

Best Practices: Immunization Strategies and Monitoring

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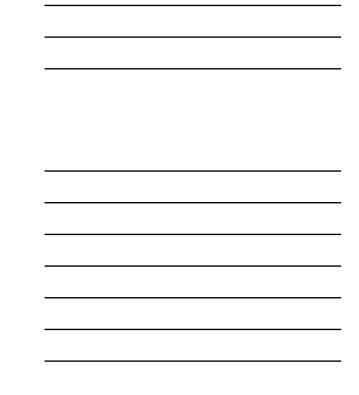
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Immunization Strategies and Monitoring *Disclosures*

- Tracey Walsh-Chocolaad None
- Maurice Alexander None
- Cathryn Jennissen None

Immunization Strategies and Monitoring Learning Objectives

- Identify clinical pearls that may be useful to consider when developing a vaccine schedule for patients post-hematopoietic stem cell transplantation (HCT)
- Explain important controversies surrounding vaccine administration post-HCT and devise strategies to individualize care



Immunization Strategies and Monitoring Learning Objectives

- Describe perspectives on immunizations following adult HCT
- Describe perspectives on immunizations following pediatric HCT



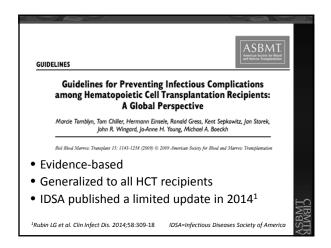
Best Practices: Immunization Strategies and Monitoring Clinical Pearls & Controversies

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Immunization Strategies and Monitoring *Overview*

- Clinical pearls
 - Monitoring for reactions following administration
 - Interference with vaccine response
 - Administering vaccines together or spread out
 - Blood products
 - Medications
- Controversies
 - Thrombocytopenia or anticoagulation
 - Recent or current immunosuppressive therapy





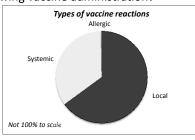
Immunization Strategies and Monitoring *U.S. Guidelines*

Advisory Committee on Immunization Practices (ACIP)

- Task force appointed by the Centers for Disease Control and Prevention (CDC)
- 15 voting members
 - Medical and public health experts
- Recommendations based on scientific evidence and expert opinion
 - Approved by CDC and published in MMWR

Morbidity and Mortality Weekly Report (MMWR) website. http://www.cdc.gov/mmwr/. Accessed January 6, 2015.

Immunization Strategies and Monitoring Clinical Pearls – Adverse Reactions Do I need to monitor my patient for a reaction following vaccine administration?



Immunization Strategies and Monitoring Clinical Pearls – Adverse Reactions

Syncope

- 80% occur within 15 minutes of vaccination
 - Sit or lie down during vaccination
 - Consider having patients wait (while sitting or lying) for 15 minutes following vaccination
 - At minimum for adolescents
 - Longer until symptoms resolve if patient feels dizzy or light headed after vaccination



Vaccine Adverse Event Reporting System (VAERS). https://vaers.hhs.gov. Accessed Dec 2, 201

Immunization Strategies and Monitoring Clinical Pearls – Adverse Reactions

Febrile seizures

- Primarily in children 6 months 5 years old
 - VZV vaccine <1 in 1,000
 - MMR vaccine 1 in 3,000

MMRV – 1 in 1,250

- DTaP vaccine 1 in 14,000
- Usually occur within 5-12 days of vaccination
- Prevention/Management
 - Acetaminophen? Requires use during entire period at risk
 - Minimize # of vaccines given at once? No evidence

DTaP-diphtheria/tetanus/acellular pertussis; MMR-measles/mumps/rubella; MMRV=MMR+varicella; VZV-varicella zoster virus MacDonald SE, et al. CMAJ. 2014;186:824-9

Immunization Strategies and Monitoring Clinical Pearls – Timing of Vaccines

Should I administer vaccines together or spread them out over multiple clinic visits?

