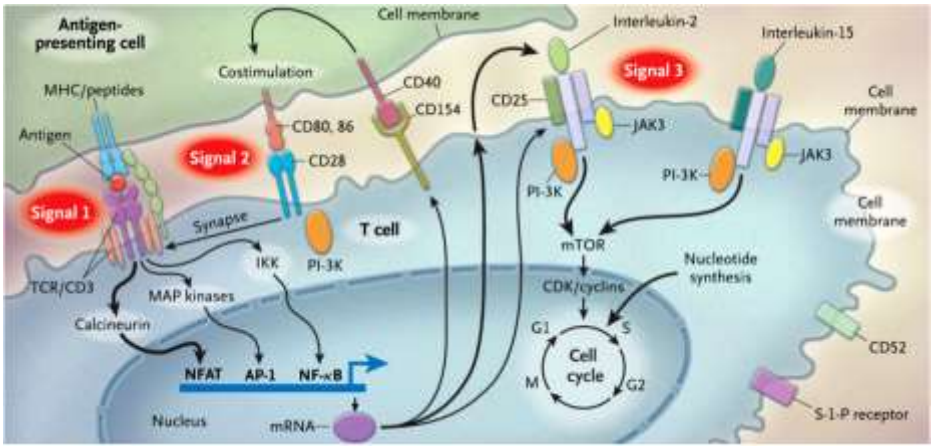
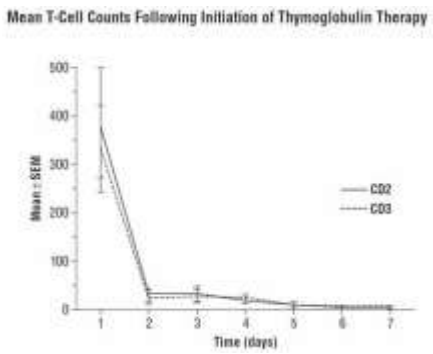


Pharmacology of Immunosuppression



Halloran et al. N Engl J Med 2004; 351:2715-2729

Induction Immunosuppression

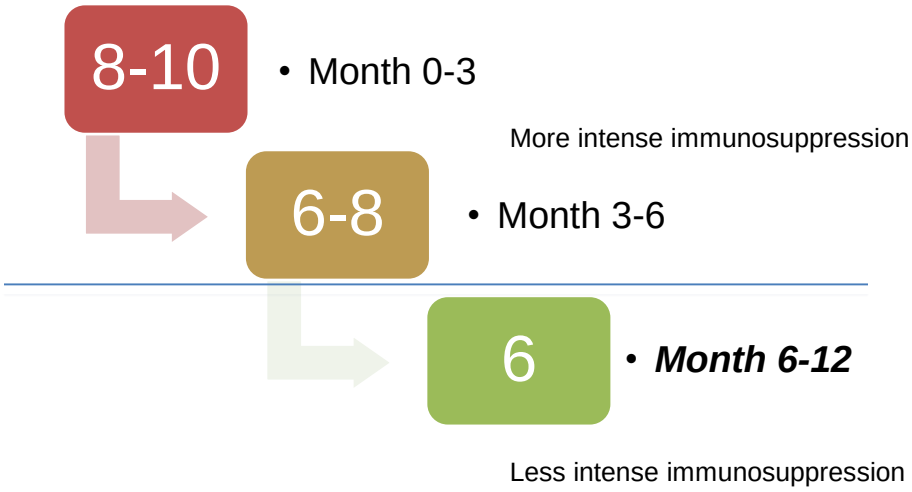


- Immunosuppressive effects agent dependent
  - Thymoglobulin vs. Basiliximab
- Thymoglobulin
  - T-cell depletion may last for months to years (2 years)

Hardinger KL, Schnitzler MA, Miller B, et al. Transplantation 78: 136-141, 2004

Thymoglobulin (antithymocyte globulin [rabbit]) [prescribing information]. Cambridge, MA: Genzyme Corporation; March 2016.

Goal Tacrolimus Levels (ng/mL)



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Corticosteroids

Steroid	Dose (mg)	Post-operative day
Methylprednisolone	500 mg (in OR)	0
Prednisone	160	1
	120	2
	80	3
	40	4
	20	5-9
	15	10-19
	10	20-24
	7.5	25-29
	5	30-on

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Clinical Concerns

1. Does vaccination increase the risk of transplant rejection?
2. Is the ability to mount an immune response impacted by the amount and/or type of immunosuppression after transplant?
3. What is the optimal time to give vaccines after transplant?

