Chapter Two: Infection Prophylaxis

Purpose: The following guidelines are intended for patients who have weakened immune systems due to treatment for hematological malignancies. Patients who are being treated and/or being prepared for stem cell transplants are at an increased risk for both pre- and post-transplant infections. Note: The bone marrow transplant team may individualize the guidelines to meet specific patient needs.

Scope: These guidelines outline the routine infection prophylaxis for patients undergoing treatment for hematological malignancies and for those undergoing hematopoietic stem cell transplantation at the University of Kentucky Markey Cancer Center.

I. Oral Care
II. Bacterial prophylaxis
III. Viral prophylaxis
IV. PCP prophylaxis
V. Fungal prophylaxis
VI. IV Gammaglobulin
VII. Procedure Prophylaxis
VIII. Nasal Washing Collection for Respiratory Battery
I. **ORAL CARE**
A. Salt and soda oral rinse four times a day for neutropenic patients.

II. **BACTERIAL PROPHYLAXIS**: Please review current protocols. Current research protocols supersede the policies listed below.

A. **Autologous Transplant Patients**:
   1. Antibacterial prophylaxis will not be routinely given unless the patient is neutropenic (ANC<500/µL).
   2. Patients with known risk for impaired humoral immunity (i.e., Hodgkin’s disease, multiple myeloma) with either hypogammaglobulinemia or recurrent sino-pulmonary infections will be considered for antibacterial prophylaxis from time of stem cell reinfusion until day +100.

B. **Antibacterial Prophylaxis for Allogeneic Transplant Patients**
   1. **Matched sibling donor**:
      a) All patients that have received an HLA-matched sibling donor transplant will receive prophylaxis until day +100.
      b) Antibacterial prophylaxis will be given at any time a patient is neutropenic (ANC<500/µL) or has acute or chronic GVHD requiring >1mg/kg/day of corticosteroid therapy. These patients will receive penicillin 500 mg po twice a day or azithromycin 250 mg po daily, if allergic to penicillin.
      c) Antibacterial prophylaxis should also be considered in patients with or without chronic GVHD that have chronic immune suppression, often manifested by hypogammaglobulinemia and/or recurrent sino-pulmonary infections.
      d) Prophylactic antibacterials will be discontinued after day +100 or when immunosuppression for prevention or treatment of GVHD is stopped.
   2. **Matched unrelated donor**:
      a) All patients that have received an HLA-matched unrelated donor transplant will receive prophylaxis until at least 3 months after immunosuppressive therapy is discontinued.
      b) Antibacterial prophylaxis will be given at any time a patient is neutropenic (ANC<500/µL) or has acute or chronic GVHD requiring >1mg/kg/day of corticosteroid therapy. These patients will receive penicillin 500 mg po twice daily or azithromycin 250 mg po daily, if allergic to penicillin.
      c) Antibacterial prophylaxis should also be considered in patients with or without chronic GVHD that have chronic immune suppression, often manifested by
hypogammaglobulinemia and/or recurrent sino-pulmonary infections.

d) Prophylactic antibacterials will be discontinued 2 months after immunosuppression for prevention or treatment of GVHD is stopped.

C. Antibacterial Prophylaxis for Hematologic Malignancy Patients

1. Leukemia/Lymphoma/Myeloma patients receiving chemotherapy will receive levofloxacin 500 mg PO daily during expected periods of neutropenia associated with the chemotherapy.

2. At the time of hospital discharge they will be given prescriptions for antibiotic prophylaxis to begin on day 8 post-treatment and continue until ANC >500; patients with extended periods of neutropenia may require 2 to 4 weeks of prophylaxis.

III. VIRAL PROPHYLAXIS

A. Adults

1. HSV:
   a) All autologous and allogeneic transplant patients receive acyclovir 400 mg po three times daily or acyclovir 250 mg/m2 IV every 12 hours in patients unable to take po from day +1. Autologous transplant patients may stop on day +30.
   b) Patients who have received an allogeneic transplant continue acyclovir 400 mg po three times a day until 3 months after immunosuppression is withdrawn.
   c) If CMV antiviral prophylaxis or treatment is given, discontinue acyclovir. Restart acyclovir when CMV prophylaxis or therapy is discontinued.
   d) Leukemia/Lymphoma/Myeloma patients receiving chemotherapy will receive acyclovir 400 mg PO three times daily during periods of neutropenia (ANC <500). At the time of hospital discharge they will be given prescriptions for antibiotic prophylaxis to begin on day 8 post-treatment and continue until ANC >500; patients with extended periods of neutropenia may require longer durations of prophylaxis.

