Guidelines on Microbiological Investigations, Antimicrobials, Vaccines, Infection Prevention and Control Practices in Haematopoietic Stem Cell Transplantation

Sri Lanka College of Microbiologists
2017

Financial support for development by WHO

Subcommittee members

Dr. Kumudu Karunaratne (Convener)	–	Consultant Microbiologist
Dr. Janaki Abeynayake	–	Consultant Virologist
Dr. Nayomi Danthanarayana	–	Consultant Virologist
Dr. Dhanushka Dasanayake	–	Consultant immunologist
Dr. Samanmalee Gunasekara	–	Consultant Microbiologist
Dr. Sunethra Gunasena	–	Consultant Virologist
Dr. Nadeeka Janage	–	Consultant Virologist
Dr. Jude Jayamaha	–	Consultant Virologist
Dr. Primali Jayasekera	–	Consultant Mycologist
Dr. Dulmini Kumarasinghe	–	Consultant Virologist
Dr. M.A.R.V. Muthugala	–	Consultant Virologist
Dr. Dilini Nakkawita	–	Consultant Microbiologist
Dr. Geethika Patabendige	–	Consultant Microbiologist
Dr. Bhagya Piyasiri	–	Consultant Microbiologist
Dr. Sagarika Samarasinghe	–	Consultant Parasitologist
Dr. Rajiva de Silva	–	Consultant Immunologist
Dr. Saranga Sumathipala	–	Consultant Virologist
Dr. Priyanka Wimalagunawardhana	–	Consultant Microbiologist

Contents Page

Abbreviations

AOC	Amoeboe, ova and cysts
BCG	Bacillus Calmette-Guerin
cGVHD	Chronic graft versus host disease
CLL	Chronic lymphocytic leukemia
CMV	Cytomegalovirus
EBV VCA	Epstein-Barr virus viral capsid antigen
EIA	Enzyme immune assay
HBs Ag	Hepatitis B Surface antigen
HBs Ab	Hepatitis B surface antibody
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HCW	Health care worker
HIV	Human immunodeficiency virus
HPV	Human papilloma virus
HSCT	Hematopoietic stem cell transplant
HSV	Herpes simplex virus
HTLV	Human T-lymphotropic virus
IG	Immunoglobulin
IVIG	Intravenous immunoglobulin
MMR	Measles, mumps and rubella
MRSA	Methicillin-resistant *Staphylococcus aureus*
MTB	*Mycobacterium tuberculosis*
NAT	Nucleic acid testing
PCP	Pneumocystis carinii pneumonia
PCR	Polymerase chain reaction
SC	Subcutaneous
TPPA	Treponema pallidum particle agglutination
VDRL	Venereal Disease Research Laboratory
VRE	Vancomycin resistant enterococci
VZV	Varicella zoster virus

1. Introduction

Hematopoietic stem cell transplantation (HSCT) involves intravenous infusion of autologous or allogeneic stem cells collected from bone marrow, peripheral blood, or umbilical cord blood to reestablish hematopoietic function in patients whose bone marrow or immune system is damaged or defective.

Stem cell transplantation has been initiated in Sri Lanka recently. Patients who go through this treatment modality experience sequential suppression of immunity, allowing various potential complications due to infections at different phases of the transplantation process. Pre and post-transplant infection surveillance and accurate diagnosis of clinically significant infection are very essential to provide optimal care.

This guideline which was developed by a comprehensive approach through contribution from microbiologists, virologists, immunologists, mycologists and parasitologists provides an overview of specific microbiological investigations, appropriate and timely antimicrobials and other specific infection prevention and control practices. It will also serve as a guide in the development of management guidelines in future by other stakeholders.

2. Laboratory Investigations

2.1 Donor screening investigations

- CMV IgG*
- EBV VCA IgG
- VZV IgG
- HSV-1 and HSV-2 IgG
- Hepatitis B surface Ag
- Hepatitis B surface Ab titre
- Hepatitis B core total Ab
- Hepatitis C (Ag + Ab) **
- HIV-1 and HIV-2 (Ag + Ab)
- HTLV-1 and HTLV-2 Ab (Optional)
- VDRL and TPPA
- Toxoplasma IgM and IgG titre
- TB - Mantoux test, Interferon gamma (QuantiFERON Gold), chest x-ray
- Malaria (thick and thin blood films)
- In donors with respiratory symptoms
    - Sputum AFB
    - Sputum culture for TB
    - TB PCR (Xpert MTB/RIF assay)

Supplementary tests for donor screening

- Toxoplasma IgG avidity
- NAT for HCV,HBV,HIV (optional depending on requirement)

*Need to confirm by an EIA with a different format

** If reactive need to confirm by PCR

Additional investigations may be necessary depending on the circumstances (travel and past medical history) to exclude brucellosis, leishmaniasis, tick borne diseases, babesiosis, Q fever etc.