- Most vaccines can be safely administered together while not interfering with efficacy
 - Avoids need for additional visits
 - Avoids risks of cancellations/non-compliance





Immunization Strategies and Monitoring Clinical Pearls – Timing of Vaccines

- History of febrile seizures Not predictive of future episodes
- Pediatric patients Involve them in the decision
- Inactive Vaccines Most can be administered simultaneously
 - Separate pneumococcal conjugate vaccine (PCV) and Menactra®, meningococcal (Groups A,C,Y & W-135) polysaccharide diphtheria toxoid conjugate vaccine, by at least 4 weeks^{1,2}

¹Prevention and Control of Meningococcal Disease: Recommendations from ACIP. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6202a1.htm. Accessed December 13, 2014. ²Menactra [package insert]. Swiftwater, PA: Sanofi Pasteur Inc; 2014.

LMAS

Immunization Strategies and Monitoring Clinical Pearls – Timing of Vaccines

Live vaccines – simultaneous administration¹⁻³

- 3-fold higher risk of varicella disease when given MMR and VZV vaccines on different visits (but within 28 days)
- Administer live vaccines together or separate ≥ 4 weeks

Live vaccines and blood products⁴

- Passive antibodies interfere with response to live vaccines
- Administer live vaccines 2 weeks prior to blood products or after passive antibody has cleared (range, 3-11 months)

¹Petralli JK, et al. N Engl J Med. 1965;273:198-201. ²Petralli JK, et al. Lancet. 1965;2:401-5. ³Verstraeten T, et al. Pediatrics. 2003;112:98-103. ⁴ACIP Vaccine Recommendations, Table 5. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm#Tab5. Accessed Dec 13, 2014.

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Immunization Strategies and Monitoring Clinical Pearls – Timing of Vaccines

Live vaccines and antiviral therapy

- Antivirals (i.e. acyclovir) may interfere with response to VZV vaccine
 - Stop antiviral therapy ≥ 24 hours before vaccine administration
 - Do not resume antiviral therapy until at least 2 weeks after vaccine administration

ACIP Vaccine Recommendations, Special Situations. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm. Accessed Dec 13, 2014



Immunization Strategies and Monitoring Controversies – Coagulation Disorders

My patient has thrombocytopenia or is on anticoagulation. Can I safely administer vaccines?

- Subcutaneous (SC) yes
 - Live vaccines
- Intramuscular (IM) controversial
 - Most inactivated vaccines
 - Adjuvant-containing

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Immunization Strategies and Monitoring Controversies - Coagulation Disorders

Vaccination – low platelets or anticoagulation

- Bleeding disorders (hemophilia, von Willebrand's)^{1,2}
 - Hepatitis B IM only; 4% mild bruising¹
 - Hepatitis B SC versus IM: similar efficacy, IM 2x more hematomas²
- Therapeutic anticoagulation^{3,4}
 - Influenza SC versus IM: similar efficacy and toxicity³
 - Influenza IM caused no local symptoms, no bleeding⁴

¹Evans DIK et al. BMJ. 1990;300:1694-5. ²Carpenter SL, et al. Haemophilia. Online Nov 7, 2014. doi:10.1111/hae.12569. ³Celipiente JC, et al. Pharmacother. 1998;18:631-6. ⁴Raj G, et al. Arch Intern Med. 1995;155:1529-31.



Immunization Strategies and Monitoring Controversies – Coagulation Disorders

Vaccination – low platelets or anticoagulation

- ACIP Give IM if physician deems it is safe
- Additional recommendations
 - Fine-gauge needle (≥ 23), apply firm pressure for 2 minutes, do not rub site

ACIP Vaccine Recommendations. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm. Accessed Dec 13, 2014.



Immunization Strategies and Monitoring Controversies - Immunosuppression

How does recent or current immunosuppressive therapy impact response to vaccinations?

- Corticosteroids
- Rituximab
- Others
 - Adalimumab
 - Etanercept
 - Infliximab

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Immunization Strategies and Monitoring Controversies - Immunosuppression

Corticosteroids post-HCT

- Post-HCT relapse
- GVHD
- BOS

Rituximab peri/post-HCT

- Conditioning
- Post-HCT maintenance
- Post-HCT relapse
- Chronic GVHD
- PTLD

BOS=bronchiolitis obliterans syndrome; GVHD=graft-versus-host disease; HCT=hematopoietic cell transplantation; PTLD=post-transplant lymphoproliferative disorder

