Superior Health Council

Vaccination in Immunocompromised (IC) patients:
Clinical cases involving
Stem cell transplant patients
(Belgian Guidelines)

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Case n°1: Rotavirus

This baby is 1 month old. Her aunt just recently (one month ago) underwent autologous stem cell transplantation for AML. She will be living under the same roof as the baby for a couple of months. The mother would like to vaccinate her child against the rotavirus (8 weeks). The aunt wants to know if she can remain in the same household during vaccination? Should she take any other precautions, and for how long?

Case n°1:Rotavirus

Can the aunt remain living in the same house with the infant who will be vaccinated against rotavirus?

a. Yes. No precautions need to be taken.

b. Yes, but the aunt should not change the infant's diapers for **4 weeks** after vaccination.

c. Yes, but the aunt should not change the infant's diapers for **8 weeks** after vaccination.

d. No. The aunt needs to move out of the house and avoid complete contact with the infant for 1 month following vaccination.

Previous version: CSS N° 8561 (2012)

- It is important to vaccinate those close to immunocompromised patients against influenza each year, including healthcare professionals, in order to improve the protection of the patients themselves.
- The following live vaccines may be administered to those living under the same roof as the patients:
- Vaccinating those living under the same roof against Measles-Mumps-Rubella and varicella is highly advisable if they have not yet acquired immunity against these infections themselves. Temporarily avoid contact with an immunocompromised patient if a vaccinated individual develops a rash after having been vaccinated against the measles and varicella.
- The rotavirus vaccine may be administered to infants under the age of 6 months who come into contact with individuals with an immune deficiency. It is advisable to take the appropriate hygiene measures (avoid contact with faeces of babies who have been vaccinated with the rotavirus vaccine).
- The yellow fever vaccine and the oral typhoid fever vaccine may be administered to thos[illegible] is indicated for them.

No information on duration!

New version:

7.2 Safety of administration of live vaccines to close contacts of immunocompromised patients

Except for oral polio, all other live vaccines are allowed to those living under the same roof of the immunocompromised patients:

Following precautions should be taken:

- **The vaccinated close contact needs to temporarily avoid contact with the immunocompromised patient if he/she develops a rash after having been vaccinated against measles and/or varicella until the rash disappears.**
- **It is advisable for the immunocompromised patient to take the appropriate hygienic measures (avoid contact with faeces of infants who have been vaccinated with the rotavirus vaccine for 4 weeks after vaccine administration).**