2.2 Recipient screening investigations

- CMV IgG*
- EBV VCA IgG
- VZV IgG
- HSV-1 and HSV-2 IgG
- Hepatitis B surface Ag
- Hepatitis B surface Ab titre
- Hepatitis B core total Ab
- Hepatitis C (Ag + Ab) **
- HIV-1 and HIV-2 (Ag + Ab)
- HTLV-1and HTLV-2 Ab (Optional)
- VDRL and TPPA
- Toxoplasma IgG
- TB – Mantoux test, Interferon gamma (QuantiFERON Gold)
- Stool AOC and Larvae – 3 consecutive samples
- Rectal swabs for resistant gram negative bacteria screening and VRE
- MRSA screening

*Need to confirm by an EIA with a different format

** If reactive need to confirm by PCR

Points to be considered

I. If the recipient is having CLL / myeloma / immunosuppressive therapy, may give false negative results in antibody based tests

II. False positive results may occur up to 3 months following IVIG/blood transfusions

- Perform aerobic and anaerobic bacterial culture of stem cell harvest after processing, prior to storage and prior to transplantation

2.3 Post-transplant investigations

I. Pre-engraftment phase (0 - 28 Days)

- CMV viral load assay
    - If pre-emptive treatment - once a week monitoring
    - if on universal prophylaxis - when clinically indicated
- EBV viral load - once a week
- Adeno viral load - once a week
- β-D glucan and galactomannan - once a week
- Septic screen for bacterial and fungal infections - when clinically indicated

II. Early post-engraftment phase (28 - 100 Days)

- CMV viral load assay
    - If pre-emptive treatment - once a week monitoring
    - if on universal prophylaxis - when clinically indicated
- EBV viral load - once a week
- Adeno viral load - once a week
- β-D glucan and galactomannan - once a week
- Septic screen for bacterial and fungal infections - when clinically indicated
- Toxoplasma PCR can be considered in patients at high risk (i.e. seropositive before transplant and who received a cord blood graft, had developed GVHD and require immunosuppressive treatment, or who are not receiving co-trimoxazole)

III. Late post-engraftment phase (after 100 Days)

- High risk patients i.e. Chronic GVHD, Cord blood transplant, CD34 selected grafts
    - CMV viral load assay - once a week
    - EBV viral load - once a week
    - Adeno viral load - once a week
- For other patients - testing offered only if clinically indicated, routine monitoring not recommended

Additional viral investigations may be required at any phase

- HHV6 viral load assay
- Parvo B19 viral load assay
- BKV viral load assay

3. Antimicrobial prophylaxis

3.1 Prophylaxis for CMV

Pre-emptive therapy is preferred.

Universal prophylaxis is only considered in situations where there are limitations to practice pre-emptive therapy.

3.2 Prophylaxis for HSV/ VZV

Aciclovir prophylaxis is considered for patients who are seropositive for HSV/ VZV and not on prophylaxis for CMV.

3.3 Prophylaxis for PCP and toxoplasmosis

Co-trimoxazole is recommended from post-engraftment period onwards.

3.4 Prophylaxis for candidiasis and aspergillosis

Fluconazole/ voriconazole/ posaconazole is recommended depending on the risk category, severity and duration of neutropenia.

4. Vaccination schedule for HSCT recipients

4.1 Children below 10 years of age

Vaccine	Months post HSCT					Comment
	6	8	10	12	24	
1.Diphtheria, Tetanus, Pertussis						
DTaP IM	√	√	√			
2. Polio Vaccine						
Inactivated polio vaccine 0.5ml IM	√	√	√			
3.*Haemophilus influenzae* type b						
IM	√	√	√			
4. Hepatitis B						
IM	√	√		√		Check HBs Ab titre 6 weeks after primary vaccination. If HBs Ab titre is <10 IU/ml, then repeat 3 dose schedule using a monovalent paediatric formulation of Hepatitis B.

