Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

EKIF
CFV

Eidgenössische Kommission für Impffragen
Commission fédérale pour les vaccinations
Commission federale per le vaccinazioni

Background document

Recommendations for immunization of solid organ transplant (SOT) candidates and recipients

February 2014

Recommendations for immunization of solid organ transplant (SOT) candidates and recipients

Authors

1st Author: Prof. Dr. med. Christoph Berger

Federal Advisory Commission on Immunisation
Members: R. Anderau, Neuchâtel; G. Bachmann, St.Gallen; C. Berger, Zürich; P. Bovier, Lausanne; M. Bouvier Gallacchi, Melide; A. Diana, Chêne-Bougerie; P. Diebold, Monthey; C. Hatz, Zürich; U. Heininger, Basel; P. Landry, Neuchâtel; D. Schorr, Liestal; C.-A. Siegrist, Genève; F. Spertini, Lausanne; S. Stronski Huwiler, Zürich. Secretariat: Federal Office of Public Health, Section Vaccination Programmes and Control Measures.

Recommendations endorsed by:
The Swiss Society for Infectious Diseases *(www.sginf.ch)*, the Swiss Transplantation Society *(www.swisstransplantationsociety.com)* and Swisstransplant *(www.swisstransplant.org)*.

Contents

1. Introduction

Solid organ transplant (SOT) recipients are at increased risk for infectious complications due to their chronic disease and to the iatrogenic immunosuppressive therapy required to prevent rejection of the allograft [1]. With respect to vaccine-preventable diseases (VPD) this risk includes:

- A higher attack rate and higher risks for severe and complicated illness, as documented e.g. for varicella [2, 3], measles [4, 5], influenza [6] and invasive pneumococcal disease (IPD) [7, 8];
- Higher risks of not having been optimally immunized, delays of routine vaccinations being frequently observed in patients with chronic organ diseases even before they become SOT candidates [9–11];
- Limited efficacy and duration of vaccine-induced protection in patients with chronic organ failure [12–14] and due to post-transplant immunosuppressive treatments [15, 16], depending on both the type of organ transplant and the immunosuppressive regimen [17, 18] and affecting the induction of primary responses more than the boosting of pre-existing immunity [19].

Two main periods are characterized with respect to the relative risks of VPD and vaccination recommendations: the pre- and the post-transplant period. During each of these periods, specific recommendations prevail:

- For the evaluation and the documentation of the immunization status
- For the immunization of the patient and his household.

These recommendations provide information on which vaccinations are indicated, on how to review and complete the vaccination status of the potential SOT candidate before transplantation, and on how to best evaluate the need for and the administration of catch-up and booster vaccinations in SOT recipients. For inactivated vaccines in SOT recipients, when specific data and recommendations are not available, the recommendations of the Swiss Immunization Plan (SIP) should be followed [20].

Sources of information: These guidelines are based on recent systematic and expert reviews and guidelines published in North America and Europe [18, 21–27]. Wherever possible and relevant, original studies have also been cited. Overall, there is only few data for evidence of protection by vaccination of SOT recipients. Immunogenicity data, if available in this population are often based on thresholds indicating protection in healthy individuals. These recommendations are made on the available specific data, the international guidelines for SOT patients. Given that the general recommendations for immunization in SOT patients are heavily based on routine schedules, this guideline draws on the SIP [20].

Off label use: Some of the recommendations for vaccinations provided here involve off label use, as no files including these patients have been submitted to the regulatory authorities. As such, limitations for reimbursement may apply and would have to be discussed with the patient. In addition, patient information leaflets accompanying vaccine preparations may contain general or specific precautions for the use of vaccines in immunocompromised or SOT patients. It must be stressed that for inactivated vaccines the safety profile is excellent and there are no known concerns substantiated by evidence that would prohibit their use in SOT patients pre- or post-transplant.

2. Prevention of vaccine-preventable diseases in the pre-transplant period

Transplant candidates frequently suffer from severe underlying chronic disease with a predictable clinical course eventually progressing to end-stage organ disease. Despite the increased risk for some VPD due to organ insufficiency even at the pre-transplant stage (e.g. hepatitis A in chronic liver disease [28], invasive pneumococcal disease in nephrotic patients [29]), these patients are often vaccinated with delay, incompletely or not at all [9–11]. Thus, updating vaccination to schedule and rapid catch-up have the highest priority before transplantation (basic and complementary vaccinations and specific at risk vaccinations). In order to achieve this aim once a chronic disease process has been diagnosed, it is necessary to define which immunizations have been completed, which are lacking or incomplete and which catch-up schedule is needed before transplantation to achieve optimal protection against VPD. In many cases an accelerated schedule may have to be used [23, 24], if SOT is expected in the near future.

This may also apply for patients who develop acute organ failure resulting in a need for emergency SOT, although time may be short to achieve full immunizations. In these patients, documentation of antibody responses to vaccines and careful prioritization of immunizations may be necessary.

2.1 Evaluation of vaccine-induced immunity in the pre-transplant period

Evaluation and documentation of the immunization status and the estimate of protection against VPD is of paramount importance as the incidence and the risk for severe or complicated VPD increases with progressing organ disease eventually requiring SOT, and persists thereafter. This evaluation and documentation is the basis and a prerequisite to define which vaccinations are to be completed, whenever possible before SOT, in order to achieve best possible protection of the SOT candidate and recipient. It relies on the documentation of immunizations received (immunization records) and on vaccine-induced immunity (serological analyses). The recommended approach is indicated in Table 1.

2.1.1 Vaccinations records:

Once a patient is identified as having an acute or chronic diseases likely to lead to SOT, it is necessary to periodically review and update documentation of immunizations (preferably including an electronic documentation which may be shared between carers, as for example on *www.meine-impfungen.ch*). This documentation must be available and reviewed at first contact in the transplantation centre and should be considered compulsory for listing. Note that pre-transplant documentation of completed immunizations by a healthcare professional is the strongest indicator for protection against VPD at the time of transplantation and indispensable for the interpretation of specific vaccine antibody titres. This documentation should include a documen-

Table 1
Evaluation of immunization status in the pre-transplant period

		Basic and complementary vaccines	Vaccines for high risks patients
		DT/dT, P_a/p_a, IPV, (Hib), HBV, HPV, MMR, VZV, (PCV13, MenC)	PCV13, influenza, HAV, MenACWY
Chronic disease state	Immunization records	Review immunizations from vaccination records, define the catch-up needed for completion and keep updated documentation available. Initiate catch-up vaccination program where necessary (Table 3).	According to underlying disease; plus seasonal influenza; HAV in patients with liver disease
	Serological analyses	Generally not recommended.	Generally not recommended.
Progression to end-stage organ disease	Immunization records	Review immunizations from vaccination records, define the catch-up needed for completion and keep updated documentation available. Initiate catch-up vaccination program where necessary (Table 3).	
	Serological analyses	Serological evaluation to document baseline and post-vaccination immunity and to guide further vaccinations (Table 2). This should be completed during the pre-transplant period and at the very latest at the first visit to the transplant centre, at listing.	
SOT candidates	Immunization records	Collect immunization status at the first visit to the transplant centre, at the latest at listing (the earlier the better) and keep up to date documentation available throughout:	
	Serological analyses	Serological evaluation to document baseline and post-vaccination immunity and to guide further vaccinations (Table 2). This should be completed during the pre-transplant period and at the very latest at the first visit to the transplant centre, at listing.	

Abbreviations for vaccines: DT/dT, diphtheria tetanus; P_a/p_a, acellullar pertussis; IPV, inactivated polio; HBV hepatitis B; HPV, human papilloma virus; MMR, measles mumps rubella; VZV, varicella; MenC, conjugated meningococcus C; PCV13, 13-valent pneumococcal conjugate vaccine; HA, hepatitis A; MenACWY, quadrivalent meningococcal conjugate vaccine.

tation of disease history where relevant, for example for hepatitis B or varicella infections.

2.1.2 Immunity against VPD (serology):
Documentation of immunity against all VPD (Table 2) should be achieved before transplantation. Because it may not be possible to assume protective immune responses even from a complete vaccination history as in healthy persons, the documentation of the vaccination status in SOT recipients as well as in SOT candidates with end-stage organ disease should be completed by the determination of specific antibody titres.
Determination of antibody levels as a surrogate marker for protection may be helpful when:

- it is unclear whether there is immunity (after disease or by immunization) against particular VPD
- the need for a booster immunization (e.g. tetanus, hepatitis B) must be assessed
- the response after completed primary or a booster immunization needs to be evaluated
- it is desirable to assess the likely (long term) protection.

