Post-Transplant Vaccination and Re-Immunisation Procedure

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Purpose
The purpose of this procedure is to ensure appropriate and timely vaccination post Haematopoietic Stem Cell Transplant (HSCT); which will provide HSCT recipients with protection against vaccine preventable diseases that is equivalent to their peers and protect against diseases that they are at higher risk of acquiring or suffering complications from.

Scope/Audience
This applies to all CDHB personnel involved in prescribing/recommending revaccination and immunisation of patients post-autologous and allogeneic HSCT, specifically Haematology Consultants and Registrars, and Bone Marrow Transplant Coordinators.

Associated documents and forms
- Post Allogeneic HSCT Vaccination Prescription (ref 5058)
Safety 1st Incident Reporting

Haematology Red Book

Definitions

Inactivated vaccines = An inactivated vaccine (or killed vaccine) consists of virus particles, bacteria, or other pathogens which are grown in culture and then killed using a method such as heat or formaldehyde. These vaccines generate an immune response, but do not cause an infection.

Live vaccines = Live virus vaccines use the weakened (attenuated) form of the virus. The measles, mumps, and rubella (MMR) vaccine and the varicella (chickenpox) vaccine are examples. Live vaccines pose risks for immunosuppressed patients.

Background

Autologous HSCT

Autologous and allogeneic HCT recipients have very different immune recovery but due to the lack of evidence both groups generally share vaccination recommendations (Torda and Alexander 2009).

For most recipients of autologous HSCT, re-immunisation is unnecessary, with the exception of Pneumococcus and seasonal influenza vaccine.

Allogeneic HSCT

Antibody titres to vaccine-preventable diseases decline over 1-10 years after autologous and allogeneic HCT (Ljungman, Cordonnier et al. 2009). Transfer of donor immunity to HCT recipients is variable and cannot be relied upon to provide long-term immunity (Torda and Alexander 2009). Although studies have shown the safety and immunogenicity of vaccines in the HCT population there is little data on the clinical outcomes.

Effective vaccination requires functional B and T lymphocytes. B cells generally return to normal 9-12 months post HCT or 6 months post rituximab. CD4+ T cells are generally <200/mm3 up to 3 months post HCT (Ljungman, Cordonnier et al. 2009). In older patients with GVHD the CD4+ T cell count may remain low for 1-2 years. T cell present up to 1 year are generally passively acquired donor T memory/effector cells that are capable of responding to antigens encountered by the donor before the HCT. Naïve T cell which are capable of responding to new antigens are only generated at 6-12 months. Similar to children, HCT recipients respond poorly to vaccination with pure polysaccharide antigens.

Similarly there is little data in RIC or haplo-identical HCT and for simplicity all patients are treated the same. GVHD is associated with prolonged immunodeficiency, an increase in bacterial infections and functional asplenia in 15% of patients (Hilgendorf, Freund et al. 2011). In chronic GVHD antibody responses to polysaccharide vaccines are poor.
**Vaccination Recommendations**

Infections can be grouped into two groups: firstly, those to which HCT recipients are more susceptible (Pneumococcus, Haemophilus, Influenza) and secondly, those for which there are standard recommendations in the healthy population (Diphtheria, Pertussis, MMR, Polio, hepatitis B, Meningococcus etc.). Inactive vaccines have been shown to be safe in HSCT recipients. Live vaccines (MMR, varicella) pose risks for immunosuppressed recipients. Immunosuppression from GVHD and its treatment means that administration of live vaccines is potentially harmful and not recommended for HSCT recipients with GVHD.

There is insufficient data to recommend the optimal time-point after transplant when vaccination should begin. 12 months is a pragmatic choice based on historical practice but vaccination may start after 6 months in selected patients, e.g. those with reduced intensity conditioning and a rapid taper of immunosuppression without evidence of GVHD.