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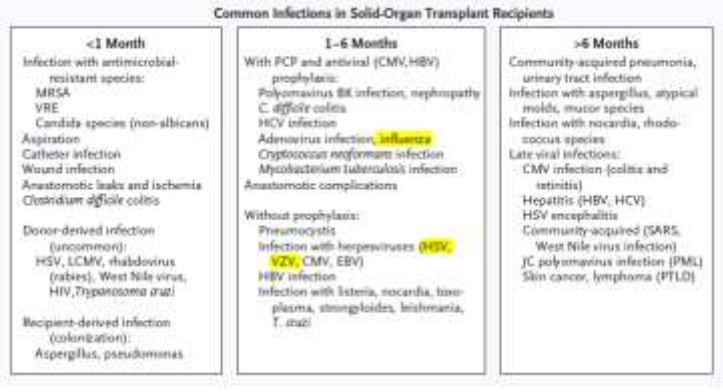
Danziger-Isakov L et al. American Journal of Transplantation 2013; 311-317

Timeline of Infection After Transplant



Common Infections in Solid-Organ Transplant Recipients

<1 Month	1–6 Months	>6 Months
Infection with antimicrobial-resistant species: MRSA VRE Candida species (non-albicans) Aspiration Catheter infection Wound infection Anastomotic leaks and ischemia *Clostridium difficile* colitis Donor-derived infection (uncommon): HSV, LCMV, rhabdovirus (rabies), West Nile virus, HIV, *Trypanosoma cruzi* Recipient-derived infection (colonization): Aspergillus, pseudomonas	With PCP and antiviral (CMV, HBV) prophylaxis: Polyomavirus BK infection, nephropathy *C. difficile* colitis HCV infection Adenovirus infection, influenza *Cryptococcus neoformans* infection *Mycobacterium tuberculosis* infection Anastomotic complications Without prophylaxis: Pneumocystis Infection with herpesviruses (HSV, VZV, CMV, EBV) HBV infection Infection with listeria, nocardia, toxoplasma, strongyloides, leishmania, *T. cruzi*	Community-acquired pneumonia, urinary tract infection Infection with aspergillus, atypical molds, mucor species Infection with nocardia, rhodococcus species Late viral infections: CMV infection (colitis and retinitis) Hepatitis (HBV, HCV) HSV encephalitis Community-acquired (SARS, West Nile virus infection) JC polyomavirus infection (PML) Skin cancer, lymphoma (PTLD)

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Fishman JA N Engl J Med 2007; 357: 2601-2614

Influenza in Transplantation

- Greater risk of morbidity and mortality*

- Cause of allograft dysfunction and acute rejection**
  - ❑ Kidney
  - ❑ Lung
- Response to the vaccine & effectiveness not well described

*Kumar D et al. Lancet Infect Dis 2010; 10: 521-526
**Cordero E et al. Clin Microbiol Infect 2012; 18: 67-73

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American Journal of Transplantation 2009; 9: 2346–2354
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2009.02787.x

Humoral and Cellular Immune Responses after Influenza Vaccination in Kidney Transplant Recipients

Patients	• 66 kidney transplant recipients (not recent)
Control	• 19 healthy individuals
Purpose	• Investigate the humoral & cellular response to influenza vaccine • To address the risk of HLA sensitization and/or allograft rejection
Outcomes	Anti-influenza antibodies (3 strains) • Positive response: **titer > 50** (seroconversion) • **3 fold** titer increase
	• T-cell enzyme-linked immunoSpot (ELISPOT) assay (cellular) influenza specific response
	• Anti-HLA antibodies (humoral) • Donor specific antibodies (DSA) – *linked to rejection*

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Candon S et al. American Journal of Transplantation 2009; 9: 2346-2354

Positive Vaccine Responses

Influenza Strain	Transplant (%)	Healthy (%)	p value
A/H1N1 (unchanged)	10	58	<0.0001
A/H3N2 (changed)	22	58	0.004
B (unchanged)	20	26	> 0.05 NS
Overall (at least 1 strain)	46	84	0.004