The correlation of antibody levels with protection is best when the level is measured 1–3 months after completion of a primary immunization series or a booster dose. Immunity from vaccines/infections that confer sustained protection (e.g. measles, VZV) may be checked at all times.
Based on data from healthy persons, correlates of protection have been established for tetanus, *Haemophilus influenzae* type b, hepatitis B, measles, rubella and varicella antibodies (Table 2) and should be determined to define which vaccinations are still needed. Antibodies to hepatitis A and yellow fever also indicate immunity. Based on these results a catch-up schedule can be designed, including required booster doses.
In patients with end-stage organ disease, antibody levels should be determined again after immunization to document vaccine-induced immunity. Specific antibody levels against other VPD such as pertussis, mumps, HPV, meningococcal infection or influenza have either not been characterized, are not established, not available, not required to demonstrate protection or lack a correlate for protection.

2.2 Immunizations in the pre-transplant period

Completion of basic and complementary immunizations for patients with a chronic organ disease likely to result in SOT is vital to ensure optimal protection against VPD. Every effort should thus be made to ensure that transplant candidates, including their close contacts, are completely vaccinated as early as possible and in any case prior to transplantation [21–26].
The need for individual catch-up vaccinations pre-transplant is the result of the evaluation of the vaccination record and of the determination of specific vaccine antibody levels. Evaluation of the immunization records should lead to:

- catch-up basic vaccinations, including those against tetanus, diphtheria, pertussis, polio (IPV), measles, mumps, rubella, as well as for children < 5 years of age also conjugated vaccines against *Haemophilus influenzae* type b, and against pneumococcal disease, and children < 5 years and adolescents 11–19 years of age against meningococcus serogroup C [20].

Table 2
Correlate of immunity to be checked, reached and documented

Vaccine	Indication for determination of specific antibody titres				Specific antibody (IgG) and unit	Interpretation of serological analyses		
	During end-stage organ disease	At pre-transplant (listing)	After catch-up immunization (pre- or post-transplant)	Post transplant		Susceptible	Some protection	Long term protection
Tetanus	Yes, if history unclear (§)	If unknown serology	Yes	At 12 months	Anti-tetanus toxoid (IU/l)	< 100	≥ 100	≥ 1000
***Haemophilus influenzae* type b**	Yes (children < 5 years)(§)	Yes, (If unknown serology in children < 5 years)	Yes (children < 5 years)	At 12 months	Anti-PRP IgG (mg/l)	< 0.15	≥ 0.15	≥ 1
Hepatitis B	Yes (#, &)	Yes, if unknown serology	Yes (#)	Every 12 months (¥)	Anti-HBs IgG (IU/l)	< 10	≥ 10 (¥)	≥ 100 (¥)
Measles	Yes	Yes, if unknown serology	Yes	At 12 months	Measles IgG, by EIA (IU/l)	< 50 (*)	50-149 (*)	≥ 150 (**)
Rubella	Yes	Yes, if unknown serology	Yes	Not if immune before SOT	Rubella IgG (IU/ml)	< 10	≥ 10	
Varicella	Yes	Yes, if unknown serology	Yes	At 12 months	VZV IgG or VZV-gp (IU/l)	< 50 (*)	50–149 (*)	≥ 150 (*, **)

§ If history unclear, check antibody titre 4 weeks after a booster dose to define whether further doses are needed.
# Check anti-HBs IgG titre if last dose given < 5 years ago, or 4–12 weeks after completion of primary series or a booster dose;
& Include HBsAg and anti-HBc to exclude current/past infection.
¥ In immunosuppressed SOT patients, the unknown contribution of immune memory requires regular booster doses to maintain anti-HBs titers ≥ 10 IU/l at all time in patients at risk of exposure.
* Measles and VZV IgG, by commercially used tests; if positive= immune, if negative or doubtful: send serum for analysis by a more sensitive test [30] to the Laboratoire de Vaccinologie des Hôpitaux Universitaires de Genève.
** Loss of pre-existing immunity to measles / VZV may occur in SOT patients.

- identify and immunize patients not yet immune against varicella and hepatitis B (importance of ascertaining infection status) and trigger their immunization.
- identify females > 9 years of age not yet immunised against HPV. Vaccination of boys against HPV may be considered given the enhanced risks of cancer in immunosuppressed patients.
- administer or catchup vaccines recommended to high-risk patients (including vaccines against influenza, pneumococcal disease, hepatitis A, as well as varicella and hepatitis B (see above) and consider particular exposition pre- and post-transplant (TBE, rabies, yellow fever etc.).

Any missing vaccinations identified before transplantation should be administered as soon as possible, as indicated in Table 3.
Table 4 shows the recommended accelerated schedule for vaccination of SOT candidates based on international recommendations and the SIP [20, 23, 24]. This schedule gives the minimal age for each particular vaccine and the scheme with the shortest possible immunization series.

Live vaccines (MMR, VZV, YF) should no longer be administered after the patient is included on an emergency transplantation list and SOT is considered as likely within 4 weeks.
Specific antibody levels have to be checked after specific vaccination, as described above in Table 2. If protective levels are not reached, additional immunizations and serological controls are recommended.
Additional information on immunizations during the pre-transplant period is included in section 5.

3. Prevention of vaccine-preventable diseases in the post-transplant period

Impaired immune response under continued immunosuppression in SOT recipients is associated with an increased incidence and risk for more severe and complicated VPD through:

- Waning (and/or delayed and partial recovery) of pre-transplant immunity [32].

Table 3
Completion of immunizations in the pre-transplant period

	Vaccine immunogenicity	Basic and complementary vaccines	Vaccines for high risks patients	Documentation of immunizations
		DT/dT, P_a/p_a, IPV, (Hib), HBV, HPV, MMR, VZV, (PCV13, MenC)	PCV13, influenza, HAV, MenACWY	
Chronic disease state	Normal or already reduced (but better than later!)	To update according to SIP [37] + include VZV and HBV vaccines already during child-hood, consider HPV for boys.	Yearly seasonal influenza; HAV immunization if liver disease (*).	Documentation of immunization status in immunization record.
Progression to end-stage organ disease	Normal or already reduced (but better than later!)	To update according to SIP and to serological analyses. Use accelerated immunization schedule if needed.	Yearly seasonal influenza; HAV immunization if liver disease (*); PCV13 if severe disease; PCV13 + MenACWY if splenic dysfunction	Documentation of immunization status and of serologies (+/–) in immunization record.
SOT candidates	Normal or already reduced (but better than later!)	To update according to SIP and to serological analyses. + Use accelerated immunization schedule if needed. + No live vaccine if included on emergency transplantationlist.	– Yearly seasonal influenza; HAV immunization if liver disease (*). + PCV13 immunization at time of listing. + MenACWY if splenic dysfunction	Documentation of immunization status and serologies (+/–) in immunization record and in the referral letter to the transplant centre.
Household contacts	Normal	To update according to SIP [37] + Including VZV vaccines already during childhood.	Yearly seasonal influenza immunization.	Documentation of immunization status in immunization record and in the referral letter to the transplant centre.

(*) Consider exposition / travel vaccines as TBE (FSME), rabies, Hepatitis A, Yellow Fever, meningococcal infections, etc. according to exposition risks before and after transplant. Special consideration should be given to yellow fever immunization which will remain contraindicated after SOT.

- Exposure to VPD through non-immune close contacts [23].

3.1 Evaluation of vaccine-induced immunity in SOT recipients

Evaluation and documentation of the immunization status and the estimate of protection against VPD is of paramount importance as the incidence and the risk for severe or complicated VPD increases with progressing organ disease eventually requiring SOT, and persists thereafter. This evaluation and documentation is the basis and a prerequisite to define which vaccinations are to be completed to achieve the best possible protection of the SOT recipient.
The approach to evaluation of immunization status in post-transplant patients is outlined in Table 5. Please refer to Table 2 for correlates of immunity to be reached and documented.

3.2 Immunizations of SOT recipients

Immunization post-transplant is necessarily limited by immunosuppression, and live vaccine in general must not be used (varicella see below). In addition, vaccine responses under transplant-associated immunosuppression are impaired to a greater extent than during the chronic disease pre-transplant stage. Nevertheless, inactivated vaccines provide some protection [18] and these should be used whenever necessary despite their limitations.

