SIOP PODC Supportive Care Education

Presentation Date: 05th September 2014

Recording Link at www.cure4kids.org:
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Email: ahmed.naqvi@sickkids.ca

IMMUNIZATION IN CHILDREN WITH CANCER

Ahmed Naqvi
SickKids, Toronto

Challenges of Vaccinating Immunocompromised Children

- Safety issues
- Immunogenecity
- Decreased vaccine efficacy
- Changing immune status
- Heterogenous patient group with variable immune deficits
- Increasing use of potent immunosuppressive regimens
- Pre-immunosuppression immunization
- Vaccination of contacts to reduce exposure of the immune-compromised child
- compliance

Basic Principles of Vaccinating Immunocompromised Children

- Determine immune status
- Carefully assess risks versus benefits
- Understand that inactivated vaccines are generally safe and play an important role
- Live vaccines are generally contraindicated
- Vaccinate contacts and healthcare workers
- Follow current vaccine recommendations
- Administer vaccines before immune-suppression when possible
- Consider antibody testing to evaluate vaccine response

Heterogeneity in Hematopoeitic Stem Cell Transplant (HSCT) Recipients

- Degree of functional immune deficit
- Recipient age
- Underlying disease
- Previous treatment
- Conditioning regimen
- Source of stem cells
- Degree of human leukocyte antigen (HLA) mismatch
- Graft-versus-host disease
- Concomitant infections
- Preexisting immunity in the donor and recipients

Timing of Live Vaccines After Steroid Therapy and Chemotherapy

Therapy	Duration of Delay
Immuno ablative therapy	
AAP Red Book	At least 3 months
United Kingdom	6 – 12 months
Australia	12 months
Canada	12 months
Steroid dose	
Topical (skin or respiratory tract)	None
Local injection	None
Physiologic	None
Systemic steroids (low or moderate dose)	None
Systemic steroids (high dose) for <2 weeks	2 weeks
Systemic steroids (high dose) for ≥2 weeks	1 month

Review Article

Guidelines on Vaccinations in Paediatric Haematology and Oncology Patients

BioMed Research International
Volume 2014, Article ID 707691, 10 pages
http://dx.doi.org/10.1155/2014/707691

Table 1: Scoring system used for the recommendations.

Strength of recommendation	Quality of evidence
A: strong evidence for efficacy and substantial clinical benefit; strongly recommended	I: evidence from at least one well-executed randomized, controlled trial
B: strong or moderate evidence for efficacy, but only limited clinical benefit; generally recommended	II: evidence from at least one well-designed clinical trial without randomization; cohort or case-controlled analytic studies (preferable more than one centre), from multiple time-series studies; dramatic results of uncontrolled experiments
C: insufficient evidence for efficacy or efficacy does not outweigh possible adverse consequences; optional	III: evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees
D: Moderate evidence against efficacy or for adverse outcome; generally not recommended	
E: strong evidence against efficacy or for adverse outcome; never recommended	

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Vaccine	During chemotherapy		After chemotherapy	
	Level of evidence	recommendation	Level of evidence	recommendation
Poliomyelitis	C III	Benefit of herd immunity Postpone if lymphocyte count <1.0 X 10^9/L	B II	Booster or vaccination 6 months after stopping chemotherapy
Diphteria and Pertussis	C III	Postpone if lymphocyte count <1.0 X 10^9/L Passive immunoprophylaxis and antibiotic prophylaxis in case of epidemic	B II	Booster or vaccination 6 months after stopping chemotherapy (for diphteria adult type vaccine for age >6 years)
Tetanus	C III	Postpone if lymphocyte count <1.0 X 10^9/L Passive immunoprophylaxis, thorough hand washing and disinfection of wound and antobiotic therapy for wounds at risk.	B II	Booster or vaccination 6 months after stopping chemotherapy

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Vaccine	During chemotherapy		After chemotherapy	
	Level of evidence	recommendation	Level of evidence	recommendation
Hepatitis A virus	C III	Vaccination of seronegative patients before starting chemotherapy in highly endemic areas; alternatively passive immuneprophylaxis	C III	Booster or vaccination 6 months after stopping chemotherapy
Hepatitis B virus	B II	As above	B II	Booster or vaccination 6 months after stopping chemotherapy
Measles, Mumps, Rubella	C III	Not administered <12 months Passive immuneprophylaxis in case of contact Vaccination of seronegative family members	B II	Booster or vaccination 6 months after stopping chemotherapy

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Vaccine	During chemotherapy		After chemotherapy	
	Level of evidence	recommendation	Level of evidence	recommendation
Influenza	B II	Vaccination yearly during fall; Postpone if lymphocyte count <1.0 X 10^9/L Vaccination of family members Not administered to infants <6 months of age		
Meningo-coccus	C III	Recommended prior to splenectomy Postpone if lymphocyte count <1.0 X 10^9/L Not recommended if age <2 years	B II	Not recommeneded if age <2 years Booster or vaccination 6 months after stopping chemotherapy Booster after 3 years if vaccinated at age 2-6 years