Rotavirus vaccines: viral shedding and risk of transmission

Evan J Anderson

Lancet Infect Dis 2008; 8: 642–49

Rotateq®

	Age	Dose	Time shedding assessed	Number of patients who shed vaccine n/N (%)*	Vaccine transmission n/N (%)	Comments
WC3 (PRV precursor)						
Clark (1988),[53] USA	Infants	$10^{7.5}$ PFU	Day 3	2/40 (5%)	No transmission to placebo	Shedding less than 10^{5} PFU
Bernstein (1990),[62] USA	Infants	10^{7} PFU	Days 3 and 5	17/103 (17%)	NR	..
W179-9, G1 only (PRV precursor)						
Clark (1990),[53] USA	Adults (25–45 years)	$10^{7.9}$ PFU	Day 3	0/4 (0%)	NR	..
Clark (1990),[53] USA	Infants	$10^{8.3}$ or $10^{8.9}$ PFU	Day 3	0/1 (0%) in $10^{8.3}$; 0/1 (0%) in $10^{8.9}$	NR	..
Clark (1990),[53] USA	Children (1–3 years)	$10^{7.9}$ PFU	Day 3	1/2 (50%)	NR	Shedding $10^{7.6}$ PFU
Clark (1990),[53] USA	Infants	$10^{7.9}$ PFU	Day 3	3/44 (7%)	NR	Shedding less than or equal to $10^{7.6}$ PFU
Clark (1990),[53] USA	Infants	$10^{7.9}$ PFU, dose 2	Day 3	2/34 (6%)	NR	..
PRV (G1 and G2), three doses						
Clark (2003),[54] USA	Infants	10^{7} PFU (combined)	Dose 1: days 3–5	18/534 (3%)	Dose 1: no transmission to placebo	Shedding ranged from 2% to 5% (different buffer solutions). 16 participants shed G1, one participant shed G2, one participant shed G1 and G2
PRV (G1–G3, P1a), three doses						
Clark (2004),[55] USA	Infants	~4×10^{7} PFU (combined)	Days 3 and 5 and subset after each dose	Dose 1: 7/161 (4%); dose 2 and 3: 0/24 (0%)	Dose 1: no transmission to placebo	Dose 1: 5/7 (71%) shed P1a, 2/7 (29%) shed recombinant G1P1a on a WC3 bovine rotavirus genome
Clark (2004),[55] USA	Infants	~4×10^{7} PFU (combined)	Anytime after a dose	Dose 1: 12/177 (7%); dose 2: 2/28 (7%); dose 3: 0/33 (0%)	NR	Dose 1: 8/12 (67%) shed P1a, 3/12 (25%) shed recombinant G1P1a, one participant shed P1a and recombinant G1P1a in one sample and recombinant G1P1a in a second sample. Dose 2: one participant shed P1a and recombinant G1P1a, one participant shed P1a. Dose 3: no shedding
PRV (G1–G4, P1a), three doses						
Vesikari (2006),[8] 11 countries	Infants	6·7–12·4×10^{7} IU (combined)	Days 4–6	Dose 1: 17/134 (13%); dose 2: 0/109 (0%); dose 3: 0/99 (0%)	NR	..
Block (2007),[66] USA and Finland	Infants	~1·1×10^{7} IU (combined)	If symptoms	ELISA 9/650 (1%) symptoms and PRV shedding. MA104 dose 1: 1/19 (5%); MA104 dose 2: 0/5 (0%); MA104 dose 3: 0/21 (0%)	No transmission to placebo	Nine participants shed (assessed by ELISA) after at least one vaccine dose. All nine were MA104-cell-culture negative supporting shedding of non-viable vaccine. Dose 1: four participants shed before day 14, two participants shed on day 14 or after. Dose 2: two participants shed before day 14, one participant shed after day 14. MA104: P1 detected in one participant on day 3 after dose 1

Owing to space considerations, studies with limited additional data about vaccine shedding are not included in the table but are included in the references.[10,11] IU=infectious units. NR=not reported. PFU=plaque-forming unit. PRV=pentavalent bovine-human reassortant vaccine. $TCID_{50}$=tissue-culture infectious dose for 50%. *Vaccine shedding detected by virus isolation in MA104-cell culture apart from Block[66] (ELISA and subset MA104).