The following principles have to be considered:

- The ability to mount and/or maintain an appropriate immune response to immunizations is impaired by immunosuppression. This affects primary vaccination series more than boosters.
- There is no evidence to associate solid organ rejection episodes to vaccination, even with live or adjuvanted vaccines [21], [30, 33–38]. In contrast, there is an association between infection including VPD as e.g. influenza and rejection episodes [39, 40]. In paediatric SOT recipients, infections exceed rejection episodes as a reason for acute hospitalisation [41].
- Live vaccines are in general contraindicated or to be used with extreme caution in SOT patients [42]. The administration of such vaccines to close contacts, however, may provide relevant protection [43]. Special considerations apply to varicella immunization (see below).
- To maximize vaccine efficacy, post-transplant immunizations should not be undertaken during the phase of maximum immunosuppression [44]. Some agents, such as mycophenolate mofetil, seem to have a strong negative effect on the ability to mount antibody responses to vaccination [45, 46]. Similarly, it is not recommended to immunize during an episode of rejection requiring intensification of immunosuppression.
- The decision when to start immunization post-transplant has to balance the higher risks of exposure and susceptibility for VPD early after SOT and the lower immune

Table 4
Recommended accelerated vaccination schedule in the pre-transplant period

Vaccine	Minimum age	# doses	Schedule (minimal interval in months)
DTP$_a$, IPV	6 weeks (>7 years dTp$_a$)	first dose <age 1 year: 4 doses ≥1 year: 3 doses	0, 1, 2, + 1x ≥12 months [1, 2] 0, 1, 6 [1, 2]
dT(p$_a$) booster	8 years	1 dose every 10 years	
Hib	6 weeks	first dose <1 year: 4 doses 12–59 months: 2 doses	0, 1, 2, + 1x ≥12 months [1] 0, 2
Hepatitis B	Birth	3 (hexavalent vaccines or rapid schedule: 4 doses; 11–15 years: 2 adult doses)	0, 1, 4 (1–3 primary doses + booster after ≥4 months)
Hepatitis A	6 months (off label <1 years)	2	0, 4
PCV13	6 weeks (off label >5 years)	first dose <1 year: 3–4 doses 1 year: 2 doses >1 year: 1 dose	0, 1, 2 + 1x ≥12 months [1]
Influenza	6 months	children <9 years: 2 doses in first season	if 2 doses: 4 weeks interval.
MMR	6 months	2 doses	0,1 [3, 4]
Varicella	6 months	2 doses	0,1 [3, 4]
HPV (women)	9 years	2 doses if first dose <15 years; 3 doses if first dose ≥15 years	0, (1), 4
MenACWY conjugate[5]	1 year (off label <11 years)	2 doses (+ booster to be considered every 5 years)	0, 2

[1] 3 doses in the first year of life: 4. dose a) >6 months after dose 3 and b) after 12 months of age.
[2] further DTP$_a$-IPV at age 4 (–7) years, see SIP
[3] not recommended if emergency listing with likelihood of SOT within 4 weeks (live attenuated vaccine)
[4] if first dose <12 months of age, give 2nd dose after 12 months of age or include a 3rd dose after 12 months of age.
[5] prefer MenACWY conjugate vaccine to polysaccharide vaccine [31]

competence under intense iatrogenic immunosuppression during the first months after SOT. Thus, at present it is recommended to wait for 6 to 12 months after SOT before revaccination (with inactivated vaccines) [23]. A notable exception is immunization against seasonal influenza, which may be recommended at all times after transplant to hopefully elicit at least partial immunity.

- Waning immunity has been recognized in previously immunized SOT recipients with positive antibody titres before and lower/undetectable titres after transplantation [24]. Breakthrough disease and liver rejection has also been documented in a previously immunized liver transplant recipient [47]. Factors such as the administration of a single instead of two vaccine doses, the type of immunosuppression (use of mycophenolate mofetil) or the failure to maintain an immunologic memory all may contribute to the observed waning of immunity [17, 24, 32, 48–51]. Despite waning immunity, immunization before transplant generates immune memory which can often be successfully boosted post-transplant.

Thus, pre- and post-transplant immunizations are important and likely to provide the best possible protection against VPD.
Table 5 indicates how to evaluate, elicit or update vaccine-induced protection in SOT recipients. Note that it is essential for every period :

1. to review immunization records to identify missing immunizations.
2. to document immunization status in the immunization record.

When vaccinations are administered post-transplant (Table 5), a normal immune response cannot be assumed. As opposed to routine immunizations in otherwise healthy individuals, it is therefore recommended to assess specific vaccine antibody responses to as surrogate markers for protection (Table 2) and to define if additional doses should be recommended.

4. Cocooning: Immunization of close contacts of SOT recipients

Close contact persons of SOT patients are the family members (persons living in the same household) as well as the health care personnel taking care of SOT recipients. The immunization status of all close contacts should be reviewed along the schedule suggested in the SIP and missing vaccinations should be completed as soon as possible. Due to the high risk of the following VPD for SOT recipients and the potentially incomplete protection of SOT recipients, the immunity of close contacts against these VPD should be checked and or induced by vaccination. Close contacts should be evaluated for immunity by history (e.g. varicella) and if immunity is unknown or the person is not immune, the following vaccinations are recommended (evidence II-2) [23]:

Table 5
Evaluation and completion of immunizations in SOT recipients

	Evaluation (see also pre-transplant evaluation)	Immune competence and vaccine responses	Basic and complementary vaccines	Vaccines for high risks patients
			DT/dT, P_a/p_a, IPV, (Hib), HBV, HPV, MMR, VZV (PCV13, MenC)	PCV13, influenza, HAV, MenACWY
6 months after SOT	Immunization record: review and identify missing vaccinations, including 1x PCV13 before SOT. Serological analyses: none	Markedly reduced	Generally not recommended	Yearly seasonal influenza; PCV13 if not received at listing
12 months after SOT	Immunization record: to review	Reduced (proportional to immunosuppression regimen)	To update according to serological analyses.	Yearly seasonal influenza
	Serological analyses: Tetanus, (Hib), HBV, measles, VZV		No live vaccine	PCV13 booster dose for all SOT recipients
Follow-up post-transplant period	Immunization record: to review Serological analyses as needed based on individual history, immunosuppression and risks of waning of vaccine-induced immunity (VZV, measles, HBV, S. pneumoniae		Catchup + update of inactivated vaccines (varicella see below) according to SIP [37] and serological analyses.	Yearly seasonal influenza immunization
Household contacts	Immunization record: to review	Normal	To update according to SIP [37] including VZV vaccines already during childhood	Yearly seasonal influenza immunization

Table 6
Immunizations for cocooning

Vaccine	Indication	Dose
Influenza	**All**	**Yearly**
Varicella	If negative history: serology* if negative serology: immunize	2 doses (interval >4 weeks)
MMR	If 2 doses are not documented: immunize	2 doses (interval >4 weeks)
Hepatitis B	All close contacts if not yet immunized	3 doses (0,1,6 months)

* not needed in young children with negative history

As a general principle, non-live vaccines should be preferred to live vaccines for close contacts of immunosuppressed patients if available (for example inactivated IPV and influenza vaccines instead of live oral polio or nasal influenza vaccines). However, there is no identified risk of transmission of MMR and minimal risk of transmission of VZV vaccines from close contacts [43]. The protection of the SOT recipient from transmission of wild type virus thus largely outweighs the only theoretical risks associated with the use of live attenuated vaccines for close contacts.

5. Recommendations for individual immunizations in the pre- or post-transplant periods

This section provides the baseline evidence on which the current recommendations are based.

5.1 Basic and complementary immunizations

dTp_a (IPV)
There are no data on the incidence or severity of tetanus, diphtheria, or pertussis in transplant recipients. Vaccination with DTP_a/dT is safe and immunogenic in paediatric populations with end-stage renal and/or end-stage liver disease and immunogenic in paediatric SOT recipients [18, 52, 53]. Antibody responses are reduced and antibodies are lost at a more rapid rate in SOT recipients compared with healthy controls [18, 52, 54]. In accordance with the SIP, DT/dT(P_a/p_a) and IPV should be administered to SOT candidates as

detailed in the general schedule. DT/dTP$_a$/p$_a$ as inactivated vaccine can be given to post-transplant patients [21–23]. Although limited, there is some evidence that this inactivated vaccine is efficacious in SOT recipients [18, 19].