2. CMV: Refer to CMV policy under Infection Therapy.

3. RSV & Common Respiratory Viral Pathogens:
   a) Follow policy below for RSV and other common respiratory pathogens control on BMT Unit. This applies to children and adults. The peak incidence is usually December through March; the policy below will be in effect these months of each year.
      (1) Diagnostic nasopharyngeal washes are required on patients suspected of having RSV or other common
respiratory viral infections. Send diagnostic nasal suction/washings to the lab before 10 am for same day turnaround.

(2) Place patients with documented or suspected RSV infection in “Protective” and “Contact” isolation

(3) Cohort nursing personnel if possible.

(4) Screen health care workers and visitors for signs/symptoms such as head colds, fever, cough, sneezing, conjunctivitis, pharyngitis, otitis media, and asthma (wheezing).
   (a) Persons suspected of active viral infection should not have direct patient contact.
   (b) Keep health care workers and visitors with suspected RSV infection out of the BMT unit.

(5) Restrict all children <10 years old from the BMT unit.

(6) If inhaled ribavirin is indicated, administration through home health is desired, whenever possible.

(7) Before taking a treated, asymptomatic patient out of isolation, retest oropharyngeal secretions for presence of virus (fluorescent antibody or EIA plus culture).

(8) In outpatient clinic, place patients with symptoms suggestive of RSV in “Contact” isolation until the disease is ruled out.

4. Varicella Zoster Prophylaxis:
   a) This information applies to all immunosuppressed patients, including those receiving chemotherapy.
   b) In patients exposed to chickenpox:
      (1) Chemotherapy and autologous transplant patients with a reliable history of chickenpox and/or positive varicella titer DO NOT require prophylactic therapy.
      (2) All allogeneic patients and those chemotherapy patients and autologous transplant patients without a definite history of chickenpox and/or a negative varicella titer should receive Varicella Zoster Immunoglobulin (VariZIG) by IM injection if eligible for study (see VariZIG protocol).
      (3) The following patient populations with a positive varicella titer should be considered for V-ZIG therapy:
         (a) All allogeneic transplant patients < 100 post transplant, patients with chronic GVHD, and patients who have received fludarabine or alemtuzumab (Campath®). The dose should be given as soon as possible after exposure for maximum protection, but no longer than 96 hours after exposure.
(4) If a patient is considered to be eligible for VariZIG, contact Cangene Corporation at 1 (800) 843-7477. (If contact information changes, contact pharmacy staff for current contact information.)

c) Historically, patients are dosed per weight as indicated below:

<table>
<thead>
<tr>
<th>Weight of Patient</th>
<th>Dose</th>
</tr>
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<tbody>
<tr>
<td>Kg</td>
<td>lb</td>
</tr>
<tr>
<td>0-10</td>
<td>0-22</td>
</tr>
<tr>
<td>10.1-20</td>
<td>22.1-44</td>
</tr>
<tr>
<td>20.1-30</td>
<td>44.1-66</td>
</tr>
<tr>
<td>30.1-40</td>
<td>66.1-88</td>
</tr>
<tr>
<td>&gt;40</td>
<td>&gt;88</td>
</tr>
</tbody>
</table>

(1) No more than 2.5 ml should be injected at any single site. (1 vial = 125 units).

(2) Watch for signs and symptoms of chickenpox for 21 days post-exposure; if signs appear, intravenous acyclovir will be initiated immediately at 500 mg/m²/dose IV every 8 hours in children and adults.

(3) Be aware that patients who receive VariZIG prophylaxis may have delayed onset of clinical chickenpox.

(a) For pregnant women with no history of chickenpox, avoid contact with patients with chickenpox or shingles. CONTACT OBSTETRICIAN IMMEDIATELY for contact with an infected patient.

d) Chicken Pox Vaccine

(1) Families with children who have not had the chickenpox should have their children immunized well in advance of transplant. The vaccination dose or doses should be completed > 4 weeks before the conditioning regimen begins or > 6 weeks before the HSCT is performed.

