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Vaccination Guidelines in Immuno-compromised children

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Why think of vaccination

- Pakistan has one of the highest death rates in children
87/1000 live births
- A third of deaths are due to vaccine preventable diseases
- One of 3 countries where polio endemic remains
- Children with cancer – highly susceptible to infections with increased morbidity/mortality
- Cancer itself and use of chemo/radiotherapy

Immunization status in Pakistan

- Comparison between findings in Pakistan Demographic and Health Survey (PDHS) 2006-07 and 2012-13

Sorry state

Fully immunised children (Who have received BCG, one dose of measles and three doses each of DPT and OPV, excluding OPV0 dose).



VACCINATION SCHEDULE

Age	Vaccinations	New schedule (2010 onwards)
At birth	BCG + Polio 0	BCG + Polio 0
6 Weeks	DPT 1 + HBV 1 + Polio 1	Pentavalent + Polio 1
10 Weeks	DPT 2 + HBV 2 + Polio 2	Pentavalent + Polio 2
14 Weeks	DPT 3 + HBV 3 + Polio 3	Pentavalent + Polio 3
9 months	Measles	Measles
12-15 months		Measles 2

Factors influencing immunosuppression

- Age of child
 - Younger the age more suppression
- Underlying disease
 - ALL/AML
 - Hodgkin's Disease
 - Burkitts
 - Sarcoma
- Type of chemotherapy
 - Steroids
 - Type/dose /duration
- Splenectomy

Does pre-cancer vaccination count?

- Most cases immunity reflects the vaccination status
- Any vaccine given 2 weeks prior to diagnosis doesn't count
- T- B cell number and function decrease
- Humoral immunity affected with decrease in IgA, IgG and IgM (in 9-50%)
- Younger patients affected more
- Although memory cells persist

Can immunization be given during chemotherapy

- Live virus vaccines CONTRAINDICATED
 - Oral polio
 - MMR
 - Yellow fever
 - Rotavirus
 - Live attenuated influenza
 - Oral typhoid
 - Varicella- during maintenance some recommend but high risk of vaccine associated complication better avoided.

Can immunization be given during chemotherapy

- Inactivated – Hepatitis A, B – Hemophilus, Pneumococcal, meningococcal, diptheria, pertussis, tetanus
 - theoretically can be given in maintenance phase but very unpredictable response
- Inactivated Influenza
 - Annually – before season (> 6 months)
 - High risk of complications from influenza
 - ALC/ANC >1000, 2-3 weeks from last chemo

Seroprotection post chemotherapy

Table 1

Percentage of children with cancer with residual protection due to previous immunisation at different times after the cessation of chemotherapy.

Authors	Period of evaluation	Tetanus (%)	Diphtheria (%)	Pertussis (%)	Polio (%)	Hib ^a (%)	Measles (%)	Mumps (%)	Rubella (%)
Mustafa et al. [6]	0-12 months off-therapy	80	88	59	100	n.e.	n.e.	n.e.	n.e.
Zignol et al. [10]	0-72 months off-therapy	86	n.e.	n.e.	93	n.e.	75	72	76
Ercan et al. [11]	3-6 months off-therapy	20	34	34	n.e.	n.e.	29	29	n.e.
Nilsson et al. [18]	2-12 years off-therapy	n.e.	n.e.	n.e.	n.e.	n.e.	60	n.e.	72
Ek et al. [19]	1-6 months off-therapy	33	17	n.e.	n.e.	100	n.e.	n.e.	n.e.
Kosmidis et al. [20]	18 months off-therapy	n.e.	n.e.	n.e.	63	n.e.	87	80	80
Brodtman et al. [21]	About 2 years off-therapy	69	88	n.e.	79	35	n.e.	46	75
Van der Does-van den Berg et al. [22]	1 year off- therapy	98	98	n.e.	95	75	n.e.	n.e.	n.e.
Feldman et al. [23]	1 year off- therapy	n.e.	n.e.	n.e.	n.e.	n.e.	77	79	64

^a Hib, *Haemophilus influenzae* type b; n.e., not evaluated.