***Haemophilus influenzae* type b (Hib)**
Immunization against *Haemophilus influenzae* type b should be considered according to recommendations for the vaccination of less than 5-year-old children in the SIP. It is not recommended in children older than 5 years and in adult SOT candidates and recipients. In children with end-stage organ disease it is recommended that antibody titres should be checked and a booster dose given if the titre is below the threshold (Table 2). Hib immunization post-transplant is expected to be less imunogenic than before. Nevertheless it is recommended in children < 5 years of age requiring catch-up, as it is reported to be effective in well-functioning paediatric renal allograft recipients [55].

MMR
In the pre-transplant period, two doses of MMR vaccine at least one month apart are recommended. The first MMR dose is usually recommended at the age of 12 months, but can be performed at the age of 6 months if required [20]. It is crucial to give two doses up to one month before transplantation, as this vaccine is contraindicated thereafter. If earlier vaccination is not documented, the adult transplant candidate (born after 1963) should be considered non-immune and receive two doses of MMR before transplantation. In cases of doubt, serological evaluation may help confirm immunity (Table 2).
Currently, there is insufficient data to generate evidence-based guidelines for the use of MMR in transplant recipients under immunosuppression. Preliminary data on efficacy and safety suggest that the use of MMR in paediatric SOT recipients could be a reasonable strategy [42, 56, 57] and one study is currently ongoing in Switzerland with liver transplant children (Posfay-Barbe, K, personal communication). Indeed, additional evidence is needed before this can be widely recommended. Meanwhile the importance of pre-transplant immunization of SOT candidates and close contacts cannot be overemphasized.

Hepatitis B
SOT recipients may have more severe and more rapidly progressive hepatitis B (HBV) infection and may also reactivate latent disease while under immunosuppression [28, 58, 59]. HBV vaccination may provide protection against donor derived infection, particularly important in settings where HBV is endemic [60–62]. HBV vaccination is recommended for patients with end-stage renal and liver disease [20, 23]. Where unknown, HBV serology including the assessment of evidence of past or active infection (presence of HBs-antigen, anti-HBs and anti-HBc) must be assessed before any further steps including immunization. If there is evidence of past or active HBV infection, further evaluation (HBV-DNA, liver biopsy, indication for antiviral treatment) of the candidate in discussion with liver and infectious diseases specialists must be undertaken. In the HBV naïve SOT candidate or recipient the standard immunisation series is to be used with 3 doses (see SIP) and anti HBs serology checked 1–3 months after completion. Since response to primary HBV vaccination may be impaired in patients with cirrhotic liver or chronic renal disease, it is particularly important to start immunizations as early as possible in these patients if HBV vaccines were not administered as part of routine immunizations [63]. As for most vaccines a poorer response has been described for patients post-transplant compared with the normal population [64, 65] with some evidence of the benefits of receiving primary HBV immunisations prior to SOT with good response to boosters in this group [66].
Since there is a strong correlation between post-vaccination titres and the protective effect of HBV immunisation, monitoring of anti-HBs serology post-immunisation is recommended in SOT candidates and recipients. If 4 weeks after the primary course the anti-HBs titre is < 10 IU/l 3 additional doses should be administered. Thereafter if the titre remains < 10 IU/l, administration of combined vaccine against Hepatitis A and Hepatitis B (Twinrix®) or high dose HBV vaccine (40ug HBs-antigen) can be tried and has variably been reported to be more or less successful [67–73]. Monitoring of anti-HBs titres after primary immunization series, at pre-transplant evaluation and after transplantation is recommended with subsequent application of booster doses if the titre is < 10 IU/l [22, 66]. An anti-HBs titre > 100 IU/l should be documented 4 weeks after boostering.

HPV
Transplant recipients with anogenital HPV infection are at 20–100-fold increased risk of cervical intraepithelial neoplasia and other anogenital malignancies [74, 75]. At the present time, no published studies of immunogenicity of this vaccine in transplant recipients and candidates are yet available [76]. Since it is an inactivated vaccine, it could theoretically be safely given after transplantation. For optimal response, it is however preferable to administer HPV vaccine to SOT candidates before transplantation to girls aged > 9 years. However, HPV vaccines are very immunogenic and should be considered for any transplant patient at risk of exposure. The use of HPV vaccine may also be considered in boys > 9 years of age.

MenC disease
Transplant recipients may be given MenC conjugate vaccine according to the SIP (1–5 years and 11–19 years). Immunization against MenACWY is recommended to patients with splenic dysfunction or other risk factors [31] see in the section immunization for high risk subjects below.

Pneumococcal disease
Immunization against invasive pneumococcal disease with 13-valent pneumococcal conjugate vaccine should be considered according to recommendations for the vaccination of less than 5-year-old children in the SIP. Immunization of groups at thigh risk for invasive pneumococcal disease including transplant candidates and recipients [77] see immunization of high risk subjects below.

Immunizations for high risk subjects

Influenza
Influenza infection in patients with chronic illness and SOT recipients is associated with increased morbidity and mortality, including severe pulmonary and extrapulmonary

complications and may lead to decompensation [36, 78–80]. Immunosuppressed patients with influenza infection have prolonged viral shedding [81, 82] and are at increased risk of allograft rejection [36, 83, 84]. In contrast, influenza immunization is not associated with a risk for development of allograft rejection after vaccination [33, 35, 36, 85, 86].
The influenza vaccine has been shown to be safe in SOT recipients, but to yield adequate antibody responses only in a part of SOT recipients [85, 87–89]. The specific immunosuppressive regimen might contribute to the size of any impairment of the response to the vaccine [45, 90–93]. Given the limited immune response to influenza vaccinations in SOT recipients, approaches to increase the immune response have been tried using intradermal application [94–96] or using, for example, MF-59 adjuvanted vaccine [97–102] with variable success.
Annual influenza vaccination is recommended for all patients with progressive chronic organ disease likely to eventually result in SOT, SOT candidates and recipients, beginning 6 months after transplantation. Earlier vaccination during the period of maximum immunosuppression during the first 6 months post-transplant has been shown to produce low antibody titres in recipients of kidney transplants [103]. To increase the immune response, SOT recipients may be given a two-dose course of influenza immunization instead of an annual single shot after individualized risk assessment, but current data do not allow for recommending an annual two dose schedule [18, 87, 104–108].

Invasive pneumococcal disease
Invasive pneumococcal infections can cause significant morbidity and mortality in SOT recipients [109]. Pneumococccal vaccination is currently recommended in patients with chronic organ disease, including e.g. cardiovascular, renal, and liver disease (see SIP) [20, 23], as well as in SOT candidates and recipients [23]. As with other vaccines, protective antibody titres are less reliably induced and known to decrease with time in patients with end-stage renal or end-stage liver disease and even more after SOT [110–112]. Thus vaccination is recommended to be given as early as indicated [77] in patients with chronic disease.
Available vaccines include the 13-valent conjugate vaccine (PCV13) and the 23-valent polysaccharide vaccine (PPSV23). Vaccination for children < 1 year at risk includes PCV13 given as a four-dose series (2, 4, 6, and 12–15 months)[20]. Children < 5 years of age and immunocompromised children of any age who have been previously fully immunized with the PCV7 should receive one supplemental dose of PCV13. The data on immune responses to PCV (PCV7) in paediatric SOT recipients show that despite a response to initial vaccination, those to subsequent doses are lower and more transient than in healthy controls [113].
While the immune response in adult SOT recipients and other immunocompromised persons after one dose of either PPSV23 or PCV7 were similar after priming with PCV7 and boosting with PPSV23 [114, 115], another study in children showed impressively good responses in children given 2–3 doses of PCV7 only after > 1 year after transplantation [116]. The available data from SOT recipients and other immunocompromised persons, including in particular those with impaired T-cell function as in HIV infection or after stem cell transplantation show increasing evidence for better efficacy and non-inferior immunogenicity of PCV in comparison with PPSV [117–123]. Based on these findings, the short and limited effect of PPSV23, the risk for hyporesponsiveness after repeated immunization with PPSV23 and the small difference in the coverage of the additional 10 serotypes only included in PPSV23 given the current epidemiology of invasive pneumococcal disease in Switzerland, PPSV23 is not recommended instead of or in addition to PCV13 in SOT candidates and recipients.
As PCV13-induced protection is also likely to be limited in time, one dose of PCV13 should be administered at listing and immunity boosted with a 2nd dose at 12 months after SOT. If a patient was not vaccinated with PCV13 before SOT, PCV13 catch-up should be given at 6 months post transplant. The booster dose at 12 months post-transplant, when immunosuppression is reduced, remains recommended regardless of the interval since the last dose.
PCV13 has been licensed by FDA and EMA (but not by Swissmedic) for immunocompromised persons with high risk for invasive pneumococcal infections and is recommended for such patients by the CDC/ACIP since 2012 [124]. Due to the lack of licensure of PCV13 use in adults by Swissmedic, this recommendation is off-label and may thus not be reimbursed by health insurances in Switzerland.

