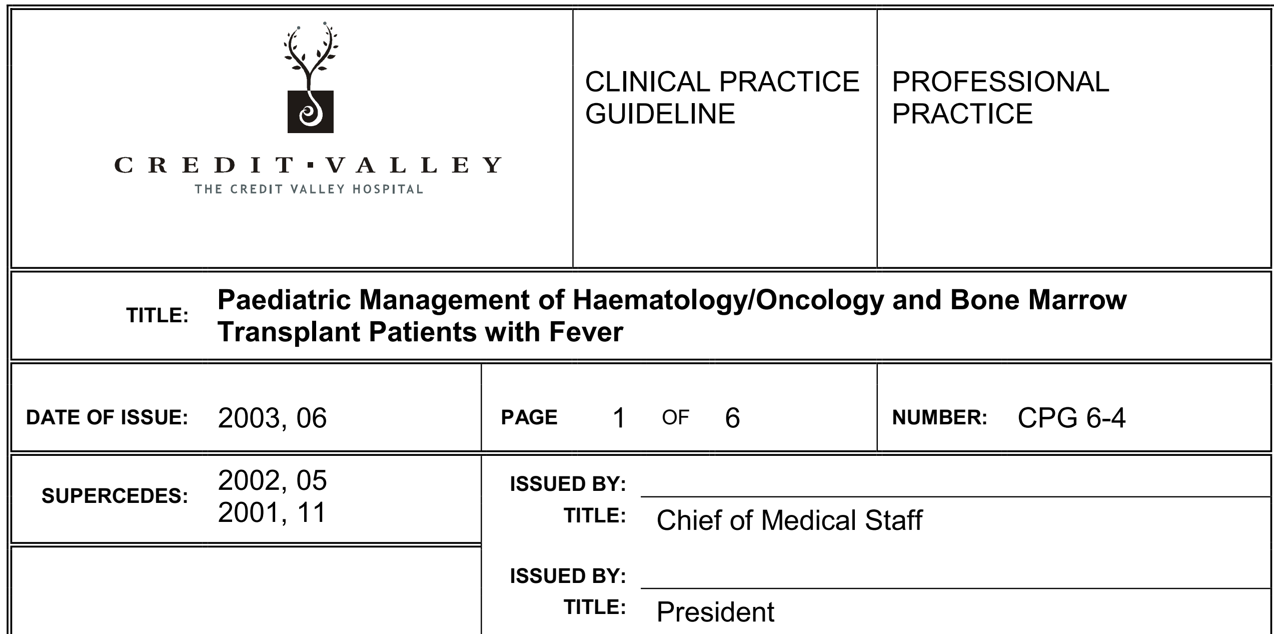

THE CREDIT VALLEY HOSPITAL	CLINICAL PRACTICE GUIDELINE	PROFESSIONAL PRACTICE
TITLE: **Paediatric Management of Haematology/Oncology and Bone Marrow Transplant Patients with Fever**		
DATE OF ISSUE: 2003, 06	PAGE 1 OF 6	NUMBER: CPG 6-4
SUPERCEDES: 2002, 05 2001, 11	ISSUED BY: TITLE: Chief of Medical Staff	
	ISSUED BY: TITLE: President	

Purpose:

To provide guidelines for the management of patients:

- with fever and neutropenia as a result of a known or suspected malignancy or the use of antineoplastics
- with fever or evidence of infection who are receiving antineoplastics or who have completed cancer therapy within 6 months **even though they are not neutropenic**.

Definitions:

Absolute neutrophil count (ANC=sum of mature polymorphs and band forms)

Selection Criteria:

- Inclusion: Temperature $\geq 38^{\circ}$ C **AND**
- ANC < 0.5 x 10^9/L, or
- ANC > 0.5 x 10^9/L and expected ANC nadir following antineoplastic administration has not yet been reached, or
- Patient is < 6 months post bone marrow transplant (BMT), or
- Patient is > 6 months post BMT and continues to take immunosuppressant agents.

In hospitalized children consider antibiotic treatment (HSC Guidelines for Initial Empiric Antibiotic Therapy 2002-2003 may be used as a reference) if:

- Temperature $\geq 38^{\circ}$ C **AND**
- ANC $\geq$ 0.5 x 10^9/L and expected ANC nadir following antineoplastic administration has already been reached, or
- Patient is > 6 months post BMT and is not taking immunosuppressant agents.

The necessity of initiating empiric antibiotic therapy in patients who **are not neutropenic,** is gauged by the severity of the presenting signs and symptoms, the results of initial investigations and the

presence/absence of a central venous catheter (CVC). **CVC cultures (all lumens) must be drawn as part of this assessment.**

Treatment and Monitoring:

EMERGENCY MANAGEMENT

Any child presenting to the emergency department or the paediatric oncology clinic with a known or suspected malignancy and a temperature of 38 degrees centigrade will have a **STAT CBC, differential and Blood Culture** via the peripheral route as per the medical directive: **Performing a Venipuncture to Obtain Blood Specimens in the Febrile Paediatric Oncology Patient (MD-22.4)**

The physician will initiate the guideline for patients that meet the inclusion criteria by completing the pre printed orders **Paediatric Haematology/Oncology and BMT Patients with Fever (Form #70002 D HR effective June 23/2003)**

Stop all antineoplastics until discussed with the staff oncologist. Consider stopping cotrimoxazole prophylaxis.