*Combined vaccination with Hexavalent (Diphtheria, Tetanus, Pertussis, Polio, *Haemophilus influenzae* type b, Hepatitis B) or Pentavalent + IPV could be considered below the age of 3 years.

Vaccine	Months post HSCT					Comment
	6	8	10	12	24	
5. *Streptococcus pneumoniae* (pneumococcus)						
pneumococcal conjugate vaccine IM	√	√	√			In patients on active immunosuppression for chronic GVHD, additional penicillin prophylaxis is recommended. (phenoxymethyl penicillin 125mg po bd for children <2 years, otherwise 250mg bd)
IM 23 valent polysaccharide vaccine IM				√		
6. *Neisseria meningitidis*						
Quadrivalent meningococcal conjugate vaccine IM	√		√			Risk factors for meningococcal disease include hyposplenism (cGVHD), asplenia, complement or properdin deficiency.
7. Influenza						
Annual seasonal formulation	√	√				Two doses of influenza vaccine should be given in the first year of post-transplant, separated by at least 4 weeks. Influenza vaccine should be administered annually.

Vaccine	Months post HSCT					Comment
	6	8	10	12	24	
8. Measles, Mumps, Rubella						
MMR deep SC					√	Give only when not on immunosuppressive therapy, no cGVHD and reconstituted cell mediated immunity. Booster dose is recommended after 6 months. A gap of 8 -11 months should be maintained after IVIG. However can be given earlier if there is a measles outbreak.
9. Varicella						
Varicella vaccine deep SC					√	Give to seronegative recipients who are without active GVHD, not on immunosuppressive therapy and reconstituted cell mediated immunity. An optional vaccine because of limited data on safety and efficacy. Two doses scheduled 6 - 8 weeks apart. A gap of 8 -11 months should be maintained after IVIG. However can be given earlier if there is a chickenpox outbreak.

4.2 Children over 10 years and adults

Vaccine	Months post HSCT					Comment
	6	8	10	12	24	
1.Influenza (inactivated)						
Seasonal Influenza formulation IM	√					First dose at 6 months post-transplant and yearly thereafter. Can be given at 4 months if there is an outbreak of influenza.
2. *Streptococcus pneumoniae* (pneumococcus)						
Pneumococcal conjugate vaccine IM	√	√	√			*For patients with chronic GVHD a 4th dose of conjugate vaccine should be given instead of polysaccharide vaccine. Pneumococcal polysaccharide vaccine boosters should be given 5 years after 1st dose. In patients on active immunosuppression, additional penicillin prophylaxis is recommended. (phenoxymethyl penicillin 250mg po bd)
Pneumococcal polysaccharide vaccine IM				√*		

Vaccine	Months post HSCT					Comment
	6	8	10	12	24	
3.Diphtheria, Tetanus, Pertussis						
DTaP IM	√	√	√			
4. Polio Vaccine						
Inactivated polio vaccine 0.5ml IM	√	√	√			
5. *Haemophilus influenzae* type b						
IM	√	√	√			
6. Hepatitis B						
IM	√	√		√		Check HBs Ab titre 6 weeks after the last dose of the vaccine. If a post vaccination anti-HBs titre of ≥10 mIU/mL is not attained, a second 3 dose schedule of high dose (40 µg) HBV vaccine should be administered (alternative: administer 1 high dose HBV vaccine after which anti-HBs is tested, if desired titre not achieved complete the 3 dose schedule)
7. *Neisseria meningitidis*						
Quadrivalent meningococcal conjugate vaccine ACYW-135 IM	√	* √				Administer booster doses at every 5 years. * Post -transplant dose at 8th month is recommended only for the allogeneic transplants.

Vaccine	Months post HSCT					Comment
	6	8	10	12	24	
8. Human papilloma virus (HPV)						
HPV IM				√*		* HPV vaccine 3 dose schedule is recommended for females at intervals of 0, 2 and 6 months commencing at 12 months post-transplant.
9. Measles, Mumps, Rubella						
MMR deep SC					√	Give only when not on immunosuppressives, no cGVHD and reconstituted cell mediated immunity. Booster dose in 6 -12 months.
10. Varicella- Optional						
Varicella vaccine deep SC					√	Give only when not on immunosuppressives, no cGVHD and reconstituted cell mediated immunity. Booster dose in 6-8 weeks.