Immunization Strategies and Monitoring Controversies – Corticosteroid Effect

Vaccine trials in post-HCT recipients taking corticosteroids:

- · Details lacking
 - Drug
 - Dose
 - Duration
- Correlations between immunosuppression and vaccine response inconsistent

Immunization Strategies and Monitoring Controversies – Corticosteroid Effect

CDC/ACIP — ok to administer LIVE vaccines to an otherwise immunocompetent person if corticosteroid therapy is:

- < 14 days duration
- < 20 mg/day or ≤ 2 mg/kg/day prednisone (or equivalent); maintenance, physiologic dose
- Alternate day treatment with short-acting steroids
- Route other than oral or intravenous
- →Otherwise, delay LIVE vaccines ≥ 1 month

ACIP Vaccine Recommendations

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm. Accessed Dec 13, 2014.

Immunization Strategies and Monitoring Controversies – Rituximab Effect

Rituximab effects on vaccine response

- Rheumatoid arthritis¹ trivalent influenza vaccine
 - <25% seroprotected (rituximab), 25-70% (methotrexate), 50-90% (healthy controls)
- Lymphoma² H1N1 influenza vaccine
 - 0% response (rituximab group) v 82% response (controls)
- Post-HCT
 - Pertussis response 0% in rituximab recipients³
 - PCV response **4** 50% in children who received rituximab⁴

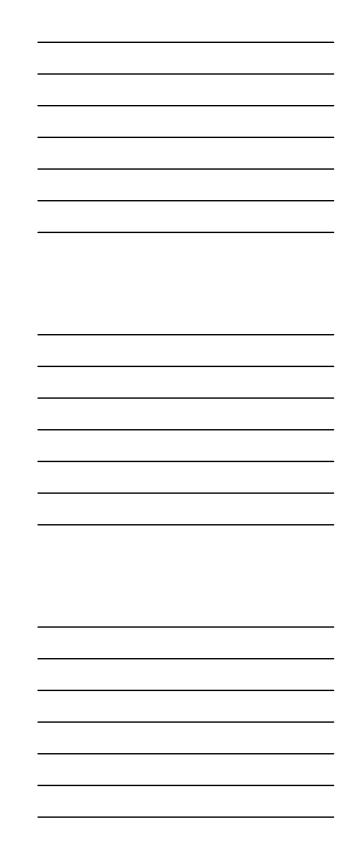
¹van Assen S, et al. Arthritis Rheum. 2010;62:75-81. ²Yri O, et al. Rituximab. Blood. 2011;118:6769-71. ³Small T, et al. BBMT. 2009;15:1538-42. ⁴Pao M, et al. BBMT. 2008;14:1022-30.

Immunization Strategies and Monitoring Controversies – Markers of Immunity

Consider measuring markers of immune competence prior to vaccination:

- B cell immunity
 - CD19+ cell # "normal" range decreases with age
 - IgG > 500 mg/dL
 - Isohemagglutinin titer ≥ 1:8
- T cell immunity
 - CD4+ > 200 cells/µL
 - Phytohemagglutinin levels >50-75% LLN

Pao M et al. Biol Blood Marrow Transplant. 2008;14:1022-30. Small TN et al. Blood. 2009;114:Abstract 1137. Kussmaul SC et al. Bone Marrow Transplant. 2010;45:1602-6.



Immunization Strategies and Monitoring *Audience Response Question #1*

Syncope following vaccine administration is most common in what age group?

- a. Young children < 5 years old
- b. Adolescents and young adults
- c. Middle aged adults
- d. Elderly
- e. Syncope is not a side effect of vaccine administration

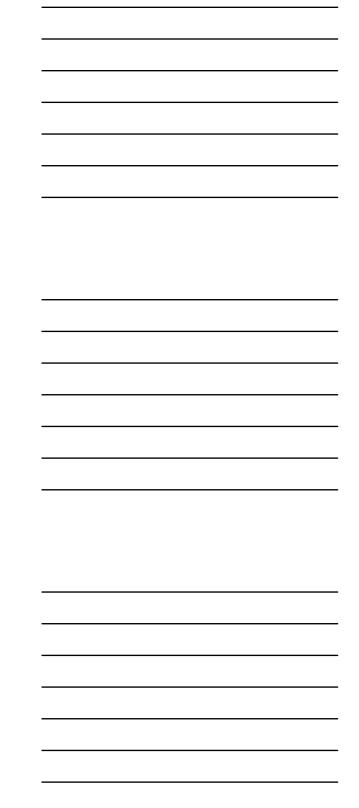
Immunization Strategies and Monitoring Audience Response Question #2

True/False: Corticosteroids only interfere with the response to LIVE vaccines. They have little impact on the response to inactivated vaccines.