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Vaccine	During chemotherapy		After chemotherapy	
	Level of evidence	recommendation	Level of evidence	recommendation
Hemophilus Influenzae	C III	Not administered if age <2 months Recommended prior to splenectomy Postpone if lymphocyte count <1.0 X 10^9/L	B II	Not administered if age <2 months Booster or vaccination 6 months after stopping chemotherapy
Pneumo-coccus	C II	Recommended prior to splenectomy Postpone if lymphocyte count <1.0 X 10^9/L	B II	Booster or vaccination 6 months after stopping chemotherapy
Varicella	C II	Vaccination of family members at risk Post exposure prophylaxis within 96 hours from contact	B II	Not administered if age <12 months Booster or vaccination 6 months after stopping chemotherapy

Contraindicated Vaccines in Immunosuppressed Children With Cancer and Hematopoeitic Stem Cell Transplant (HSCT) recipients

Vaccine type	Contraindicated Vaccines
Live bacteria	BCG, Ty21a Salmonella typhi
Live virus	LAIV, MMR, varicella, OPV, yellow fever, rotavirus (RV1, RV5)

Pediatr Blood Cancer

REVIEW

Vaccination Guidelines for Children With Cancer and Hematopoietic Stem Cell Transplantation Living in Resource-Poor Countries

Ahmed Naqvi, MBBS, DCH, MCPS, MRCP (UK), FRCPCH (UK),* Zehra Fadoo, MBBS, DABP, and Saima Alvi, MBBS, FCPS

TABLE I. Recommended Routine Immunization Program for Children Under the Age of 5 Years in Pakistan

Vaccine	Minimum age of first dose	Dose 1	Dose 2	Dose 3
Bacille–Calmette–Guerin (BCG)	At birth (single dose)	—	—	—
Diphtheria, Pertussis, Tetanus (DPT)[a]	6 weeks	6 weeks	10 weeks	14 weeks
Polio (OPV)[b]	At birth	6 weeks	10 weeks	14 weeks
H. influenzae type-b (Hib)	6 weeks	6 weeks	10 weeks	14 weeks
Hepatitis B	6 weeks	6 weeks	10 weeks	14 weeks
Measles	9 months	12 months	18 months	—

[a]DT should be used whenever there is a contraindication to pertussis vaccine; [b]Dose zero is given at birth. Quinvaxem® (Pentavalent vaccine: Diphtheria, Tetanus, Pertussis, Hepatitis B, and *Haemophilus influenzae* type-b) is now included in Expanded Program of Immunization for Pakistan.

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TABLE II. Recommended Catch up Schedule for Immunocompromised Children (Except HSCT Recipients) <7 Years of Age Who Start Late or are 1 Month Behind

Vaccine	Minimum age for first dose	Recommended minimum interval between doses		
		Dose 1–2	Dose 2–3	Dose 3–4
Bacille–Calmette–Guerin (BCG)[a]	At birth	Only one dose at first encounter	—	—
Diphtheria, Tetanus, Pertussis (DTaP or DPT[b])	6 weeks	4 weeks	4 weeks	6 months[c]
Haemophilus influenzae type-b (Hib)	6 weeks	4 weeks (if first dose given at age <12 months) 8 weeks (as final dose if first dose given at age 12–14 months, no further doses needed if first dose given at ≥15 months)	4 weeks (if current age is <12 months) 8weeks (as final dose if current age is ≥12 months and second dose given at <15 months of age. No further doses given if previous dose given at age ≥15 months)	8 weeks (as final dose, only for children aged 12–59 months who received less than three doses before 12 months of age)
Pneumococcal[f]	6 weeks	4 weeks (if first dose given at age <12 months) 8 weeks (if first dose given at age ≥12 months or current age 24–59 months)	4 weeks (if current age is <12 months) 8 weeks (if first dose given at age ≥12 months)	8 weeks (as final dose, only for children 12–59 months who already received three doses before age 12 months)
Hepatitis B[d]	Birth	4 weeks	8 weeks	—
Inactivated polio[a]	6 weeks	4 weeks	4 weeks	—
Measles–Mumps–Rubella[e]	12 months	4 weeks	—	—
Varicella[a]	12 months	3 months	—	—
Hepatitis A[a]	12 months	6 months	—	—
Influenza[a]	6 months		Should be given yearly	
Typhoid[a]	24 months		A single dose at first encounter	

[a]See text; [b]Any child more than 2 years of age should receive DT only, if DTaP is not available; [c]Fifth dose is required if fourth dose is given at ≤4 years of age. Interval between fourth and fifth doses is 6 months; [d]Unvaccinated children will receive three doses; [e]Second dose is recommended at 4–6 years of age. For unvaccinated children two doses can be given with a minimum of 4 weeks interval; [f]For children between 24 and 59 months, administer one dose of Pneumococcal vaccine if three doses were given previously or two doses at least 8 weeks apart if fewer than three doses were given previously.