Optional vaccines

1. Hepatitis A vaccine
2. Rabies vaccine(in special circumstances)
3. Varicella vaccine

Contraindicated vaccine

1. BCG
2. Oral polio vaccine
3. Rota virus vaccine
4. Zoster vaccine(different from varicella vaccine)
5. Intra nasal influenza vaccine

5. Hospital infection prevention and control

Minimizing opportunistic and life threatening infections require stringent infection prevention and control in many areas with evidence based recommendations.

Room ventilation

HSCT recipients especially during conditioning and pre-engraftment period should be placed in single patient rooms with protective isolation that incorporate the following features:

- ≥12 air exchanges/hour
- Point-of-use or central HEPA filters with 99.97% efficiency for removing particles ≥0.3µm in diameter

Efficiency of HEPA filters should be checked every 3 months by performing a particulate count preferably by a third party. Filters should be replaced based on the efficiency report and on manufacturers' recommendations. When there is ongoing construction, filtration efficiency should be monitored frequently to determine appropriate time for replacement.

- Mixed air (recirculating: fresh air 70 - 75%: 30 - 25%) or fresh air 100% to be circulated
- Positive pressure in rooms should be maintained between 10 - 20Pa. Meter indicating the pressure should be available for monitoring purposes
- Consistent positive air pressure differential between the patient's room and the hallway or ante-rooms should be maintained
- Pressure in the adjoining toilet should be maintained less than the room (by using an exhaust fan)
- Backup emergency power and redundant systems should be provided to maintain room pressurization and a constant number of air exchanges in HSCT units when the ventilation system is shut-off for maintenance, repair or in the event of a power failure

- Well sealed rooms without gaps between walls and windows, outlets, floor and ceiling should always be used in HSCT units. This will prevent infiltration of air from outside the room that could allow entry of spores and hinder maintenance of proper pressure differential
- Continuous pressure monitoring is required especially while rooms are occupied. There should be an alarm system to alert staff when there is a pressure differential problem
- Air handling system should never be shut off even when the room is not occupied. Consider set back mode for energy conservation purpose
- Self-closing doors to maintain constant pressure differentials. Glass panels can be installed in either the door or the wall of the HSCT recipient's room to enable the nursing staff to observe the patient even when the doors are closed
- Following monitoring records should be maintained
    - Pressure
    - Temperature
    - Humidity
    - Number of air exchanges per hour
    - Efficiency of HEPA filters
    - Alarm checks (on pressure gauges)
    - General house keeping
    - Electrical maintenance
    - Plumbing and carpentry
- Air sampling surveys should be conducted every 6 months. Additional sampling in an outbreak of fungal infection, every 3 months during periods of hospital reconstruction
- Room temperature should be maintained between 22-25^{0}C

Water quality

- Water quality should be monitored every 3 months
- Water to the wash room should pass through a UV light. Life span of the UV bulb should be monitored
- Disposable shower-heads with inbuilt bacterial filters should be used. It should be disposed according to manufacturers' recommendation

Construction and renovation

- Planning for construction or renovation should include strategies for intensified mould control measures (Appendix I)
- Whenever possible, HSCT recipients should avoid construction and renovation areas
- Avoid transporting equipment and supplies to be used by HSCT recipients through construction and renovation areas
- During hospital construction or renovation, should construct rigid, dust-proof barriers with airtight seals between patient care areas and construction or renovation areas to prevent dust from entering patient care areas
- During periods of construction HSCT recipients may benefit from wearing N95 respirators while outside the HEPA filtered areas
- Whenever possible false ceilings should be avoided
- Areas above false ceilings located under or adjacent to construction areas, should be routinely vacuumed

Building cleaning

- Permanent trained staff should be appointed to the unit. Preferable to demonstrate competency prior to allocation of the task