- a. True
- b. False

Immunization Strategies and Monitoring Conclusions

- Monitor for reactions for 15 minutes following vaccine administration in adolescents
- Consider products that interfere with vaccine response and adjust timing of vaccines accordingly
- Do not alter the U.S. FDA-approved route of vaccine administration unless the risk outweighs the benefit
- Avoid live vaccines in patients on extraphysiologic doses of corticosteroids or within 6 months of rituximab. Avoid inactive vaccines, except in cases of outbreaks





Best Practices: Immunization Strategies and Monitoring Adult Perspectives

Maurice Alexander, PharmD, BCOP, CPP Clinical Pharmacist Practitioner, Heme/Onc/BMT University of North Carolina Medical Center

University of North Carolina BMT Program

- Staff
 - 7 Attending physicians
 - 6 Advanced Practice Professionals (NP/PA)
 - 3 Pharmacy FTEs
- Capacity
 - 16-bed inpatient unit
 - ~180 transplants per year
 - Outpatient Clinic
 - Pharmacy presence since 2010

Bone Marrow and Stem Cell Transplant Manual Policy Name BMT Program Immunization Policy Policy Number BMT 0018 Policy Number BMT 0018 Responsible for Content BMT Program • Outlines: Recommended vaccines Recommended vaccine schedule

Immunization Screening Strategies

- Daily clinic huddle
 - Identification of patients scheduled for vaccines
- Review of clinic schedule
 - Post-transplant timing
 - Immune status
 - Post-transplant complications
 - Current or recent medications

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Patient Screening and Assessment High Risk Immunosuppression

Steroid therapy	≥ 20 mg prednisone or equivalent x 14 days
Biologic immune modulators	Rituximab, TNF-α-inhibitors, IL-2 inhibitors
Active chemotherapy	2 weeks prior 3 months after
CD4 T-lymphocyte count	<200 cells/mm³

Rubin et al. Clin Infect Dis. 2014 Feb;58(3):e44-100.

Patient Screening and Assessment

- Acute illness
 - Vaccination not contraindicated: Mild illnesses (diarrhea, URI with or without low grade fever, other low-grade febrile illness)
 - Sufficient reason to postpone: moderate to severe acute illness
- Concerns
 - Superimposing adverse events of vaccine on underlying illness
 - Attributing symptoms of illness to vaccine

ACIP Vaccine Recommendations, Contraindications and Precautions http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm. Accessed Dec 14, 2014.



Patient Screening and Assessment

Anti-infectives

Antibacterials

May interfere with response to oral typhoid

Antivirals for Herpes Viruses

May interfere with response to varicella-containing vaccines

Antivirals for Influenza Virus

May interfere with response to live attenuated influenza vaccine

ACIP Vaccine Recommendations, Special Situations. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm. Accessed Dec 14, 2014.

Patient Screening and Assessment

Blood Products

2 weeks prior 3-11 months after

Intervals relevant for live vaccine administration only

Thrombocytopenia

Platelets $\geq 50 \times 10^9/L$ Absence of bleeding complications

Anticoagulation

Platelets ≥ 50 x 10⁹/L
Absence of bleeding complications

ACIP Vaccine Recommendations, Spacing of Vaccines and Antibody-Containing Products. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm. Accessed Dec 14, 2014.