- Response largely due to an ↑ in antibody titers except for H3N2
- Vaccine response significantly lower for A/H1N1 and A/H3N2 in immunosuppressed transplant patients than in healthy controls
- Similar response to B strain

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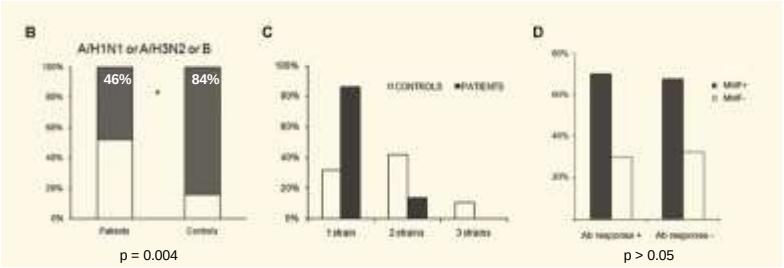
Candon S et al. American Journal of Transplantation 2009; 9: 2346-2354

Factors Effecting Response



B. Total proportion of individuals responding to at least one strain (dark bars)
C. Individuals mounting an antibody response toward one, two or three strains
D. Patients +/- MMF according to humoral postvaccinal response

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Candon S et al. American Journal of Transplantation 2009; 9: 2346-2354

Immunosuppression

- No influence of maintenance immunosuppression
  - Mycophenolate mofetil dose
  - Steroid dose
  - Trough levels of sirolimus or tacrolimus
- Did not assess induction therapy

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Candon S et al. American Journal of Transplantation 2009; 9: 2346-2354

Influenza Specific T-Cell activity

- Important for viral clearance during ongoing infection
  - Provision of T-helper component of humoral immunity
- Significant response detected in transplant patients
- Included response to major antigens in vaccine
  - Transplant: 13 out of 46 (28%)
  - Control: 3 out of 12 (25%)
    - $p > 0.05$
- This did not impact antibody response

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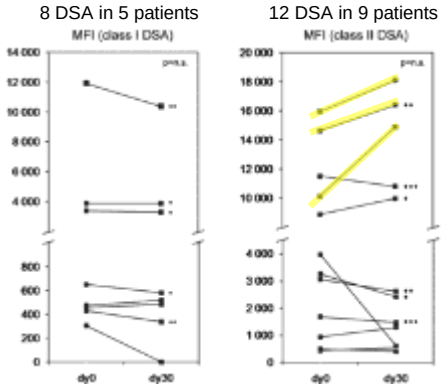
Candon S et al. American Journal of Transplantation 2009; 9: 2346-2354

Donor Specific Antibodies (DSA)

- DSA day 0 (baseline):
  - ➢ n = 14 (22%)
    - Class I: n = 5
    - Class II: n = 9
  - ➢ All detected at day 30
    - ➢ Not significantly changed
    - ➢ No enhancement of anti-donor sensitization
    - ➢ ↑ in 3 class II DSA with high MFI value (>10,000)



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Candon S et al. American Journal of Transplantation 2009; 9: 2346-2354

Sensitization after Vaccination

- *de novo* DSA (day 30): n = 3 (4.8%)
  - – Low MFI for all three
    - Patient 1: 482
    - Patient 2: 322
    - Patient 3: 624

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Candon S et al. American Journal of Transplantation 2009; 9: 2346-2354

Rejection Episodes

- No clinical or biological signs of rejection at 3 months
  - Including those with baseline & *de novo* DSA
- Serum creatinine:
  - 1.59 ± 0.77 mg/dL (day 0)
  - 1.55 ± 0.58 mg/dL (day 90)
    - p >0.05

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Candon S et al. American Journal of Transplantation 2009; 9: 2346-2354

Decreased Antibody Response to Influenza Vaccination in Kidney Transplant Recipients: A Prospective Cohort Study

Kelly A. Birdwell, MD, MSCI,[1] Mine R. Ikizler, MS,[2] Edith C. Sannella, MT,[2] Li Wang, MS,[3] Daniel W. Byrne, MS,[3] T. Alp Ikizler, MD,[1] and Peter F. Wright, MD[2,4]