Table 3: PRV shedding

Rotarix®

	Age	Dose	Time shedding assessed	Number of patients who shed vaccine n/N (%)*	Vaccine transmission n/N (%)	Comments
89-12 (HRV precursor), one dose						
Bernstein (1998),[45] USA	Adults	10^{5} PFU	Days 4 and 7	0/20 (0%)	No transmission to placebo	..
Bernstein (1998),[45] USA	Seropositive children (2–12 years)	10^{5} PFU	Days 4 and 7	3/20 (15%)	No transmission to placebo	..
Bernstein (1998),[45] USA	Infants	10^{6} PFU	Days 4 and 7	3/6 (50%)	NR	..
89-12, two doses (HRV precursor)						
Bernstein (1998),[45] USA	Infants	10^{5} PFU	Days 4 and 7	Dose 1: 14/20 (70%); dose 2: 5/20 (25%)	No transmission to placebo	Shedding after either dose was 85%. HRV shedding less than wildtype by ELISA
RIX4414 (HRV), one dose						
Vesikari (2004),[46] Belgium	Adults (18–44 years)	$10^{6.1}$ FFU	Days 0 and 7	0/22 (0%)	No transmission to placebo	..
Vesikari (2004),[46] Germany	Seropositive children (1–3 years)	$10^{6.1}$ or $10^{6.4}$ FFU	Days 0 and 7	0/11 (0%) in $10^{6.1}$ FFU; 2/6 (33%) in $10^{6.4}$ FFU	No transmission to placebo	..
Zibrik (2007),[47] UK	Adults (20–45 years)	10^{6} $TCID_{50}$	Days 1–14	1/10 (10%)	NR	One participant was ELISA-positive on day 3 but MA104-cell-culture negative
RIX4414, two doses (HRV)						
Vesikari (2004),[46] Finland	Infants	$10^{6.1}$ FFU	Days 0 and 7	~40%†	No transmission to placebo	..
Vesikari (2004),[46] Finland	Infants	$10^{6.1}$, $10^{6.4}$, or $10^{6.6}$ FFU	Days 0 and 7	9/24 (38%) in $10^{6.1}$ FFU; 18/30 (60%) in $10^{6.4}$ FFU; 16/29 (55%) in $10^{6.6}$ FFU	No transmission to placebo	Dose 2 shedding less than 15% and mainly in those without response to a first dose; rotavirus detected in diarrhoeal stools from two participants given $10^{6.1}$ FFU and two participants given $10^{6.4}$ FFU collected up to 11 days after vaccination in addition to predetermined timepoints
Dennehy (2005),[48] USA and Canada	Infants	$10^{6.1}$ FFU	Days 0 and 7	92/170 (54%)		Dose 1 shedding was 48%; one participant shed 2 months after dose 1
Dennehy (2005),[48] USA and Canada	Infants	$10^{6.4}$ FFU	Days 0 and 7	92/158 (58%)	2/78 (3%)	Dose 1 shedding was 55%; one participant shed 2 months after dose 1. Two placebo recipients shed vaccine and developed IgA response (both had twin siblings in $10^{6.4}$ FFU group)
Phua (2005)[49] Singapore	Infants	$10^{6.1}$, $10^{6.4}$, or $10^{6.6}$ FFU	Dose 1: days 0, 7, 15, and 30; dose 2: days 7 and 15	Dose 1, day 7: 76–80%; dose 1, day 30: 18–24%. Dose 2, day 7: 18–29%; dose 2, day 15: 11–16%‡	3/50 (6%)	Transmission to 3/50 placebo recipients (two seroconversions). Timing of transmission—participant 1: dose 1, day 7; participant 2: dose 1, day 30 and dose 2, day 7; and participant 3: dose 2, days 7 and 15
Salinas (2005)[50] Brazil, Mexico, Venezuela	Infants	$10^{6.1}$, $10^{6.4}$, or $10^{6.6}$ FFU	Days 0 and 7	Dose 1: 35–44%; dose 2: 11–21%§	No transmission to placebo	One infant in $10^{6.6}$ FFU group shed vaccine 60 days after dose 1
Ruiz-Palacios (2007),[51] Mexico	Infants	$10^{6.1}$ FFU	Days 0 and 7	Dose 1: 43%; dose 2: 11%¶	No transmission to placebo	..
Ruiz-Palacios (2007),[51] Mexico	Infants	$10^{6.1}$ FFU	Days 0 and 7	Dose 1: 21%; dose 2: 12%‖	No transmission to placebo	..
Ruiz-Palacios (2007),[51] Mexico	Infants	$10^{6.4}$ FFU	Days 0 and 7	Dose 1: 61%; dose 2: 14%**	No transmission to placebo	One infant shed 60 days after dose 1

Owing to space considerations, studies with limited additional data about vaccine shedding are not included in the table but are included in the references.[47,48] FFU=focus-forming units. HRV=human attenuated rotavirus vaccine. NR=not reported. PFU=plaque-forming units. $TCID_{50}$=tissue-culture infectious dose for 50%. *Vaccine shedding detected by ELISA, apart from Zibrik[47] (ELISA and MA104-cell culture). †Number of vaccinated participants assessed for shedding not reported. §50 participants assessed for shedding in each group. ¶400 participants assessed for shedding. ¶Number of participants assessed for shedding dose 1: 51; dose 2: 38. ‖Number of participants assessed for shedding dose 1: 43; dose 2: 33. **Number of participants assessed for shedding dose 1: 44; dose 2: 35.