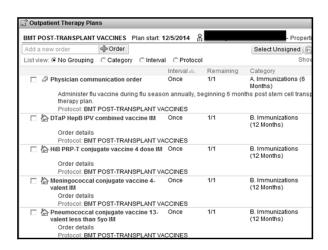
Immunization Schedule

- Initiation of immunization series
 - 6 months post-transplant influenza vaccine
 - 1 year post-transplant for other vaccines
- Timing considerations
 - Autologous vs. allogeneic patients
 - Early vs. late vaccination
 - Simplify screening efforts
- Together vs. separate
 - Each vaccine series administered together



Vaccination	6 month	12 month	14 month	16 month	24 month
DTaP		х	х	Х	
Tdap		Х	Х	Х	
Нер В		Х	Х	Х	
Hib		х	х	X	
IPV		X	Х	X	
MCV4		X	х	X	
PCV-13		X	х	х	
PPSV-23					х
MMR					х
Influenza	х				

	irus Inactivate		5 mL intramu	scularly – adı	minister durin	g flu season	annually,
beginning 6	months post	-SCT					
	Date/Lot						
DTaP, Hep	atitis B and In	activated Pol		Pediarix®) 0.		cularly - inac	tive
	Date/Lot		Date/Lot		Date/Lot		
12 month		14 month		16 month			
Haemophilu	is influenzae	type b (Hib) o		cine 0.5 mL i		ly - inactive	
	Date/Lot		Date/Lot		Date/Lot		
12 month		14 month		16 month			
Pneumocoo	ccal conjugate	vaccine (PC		-13®) 0.5 ml		arly - inactive	•
	Date/Lot		Date/Lot		Date/Lot		
12 month		14 month		16 month			
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Vaccine Monitoring

- Adverse events
 - Monitored in clinic after RN administration
- Antibody titers
 - Not routinely monitored
 - Lack of standard threshold for adequate response and subsequent revaccination
 - Vaccination timing

Donors and Household Contacts

- Donor vaccination
 - No standard donor vaccine program
 - Practical and ethical concerns
- Household contacts
 - No formal program
 - Recommend to all patients that family and close contacts follow recommended vaccine schedules

Successes and Challenges

- Screening efforts
 - Must commit to daily patient review
 - Opportunity for students and residents
- Immunization passport
- Billing and reimbursement
 - Reimbursement for pediatric vaccines?
 - Clinic nursing productivity for vaccine administration
- EMR updates
 - Transition from paper to electronic templates
 - Formulary management and template maintenance

Immunization Strategies and Monitoring *Audience Response Question #3*

JG is a 67 YOM 4 months post-allogeneic HCT . He has not begun receiving his post-HCT vaccines. He has cutaneous GVHD and has been stable on prednisone 10 mg PO daily for 3 weeks . His physician asks you about giving him DTaP, Hep B, IPV, Hib, and PCV13 vaccines today in clinic. JG also informs you that his 5-year old nephew is coming to visit and is due for his last set of booster vaccines.

What would your recommendations be regarding vaccines for JG and his nephew?

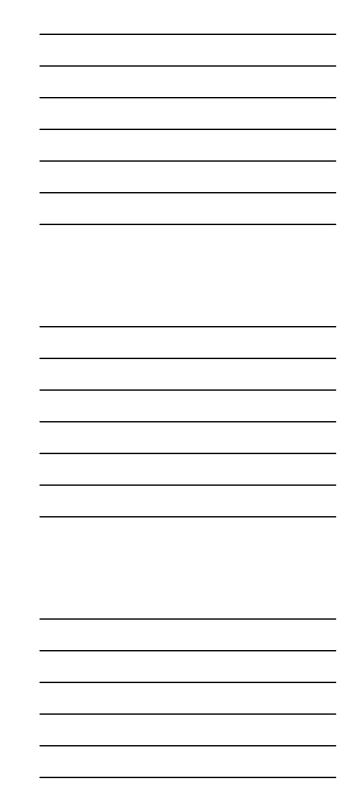
Immunization Strategies and Monitoring *Audience Response Question #3*

- a. Give all vaccines to JG and clear his nephew to receive his booster vaccines.
- b. Delay all vaccines for both JG and his nephew until he is at least 6 months post-HCT.
- Delay all vaccines for JG until he is at least 6 months post-HCT, but clear his nephew to receive his booster vaccines.
- d. Give all vaccines to JG, but delay his nephew until he is at least 6 months post-transplant.