Invasive meningococcal disease
Immunization against MenACWY should be recommended to all SOT candidates and recipients with splenic dysfunction. The conjugate vaccine (Menveo®, Novartis vaccines) is more immunogenic and should be preferred to the polysaccharide vaccine (Mencevax®). Booster doses should be considered every 5 years , especially if there is an exposition to mennigococi serogroup A [31].

Varicella
Varicella is known to cause severe disease especially in immunocompromised hosts [125]. Despite the availability of a life-attenuated varicella zoster virus (VZV) vaccine (Varilrix®, Varivax®) with an efficacy of 70–90% against chickenpox and > 95% against severe disease in healthy hosts, VZV circulation is definitely persisting in the community, thus posing a risk for susceptible SOT recipients, children in particular.
Live-attenuated VZV immunization in end-stage renal diseases and in SOT candidates is safe and effective [51, 126, 127]. As most adult transplant candidates are already immune to varicella, the disease history however is rarely documented. VZV serology (IgG) is thus recommended for all candidates. If VZV IgG is negative (Table 2) – and for children > 9 months of age without a history of chickenpox – immediate VZV vaccination (two doses one month apart) is highly recommended.
Varicella vaccination before transplantation is essential as, SOT candidates and recipients are a high-risk group, vaccine responses are better before than after SOT, and the live attenuated VZV vaccine is officially contraindicated in immunocompromised patients. However, varicella vaccination has been studied in paediatric SOT recipients and accumulating evidence shows this vaccine to be safe and immunogenic in SOT recipients. While a vaccine response (protective antibody titre and cellular immunity) was seen in > 70% up to 100% of paediatric SOT recipients (kidney and liver), unwanted local and systemic effects including

vaccine-induced varicella were mild and transient [18, 30, 57, 128–130]. Breakthrough disease was reported with a cumulative incidence of 0–25%, was mostly mild, rarely requiring hospital admission or antiviral treatment and occurred only in VZV antibody-negative SOT recipients [131]. Although these studies are and will remain underpowered to assess efficacy and severe adverse events, they allow considering varicella immunization in seronegative SOT recipients with minimal immunosuppression, the expected benefits (protection from varicella in countries where viral circulation is widespread) outweighing the theoretical risks of VZV vaccination (extensive viral replication, which could be controlled by antivirals).
Varicella vaccine is thus not only a first priority in susceptible SOT candidates but also to be considered and recommended in stable VZV-seronegative SOT recipients with minimal immunosuppression if immunization before SOT did not occur and/or VZV immunity has waned.

Herpes zoster
Reactivation of VZV after primary infection, or herpes zoster infection, occurs with increased incidence in immunocompromised hosts, including SOT recipients[132–134]. For prevention or mitigation of herpes zoster, a live attenuated zoster vaccine was developed. This vaccine is composed of the same viral strain (Oka) as the varicella vaccine but has a distinct (i.e.14-fold) higher virus titre. This vaccine should not be used in varicella naïve persons or person previously immunized with varicella vaccine. Despite the ACIP statement [135], it is currently neither available nor recommended in Switzerland – and clearly contraindicated after transplantation [136].

Hepatitis A
Hepatitis A virus (HAV) can cause severe disease and fulminant hepatitis in patients with chronic viral hepatitis and in end-stage liver disease [137–140]. Vaccination against hepatitis A is thus recommended [20, 23] for patients with end-stage liver disease and may be considered in all SOT candidates at risks of exposure (travel) [28]. Antibody titres in response to hepatitis A vaccination are lower in patients with end-stage liver disease, and even more after SOT, compared to healthy subjects and may more rapidly decrease after SOT [16, 65, 141–143]. If immunization is performed after SOT, HAV responses should thus be assessed 1–3 months after the second dose and a single HAV booster be administered to non-responders [22, 23, 143].

Other vaccinations (risk based assessment)
Every inactivated vaccine can be safely administered to SOT candidates and recipients. The potentially risks of poorer vaccine responses has to be taken into account, in particular in immunosuppressed SOT recipients. An individual discussion is strongly recommended to define the risk of exposure and discuss the possibility of providing protection against other vaccine-preventable disease. This may include vaccinations against TBE (FSME), hepatitis A, rabies, meningococcal disease or yellow fever (only before SOT) when travel-associated exposure may be relevant.
In general, unless specifically indicated otherwise in this document, live vaccines are contraindicated after SOT.