- Tetanus – 64%, range 20-98%
- Diphtheria – 65%, range 17-98%
- Pertussis – 46.5%, range 34-59%
- Polio – 86%, range 63-100%
- Hib – 70%, range 35 – 100%
- Measles – 65%, range, 29-87%
- Mumps – 61%, range, 29-80%
- Rubella – 73%, range, 64-80%

Seroprotection Post Chemotherapy

- Younger the age higher risk of loss of antibodies
 - Incomplete primary series
 - Immature B lymphocytes
- Even though Ab level low below protective range – presence of “memory cells”

Immune system recovery post chemotherapy

- Lymphocyte count return to normal within 3 months
- NK cells recovery in solid tumor – 3mths, in ALL within 1 month
- B cells recovery quickly
- CD8 and CD4 T cells require >3 mths
- Immunoglobulin levels >3mths

TABLE I. Recommended Vaccinations According to Time of Chemotherapy

Time of therapy	Recommended vaccinations
During treatment or within 6 months from the end of therapy	No vaccinations are recommended ^a Live vaccines have to be completely avoided
6 Months and later	Start a new vaccination schedule in children under 1 year of age who have never been vaccinated or who have received just one dose of vaccine Booster dose followed by the regular vaccination schedule for all the other children

^aThe administration of nonlive vaccines should be evaluated case by case according to social or epidemiological data based on the risk of contracting vaccine preventable diseases.

What schedule to follow

- For children with completed primary series
 - Check titers and then give boosters
 - Or give boosters to everyone
- For children with incomplete primary series
 - If no vaccination then according to age recommendation
 - If partially vaccinated then boosters and catch up immunization

TABLE II. Specific Recommendations for Each Vaccine

Vaccine	Recommended administration schedule
Influenza	In all immunocompromised patients, even receiving chemotherapy, especially when administered more than 3 weeks after the last chemotherapy treatment
Meningococcal ^a	6 Months from the end of therapy
Pneumococcal ^a	6 Months from the end of therapy
Hepatitis A and B ^a	6 Months from the end of therapy
HiB ^a	6 Months from the end of therapy
Diphtheria, tetanus, acellular pertussis, inactivated polio (Salk) ^a	6 Months from the end of therapy
Measles, mumps, and rubella	At least 6–12 months from the end of chemotherapy
Oral Polio (Sabin), yellow fever, and oral typhoid vaccine	Contraindicated in patients with cancer
Varicella	The vaccination should not be routinely administered. Children with ALL should not receive routinely vaccination where the incidence of varicella zoster virus (VZV) infection is decreasing. The immunization should be undertaken only at least 1 year after cessation of chemotherapy

^aThe administration of nonlive vaccines in children receiving therapy, or within the first 6 months after cessation of therapy, should be evaluated case by case according to social or epidemiological data based on the risk of contracting vaccine preventable diseases.

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
<i>Haemophilus influenzae</i> 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) 8 weeks (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	

^aSee text; ^bAny child more than 2 years of age should receive DT only, if DTaP is not available; ^cFifth dose is required if fourth dose is given at ≤4 years of age. Interval between fourth and fifth doses is 6 months; ^dUnvaccinated children will receive three doses; ^eSecond dose is recommended at 4–6 years of age. For unvaccinated children two doses can be given with a minimum of 4 weeks interval; ^fFor 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.

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

Vaccine	Minimum interval between doses		
	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	

^aSee text; ^bIf available; ^cUn-vaccinated immunocompromised children will receive three doses; ^dAdminister two doses with 28 days interval if not previously vaccinated.

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

Vaccine/Toxoid	Time after HSCT		
	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)	Pediatr Blood Cancer 2010;54:3–7 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

^aSee text; ^bBooster doses of Td should be given every 10 years; ^cIt is recommended for HSCT recipients of all ages.

Pediatr Blood Cancer 2010;54:3–7

Special considerations for Pakistan

- All children should be regarded as never immunized
- Acute shortage/unavailability – Hexa/Infranrix
- Pentavalent – DPT/HIB/Hep B – variable availability only till 14 weeks
- BCG - at least one dose
- Typhoid - injectable
- OPV – no literature available for its use

Household contacts

- All should receive their routine vaccinations
- All may receive inactivated vaccines
- All may receive MMR
- All may receive rotavirus vaccine
- All may receive varicella vaccine
- All may receive annual inactivated influenza
- **SHOULD NOT RECEIVE ORAL POLIO**
 - IPV indicated , if given strict hand washing, physical contact avoided at least 4 weeks

Household contacts – Special precautions

- Varicella vaccine
 - If vaccinee develops rash, avoid direct contact
 - if exposure no VZIG/IVIG indicated
 - If illness develops – antiviral therapy
- Rotavirus vaccine
 - All household contacts use hand hygiene measures after contact with rotavirus vaccinated infant for atleast one week.

Health Care Personnel

- All should be vaccinated
 - MMR
 - Hep B / A
 - Influenza
 - Varicella
 - TB