Best Practices: Immunization Strategies and Monitoring -Pediatric Perspectives

Cathryn Jennissen, PharmD, BCOP Pediatric Clinical Pharmacist Hematology/Oncology/Hematopoietic Stem Cell Transplant University of Minnesota Masonic Children's Hospital



University of Minnesota Blood and Marrov Transplant Program - Pediatric

- 10 Attending physicians
- 5 Advanced Practice Professionals (NP/PA)
- 2 Pharmacy FTEs
- ~90 transplants per year
- 24-bed inpatient unit
- Outpatient Clinic
 - Pharmacy presence since 2007

ASBMI

University of Minnesota Blood and Marrow **Transplant Vaccination Guidelines** 14 months post HCT 12 months post DTaP Х Х Х < 7 years of age Tdap ≥ 7 years of age Х Х Х PCV13 х х IPV X X Meningococcal 11-21 years of age Quadrivalent HPV MMR Varicella Influenza (not live) Yearly administration recommended beginning pre-HCT and resuming ≥ 60 days post-HCT HPV = Human papilloma virus

Immunization Schedule

- Vaccine orders in Epic therapy plans for anniversary visits
- First vaccine: Influenza
 - >/= 60 days post-transplant (range 2-6 months)
- Other vaccinations
 - 12 months post-transplant
- Allogeneic vs. Autologous

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Future Schedule Updates

- Remove age differences and administer DTaP to all patients
 - FDA approved: 6 months to <7 years of age due to increased adverse effects to DT if > 7 years of age
 - Tdap with poor response in study with autologous patients regardless of timing to transplant 1,2
 - Adult HCT patients received DT with lower rate of local side effects compared to previously vaccinated immunocompetent adults³
 - Consistent with IDSA, ASBMT, and CIBMTR recommendations^{3,4}

IDSA = Infectious Disease Society of America, ASBMT = American Society of Blood and Marrow Transplantation, CIBMTR = Center for International Blood and Marrow Transplant Research

- . Small TN et al. Biol Blood Marrow Transplant. 2009;15:1538-1542 Papadopoulos E et al. Blood. 2008;112:2214. Rubin LG et al. Clin Infect Dis. 2014;58:e44-e100. . Tomblyn M et al. Biol Blood Marrow Transplant. 2014;15:1143-1238.

Future Schedule Updates

- Add PPSV23 as a fourth pneumococcal dose and consider giving PCV13 earlier (6 or 9 months?)
 - Study demonstrated that PPSV23 administered after 3 dose series conjugate vaccine increased response rate (RR)¹
 - Consistent with IDSA, ASBMT, and CIBMTR recommendations^{2,3}
 - Study also demonstrated that late immunization (6-9 months vs. 3 months) offers a better long-lasting response yet delays protection after HCT1
 - Is 12 MONTHS too late?
- Add 2nd MMR dose in our pediatric population
 - Multiple studies have demonstrated higher response rate to MMR in aduthan children post HSCT⁴⁻⁷
 - Consistent with IDSA, ASBMT, and CIBMTR recommendations^{2,3}

Cordonnier C et al. Clin Infect Dis. 2009;48:1382-1401.
 Rubin LG et al. Clin Infect Dis. 2014;58:e44-e100.
 Tomblyn M et al. Riol Blood Marrow Tronsplant. 2014;15:1143-1238.
 Alachado CM et al. Rone Morrow Transplant. 2005;15:787-791.
 Spoulou V et al. Rone Morrow Transplant. 2004;33:1187-1190.
 6. King SM et al. Bone Morrow Transplant. 1906;17:333-636.
 7. Lympan P et al. Jinject Dis. 1895;13:56:10-615.

Typical day of vaccination

"How many shots am I getting???"

- 12-month visit
 - DTaP-hepatitis B recombinant-IPV (Pediarix®)
 - Haemophilus B conjugate (ActHIB®)
 - Pneumococcal conjuate(Prevnar 13®)
 - Meningococcal conjugate (Menactra®)*
 - Quadrivalent HPV (Gardasil®)*
- · 24 month visit
 - DTaP-hepatitis B recombinant-IPV (Pediarix®)
 - Haemophilus B conjugate (ActHIB®)
 - Pneumococcal conjugate (Prevnar 13®)
 - Measles, mumps and rubella (MMR)
 - Varicella virus live (Varivax®)

*Based on age

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Patient assessment and screening