**Influenza vaccine**  
From 4 months post HSCT  
- Annual vaccination  
- Prior to influenza season

**Other non-live vaccines**  
From 12 months post *Allogeneic* HSCT  
- Non-live vaccines should not be delayed in patients with GVHD  
- Vaccination may be postponed up to 3 months but not longer in patients receiving >0.5mg/kg prednisone or triple agent GVHD regimen  
- Conjugated vaccines are preferred over polysaccharide vaccines

**Live vaccines**  
No sooner than 24 months post *Allogeneic* HSCT  
- Live vaccines are contra-indicated in patients with GVHD  
- Is not taking immunosuppressive medication and  
- Has not received intravenous immunoglobulin in the preceding 8 months  
- Where the patient has extensive GVHD, and/or is taking significant immunosuppression medication, and has not received IVIG in the preceding 8 months, individual risk benefit assessment is recommended at 24 months post HSCT

It is recommended that patients complete their full vaccination schedule (refer to Appendix A or the *Post Allogeneic HSCT Vaccination Prescription Form* (ref 5058). with the same provider - however if this has not occurred, confirmation documentation must be sought confirming vaccinations were administered.
Procedure

1. Procedure for In-Hospital Vaccination Administration

1.1. Doctor assesses patient at 6 months and confirms vaccination can start, records decision in clinical notes and communicates to GP when vaccination is to commence.

1.2. Doctor prescribes vaccines on Post Allogeneic HSCT Vaccination Prescription Form (ref 5058).

1.3. Vaccines are obtained from pharmacy and administered by out-patient nursing staff.

1.4. Nursing staff sign and date the Post Allogeneic HSCT Vaccination Prescription Form (ref 5058) before placing in patient’s medical records.

1.5. Upon completion of the Vaccination Prescription (ref 5058) send the completed form to the patient’s GP, patient’s primary haematologist if not in the CDHB and upload copy to patient’s CDHB electronic record.

2. Procedure for Vaccination Administration Outside of CDHB

2.1. Doctor assesses patient at 6 months and confirms vaccination can start, records decision in clinical notes and communicates to GP when vaccination is to commence.

2.2. Medical staff to prescribe vaccination on Post Allogeneic HSCT Vaccination Prescription Form (ref 5058).

2.3. Give the Post Allogeneic HSCT Vaccination Prescription Form (ref 5058) to the patient or post to patient’s GP with a request to return a copy of the completed form.

3. Administration and Monitoring

3.1. Patient should remain in the clinical area under observation for 20 minutes after vaccination.

3.2. Ensure patients are aware of reactions to observe for, and follow up required if adverse reaction occurs.

References


FACT-JAICE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration: Part B, section B7.7.3
### Appendix A – Vaccination Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Influenza</th>
<th>Tetanus, Diptheria &amp; Perfsiss</th>
<th>Pneumococcal conjugate (PCV13)</th>
<th>Haemophilus Influenzae B</th>
<th>Meningococcal Conjugate (MCV4-D)</th>
<th>Pneumococcal polysaccharide (PPV23)</th>
<th>Measles, Mumps, Rubella (live)</th>
<th>Varicella (live)</th>
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<tbody>
<tr>
<td>4 months</td>
<td>Boostrix</td>
<td>Prevenar 13</td>
<td>Act-HIB</td>
<td>Menactra</td>
<td>Pneumavax 23</td>
<td>MMR II</td>
<td>Varilrix</td>
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<td>12 months</td>
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**Notes:**
- * Consider 2nd dose of Pneumococcal conjugate (PCV13) in patients with cGVHD
  + Check measles antibody titres at 2 years
  ++ MMR vaccine for seronegative patients only
  +++ Check antibody titres after 6-8 weeks
  ++++ 2nd MMR if non-immune
  ‡ Check varicella antibody titres at 2 years
  ‡‡ Varicella vaccine for seronegative patients only
  ‡‡‡ If Varicella non-immune VZIG prophylaxis will still be required post exposure

1. Immunisation at 6 months post SCT is the general recommendation. May be considered in patients with cGVHD but responses may be impaired. Better responses are likely to be seen in patients off both calcineurin inhibitors and corticosteroids (>4 weeks), 6 months post rituximab and in those with evidence of lymphocyte recovery.

2. Live vaccines (MMR / Varicella): Consider herd immunity and likely risk of exposure. Test for measles and varicella antibodies and offer vaccination only to seronegative patients without active cGVHD. Wait for 8 and 5 months respectively after IVIg and VZIG therapy. Test for measles antibody response 4-6 weeks post MMR.
## Appendix B – Amendment History

<table>
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