Start intravenous and give fluids at about 1.5 x maintenance rate. If not able to immediately access an indwelling central venous catheter (CVC) start a peripheral IV. Use the CVC as soon as possible.

Order a chest x-ray (if clinically warranted), renal function tests (creatinine, urinalysis) and the following cultures:

a) Blood from peripheral site (as per medical directive)
b) Blood from all lumens of indwelling central venous line(s)
c) Urine
d) Any apparent site of infection

Always consider the patient’s past history regarding resistance patterns of **previously cultured organisms** and clinical status (eg septic shock) when selecting antibiotics. Standard initial antibiotics for the stable patient may not be appropriate in a patient who has a history of serious infection due to an antibiotic resistant organism.

Catheter associated infection may present as fever related to manipulation of the CVC, infection at the catheter exit site or as infection along the subcutaneous course of the catheter. If this is the case, antibiotics directed at this site of infection (usually vancomycin) should be initiated IN ADDITION to the broad spectrum empiric antibiotic regimen. If CVC cultures confirm infection, a full course of antibiotics, alternated through all lumens, is indicated. Removal of the catheter is often required. Consultation with Infectious Diseases is recommended to facilitate this decision.

Administer **ANTIBIOTICS STAT** (should be given prior to patient transfer to any other area and prior to administration of blood products) according to the Antibiotic Dosing Guideline **Table 1.**

Table 1. Antibiotic Dosing Guideline

STABLE PATIENTS: No significant beta-lactam allergy

Drug, Route and Frequency	Dosing Guideline	Maximum
TAZOCIN ® (piperacillin-tazobactam) IV q8h	80 mg piperacillin/kg/dose	Max single dose: 4 g
GENTAMICIN IV q8h	Leukemia: 1 month to < 1 year: 2.5 mg/kg/dose 1 to < 5 years: 3 mg/kg/dose 5 to < 12 years: 2.7 mg/kg/dose ≥ 12 years: 2.3 mg/kg/dose Other Malignancy: 2.5 mg/kg/dose	Max single dose: Leukemics ≥ 12 years: 150 mg Others: 120 mg
The combination of Tazocin ® and gentamicin usually provides adequate empiric coverage against Gram positive organisms including *viridans streptococci*. However, if additional coverage against Gram positive organisms is desired, the addition of clindamycin is recommended. Consider discontinuation of clindamycin once C&S results are available.		

STABLE PATIENTS: Significant beta-lactam allergy (ie anaphylaxis)

Drug, Route and Frequency	Dosing Guideline	Maximum
CIPROFLOXACIN IV q12h	10 mg/kg/dose	Max single dose: 400mg
GENTAMICIN IV q8h	Dose as per above	
CLINDAMYCIN IV q8h	8 mg/kg/dose	Max: 600 mg/dose
Consider discontinuation of clindamycin once C&S results are available.		

UNSTABLE PATIENTS INCLUDING SEPSIS SYNDROME: No significant beta-lactam allergy

Drug, Route and Frequency	Dosing Guideline	Maximum
MEROPENEM IV q8h	20 mg/kg/dose	Max single dose: 1 g
GENTAMICIN IV q8h	Dose as per above	
VANCOMYCIN IV q6h	15 mg/kg/dose	Max single dose: 1 g

UNSTABLE PATIENTS INCLUDING SEPSIS SYNDROME: Significant beta-lactam allergy (ie. anaphylaxis)

Drug, Route and Frequency	Dosing Guideline	Maximum
CIPROFLOXACIN IV q12h	10 mg/kg/dose	Max single dose: 400mg
AMIKACIN IV q8h	10-15 mg/kg/dose	
VANCOMYCIN IV q6h	Dose as per above	

- Consider anaerobic coverage in patients who have signs of perirectal infection if not already receiving Tazocin® or meropenem.

- Consider discontinuation of vancomycin once C&S results are available.

Monitor the patients vital signs q1h until stable then q4h and/or as indicated.

Acetaminophen is the preferred antipyretic agent. Ibuprofen is not recommended for neutropenic patients.

Contact the Haematology/Oncology fellow on call at The Hospital for Sick Children to discuss the patient. If the patient is stable this can wait until the next day.

Patients who become **UNSTABLE** or appear to be progressively deteriorating, immediately contact the Haematology/Oncology fellow on call at The Hospital for Sick Children to discuss indications for transfer.

ADMISSION MANAGEMENT

Antibiotic Management

Continue antibiotics according to Antibiotic Dosing Guideline **Table 1.** or see Emergency Management for antibiotic selection and dosing guidelines.

Patients with **multi-lumen CVC's** should have their antibiotic therapy alternated among all lumens for the duration of antibiotic therapy.