Patients	53 kidney transplant recipients (single center: Vanderbilt University) 36% (19 out of 53) < 6 months post-transplant	
Control	106 healthy participants	
Purpose	Antibody response to inactivated influenza vaccine is not well described in this population ***using newer & commonly used immunosuppressive agents***	
Hypothesis	Tacrolimus based immunosuppression would result in decreased antibody response compared to healthy controls using 2006-2007 standard trivalent inactivated vaccine	
Outcomes	Primary	Proportion of patients achieving: • Seroresponse (**4** fold increase in titer) • Seroprotection (antibody titer **> 1:32**) *Influenza types: A/H1N1, A/H3N2, B* *Assessed at 1 month post vaccination*
	Secondary	Associations of antibody response with: • Gender • Age • Immunosuppression • Time from transplant • Kidney function (SCr at 1 month)

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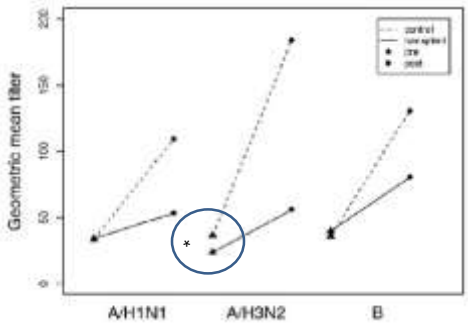
Birdwell et al. Am J Kidney Dis 2009; 54:112-121



Serological Response (antibody titers)

- Post-vaccination titers increased significantly from baseline for all stains in each group
- Mean change (pre vs. post vaccination titers) significantly different between healthy (control) & transplant group for all 3 strains

Birdwell et al. Am J Kidney Dis 2009; 54:112-121

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Percentages and Odds Ratios of Developing Antibody Response to the 2006-2007 Influenza Vaccine in All Participants

	Controls (%) (n = 106)	Transplant Recipients (%) (n = 53)*	Unadjusted Odds Ratio	95% Confidence Interval	P
Seroresponse (4-fold increase)					
A/H1N1	32.1	22.6	0.62	0.29-1.33	0.2
Transplantation < 6 mo		5.3	0.12	0.02-0.92	0.04
Transplantation > 6 mo		32.4	1.01	0.44-2.31	0.9
A/H3N2	62.3	34.0	0.31	0.16-0.62	0.001
Transplantation < 6 mo		21.1	0.16	0.05-0.52	0.002
Transplantation > 6 mo		41.2	0.42	0.19-0.93	0.03
B	48.1	35.8	0.60	0.31-1.12	0.1
Transplantation < 6 mo		15.8	0.20	0.06-0.74	0.02
Transplantation > 6 mo		47.1	0.96	0.44-2.08	0.9
Seroprotection (postvaccination titer ≥ 1:32)					
A/H1N1	83.0	69.8	0.47	0.22-1.03	0.06
Transplantation < 6 mo		63.2	0.35	0.12-1.01	0.05
Transplantation > 6 mo		73.5	0.57	0.23-1.42	0.2
A/H3N2	91.5	69.8	0.22	0.09-0.53	0.001
Transplantation < 6 mo		68.4	0.20	0.06-0.66	0.008
Transplantation > 6 mo		70.6	0.22	0.08-0.61	0.003
B	92.5	86.8	0.54	0.18-1.57	0.3
Transplantation < 6 mo		89.5	0.69	0.14-3.55	0.7
Transplantation > 6 mo		85.3	0.47	0.14-1.56	0.2

Birdwell et al. Am J Kidney Dis 2009; 54:112-121

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Percentages and Odds Ratios of Developing Antibody Response to the 2006-2007 Influenza Vaccine in Participants Without Baseline Seroprotection