References

1. Fishman, J.A., Infection in Solid-Organ Transplant Recipients. New England Journal of Medicine, 2007. 357(25): p. 2601–2614.
2. Rodriguez-Moreno, A., et al., Varicella infection in adult renal allograft recipients: experience at one center. Transplantation Proceedings, 2006. 38(8): p. 2416–8.
3. Furth, S.L., et al., Varicella in the first year after renal transplantation: a report of the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS). Pediatric Transplantation, 1997. 1(1): p. 37–42.
4. Kalman, S., et al., Measles: a rare communicable disease in a child with renal transplantation. Pediatric Transplantation, 2002. 6(5): p. 432–4.
5. Kidd, I.M., et al., Measles-associated encephalitis in children with renal transplants: a predictable effect of waning herd immunity? Lancet, 2003. 362(9386): p. 832.
6. Kumar, D., et al., Outcomes from pandemic influenza A H1N1 infection in recipients of solid-organ transplants: a multicentre cohort study. The Lancet Infectious Diseases, 2010. 10(8): p. 521–526.
7. de Bruyn, G., et al., Invasive pneumococcal infections in adult lung transplant recipients. American Journal of Transplantation, 2004. 4(8): p. 1366–71.
8. Tran, L., et al., Invasive pneumococcal disease in pediatric organ transplant recipients: a high-risk population. Pediatric Transplantation, 2005. 9(2): p. 183–6.
9. Dehghani, S.M., et al., Vaccination status in pediatric liver transplant candidates. Pediatric Transplantation, 2009. 13(7): p. 820–2.
10. Genc, G., et al., Vaccination status of children considered for renal transplants: missed opportunities for vaccine preventable diseases. Experimental & Clinical Transplantation: Official Journal of the Middle East Society for Organ Transplantation, 2012. 10(4): p. 314–8.
11. Chesi, C., et al., Immunization of liver and renal transplant recipients: a seroepidemiological and sociodemographic survey. Transplant Infectious Disease, 2009. 11(6): p. 507–12.
12. Castells, L. and R. Esteban, Hepatitis B vaccination in liver transplant candidates. European Journal of Gastroenterology & Hepatology, 2001. 13(4): p. 359–61.
13. Neu, A.M., Immunizations in children with chronic kidney disease. Pediatric Nephrology, 2012. 27(8): p. 1257–63.
14. Wu, J.-F., et al., Humoral immunogenicity to measles, rubella, and varicella-zoster vaccines in biliary atresia children. Vaccine, 2009. 27(21): p. 2812–5.
15. Smith, K.G., et al., Suppression of the humoral immune response by mycophenolate mofetil. Nephrology Dialysis Transplantation, 1998. 13(1): p. 160–4.
16. Gunther, M., et al., Rapid decline of antibodies after hepatitis A immunization in liver and renal transplant recipients. Transplantation, 2001. 71(3): p. 477–9.
17. Gangappa, S., et al., Immune responsiveness and protective immunity after transplantation. Transplant International, 2008. 21(4): p. 293–303.
18. Eckerle, I., et al., Serologic Vaccination Response after Solid Organ Transplantation: A Systematic Review. PLoS ONE [Electronic Resource], 2013. 8(2): p. e56974.
19. Pedrazzi, C., et al., Duration of immunity to diphtheria and tetanus in young kidney transplant patients. Pediatric Transplantation, 1999. 3(2): p. 109–14.
20. Bundesamt fuer Gesundheit and Eidgenoessische Kommision fuer Impffragen (EKIF), Schweizerischer Impfplan 2013. Richtlinien und Empfehlungen, Bundesamt fuer Gesundheit, Editor 2013: Bern.
21. Avery, R.K. and M. Michaels, Update on immunizations in solid organ transplant recipients: what clinicians need to know. American Journal of Transplantation, 2008. 8(1): p. 9–14.
22. Chow, J. and Y. Golan, Vaccination of Solid-Organ Transplantation Candidates. Clinical Infectious Diseases, 2009. 49(10): p. 1550–1556.
23. Danzinger-Isakov, L., D. Kumar, and A.S.T.I.D.C.o.P. the, Guidelines for Vaccination of Solid Organ Transplant Candidates and Recipients. American Journal of Transplantation, 2009. 9: p. S258–S262.
24. Abuali, M.M., R. Arnon, and R. Posada, An update on immunizations before and after transplantation in the pediatric solid organ transplant recipient. Pediatric Transplantation, 2011. 15(8): p. 770–777.
25. Verma, A. and J.J. Wade, Immunization issues before and after solid organ transplantation in children. Pediatric Transplantation, 2006. 10(5): p. 536–548.
26. Ballout, A., et al., Vaccinations for adult solid organ transplant recipient: current recommendations. Transplantation Proceedings, 2005. 37(6): p. 2826–7.
27. Danziger-Isakov, L. and D. Kumar, Vaccination in solid organ transplantation. American Journal of Transplantation, 2013. 13 Suppl 4: p. 311–7.
28. Keeffe, E.B., Hepatitis A and B superimposed on chronic liver disease: vaccine-preventable diseases. Transactions of the American Clinical & Climatological Association, 2006. 117: p. 227–37; discussion 237–8.
29. Tain, Y.L., G. Lin, and T.W. Cher, Microbiological spectrum of septicemia and peritonitis in nephrotic children. Pediatric Nephrology, 1999. 13(9): p. 835–7.
30. Posfay-Barbe, K.M., et al., Varicella-zoster immunization in pediatric liver transplant recipients: safe and immunogenic. American Journal of Transplantation, 2012. 12(11): p. 2974–85.
31. Eidgenoessische Kommision fuer Impffragen (EKIF) and Bundesamt fuer Gesundheit, Aktualisierung der Impfempfehlung gegen Meningokokken: Einfuehrung eines quadrivalenten Konjugatimpfstoffs. BAG Bulletin, 2011. 34: p. 711–717.
32. Warmington, L., B.E. Lee, and J.L. Robinson, Loss of antibodies to measles and varicella following solid organ transplantation in children. Pediatric Transplantation, 2005. 9(3): p. 311–314.
33. Kimball, P., et al., Influenza vaccination does not promote cellular or humoral activation among heart transplant recipients. Transplantation, 2000. 69(11): p. 2449–51.
34. Kobashigawa, J.A., et al., Influenza vaccine does not cause rejection after cardiac transplantation. Transplant Proc, 1993. 25(4): p. 2738–9.
35. Hurst, F.P., et al., Outcomes associated with influenza vaccination in the first year after kidney transplantation. Clinical Journal of The American Society of Nephrology: CJASN, 2011. 6(5): p. 1192–7.
36. Kunisaki, K.M. and E.N. Janoff, Influenza in immunosuppressed populations: a review of infection frequency, morbidity, mortality, and vaccine responses. The Lancet Infectious Diseases, 2009. 9(8): p. 493–504.
37. Kobashigawa, J.A., et al., Influenza vaccine does not cause rejection after cardiac transplantation. Transplantation Proceedings, 1993. 25(4): p. 2738–9.
38. Siegrist, C.A., et al., Responses of solid organ transplant recipients to the AS03-adjuvanted pandemic influenza vaccine. Antiviral Therapy, 2012. 17(5): p. 893–903.
39. Cainelli, F. and S. Vento, Infections and solid organ transplant rejection: a cause-and-effect relationship? The Lancet Infectious Diseases, 2002. 2(9): p. 539–549.
40. Shepherd, R.W., et al., Risk Factors for Rejection and Infection in Pediatric Liver Transplantation. American Journal of Transplantation, 2008. 8(2): p. 396–403.
41. Dharnidharka, V.R., D.M. Stablein, and W.E. Harmon, Post-Transplant Infections Now Exceed Acute Rejection as Cause for Hospitalization: A Report of the NAPRTCS1. American Journal of Transplantation, 2004. 4(3): p. 384–389.
42. Danerseau, A.M. and J.L. Robinson, Efficacy and safety of measles, mumps, rubella and varicella live viral vaccines in transplant recipients receiving immunosuppressive drugs. World Journal of Pediatrics, 2008. 4(4): p. 254–8.
43. Diaz, P.S., et al., Lack of transmission of the live attenuated varicella vaccine virus to immunocompromised children after immunization of their siblings. Pediatrics, 1991. 87(2): p. 166–70.
44. Halloran, P.F., Immunosuppressive Drugs for Kidney Transplantation. New England Journal of Medicine, 2004. 351(26): p. 2715–2729.
45. Mulley, W.R., et al., Mycophenolate and lower graft function reduce the seroresponse of kidney transplant recipients to pandemic H1N1 vaccination. Kidney International, 2012. 82(2): p. 212–9.
46. Rose, M.L., et al., Mycophenolate mofetil decreases antibody production after cardiac transplantation. Journal of Heart & Lung Transplantation, 2002. 21(2): p. 282–5.
47. Sternfeld, T., et al., Acute measles infection triggering an episode of liver transplant rejection. Int J Infect Dis, 2010. 14(6): p. e528–30.
48. Abuali, M.M., R. Arnon, and R. Posada, An update on immunizations before and after transplantation in the pediatric solid organ transplant recipient. Pediatr Transplant. 15(8): p. 770–7.
49. Gangappa, S., et al., Immune responsiveness and protective immunity after transplantation. Transpl Int, 2008. 21(4): p. 293–303.
50. Warmington, L., B.E. Lee, and J.L. Robinson, Loss of antibodies to measles and varicella following solid organ transplantation in children. Pediatr Transplant, 2005. 9(3): p. 311–4.
51. Broyer, M., et al., Varicella and zoster in children after kidney transplantation: long-term results of vaccination. Pediatrics, 1997. 99(1): p. 35–9.
52. Balloni, A., et al., Immunity to poliomyelitis, diphtheria and tetanus in pediatric patients before and after renal or liver transplantation. Vaccine, 1999. 17(20–21): p. 2507–11.
53. Enke, B.U., et al., Response to diphtheria and tetanus booster vaccination in pediatric renal transplant recipients. Transplantation, 1997. 64(2): p. 237–41.
54. Ghio, L., et al., Immunity to diphtheria and tetanus in a young population on a dialysis regimen or with a renal transplant. Journal of Pediatrics, 1997. 130(6): p. 987–9.
55. Sever, M.S., et al., Immune response to Haemophilus influenzae type B vaccination in renal transplant recipients with well-functioning allografts. Nephron, 1999. 81(1): p. 55–9.
56. Mori, K., et al., Responses in children to measles vaccination associated with perirenal transplantation. Pediatrics International, 2009. 51(5): p. 617–20.
57. Shinjoh, M., et al., Effective and safe immunizations with live-attenuated vaccines for children after living donor liver transplantation. Vaccine, 2008. 26(52): p. 6859–63.
58. Kanaan, N., et al., Significant rate of hepatitis B reactivation following kidney transplantation in patients with resolved infection. Journal of Clinical Virology, 2012. 55(3): p. 233–8.
59. Phillips, M.J., et al., Post-transplant recurrent hepatitis B viral liver disease. Viral-burden, steatoviral, and fibroviral hepatitis B. Am J Pathol, 1992. 140(6): p. 1295–308.
60. Kwon, C.H.D., et al., Long-term protection against hepatitis B in pediatric liver recipients can be achieved effectively with vaccination after transplantation. Pediatric Transplantation, 2006. 10(4): p. 479–86.
61. Barcena Marugan, R., et al., Prevention of de novo hepatitis B infection in liver allograft recipients with previous hepatitis B infection or hepatitis B vaccination. American Journal of Gastroenterology, 2002. 97(9): p. 2398–401.
62. Su, W.-J., et al., High-titer antibody to hepatitis B surface antigen before liver transplantation can prevent de novo hepatitis B infection. Journal of Pediatric Gastroenterology & Nutrition, 2009. 48(2): p. 203–8.
63. Pascasio, J.M., et al., Response to a vaccination schedule with 4 doses of 40 microg against hepatitis B virus in cirrhotic patients evaluated for liver transplantation. Transplantation Proceedings, 2008. 40(9): p. 2943–5.
64. Loinaz, C., et al., Hepatitis B vaccination results in 140 liver transplant recipients. Hepato-Gastroenterology, 1997. 44(13): p. 235–8.
65. Martin, K., et al., Response to hepatitis A and B vaccination after pediatric heart transplant. Pediatric Transplantation, 2012. 16(7): p. 699–703.