If **initial blood cultures (peripheral or central venous line) are positive**, then repeat cultures should be drawn when this result becomes known. Antibiotics specifically directed toward the identified organism should be **added to** the broad spectrum therapy if the initial antibiotics do not provide adequate coverage. **Broad spectrum coverage must not be replaced by specific antibiotic(s) alone in the neutropenic patient.**

Patients who remain febrile after initiation of appropriate antibiotic therapy ordinarily should have CVC cultures drawn no more than once daily. Peripheral cultures are of limited value and should not be routinely drawn under most circumstances.

Therapeutic drug monitoring

Pre and post levels should be ordered with the third dose of gentamicin. A post level of 7-9 mg/L should be targeted. Subsequently, a pre level should be ordered once weekly to detect gentamicin accumulation. If the patient is receiving concurrent nephrotoxic drugs (e.g. amphotericin, acyclovir) or has unstable renal function, twice weekly pre levels may be warranted.

For patients on amikacin or vancomycin therapeutic drug monitoring should be ordered pre and post the third dose for amikacin and pre and post the fourth dose for vancomycin. For additional information refer to The Hospital for Sick Children Formulary.

Alternative Antibiotic Management

PATIENTS WHO ARE PERSISTENTLY FEBRILE but STABLE should continue to receive the initial empiric antibiotic regimen according to **Table 1**. If the patient's condition indicates evolving infection at a particular site (e.g. abdominal pain, severe mucositis, pneumonia), antibiotics directed toward possible causative organism should be added to the broad spectrum coverage. After 5 to 7 days of persistent fever, consider the addition of AMPHOTERICIN.

Consider an Infectious Disease consult.

Contact the Haematology/Oncology fellow at The Hospital for Sick Children to discuss indications for transfer.

PATIENTS WHO DETERIORATE (i.e. are hemodynamically unstable or show other signs of sepsis) should have their antibiotics reassessed and changed to dosing regimes for UNSTABLE PATIENTS INCLUDING SEPSIS SYNDROME according to **Table 1**.

Consider an Infectious Disease consult.

Consider the addition of AMPHOTERICIN after 5 to 7 days of persistent fever.

Immediately contact the Haematology/Oncology fellow at The Hospital for Sick Children to discuss indications for transfer.

Duration of Antibiotic Therapy

Patient Parameters	**Plan**
Afebrile, ANC > 0.5 X 10^9/L, cultures negative	DISCONTINUE antibiotics
Afebrile, ANC < 0.5 X 10^9/L, cultures negative, IV antibiotic duration > 48 hours	CONSIDER discontinuing antibiotics (see criteria in Management on Discharge section)
Afebrile, ANC < 0.5 X 10^9/L, cultures negative, IV antibiotic duration > 7 days	CONSIDER discontinuing antibiotics
Afebrile, ANC > 0.5 X 10^9/L, cultures positive	CONSIDER discontinuing broad spectrum coverage, CONTINUE specific therapy

Management on Discharge

After a minimum of 48 hours of IV antibiotic therapy, it may be reasonable to consider stopping antibiotics and discharging patients who meet the following criteria, even though the ANC is less than 0.5 x 10^9/L:

1. Not on induction therapy for a malignancy known to significantly involve the bone marrow;
2. Did not present with clinical sepsis;
3. Negative blood cultures (CVC and peripheral);
4. Afebrile for a minimum of 24 hours;
5. Fever did not persist beyond 96 hours;
6. Clinically well and not in need of other inpatient care;
7. Evidence of bone marrow recovery: increased monocyte, increased neutrophil or increased platelet counts; and
8. No known or suspected non-compliance with follow-up instructions.

Discharge of patients with **localized sites of infection** and who meet the above criteria should be considered on a case by case basis.

NOTE: It is not necessary to keep the patient in hospital for 24 hours following discontinuation of IV therapy. Families must be advised to continue strict follow-up with their treatment team. Any recurrence of fever should be approached as a *de novo* (brand new fever) in a immunocompromised host and requires immediate evaluation.

If at any point the patient becomes UNSTABLE or appears to be PROGRESSIVELY DETERIORATING the Haematology/Oncology fellow at The Hospital for Sick Children should be contacted immediately to discuss indications for transfer.

Evaluation:

An audit will be done to determine compliance and outcomes of the CPG after it has been in place for 1 year.

References:

The 2002-2003 Hospital for Sick Children Formulary of Drugs: Child Health Network Website (www.echn.ca)
The Hospital for Sick Children Guideline: Management of Haematology/Oncology and Bone Marrow Transplant Patients with Fever
The Hospital for Sick Children Therapeutic Drug Monitoring Guidelines

Approval:

Oncology Advisory Committee and The Department of Paediatrics: May 28, 2003 / May 27, 2003
Paediatric Programme Steering Committee: June 23, 2003
Pharmacy and Therapeutics Committee: June 10, 2003
Clinical Quality Care Committee: June 18, 2003
Professional Practice Committee: June 23, 2003
Medical Advisory Committee: September 08, 2003