Table 2: HRV shedding

Viral shedding: particularly during the

- 1st **2 weeks** after 1st dose of Rotateq®
- 1st **4 weeks** after dose of Rotarix®

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Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Horizontal transmission of a human rotavirus vaccine strain—A randomized, placebo-controlled study in twins☆

Luis Rivera[a,*], Lourdes Mendez Peña[a], Isabelle Stainier[b], Paul Gillard[b], Brigitte Cheuvart[b], Igor Smolenov[b], Eduardo Ortega-Barria[c], Htay Htay Han[b]

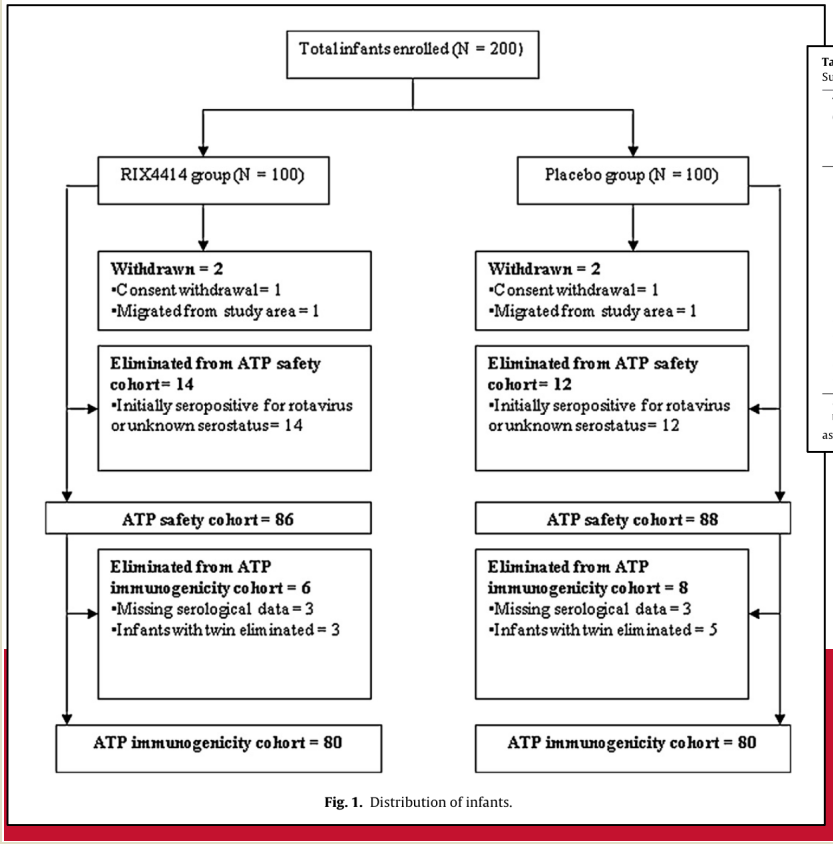

Fig. 1. Distribution of infants.

Table 1
Summary of the transmission cases.

Transmission case, *N*	Previous dose(s) of vaccine/placebo[a]	Twin receiving HRV		Twin receiving placebo		
		Start day of shedding	Duration of shedding[b]	Day of transmission	Duration of shedding[a]	Live HRV virus detected (yes/no)
1	1	Day 4	8 (D4–D16)	Day 10	8 (D10–16)	Yes
2	1	Day 2	14 (D2–D28)	Day 6	14 (D6–D28)	No
3	2	Day 8	8 (D8–D32)	Day 24	2 (D24)	No
4	1	Day 2	14 (D2–D16)	Day 14	8 (D14–D20)	Yes
5	1	Day 6	16 (D6–D34)	Day 10	4 (D10–12)	No
6	2	Day 10	4 (D10–D12)	Day 12	2 (D12)	No
7	2	Day 2	4 (D2–D4)	Day 8	2 (D8)	No
8	2	Day 2	2 (D2)	Day 8	6 (D8–D12)	No
9	1	Day 2	14 (D2–D18)	Day 14	2 (D14)	No
10	2	Day 4	16 (D4–D36)	Day 30	2 (D30)	No
11	2	Day 10	8 (D10–D16)	Day 8	2 (D8)	No
12	1	Day 10	2 (D10)	Day 8	2 (D8)	No
13	1	Day 8	10 (D8–D16)	Day 4	4 (D4–D6)	Yes
14	1	Day 2	10 (D2–D14)	Day 2	10 (D2–D14)	No
15	2	Day 6	2 (D6)	Day 2	2 (D6)	No