	Control (%)	Transplant (%)	Unadjusted Odds Ratio	95% Confidence Interval	*P*
Seroresponse (4-fold increase)					
A/H1N1*	58.3	38.1	0.44	0.15-1.26	0.1
Transplantation < 6 mo		12.5	0.10	0.01-0.90	0.04
Transplantation > 6 mo		53.8	0.83	0.24-2.86	0.8
A/H3N2†	88.9	55.2	0.15	0.04-0.55	0.004
Transplantation < 6 mo		36.4	0.07	0.01-0.36	0.001
Transplantation > 6 mo		66.7	0.25	0.06-1.04	0.06
B‡	75.0	50.0	0.33	0.11-1.01	0.05
Transplantation < 6 mo		28.6	0.13	0.02-0.79	0.03
Transplantation > 6 mo		61.5	0.53	0.14-1.98	0.4
Seroprotection (postvaccination titer ≥ 1:32)					
A/H1N1*	62.5	23.8	0.19	0.06-0.60	0.005
Transplantation < 6 mo		12.5	0.09	0.01-0.76	0.03
Transplantation > 6 mo		30.8	0.27	0.07-0.99	0.05
A/H3N2†	75.0	44.8	0.27	0.10-0.78	0.02
Transplantation < 6 mo		45.5	0.28	0.07-1.13	0.07
Transplantation > 6 mo		44.4	0.27	0.08-0.88	0.03
B‡	84.1	65.0	0.35	0.10-1.19	0.09
Transplantation < 6 mo		71.4	0.47	0.08-2.94	0.4
Transplantation > 6 mo		61.5	0.30	0.08-1.20	0.09

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Birdwell et al. Am J Kidney Dis 2009; 54:112-121

Other Studies: Immunosuppression

Experimental	Control	Findings	Citation
Cyclosporine (CSA)	Azathioprine (AZA)	• (CSA) group ↓ antibody response to influenza vaccine	1 & 2

Cyclosporine (CSA)
Mycophenolate (MMF)
Prednisone (PRED)
	Cyclosporine (CSA)
	Azathioprine (AZA)
	Prednisone (PRED)
		• **Transplant patients < 6 months excluded**
		• Similar seroresponse and seroprotection
		• MMF had effect on vaccine response (H1N1)
		• Lower probability of protective titers with
		  • ↑ PRED doses (A/H1N1)
		  • ↑ CSA doses (A/H3N2)
			3

Multiple regimens	Healthy controls	• **Transplant patients < 6 months excluded** • Similar seroresponse and seroprotection • Major impact of MMF (> 2 g) for all viral strains	4

1. Huang KL et al. Infect Immun 40: 421-424, **1983**
2. Versluis DJ et al. Transplantation 42: 376-379, **1986**
3. Keshtkar-Jahromi et al. Am J Nephrol 28:654-660, **2008**
4. Scharpe et al. Am J Transplant 8: 332-337, **2008**

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Other Factors Effecting Vaccine Response

- Chronic Kidney Disease
- End Stage Renal Disease (Hemodialysis)
- Type of transplant*

Dinits-Pensy M et al. Am J Kidney Dis 2005; 46: 997-1011
Osanloo EO et al. Kidney Int 1978; 14: 614-618
Danziger-Isakov L. et al. American Journal of Transplantation 2013; 13: 311–317

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Other Vaccines With Impaired Immunogenicity

- Hepatitis B[1,2]
- HPV[3]
- Tetanus[4]
- Varricella[5]

1. Jacobson IM et al. Transplantation 1985; 39: 393-395
2. Lefebure AF et al. Vaccine 1993; 11: 397-399
3. Kumar D et al. Am J of Transplantation 2013; 13: 2411–2417
4. Puissant-Lubrano et al. Exp Clin Transplant 2010; 8: 19-28
5. Gershon AA et al. Infect Dis Clin Noth Amer 1996; 10: 583-594

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Results Applied to Guidelines & the Practice of Vaccination

Birdwell et al.
Am J Kidney Dis 54:112-121

- Time post-transplant
- Maintenance immunosuppressants
- Type of strain
- Baseline seroprotection
- Age, gender, and race

Candon S et al.
A J Transplantation 2009; 9: 2346-54

- Time post-transplant
- Maintenance immunosuppressants
- Sensitization & rejection
- T-cell & humoral response
- New Influenza antigens
- Age, gender

Possible increased susceptibility to influenza in this population despite vaccination

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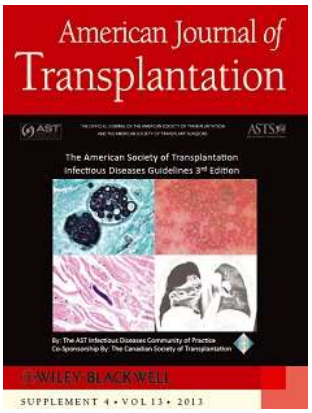
Vaccination Recommendations