- Environmental cleaning
    - Exhaust vents and all horizontal surfaces should be cleaned daily with detergent and disinfectant using a sterile towel and disinfected mop heads. Terminal cleaning after patient discharge should be done using a disinfectant (chlorine based solutions should have 1000 ppm available chlorine)
    - Walls should be cleaned weekly with a disinfectant
    - Floor should be disinfected twice daily by wet mopping using a solution with 1000 ppm available chlorine
    - Bathroom/toilet should be cleaned and disinfected (twice a day) with phenolic disinfectants
    - Thorough cleaning during and after any construction activity, including minor renovation projects, is critical
- Damp dusting should be practised to avoid generation of aerosolized dust
- Floor surfaces and finishes should be smooth, nonporous, and scrubbable (e.g. vinyl) to minimize dust levels
- Carpeting should not be installed in HSCT center hallways, outside of patient rooms or inside the rooms. HSCT recipients should not be exposed to vacuuming
- Water leaks should be cleaned up and repaired as soon as possible but within 72 hours to prevent mould proliferation in floor, wall coverings, ceiling tiles, cabinetry and in around all HSCT patient care areas. If cleanup and repairs are delayed ≥72 hours after the water leak, the involved materials should be assumed to contain fungi and handled accordingly (e.g. discarded preferably or cleaned)
- Design and selection of furnishings should focus on creating and maintaining a dust-free environment. Upholstery should be smooth, nonporous and easily cleanable

- Finishes (i.e. wall coverings, window shades and countertops) used in HSCT centers should also be scrubbable, nonporous, and easily disinfected to minimize dust accumulation
- Defects in roofing, tiling, flooring, walls, windows, fixtures or seals that manifest as ingress of water and dust should result in an immediate notification for corrective action
- Once a patient is discharged from the unit, a thorough terminal cleaning and disinfection must be done (Appendix II)
- Spill management – refer Sri Lanka College of Microbiologists (SLCM) Infection Control Manual

Isolation and barrier precautions

- When indicated, HSCT recipients should also be placed on airborne, droplet, or contact precautions in addition to standard precautions
- Each room is made up of three main areas: the ante-room (optional), the main room and bath room. The door to the room and the door to the bath room must be closed all the time. The main door and ante-room door should never be opened at the same time
- Door signage with protective precautions to be clearly displayed at entry to patient's room
- Restricted entry has to be ensured (No visitors unless essential for patient management)
- Those who have signs and symptoms of community respiratory viral infection, skin rash, vomiting or diarrhoea within last 48 hours should not be granted access including staff and visitors
- Hand washing facilities must be available at the entrance of each patient room with single use hand towels. Hand driers are not recommended

- Trolley for PPE should be set up outside single room (ante room) with alcohol hand rub, gowns, gloves, masks, neutral detergent wipes for cleaning and 70% isopropyl alcohol wipes for disinfection
- Alcohol hand rubs to be placed at bedside and on entry to the room
- HSCT recipients may benefit from wearing N95 respirators (during hospital construction) especially during the pre-engraftment period when they are outside the room

Hand hygiene

- Hand hygiene is the single most effective procedure for preventing nosocomial infections
- Everyone including HCWs should wash hands on entering and after leaving rooms of HSCT recipients and candidates
- All HCWs should practice hand hygiene adhering to WHO five moments of hand hygiene, before wearing and after removing gloves. Hand washing is preferable over use of alcohol hand rub
- Health-care workers wearing gloves should put them on in the patient's room after hand washing and then discard them in the same patient's room before washing hands again on exiting the room
- Gloves should always be changed after touching a dirty area of the body
- In suspected or confirmed *Clostridium difficile* infections and other diarroheal infections, hand washing should be practiced
- HSCT recipients and bystanders of children should be encouraged to practice good hand hygiene (e.g. washing hands before eating, after using the toilet, before and after touching a wound)

Equipment

- Dedicated patient equipment in each room must be cleaned and disinfected appropriately prior to reuse after patient discharge (refer SLCM Infection Control Manual)
- All non-dedicated equipment should be cleaned and disinfected appropriately after use

Toys

- Toys that cannot be washed or disinfected after use should be avoided. Toys provided in an individual patient room should be thoroughly washed before they are brought into the room and thereafter at least once weekly or as required
- Water-retaining bath toys should not be used by immunocompromised HSCT recipients
- Toys should not be shared

Plants

- Fresh or dried flower arrangements should not be allowed in the unit

Health care Personnel

- Immunization of all HCWs with following vaccines is recommended to prevent transmission of vaccine preventable diseases to HSCT recipients
    - Hepatitis B (Immunity should be checked)
    - MMR (Measles, Mumps and Rubella)
    - dTpa (Diptheria, Tetanus and Pertussis)
    - Varicella (if no evidence of protection – not vaccinated or past history of infection)
    - Annual Influenza
- HCWs caring for HSCT recipients should preferentially receive inactivated vaccines (e.g. inactivated influenza vaccine,

inactivated polio vaccine) to minimize the theoretical risks of transmission of vaccine virus to HSCT recipients