[a] Mean age at Dose 1 was 8.2 ± 1.80 weeks and mean age at Dose 2 was 14.2 ± 1.82 weeks.
[b] Duration of shedding in days was derived as 2 times the number of RV positive stools (the days of the first and last sample positive for RV are presented in brackets). No associated GE symptoms were reported.

Vaccine. 2011. 29: 9508-13.

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Case n°2: Vaccination post HSCT

- The aunt has been told that now that she has completed her HSCT, she needs to be re-vaccinated against many diseases. And….there are cases of measles at her niece's school.
- She makes an appointment at the consultation for "Vaccination for immunocompromised patients" and she comes to see you.
- We are now in October, and she is only 2 months post completing autologous HSCT.

Case n°2: Vaccination post HSCT

What vaccines would you administer to the patient at this time ?

a. The tetravalent vaccine against influenza in November + December.

b. A vaccine against measles (Priorix®) in November.

c. Boostrix® in October.

d. The Prevenar-13® vaccine in November.

e. a + d

Previous version: CSS N° 8561 (2012)

DISORDERS (footnotes) / VACCINES (general observations, cf. 2.4.0)	HIV CD4 < 200/mm³ (2.4.1.)	HIV CD4 200-500/mm³ (2.4.1.)	Solid organ transplantation (SOT): Heart, liver, kidney, pancreas, lung, intestine (2.4.2)	PRIOR TO bone marrow or stem cell transplantation (2.4.3.)	AFTER bone marrow or stem cell transplan-tation (2.4.3.)	Immune-mediated inflammatory diseases treated with immune modulators (2.4.4.)	Haematological malignancies & influence of chemotherapy: oncological chemotherapy (2.4.5.)
INACTIVATED VACCINES							
dTpa	S	S	S	S	A	S	S
IPV	R	R	R	S	A	R	R
Haemophilus influenzae b	NA	NA	NA	S	A	NA	NA
Hepatitis A (2.4.0.)	R	R	R	R	R	R	R
Hepatitis B (2.4.0.)	A	A	A	A	A	R	R
Influenza (annually) (2.4.0.)	A	A	A	A	A	A	A
Pneumococcal vaccine (2.4.0.)	A	A	A	A	A	A	A
Meningococcal C (conjugate) vaccine (2.4.0.)	S up to the age of 18	S up to the age of 18	S up to the age of 18	S up to the age of 18	A up to the age of 18	S up to the age of 18	S up to the age of 18
HPV (2.4.0.)	R	R	R	R	R	R	R

The full basic vaccination schedule has to be reinitiated with the **inactivated vaccines**, starting **6 to 12 months** after the transplantation, depending on the degree of cellular immunosuppression. For the actual vaccination schedules, also consult the SHC factsheet "catch-up vaccinations" (www.health.belgium.be , click on: Nl / Fr; keyword: Vaccin).

New version:

AFTER HSCT

- The same rules apply to **autologous**, and to **allogenic** HSCT.
- The full basic vaccination schedule has to be reinitiated with the **inactivated vaccines**, starting **3 to 12 months** after the transplantation, depending on the degree of cellular immunosuppression. Because of the risk of serious infections following HSCT, influenza and pneumococcal vaccinations should be initiated within the 3-6 months following HSCT. However, for vaccines against tetanus, diphteria, pertussis, HBV, and HPV, vaccination can be done at 6-12 months following HSCT, in order to obtain better immunological responses.
- Yearly influenza vaccination is recommended until complete immune recovery.