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TABLE III. Recommended Catch up Schedule for Immunocompromised Children (Except HSCT Recipients) 7–18 Years of Age Who Start Late or are 1 Month Behind

	Minimum interval between doses		
Vaccine	Dose 1–2	Dose 2–3	Dose 3–4
Bacille–Calmette–Guerin[a]		Only one dose to be given at first contact	
Tetanus diphtheria (Td)[b]	4 weeks	4 weeks (if first dose given at age <12 months) 6 months (if first dose given at age ≥12 months)	6 months (if first dose given at age <12 months)
Hepatitis B[ac]	4 weeks	8 weeks	—
Inactivated polio[a]	4 weeks	4 weeks	4 weeks
Measles–Mumps–Rubella[d]	4 weeks	—	—
Varicella	3 months (for children <13 years of age) 4 weeks (for children ≥13 years of age)	—	—
Hepatitis A	6 months	—	—
Influenza		Annually after 6 months of age	
Typhoid[a]		Single dose to be given at first encounter	

[a]See text; [b]If available; [c]Un-vaccinated immunocompromised children will receive three doses; [d]Administer two doses with 28 days interval if not previously vaccinated

REVIEW

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TABLE IV. Re-Immunization Schedule for Allogeneic and Autologous Hematopoietic Stem Cell Transplant Recipients (HSCT)

	Time after HSCT		
Vaccine/Toxoid	12 months	14 months	24 months
Diphtheria, Pertussis, Tetanus			
Children <7 years	DPT/DTaP or DT	DPT/DTaP or DT	DPT/DTaP or DT
Children >7 years[b]	Td	Td	Td
Hepatitis B	Hepatitis B	Hepatitis B	Hepatitis B
Hib conjugate[c]	Hib conjugate	Hib conjugate	Hib conjugate
Influenza (inactivated)	Lifelong seasonal administration starting before and resuming at ≥6 months after HSCT		
Pneumococcal[a]	23PS	—	23PS
IPV	IPV	IPV	IPV
MMR	—	—	MMR
Varicella[a]	—	—	Varicella
Hepatitis A[a]	Hepatitis A	—	—
Bacille–Calmette–Guerin (BCG)[a]	—	—	BCG

[a]See text; [b]Booster doses of Td should be given every 10 years; [c]It is recommended for HSCT recipients of all ages.

Live Viral Vaccines: Oral Poliovirus Vaccine (OPV)

- Contraindicated in patients and their household contacts because of the risk of vaccine-associated polio in immunocompromised children
- Viral shedding may occur in OPV recipients for 8 – 12 weeks after vaccine administration.
- If OPV is introduced into the household of an immunocompromised child , the vaccinee should practice proper hand hygiene

Live Viral Vaccines: Varicella Vaccine

- Immunosuppressed patients are at a high risk of complications from varicella infection
- Should not be routinely administered to children who have T-lymphocyte immunodeficiency, including those with leukemia, lymphoma, and other malignant neoplasms affecting the bone marrow
- Patients who have received high dose steroids for ≥14 days should not receive varicella vaccine at least for a month
- The timing of vaccine administration is controversial
- Patient in continuous remission for at least one year with lymphocyte counts of $>0.7 \times 10^9/L$ and platelet counts of $>100 \times 10^9/L$

Live Viral Vaccines: MMR Vaccine

- Should be withheld for at least 3 months after therapy is completed
- Already immunized should receive a booster dose 6 months after therapy is completed
- Immune response 3-6 months after the completion of chemotherapy is similar to age matched healthy children
- Exposure to measles in unimmunized child Ig should be given
- Revaccination after HSCT should be delayed for at least 24 months who are no longer on immune suppression and do not have GVHD.

Live Virus Vaccines: Rotavirus Vaccine

- Contraindicated in patients with SCIDS
- Unproven safety in infants with immune deficiency

Recommendations for household contacts and health-care personnel

- All routine age-specific vaccines be given according to the local immunization schedules
- Administer MMR to all children aged ≥12 months who are likely to come in contact
- Administer inactivated influenza vaccine annually to all household members more than 6 months of age
- Immunize all contacts at risk for chicken pox with varicella vaccine. Transmission of infection after vaccination can occur rarely. If vaccine recipient develops a rash, should avoid contact with patient. In case of any symptoms of varicella in patient, consider acyclovir.

Recommendations for household contacts and health-care personnel

- Administer all household contacts with Rota virus vaccine
- All health care givers, who are non-immunized against tuberculosis, hepatitis B, Measles, Mumps, Rubella, Influenza, and varicella should be vaccinated for these diseases
- Pregnant women can safely receive adult-type tetanus and Diphtheria toxoid (Td), inativated influenza, pneumococcal, hepatitis A, and hepatitis B vaccines. All live vaccines including MMR, varicella, and live influenza are contraindicated