(2) HSCT recipients and candidates undergoing conditioning therapy should avoid any contact with any vaccine recipient for a period of 4-6 weeks especially a vaccine recipient who experiences a rash after vaccination. The rash normally appears 5-35 days after vaccination (median 22 days).
IV. **PCP PROPHYLAXIS**

A. **Adults**
   1. Autologous transplant patients will receive PCP prophylaxis starting once engraftment is stable and continued until day +100 if they have been conditioned with a TBI-containing regimen, have suspected humoral immunodeficiency or hypogammaglobulinemia, or prolonged cytopenias following autologous engraftment.
   2. Allogeneic transplant recipients will receive PCP prophylaxis for at least 6 months and until after the discontinuation of any immunosuppressive therapy for the prevention or treatment of GVHD. Bactrim/Septra DS po bid every Sat/Sun starting when ANC > 0.5 x 10⁹/l.
   3. Transplant recipients with chronic GVHD receiving immunosuppressive therapy continue PCP prophylaxis until discontinuation of all immunosuppressive agents for chronic GVHD.
   4. For patients allergic or intolerant to Septra, dapsone 200 mg, leucovorin 25 mg & pyrimethamine 75 mg weekly may be administered in patients’ without G6PD deficiency. Dapsone 100 or 200 mg daily, Atovaquone 1500 mg daily or inhaled/IV pentamidine 300 mg every 4 weeks, pre-med with albuterol MDI 2-3 puffs are additional options.

V. **FUNGAL PROPHYLAXIS**

A. **Adult Recipients of Autologous Stem Cells:**
   1. Fluconazole 400 mg po daily is given to all patients from day +1 until ANC>500/μL.

B. **Adult Recipients of Allogeneic Stem Cells:**
   1. Fluconazole 400 mg po daily is given to all patients from day +1 until day 100 in patients without GVHD.
   2. Posaconazole 200 mg po TID through at least day +100 in patients with acute GVHD requiring ≥ 1 mg/kg prednisone (or equivalent) or in patients with chronic GVHD. Posaconazole will be discontinued when steroids are tapered off. Posaconazole should be administered with a high fat meal or high fat meal or high fat enteral nutritional supplement. (Voriconazole may be used in substitution depending on patient’s ability to tolerate posaconazole.)
   3. Selected patients with poor engraftment, extensive chronic graft-versus-host disease, or those being managed with monoclonal antibodies or other anti-lymphocyte monoclonal antibody therapy or combination immunosuppressive therapy may continue antifungal prophylaxis until immunosuppression is withdrawn.
4. Voriconazole 200 mg po BID is given from day +1 until day 100 in patients with a history of invasive aspergillus prior to allogeneic stem cell transplant.

C. Antifungal Prophylaxis for Patients with Hematologic Malignancies:
1. De novo patients with AML or MDS will be treated with posaconazole 200 mg po TID for prophylaxis during the period of ANC < 500. They will be discharged with prescriptions to begin posaconazole 200 mg po TID on day 8 and continue until ANC >500. Patients with extended periods of neutropenia may require 2-4 weeks of prophylaxis. Posaconazole should be administered with a high fat meal or a high fat enteral nutritional supplement. Patients unable to tolerate posaconazole will receive fluconazole 400 mg po daily during period of neutropenia.
2. Primary refractory or refractory relapsed AML patients will be treated with posaconazole 200 mg po TID during the period of ANC < 500. Posaconazole should be administered with a high fat meal or a high fat enteral nutritional supplement. Patients unable to tolerate posaconazole will receive voriconazole 200 mg po BID during period of neutropenia.
3. Patients with hematologic malignancies other than AML or MDS will receive fluconazole 400 mg po daily during periods of neutropenia.

VI. INTRAVENOUS GAMMA GLOBULIN

A. Adults
1. IVIG is not recommended for prophylaxis unless the patient is an unrelated marrow recipient with severe hypogammaglobulinemia (serum IgG < 400 mg/dL) beyond the first 100 days post-transplant.

VII. PROPHYLAXIS PRIOR TO PROCEDURES:
A. Prophylaxis should be given to neutropenic patients and to patients with indwelling lines and patients on immunosuppressive therapy.