New Table

Standard vaccination for all HSCT recipients (auto/allo)

Organism	Type of vaccine	Schedule	Time after HSCT	Comments
Pneumococcus	Inactivated conjugate vaccine 13-valent (PCV13)	3 doses schedule 0-1- 2 months	3 – 6 months	
Pneumococcus	Inactivated polysaccharide vaccine (PPSV23)	1 doses schedule (at least 6 months after the last PCV13 vaccine)	6 months	In case of chronic GVHD, replace PPSV23 vaccine with a fourth dose of PCV13 (poor response to PPSV23)

Standard vaccination for all HSCT recipients (auto/allo)

Organism	Type of vaccine	Schedule	Time after HSCT	Comments
Diphteria **Tetanos** **Pertussis** **Polio** **Hib**	Combined vaccine DTPa-IPV-Hib	4 doses schedule 0 – 1 - 2 – 12 months	6 months	• Regardless of the age, paediatric formulation is mandatory because of higher antigen concentration • Tetanus Ab titre may be checked after vaccination if poor response is suspected
Hepatits B	Inactivate vaccine	3 doses schedule 0 – 1 - 6 months	6 – 12 months	• Antigen concentration may be adapted regarding the patient age • Hexavalent vaccine could be used • HBsAb may be measured 1 month after 3d dose
Influenza	Tetravalent inactivated vaccine	• Age < 9y: 2 doses (1 month interval) • Age > 9y and delay from HSCT more than 6 months: 1 dose • (2 doses if delay < 6 months)	3 – 6 months	• During the flu season
MMR	Live-attenuated vaccine	2 doses schedule 0 – 1 month	Min 24 months*	In seronegative patients and min 8 to 11 months after last IVIG injection * Contra-indicated if • GVHD • Immunosuppressive therapy (until 2 months before vaccination) • CD4 < 200/µl
Varicella	Live-attenuated vaccine	2 doses schedule 0 – 1 month	Min 24 months*	In seronegative patients and min 8 to 11 months after last IVIG injection * Contra-indicated if • GVHD • Immunosuppressive therapy (until 2 months before vaccination) • CD4 < 200/µl

Why?

- Risk of invasive pneumococcal disease [1-2]:
  - **Autologous HSCT: 3.8-5/1000 Tx cases**
  - **Allogenic HSCT: 8.2-9/1000 Tx cases**
- 6 m post Tx, 85% of patients are unprotected[3]
- Response to PPSV23 is poor: 20-30% (6-12 m post Tx)[4]
- If given 12-18m after 3 doses of PCV7 → response in >80% of patients[5]
- Response to 3 doses of PCV: 64-98% (comparable between patients vaccinated at 3m and 9 m post-Tx)[3,6-7]
- 4th dose of PCV13 at 9-12 months post HSCT increased immunological response[7]

1. Engelhard D et al. Br J Haematol. 2002. 117: 444-50.
2. Youssef S. Medicine. 2007. 86: 69-77.
3. Cordonnier C et al. Clin Infect Dis. 2009. 48: 1392-401.
4. Parkkali T et al. Bone Marrow Transplant. 1996. 18: 961-7.
5. Cordonnier C et al. Vaccine. 2010. 28: 2730-34.
6. Meisel R et al. Blood. 2007. 109: 2322-26.
7. Cordonnier C et al. Clin Infect Dis. 2015. 61: 61: 313-23
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Why?