66. Ni, Y.-H., et al., Response to booster hepatitis B vaccines in liver-transplanted children primarily vaccinated in infancy. Transplantation, 2008. 86(11): p. 1531–5.
67. Arslan, M., et al., Double-dose accelerated hepatitis B vaccine in patients with end-stage liver disease. Liver Transplantation, 2001. 7(4): p. 314–20.
68. Aziz, A., et al., Efficacy of repeated high-dose hepatitis B vaccine (80 microg) in patients with chronic liver disease. Journal of Viral Hepatitis, 2006. 13(4): p. 217–21.
69. Hayney, M.S., et al., High-dose hepatitis B vaccine in patients waiting for lung transplantation. Pharmacotherapy:The Journal of Human Pharmacology & Drug Therapy, 2003. 23(5): p. 555–60.
70. Dominguez, M., et al., Vaccination against hepatitis B virus in cirrhotic patients on liver transplant waiting list. Liver Transplantation, 2000. 6(4): p. 440–2.
71. Horlander, J.C., et al., Vaccination against hepatitis B in patients with chronic liver disease awaiting liver transplantation. American Journal of the Medical Sciences, 1999. 318(5): p. 304–7.
72. Rosman, A.S., et al., Efficacy of a high and accelerated dose of hepatitis B vaccine in alcoholic patients: a randomized clinical trial. American Journal of Medicine, 1997. 103(3): p. 217–22.
73. Mitwalli, A., Responsiveness to hepatitis B vaccine in immunocompromised patients by doubling the dose scheduling. Nephron, 1996. 73(3): p. 417–20.
74. Savani, B.N., S. Goodman, and A.J. Barrett, Can routine posttransplant HPV vaccination prevent commonly occurring epithelial cancers after allogeneic stem cell transplantation? Clinical Cancer Research, 2009. 15(7): p. 2219–21.
75. Chin-Hong, P.V., E.J. Kwak, and A.S.T.I.D.C.o.P. the, Human Papillomavirus in Solid Organ Transplantation. American Journal of Transplantation, 2013. 13(s4): p. 189–200.
76. Wong, G., et al., The health and economic impact of cervical cancer screening and human papillomavirus vaccination in kidney transplant recipients. Transplantation, 2009. 87(7): p. 1078–91.
77. Eidgenoessische Kommision fuer Impffragen (EKIF) and Bundesamt fuer Gesundheit, Pneumokokkenimpfung: Empfehlungen zur Verhinderung von invasiven Pneumokokkenerkrankungen bei Risikogruppen. BAG Bulletin, 2014. (in press).
78. Cordero, E., et al., Pandemic influenza A(H1N1) virus infection in solid organ transplant recipients: impact of viral and non-viral co-infection. Clinical Microbiology & Infection, 2012. 18(1): p. 67–73.
79. Martin, S.T., M.J. Torabi, and S. Gabardi, Influenza in solid organ transplant recipients. Annals of Pharmacotherapy, 2012. 46(2): p. 255–64.
80. Vilchez, R.A., et al., Influenza Virus Infection in Adult Solid Organ Transplant Recipients. American Journal of Transplantation, 2002. 2(3): p. 287–291.
81. Weinstock, D.M., L.V. Gubareva, and G. Zuccotti, Prolonged shedding of multidrug-resistant influenza A virus in an immunocompromised patient. N Engl J Med, 2003. 348(9): p. 867–8.
82. Pinsky, B.A., et al., Long-term shedding of influenza A virus in stool of immunocompromised child. Emerg Infect Dis, 2010. 16(7): p. 1165–7.
83. Mauch, T.J., et al., Influenza B virus infection in pediatric solid organ transplant recipients. Pediatrics, 1994. 94(2 Pt 1): p. 225–9.
84. Gabriel, R., et al., Virus infections and acute renal transplant rejection. Nephron, 1976. 16(4): p. 282–6.
85. Magnani, G., et al., Safety and efficacy of two types of influenza vaccination in heart transplant recipients: a prospective randomised controlled study. Journal of Heart & Lung Transplantation, 2005. 24(5): p. 588–92.
86. Sanchez-Fructuoso, A.I., et al., Influenza virus immunization effectivity in kidney transplant patients subjected to two different triple-drug therapy immunosuppression protocols: mycophenolate versus azathioprine. Transplantation, 2000. 69(3): p. 436–9.
87. Blumberg, E.A., et al., The immunogenicity of influenza virus vaccine in solid organ transplant recipients. Clinical Infectious Diseases, 1996. 22(2): p. 295–302.
88. Madan, R.P., et al., A prospective, comparative study of the immune response to inactivated influenza vaccine in pediatric liver transplant recipients and their healthy siblings. Clinical Infectious Diseases, 2008. 46(5): p. 712–8.
89. Scharpe, J., et al., Influenza vaccination is efficacious and safe in renal transplant recipients. American Journal of Transplantation, 2008. 8(2): p. 332–7.
90. Hayney, M.S., et al., Influenza vaccine antibody responses in lung transplant recipients. Progress in Transplantation, 2004. 14(4): p. 346–51.
91. Keshtkar-Jahromi, M., et al., Antibody response to influenza immunization in kidney transplant recipients receiving either azathioprine or mycophenolate: a controlled trial. American Journal of Nephrology, 2008. 28(4): p. 654–60.
92. Nailescu, C., et al., Influenza vaccine after pediatric kidney transplant: a Midwest Pediatric Nephrology Consortium study. Pediatric Nephrology, 2011. 26(3): p. 459–67.
93. Salles, M.J.C., et al., Influenza virus vaccination in kidney transplant recipients: serum antibody response to different immunosuppressive drugs. Clinical Transplantation, 2010. 24(1): p. E17–23.
94. Manuel, O., et al., Low-dose intradermal versus intramuscular trivalent inactivated seasonal influenza vaccine in lung transplant recipients. Journal of Heart & Lung Transplantation, 2011. 30(6): p. 679–84.
95. Morelon, E., et al., Immunogenicity and safety of intradermal influenza vaccination in renal transplant patients who were non-responders to conventional influenza vaccination. Vaccine, 2010. 28(42): p. 6885–90.
96. Mossad, S.B., Larger dose of intradermal influenza vaccination may be more immunogenic in transplant recipients. American Journal of Transplantation, 2008. 8(5): p. 1073; author reply 1074.
97. Esposito, S., et al., An open-label, randomized clinical trial assessing immunogenicity, safety and tolerability of pandemic influenza A/H1N1 MF59-adjuvanted vaccine administered sequentially or simultaneously with seasonal virosomal-adjuvanted influenza vaccine to paediatric kidney transplant recipients. Nephrology Dialysis Transplantation, 2011. 26(6): p. 2018–24.
98. Felldin, M., et al., The antibody response to pandemic H1N1 2009 influenza vaccine in adult organ transplant patients. Transplant International, 2012. 25(2): p. 166–71.
99. Siegrist, C.-A., et al., Responses of solid organ transplant recipients to the AS03-adjuvanted pandemic influenza vaccine. Antiviral Therapy, 2012. 17(5): p. 893–903.
100. Leroux-Roels, I., et al., Antigen sparing and cross-reactive immunity with an adjuvanted rH5N1 prototype pandemic influenza vaccine: a randomised controlled trial. Lancet, 2007. 370(9587): p. 580–9.
101. Vesikari, T., et al., Enhanced immunogenicity of seasonal influenza vaccines in young children using MF59 adjuvant. Pediatric Infectious Disease Journal, 2009. 28(7): p. 563–71.
102. Waddington, C.S., et al., Safety and immunogenicity of AS03B adjuvanted split virion versus non-adjuvanted whole virion H1N1 influenza vaccine in UK children aged 6 months–12 years: open label, randomised, parallel group, multicentre study. BMJ, 2010. 340: p. c2649.
103. Birdwell, K.A., et al., Decreased antibody response to influenza vaccination in kidney transplant recipients: a prospective cohort study. American Journal of Kidney Diseases, 2009. 54(1): p. 112–21.
104. Bundesamt fuer Gesundheit, Eidgenoessische Kommision fuer Impffragen (EKIF), and Arbeitsgruppe Influenza (AGI), Richtlinien und Empfehlungen. Empfehlungen zur Grippeimpfung, Bundesamt fuer Gesundheit, Editor 2011: Bern.
105. Kumar, D., et al., Influenza vaccination in the organ transplant recipient: review and summary recommendations. American Journal of Transplantation, 2011. 11(10): p. 2020–30.
106. Admon, D., et al., Antibody response to influenza immunization in patients after heart transplantation. Vaccine, 1997. 15(14): p. 1518–22.
107. Manuel, O., et al., Immunogenicity and safety of an intradermal boosting strategy for vaccination against influenza in lung transplant recipients. American Journal of Transplantation, 2007. 7(11): p. 2567–72.
108. Soesman, N.M., et al., Efficacy of influenza vaccination in adult liver transplant recipients. Journal of Medical Virology, 2000. 61(1): p. 85–93.
109. Amber, I.J., et al., Increased risk of pneumococcal infections in cardiac transplant recipients. Transplantation, 1990. 49(1): p. 122–5.
110. McCashland, T.M., L.C. Preheim, and M.J. Gentry, Pneumococcal vaccine response in cirrhosis and liver transplantation. Journal of Infectious Diseases, 2000. 181(2): p. 757–60.
111. Sarmiento, E., et al., Impaired anti-pneumococcal polysaccharide antibody production and invasive pneumococcal infection following heart transplantation. International Immunopharmacology, 2006. 6(13-14): p. 2027–30.
112. Linnemann, C.C., Jr., M.R. First, and G. Schiffman, Revaccination of renal transplant and hemodialysis recipients with pneumococcal vaccine. Arch Intern Med, 1986. 146(8): p. 1554–6.
113. Lin, P.L., et al., Safety and immunogenicity of the American Academy of Pediatrics-recommended sequential pneumococcal conjugate and polysaccharide vaccine schedule in pediatric solid organ transplant recipients. Pediatrics, 2005. 116(1): p. 160–7.
114. Kumar, D., et al., A randomized, double-blind, placebo-controlled trial to evaluate the prime-boost strategy for pneumococcal vaccination in adult liver transplant recipients. Clinical Infectious Diseases, 2008. 47(7): p. 885–92.
115. Kumar, D., et al., Immunogenicity of pneumococcal vaccine in renal transplant recipients-three year follow-up of a randomized trial. American Journal of Transplantation, 2007. 7(3): p. 633–8.
116. Barton, M., et al., Seven-valent pneumococcal conjugate vaccine in pediatric solid organ transplant recipients: a prospective study of safety and immunogenicity. Pediatric Infectious Disease Journal, 2009. 28(8): p. 688–92.
117. French, N., et al., A trial of a 7-valent pneumococcal conjugate vaccine in HIV-infected adults. N Engl J Med, 2010. 362(9): p. 812–22.
118. French, N., et al., 23-valent pneumococcal polysaccharide vaccine in HIV-1-infected Ugandan adults: double-blind, randomised and placebo controlled trial. Lancet, 2000. 355(9221): p. 2106–11.
119. Feikin, D.R., et al., High rate of pneumococcal bacteremia in a prospective cohort of older children and adults in an area of high HIV prevalence in rural western Kenya. BMC Infect Dis, 2010. 10: p. 186.
120. Crum-Cianflone, N.F., et al., A randomized clinical trial comparing revaccination with pneumococcal conjugate vaccine to polysaccharide vaccine among HIV-infected adults. Journal of Infectious Diseases, 2010. 202(7): p. 1114–25.
121. Lesprit, P., et al., Immunological efficacy of a prime-boost pneumococcal vaccination in HIV-infected adults. AIDS, 2007. 21(18): p. 2425–34.
122. Kumar, D., et al., A randomized, double-blind trial of pneumococcal vaccination in adult allogeneic stem cell transplant donors and recipients. Clinical Infectious Diseases, 2007. 45(12): p. 1576–82.
123. Cordonnier, C., et al., Randomized study of early versus late immunization with pneumococcal conjugate vaccine after allogeneic stem cell transplantation. Clinical Infectious Diseases, 2009. 48(10): p. 1392–401.