- If a live vaccine (Varicella, MMR) is given HCW should avoid working in HSCT units for a minimum of 4 weeks
- All HCWs with infections that are potentially transmissible to HSCT recipients or candidates should be restricted from direct patient care activities
- On significant exposures to fever rash illness, HCW should be assessed for quarantine purposes
- HCWs with draining skin and soft tissue infections or other skin or mucous membrane lesions (e.g. HSV lip lesions) that cannot be completely covered, should be restricted from patient contact
- The extent of work restrictions (e.g. leave from work versus temporary reassignment to non-patient care duties) will depend on the specific infection
- Work exclusion policies should be designed to encourage HCWs to report their illnesses or exposures to Infection Control Unit

HSCT centre visitors

- No visitors allowed unless essential for patient management. Generally children less than 12 years of age are not permitted entry to the unit
- HSCT centers should have written policies regarding the screening of all visitors for communicable infections. Trained personnel (e.g. administrative or nursing personnel) should perform active screening daily at key entry points to the units, particularly during the respiratory virus season
- Visitors with signs or symptoms suggestive of communicable infections (e.g. fever, upper respiratory infection or flu-like symptoms, diarrhea, *Varicella zoster*-like rash) or for recent exposures to communicable infections (e.g. chickenpox, mumps, measles, pertussis) should be excluded from entry

- Visitors who received live vaccines recently (e.g. within 6 weeks of receiving a chickenpox vaccine, or a history of receiving an oral polio vaccine within the previous 3 to 6 weeks) should not visit the unit
- All visitors must follow hand hygiene and isolation precautions
- Annual vaccination with influenza vaccine is recommended for all family members
- >6 months of age and household contacts of these patients

Patient Skin Care

- HSCT recipients should take daily showers or baths using a mild soap during and after transplantation depending on the clinical status
- For patients with GVHD, regular lubrication of dry, intact skin with emollients may decrease pruritus and maintain skin integrity. Ointments and creams are more effective than lotions and less likely to sting when applied to sensitive skin
- Routine inspection of skin sites likely to be portals of infection (e.g. perineum, intravascular access sites) is recommended during neutropenia
- Should maintain good perineal hygiene to minimize loss of skin integrity and risk for infection. (Gentle but thorough perineal cleaning after each bowel movement and thorough drying of the perineum after each episode of urination. After using the toilet, females should always wipe the perineum from front to back to prevent fecal contamination of the urethra and urinary tract infections)
- The use of rectal thermometers, enemas, or suppositories; internal rectal examinations; are contraindicated among HSCT recipients because of the risk for skin or mucosal breakdown
- Nails of the patient should be cut short

Patient Oral Care

To reduce the risk of oral and dental infections, all HSCT candidates and their caregivers should be educated regarding the importance of maintaining good oral and dental hygiene.

- All HSCT candidates should receive a dental evaluation and relevant treatment before conditioning therapy begins
- Elective dentistry should be postponed until the patient has demonstrated substantial immune recovery
- HSCT recipients with mucositis and HSCT candidates undergoing conditioning therapy should maintain oral hygiene by performing oral rinses 4 to 6 times/day with 4% chlorhexidine, sterile water, normal saline, or sodium bicarbonate solutions
- HSCT recipients and candidates should brush their teeth 2 to 3 times a day with a soft regular toothbrush which should be replaced regularly. If the recipient cannot tolerate a toothbrush, a foam tooth swab can be used
- Routine dental supervision to monitor and guide the patient's maintenance of oral and dental hygiene should be provided.
- HSCT recipients and candidates should not wear fixed orthodontic appliances or space maintainers from the start of conditioning therapy until pre-engraftment mucositis resolves
- If wearing dentures, use them only while eating. Clean them twice daily with a soft toothbrush. When not wearing them, soak dentures in antiseptic denture soaking solution. The solution should be changed daily
- Patients with GVHD of the oral cavity should undergo frequent dental evaluation because of the accelerated pace of dental caries in those patients

Vaccination

- Recommend VZV vaccination for at risk household contacts of candidates to be completed 3 months prior to transplant
- Annual influenza vaccine
- Avoid oral polio vaccine