- No evidence of allograft rejection (Grading II-2)
- Vaccinate early
  - Document pre-transplant
  - Live vaccines prior to transplant
  - Refer for vaccination at the time of listing
- Vaccinate after transplant
  - 3-6 months post-transplant
  - Inactivated vaccines safe
  - live contraindicated



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Danziger-Isakov L. et al. American Journal of Transplantation 2013; 13: 311–317

Adult Recommendations: AST

Live Attenuated Vaccines	Inactive vaccines
• **Influenza (LAIV)** • **Varicella◊♠ (Varivax*, Zostavax)** • **Measles, Mumps, Rubella (MMR◊♠)** • **BCG (TB)**	• **Influenza** • **Hepatitis A* & B*◊** • **Pertussis** • **Tetanus*** • **Inactivated polio** • ***S. pneumoniae* (Pneumovax23 – polysaccharide & Prevnar13-conjugated)*** • ***N. Meningitidis*** • **Human papillomavirus (HPV)** • **Rabies***

*Monitor titers after vaccination
◊ Check serology prior to transplant: if (–) dose x1 check serology post-vaccination
♠ Delay for 3 months if administered intravenous immunoglobulin (IVIG)

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Danziger-Isakov L. et al. American Journal of Transplantation 2013; 13: 311–317

IDSA GUIDELINES

2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

- Prior to planned immunosuppression if feasible (strong, moderate)
- Live vaccines
  - ❑ Administer ≥ 4 weeks prior to immunosuppression (strong, low)
  - ❑ Avoid within 2 weeks of initiation of immunosuppression (strong, low)
- Inactive vaccines
  - ❑ Administer ≥ 2 week prior to immunosuppression (strong, moderate

Clinical infectious disease (CID) 2014; 58: e44-e100

CMS Recommendations: Influenza

- Not vaccinating may leave a transplant recipient vulnerable to infection
- All patients ***(including transplant***) should be immunized prior to discharge
- Immunization very early post-transplant
  - Decreased immune response to the vaccine

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Antiviral Prophylaxis

Oseltamavir 75 mg daily for 12 weeks

Use when vaccine is contraindicated or patient may have insufficient response; start at the beginning of influenza season
(grade I)

If live attenuated vaccine administered inadvertently: anti-viral therapy and subsequent revaccination with inactivated vaccine can be considered
(grade III)

O Manuel et al. Am J of Transplantation. 2013; 13: 212-219
Kumar D et al. Am J Transplant 2011; 11: 2020-2030

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Oseltamivir Treatment Considerations

- Prolonged viral replication in transplant patients
  - Extend course beyond 5 days to 10-14 days
  - Viral replication (PCR) may guide duration of therapy
- Dosing during severe cases
  - Doubling of the dose sometimes recommended
    - 150 mg twice daily (normal kidney function)
- Renal dosing recommendations vary (CrCl <30 ml/min):
  - Drug information database: 30 mg once daily
  - Guidelines and package insert: 75 mg once daily
- No clinically relevant interactions with immunosuppressants

O Manuel et al. Am J of Transplantation. 2013; 13: 212-219
Khana N et al. Transplant Infect Dis 2009; 11: 100-105
Lam et al. Ther Drug Monit 2011; 33: 699-704
Tamiflu (oseltamivir) [prescribing information]. South San Francisco, CA: Genentech, Inc; June 2016.

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Household Contacts

- Family members should be fully vaccinated
  - Influenza vaccine yearly (inactive preferred)
- Live vaccines if it is the only option
  - Measles, mumps, rubella, and varicella
  - Except: oral polio and small pox
- Live attenuated influenza vaccine (LAIV) & Rotavirus
  - Good use of infection prevention

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Counseling Patients

- They are safe, effective, & important to outcomes
- You may have reduced response to vaccines
- Local pharmacies can increase access to vaccination
- Ensure that you and your family members are properly vaccinated after your transplant
- Take extra precaution during flu season

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Pets

- Pets should be fully immunized
  - Little or no risk of transmission following immunization of pets with live vaccines
    - (*canine bordetella bronchiseptica intranasal*)

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Unanswered Questions & Prospective Research

- Immunosuppression
- Chronic Kidney Disease
- Impact of new viral strains
- Strategies for early vaccination (i.e. booster)
- Cost effectiveness of early vaccination
- Study Design
- Outcomes

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Care for kidney transplant patients: treatment and vaccination guidance

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