- 33% of HSCT recipients that are infected with influenza,
  - develop lower respiratory disease
  - High mortality, despite antivirals[1-2]

- One dose of the trivalent inactivated influenza vaccine (IIV) in a cohort of HSCT recipients vaccinated 6 m post Tx:
  - 10-40% response rate within 6 months of Tx[3-5,8]
  - 10-72% response rate > 6 m (close to responses obtained from healthy individuals 2 years post Tx [6-8]

- Poor response was observed in patients with[5,8]:
  - Lymphopenia
  - GvHD
  - Rituximab
  - Hypogammaglobulinemia

Benefit of 2 doses instead of 1 has been suggested, but not demonstrated in a randomized study[5]

1. Choi SM et al. Blood. 2011. 117: 5050-56.
2. Nichols WG et al. Clin Infect Dis. 2004. 39: 1300-06.
3. Machado CM et al. Bone Marrow Transplant. 2005. 36: 897-900.
4. Ambati A et al. Transpl Infect Dis. 2015. 17: 371-79.
5. Engelhard D et al. Bone Marrow Transplant. 1993. 11: 1-5.
6. Karras NA et al. Biol Blood Marrow Transplant 2013. 19: 109-16.
7. Pauksen K et al. Clin Infect Dis. 2000. 30: 342-48.
8. Cordonnier C et al. Lancet Infect Dis. 2019. 19: e200-12.

Case n°2: Vaccination post HSCT

How would you re-vaccinate against tetanus, if the patient had received a Boostrix just 1 year before being diagnosed with AML?

a. Boostrix® in 1 month.

b. Revaxis® in 2 months.

c. Hexavalent® in 4 m + 5 m + 6 m + 16 m.

d. Boostrix, 10 years after last Boostrix®.

Previous version: CSS N° 8561 (2012)

dTpa – IPV-Hib - Hep B	**The hexavalent paediatric vaccine** may be used, even though it contains a higher dosage of **DTPa components**, because the immune system is once again "naïve", as is the case in children.

New version:

DTpa - IPV - Hib - Hep B	**The hexavalent paediatric vaccine** should be used, even though it contains a higher dosage of **DTPa components**, because the immune system is once again "naïve", as is the case in children.

Standard vaccination for all HSCT recipients (auto/allo)

Organism	Type of vaccine	Schedule	Time after HSCT	Comments
Diphteria **Tetanos** **Pertussis** **Polio** **Hib**	Combined vaccine DTPa-IPV-Hib	4 doses schedule 0 – 1 - 2 – 12 months	6 months	• Regardless of the age, paediatric formulation is mandatory because of higher antigen concentration • Tetanus Ab titre may be checked after vaccination if poor response is suspected
Hepatits B	Inactivate vaccine	3 doses schedule 0 – 1 - 6 months	6 – 12 months	• Antigen concentration may be adapted regarding the patient age • Hexavalent vaccine could be used • HBsAb may be measured 1 month after 3d dose
Influenza	Tetravalent inactivated vaccine	• Age < 9y: 2 doses (1 month interval) • Age > 9y and delay from HSCT more than 6 months: 1 dose • (2 doses if delay < 6 months)	3 – 6 months	• During the flu season
MMR	Live-attenuated vaccine	2 doses schedule 0 – 1 month	Min 24 months*	In seronegative patients and min 8 to 11 months after last IVIG injection * Contra-indicated if • GVHD • Immunosuppressive therapy (until 2 months before vaccination) • CD4 < 200/µl
Varicella	Live-attenuated vaccine	2 doses schedule 0 – 1 month	Min 24 months*	In seronegative patients and min 8 to 11 months after last IVIG injection

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Why?

- 50% of patients lose their protection against during the 1st year after TX, irrespective of donor's and recipient's serology.[1]
- The response to tetanus vaccine (3 doses), administered 6-12 months after transplantation: 85-100%[1-4]
- The response rate to diphteria vaccine (3 doses) from 3 months after allogenic HSCT, and 18 m after autologous HSCT: 70-100%[1-2]
- High doses of diphteria toxoid (DT) instead of low doses (dT):
  - **Not recommended for healthy adults, because of increased risk of adverse events**
  - **They may provide better protection than low-dose toxoid vaccines in** allogenic HSCT recipients[1]
-

1. Ljungman P et al. J Infect Dis. 1990. 162: 496-500.
2. Parkkali T et al. Bone Marrow Transplant 2007. 39: 179-88.
3. Inaba H et al. Br J Haematol.2012. 156: 109-17.
4. Parkkali T et al. BMT. 1997. 19: 933-38.

Thank you for your attention!