- Consider vaccination delay in patients with high risk immunosuppression
 - Active treatment of acute GVHD
 - No vaccines (especially live) until 6 months off immunosuppression
 - Exception: yearly influenza vaccine
 - Current chemotherapy
 - Consider delaying until 3 months post-chemotherapy
 - Biologic immune modulators
 - Within 6 months of rituximab

Patient assessment and screening

- Thrombocytopenia and/or anticoagulation
 - Physician decision on a per patient basis
- Meningococcal vaccine: Who should receive it?
 - All patients 11-21 years of age
 - Patients >21 years of age living in dormitory setting or military barracks
 - Sickle cell patients ("functional asplenia") and patients with anatomic asplenia >1 year of age

Patient assessment and screening

- · Quadrivalent HPV vaccine: Who should receive it
 - Our current protocol:
 - Females > 11 years of age and <26 years who are withou evidence of the papilloma virus
 - $1^{\rm st}$ dose: 12 months post HCT, $2^{\rm nd}$ dose: 14 months post HCT and $3^{\rm rd}$ dose: 18 months post HCT
 - No data regarding HPV vaccine in HCT recipients, so no recommendations from IDSA, ASBMT or CIBMTR
 - Next protocol update: include male HCT recipients be in line with ACIP/CDC recommendations



Vaccine Monitoring

- Adverse events
 - Monitored in clinic after RN administration
- Antibody titers
 - Not routinely monitored
 - Lack of standard threshold for adequate response and subsequent revaccination
 - Vaccination timing

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Donors and Household Contacts

- Donor vaccination
 - No standard donor vaccine program
- Household contacts

Recommendations for Use
Routine hepatitis A Vaccination is recommended in endemic areas or during outbreaks, according to existing ACIP guidelines.
Hausshird contexts: Influenza varientation is strongly recommended during sechs influenza seasone beginning in the season before the transpolar and continuing up to a least 24 nonethy no-NFCT. All household contexts of immune compromised HCT recipients should be vaccinated annually as long as these conditions persuit. Use of Philds, the nanal form of the vaccine should not be administered to the properties of the properties of the properties of the properties of the properties of the should not be in context with HCT patients for 7 days port-vaccination, as this may pose a transmission size of the virus to patient.
Vaccine (not routinely recommended for adults) should be given when indicated per ACIP guidelines. Injectable inactivated polio vaccine (IPV) is to be used.
MMR vaccination is recommended for all persons who are \geq 12 months old and who are not pregnant or immunocompromised.
If a household contact of a HCT recipient develops a post-vaccination rash within 42 days of varicella vaccination, contact precautions should be implemented. Direct chicken pox exposure in a HCT recipient with no history of chicken pox or prior vaccination should have VZV serology test and should receive antivarial therapy (acyclovar) until seropositivity is confirmed.

VACCINATIONS FOR HOUSEHOLD CONTACTS

Family Immunization Program at UMMCH

- Influenza and pertussis vaccines (when appropriate) offered free of charge to family members
 - Inactivated Influenza only
 - Specific to families that are unable to access their primary caregiver, local outpatient clinic, or local pharmacy
- Unit nurses assess families for vaccination statu



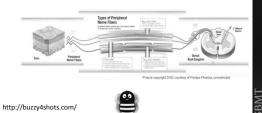
Strategies for successful vaccination in pediatric patients

"No, I don't want a shot! It will hurt!!!"

- Distraction
 - Play games
 - Watch movies
 - Child Family Life
- Schedule vaccines with sedated procedure
- Give patient control
- Numbing cream, e.g. lidocaine/prilocaine cream (EMLA®)

Strategies for successful vaccination in pediatric patients

- Other tools
 - Buzzy® "physiologic pain blocker"
 - Vibrations and cold confuse nerve fibers according to the Gate Control Theory



Audience Response Question #4

Which of the following is a recommended strategy used in the pediatric population to help provide a more "pleasant" vaccination experience?

- a. Distraction with movies and games
- b. Coordination of vaccinations with a sedated procedure
- c. Allow the child to choose which vaccines he/she will receive and which ones he/she will not
- d. Application of numbing cream prior to vaccine
- e. Answers a, b and d
- f. All of the above