124. Bennet, N.M., et al., Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morbidity and Mortality Weekly Report, 2012. 61(40): p. 816–819.
125. Lynfield, R., J.T. Herrin, and R.H. Rubin, Varicella in pediatric renal transplant recipients. Pediatrics, 1992. 90(2 Pt 1): p. 216–20.
126. Broyer, M. and B. Boudailliez, Varicella vaccine in children with chronic renal insufficiency. Postgrad Med J, 1985. 61 Suppl 4: p. 103–6.
127. Webb, N.J., et al., Immunisation against varicella in end-stage and pre-end-stage renal failure. Trans-Pennine Paediatric Nephrology Study Group. Arch Dis Child, 2000. 82(2): p. 141–3.
128. Weinberg, A., et al., Safety and immunogenicity of varicella-zoster virus vaccine in pediatric liver and intestine transplant recipients. Am J Transplant, 2006. 6(3): p. 565–8.
129. Zamora, I., et al., Attenuated varicella virus vaccine in children with renal transplants. Pediatr Nephrol, 1994. 8(2): p. 190–2.
130. Khan, S., J. Erlichman, and E.B. Rand, Live virus immunization after orthotopic liver transplantation. Pediatr Transplant, 2006. 10(1): p. 78–82.
131. Mizuta, K., et al., Varicella zoster virus disease after pediatric living donor liver transplantation: is it serious? Transplantation Proceedings, 2012. 44(3): p. 780–3.
132. Luby, J.P., et al., A longitudinal study of varicella-zoster virus infections in renal transplant recipients. J Infect Dis, 1977. 135(4): p. 659–63.
133. Rand, K.H., et al., Cellular immunity and herpesvirus infections in cardiac-transplant patients. N Engl J Med, 1977. 296(24): p. 1372–7.
134. Gourishankar, S., et al., Herpes zoster infection following solid organ transplantation: incidence, risk factors and outcomes in the current immunosuppressive era. Am J Transplant, 2004. 4(1): p. 108–15.
135. Harpaz, R., I.R. Ortega-Sanchez, and J.F. Seward, Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep, 2008. 57(RR–5): p. 1-30; quiz CE2–4.
136. Guidelines for vaccination of solid organ transplant candidates and recipients. Am J Transplant, 2009. 9 Suppl 4: p. S258–S262.
137. Worns, M.A., et al., Incidence of HAV and HBV infections and vaccination rates in patients with autoimmune liver diseases. American Journal of Gastroenterology, 2008. 103(1): p. 138–46.
138. Vento, S., et al., Fulminant hepatitis associated with hepatitis A virus superinfection in patients with chronic hepatitis C. N Engl J Med, 1998. 338(5): p. 286–90.
139. Lefilliatre, P. and J.P. Villeneuve, Fulminant hepatitis A in patients with chronic liver disease. Can J Public Health, 2000. 91(3): p. 168–70.
140. Keeffe, E., Hepatitis A in patients with chronic liver disease – severity of illness and prevention with vaccination. Journal of Viral Hepatitis, 2000. 7 Suppl 1: p. 15–7.
141. Arslan, M., et al., Safety and efficacy of hepatitis A vaccination in liver transplantation recipients. Transplantation, 2001. 72(2): p. 272–6.
142. Dumot, J.A., et al., Immunogenicity of hepatitis A vaccine in decompensated liver disease. American Journal of Gastroenterology, 1999. 94(6): p. 1601–4.
143. Stark, K., et al., Immunogenicity and safety of hepatitis A vaccine in liver and renal transplant recipients. Journal of Infectious Diseases, 1999. 180(6): p. 2014–7.