6. Diet for Transplant recipient

- The diet has been designed to reduce the bacterial content of the food. This diet should be followed until 3 months after transplant. Allogeneic transplant patients should follow the diet until all immunosuppressive therapy is discontinued
- It is also important to follow good food hygiene and personal hygiene when preparing food. Store them appropriately and safely. Food should be well cooked and freshly prepared. Expiry date of food should be checked. Never leave hot food to cool on the table or cold food to warm. Eat hot food hot (>60^0C) and cold food cold (<50^0C).Preferable to eat food within one hour of preparation
- Fruits with peels can be allowed, it has to be freshly cut
- Transplant recipients should use boiled cooled water for drinking purposes and for preparation of fruit juices and milk. Avoid bottled water
- All food and water consumed by the patient is preferred to be pressure cooked
- High risk foods
    - Raw and undercooked seafood, meat and poultry
    - Pro-biotic yoghurts, probiotic capsules
    - Raw or partially cooked egg
    - Cold smoked sea food
    - Raw sprouts and salads
    - Pre-cut fruits
    - Pate and meat spreads
    - Soft and semisoft cheese
    - Unpasteurized milk and dairy products made from unpasteurized milk
    - Well water and tank water unless regularly tested for water quality
    - Raw or non-heat treated honey
    - Raw nuts and nuts in shell

7. List of immunoglobulin

- VZV specific IG
- HBV specific IG
- CMV specific IG
- IVIG
- Rabies specific IG (human/ equine)

8. List of antimicrobials

8.1 Antivirals

- Intravenous aciclovir
- Oral aciclovir (adult)
- Syrup aciclovir (paediatric)
- Syrup valganciclovir
- Intravenous ganciclovir
- Oral Valganciclovir
- Intravenous cidofovir
- oral probenecid
- Intravenous foscarnet
- Oral oseltamivir (adult)
- Syrup oseltamivir (paediatric)
- Inhalational zanamivir
- Nebulized ribavirin
- Oral ribavirin
- Oral tenofovir
- Peginterferon alpha
- Oral valaciclovir (adult)
- Oral lamivudine
- Oral famciclovir
- Oral sofosbuvir

8.2 Antifungal

- Oral fluconazole
- Intravenous fluconazole
- Itraconazole suspension
- Intravenous itraconazole
- Intravenous amphoterecin B deoxycholate
- Intravenous liposomal amphoterecin B
- Intravenous caspofungin
- Intravenous anidulafungin
- Intravenous micafungin
- Oral voriconazole
- Intravenous voriconazole
- Oral posaconazole
- Oral flucytosine
- Intravenous flucytosine

8.3 Antiparasitic

- Inhalational pentamidine isothionate
- Oral sulfadiazine
- Oral pyrimethamine
- Oral folinic acid
- Oral mebendazole
- Oral albendazole
- Oral metronidazole
- Oral levamisole
- Oral thiabendazole
- Oral ivermectin
- Oral cotrimoxazole

8.4 Antibiotics

Specifically needed in addition to the available antibiotics

- Intravenous tigecycline
- Intravenous colistimethate sodium
- Intravenous ertapenam
- Oral trimethoprim
- Intravenous co-trimoxazole
- Intravenous moxifloxacin
- Oral moxifloxacin
- Intravenous linezolid
- Oral linezolid
- Oral vancomycin
- Intravenous aztreonam

References:

- Accreditation advisory council, Australian Government Department of Health (2014) Requirements for procedures related to the collection, processing, storage and issue of Haemopoietic progenitor cells. 5th ed.
- Blood and marrow transplant network, NSW. (2013) Post-transplant vaccine guidelines.
- British Transplantation Society Guidelines (2015) The Prevention and Management of CMV Disease after Solid Organ Transplantation. 3rd ed. pp 1-55. www.bts.org.uk
- Christian Medical College, Vellore (2015) Hospital infection control manual. 6th ed.
- Department of Hematology and BMT BGS Global Hospital, Bangalore. Worksheet for immunization of HSCT recipients.
- Department of Hematology, Rajeev Gandhi Cancer Institute and research Centre, Delhi. Post stem cell transplant vaccination schedule
- Dignan F, Clark A, Aitken C, Gilleece M, Jayakar V, Krishnamurthy P *et al.* (2016) BCSH/BSBMT/UK clinical virology network guideline: diagnosis and management of common respiratory viral infections in patients undergoing treatment for haematological malignancies or stem cell transplantation. Br J Haematol. 173(3) pp 380-93. doi: 10.1111/bjh.14027. Epub 2016 Apr 7.
- Dykewicz C (2001) Hospital Infection Control in Hematopoietic Stem Cell Transplant Recipients. Emerging Infectious Diseases. 7(2) pp 263-267. doi:10.3201/eid0702.700263.
- Emery V, Zuckerman M, Jackson G, Aitken C, Osman H, Pagliuca A *et al*. (2013) Management of cytomegalovirus infection in haemopoietic stem cell transplantation. Br J of Haematol. 162 pp 25–39
- Japan Society for Hematopoietic Stem Cell Transplantation (JSHCT) https://www.jshct.com/english/