### Prophylactic Regimens for Dental, Oral, Respiratory Tract, or Esophageal Procedures

<table>
<thead>
<tr>
<th>Situation</th>
<th>Agent</th>
<th>Regimen *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard general prophylaxis</td>
<td>Amoxicillin</td>
<td>Adults: 2 g; children: 50 mg/kg orally 1 h Before procedure</td>
</tr>
<tr>
<td>Unable to take oral medications</td>
<td>Ampicillin</td>
<td>Adults: 2 g intramuscularly (IM) or intravenously (IV); children: 50 mg / kg IM or IV within 30 min before procedure</td>
</tr>
<tr>
<td>Allergic to penicillin</td>
<td>Clindamycin or Cefadroxil Or Cefazolin†</td>
<td>Adults: 600 mg; children: 20 mg/kg orally 1 h before procedure</td>
</tr>
<tr>
<td>Allergic to penicillin and unable to take oral medications</td>
<td>Clindamycin Or Cefazolin†</td>
<td>Adults: 600 mg; children: 20 mg/kg IV within 30 min before procedure</td>
</tr>
</tbody>
</table>

* In patients with platelet counts <100,000 discuss platelet support with dentist.

### Prophylactic Regimens for Genitourinary and Gastrointestinal Procedures

<table>
<thead>
<tr>
<th>Situation</th>
<th>Agents*</th>
<th>Regimen†</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk patients, coverage for bowel procedures, ANC &lt;500, indwelling catheter</td>
<td>Ampicillin plus Gentamicin</td>
<td>Adults: ampicillin 2 g intramuscularly (IM) or intravenously (IV) plus gentamicin 1.5 mg/kg (not to exceed 120 mg) within 30 min of starting the procedure; 6 h later, ampicillin 1 g IM/IV or amoxicillin 1 g orally. Children: ampicillin 50 mg/kg IM or IV (not to exceed 2 g) plus gentamicin 1.5 mg/kg within 30 min of starting the procedure; 6 h later, ampicillin 25 mg/kg IM/IV or amoxicillin 25 mg/kg orally.</td>
</tr>
<tr>
<td>High-risk patients allergic to Ampicillin/amoxicillin</td>
<td>Vancomycin plus Gentamicin</td>
<td>Adults: vancomycin 1 g IV over 1-2 h plus gentamicin 1.5 mg/kg IV/IM (not to exceed 120 mg); complete injection/infusion within 30 min of starting the procedure. Children: vancomycin 20 mg/kg IV over 1-2 h plus gentamicin 1.5 mg/kg IV/IM; complete injection/infusion within 30 min of starting the procedure.</td>
</tr>
<tr>
<td>Moderate-risk patients</td>
<td>Amoxicillin or Ampicillin</td>
<td>Adults: amoxicillin 2 g orally 1 h before procedure, or ampicillin 2 g IM/IV within 30 min of starting the procedure. Children: amoxicillin 50 mg/kg orally 1 h before procedure, or ampicillin 50 mg/kg IM/IV within 30 min of starting the procedure.</td>
</tr>
<tr>
<td>Moderate-risk patients allergic to Ampicillin/amoxicillin</td>
<td>Vancomycin</td>
<td>Adults: vancomycin 1 g IV over 1-2 h; complete infusion within 30 min of starting the procedure. Children: vancomycin 20 mg/kg IV over 1-2 h; complete infusion within 30 min of starting the procedure.</td>
</tr>
</tbody>
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**VIII. NASAL WASHING COLLECTION FOR RESPIRATORY BATTERY**

### A. Adults

**Supplies**

Reviewed and Revised 11/2012

Minimal content changes made.
Minimal content changes made.

- 10ml Syringe
- Normal saline
- Sterile specimen cup
- Viral culterette swab
- Kleenex
- Clean Gloves

**Procedure**

- Wash hands
- Don clean gloves
- Using 10ml syringe, draw up 10ml normal saline
- Hand patient opened specimen cup
- Instruct patient to tilt head back and hold their breath
- Using normal saline filled syringe, squirt 5ml normal saline in the patient's nostril
- Instruct patient to tilt head down and gently blow normal saline into specimen cup
- Using same instructions, squirt the remaining 5ml of normal saline in patient's opposite nostril
- Using viral culterette, swab patient's throat
- Swirl the swab in the normal saline/nasal secretion specimen cup and then discard swab
- Send specimen to lab on ice
- Mark microbiology requisition for respiratory battery and write in nasal/throat secretion for source of specimen

* Try to allow all the normal saline to drip out of each nostril for complete specimen
REFERENCES:

Section I: Oral Care

Section II: Bacterial Prophylaxis


Section III: Viral Prophylaxis

Section IV: Pneumocystis jirovecii Prophylaxis

Section V: Fungal Prophylaxis


**Section VI: Intravenous Gammaglobulin**