- Lin R and Liu Q (2013) Diagnosis and treatment of viral diseases in recipients of allogeneic hematopoietic stem cell transplantation. J Hematol Oncol. 6 pp 94
- Ljungman P, Cordonnier C, Einsele H, Englund J, Machado CM, Storek J et a*l* (2009) Vaccination of hematopoietic cell transplant recipients. Bone Marrow Transplant. 44 pp 521-526. doi: 10.1038/bmt.2009.263.
- National Pathology accreditation advisory council, Australian Government, Department of Health (2014) Requirements for procedures related to the collection, processing, storage and issue of Heamopoietic progenitor cells. 5th ed.
- RNSH, Northern Sydney Local Health District (2015) Protection of HSCT recipients from exposure to transmissible pathogens
- Rubin L, Levin M, Ljungman P, Davies E, Avery R, Tomblyn M *et al*. (2014) 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host. Clin Infect Dis. 58(3) pp 309-18. doi: 10.1093/cid/cit816.
- St Vincent's & Mater Health Sydney (2010) Immunosuppresses diet.
- Tomblyn M, Chiller T, Einsele H, Gress R, Sepkowitz K, Storek *et al*. (2009) Guidelines for Preventing Infectious Complications among Hematopoietic Cell Transplantation Recipients: A Global Perspective. Biol Blood Marrow Transplant. 15 pp 1143-1238
- Tomblyn M, Chiller T, Einsele H, Gress R, Sepkowitz, Storek J *et al*. (2009) Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. Biol Blood Marrow Transplant. 44 pp 453–558.
- Western Sydney Local Health District (2016) West mead Hospital High Risk Wards: Environmental Monitoring in Haematology, Renal, NICU and Operating Theatres.
- Winnie W and Qasim W. (2013) Management of Adenovirus in Children after Allogeneic Hematopoietic Stem Cell Transplantation. Adv Hematol. 2013; 176418. doi: 10.1155/2013/176418

Appendix I

Strategies for mould control during construction and renovation

1. HEPA filtration of incoming air
2. Directed room air flow
3. Positive room air pressure relative to the corridor
4. Well sealed rooms
5. High rates of room air changes

Appendix II

CDC Environmental Checklist for Monitoring Terminal Cleaning[1]

Date:	
Unit:	
Room Number:	
Initials of ES staff[2] (optional):	

Evaluate the following priority sites for each patient room:

High-touch Room Surfaces[3]	Cleaned	Not Cleaned	Not Present in Room
Bed rails / controls			
Tray table			
IV pole (grab area)			
Call box / button			
Telephone			
Bedside table handle			
Chair			
Room sink			
Room light switch			
Room inner door knob			
Bathroom inner door knob / plate			
Bathroom light switch			
Bathroom handrails by toilet			
Bathroom sink			
Toilet seat			
Toilet flush handle			
Toilet bedpan cleaner			

Evaluate the equipment present in the room:

High-touch Room Surfaces[3]	**Cleaned**	**Not Cleaned**	**Not Present in Room**
IV pump control			
Multi-module monitor controls			
Multi-module monitor touch screen			
Multi-module monitor cables			
Ventilator control panel			

Mark the monitoring method used:	
☐ Direct observation	☐ Fluorescent gel
☐ Swab cultures	☐ ATP system
☐ Agar slide cultures	

[1]Selection of detergents and disinfectants should be according to institutional policies and procedures

[2]Hospitals may choose to include identifiers of individual environmental services staff for feedback purposes.

[3]Sites most frequently contaminated and touched by patients and/or healthcare workers