**Febrile Neutropenic Patients Considered at Low Risk of Complications:**

The following patients have been identified as being at low risk of mortality, and may qualify for initial treatment with oral antibiotic therapy.

- patients presenting as outpatients
- no clinical evidence of any specific infection (e.g., normal CXR, catheter site infection/inflammation)
- no signs or symptoms of systemic infection (e.g., hypotension, rigors, respiratory insufficiency, dehydration) other than fever
- no significant comorbid illness (e.g., COPD, liver or renal dysfunction, diabetes)
- ANC greater than 100 cells/mm³
- recovery of neutrophils expected within 7 days
- peak temperature less than 39°C
- no neurologic or mental status changes
- respiratory rate less than 24
- no nausea, vomiting, diarrhea, or severe mucositis
- ECOG performance status of 0 or 1

In addition, the following patients are **excluded** from consideration of treatment with oral antibiotics:

- patients considered to have “uncontrolled” cancer/malignancy
- allogeneic BMT patients
- patients who require acute hospital care for reasons other than fever/neutropenia (e.g., pain control, dehydration)
- patients who have received antibiotics (IV or PO) within the past 7 days
- patients with allergy to penicillins or quinolones, and/or patients receiving concomitant therapy with agents likely to complicate oral antibiotic therapy (e.g., antacids, sucralfate, iron, theophylline, allopurinol)

**References:**

TOH INPATIENT MANAGEMENT OF NEUTROPENIC FEVER
(Oncology – Hematology, except BMT and acute leukemia patients)

**Fever ≥ 38°C + Neutropenia** (< 1000 neutrophils/mm³)

**Evaluate**

**History and Physical Examination**
Physical signs may be minimal or absent due to decreased neutrophils, which generate the inflammatory reaction. E.g., no redness or swelling of skin, no infiltrate on chest X-ray.

**Blood Work** (Stat then daily x 7 days)
CBC, differential, platelet count, biochemistry as indicated (usually lytes, BUN, creatinine ± LTFs).

**Radiology**
Chest X-ray

**Cultures** (Do not delay treatment > 1 hour to collect all cultures)
Urine, sputum, swabs, diarrhea stool, blood: 2 sets total (all peripheral or peripheral x 1 + 1 from each CVC lumen)

Give first dose of antibiotic as soon as possible

- **Low Risk***
  - Oral
    - Ciprofloxacin 750mg PO BID
    - Amoxicillin + clavulanate 500mg PO TID

- **High Risk**
  - IV
    - Piperacillin/tazobactam 3.375g IV q6h

**For known or suspected pseudomonal infections or patient extremely ill** (e.g., unstable, hypotensive patient, T > 39°C and/or neutrophils < 100/mm³ or less)

**Consider adding Tobramycin**
2 mg/kg/dose IV. Interval based on estimated CrCl (see dosing chart)

**If ANY of the following apply:**
- Signs and symptoms or high suspicion of venous access device infection
- Blood culture positive for gram positive bacteria pending identification
- Hypotensive, hemodynamically unstable
- Known colonization with MRSA

**Consider adding Vancomycin**
1g IV q12h for patients less than 75 yo with CrCl of 40 mL/min or greater
1g IV q24h for patients 75 yo or older or CrCl less than 40 mL/min

**If Penicillin Allergy:**
1. Life threatening allergy to penicillin – e.g., anaphylaxis, throat swelling, shortness of breath:
   - Levofoxacin 750 mg IV q24h
2. Non severe penicillin allergy or has previously tolerated a cephalosporin: Ceftazidime 2 g IV q8h

All these antibiotics need a **dose** or **interval** adjustment in patients with impaired renal function. Please see dosing chart (CrCl must be calculated).

* See definition of low risk patients on the previous page.

Note: These are guidelines ONLY; modification may be necessary depending on individual patient characteristics, underlying causes, type of infection, and local susceptibility patterns.
ANTIBIOTIC DOSING CHART FOR FEBRILE NEUTROPENIC PATIENTS WITH IMPAIRED RENAL FUNCTION

Creatinine clearance must be calculated (see notes at the bottom):

\[
\text{CrCl (mL/sec): } \frac{(140 - \text{age}) \times \text{weight (kg)} \times \text{IBW}}{50 \times \text{serum creatinine (μmol/L)}}
\]

\[
\text{CrCl (mL/min) } = \text{CrCl (mL/sec) } \times 60
\]

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIPROFLOXACIN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PO</td>
<td>CrCl (\geq) 30 mL/min</td>
<td>750 mg PO q 12 h</td>
</tr>
<tr>
<td>CrCl &lt; 30 mL/min</td>
<td>750 mg PO q 24 h</td>
<td></td>
</tr>
<tr>
<td>AMOXICILLIN/CLAVULANIC ACID</td>
<td>PO</td>
<td></td>
</tr>
<tr>
<td>CrCl 10 – 30 mL/min</td>
<td>500 mg PO q 12 h</td>
<td></td>
</tr>
<tr>
<td>CrCl &lt; 10 mL/min</td>
<td>500 mg PO q 24 h</td>
<td></td>
</tr>
<tr>
<td>LEVOFLOXACIN</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>CrCl 20 – 49 mL/min</td>
<td>500 mg IV q24h</td>
<td></td>
</tr>
<tr>
<td>CrCl &lt; 20 mL/min</td>
<td>750 mg IV x 1, then 500 mg IV q48h</td>
<td></td>
</tr>
<tr>
<td>PIPERACILLIN/TAZOBACTAM</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>CrCl 20 – 40 mL/min</td>
<td>2.25 g IV q 6 h</td>
<td></td>
</tr>
<tr>
<td>CrCl &lt; 20 mL/min</td>
<td>2.25 g IV q 8 h</td>
<td></td>
</tr>
<tr>
<td>TOBRAMYCIN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl mL/min</td>
<td>72</td>
<td>42 – 72</td>
</tr>
<tr>
<td>Interval (h)</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>VANCOMYCIN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl mL/min</td>
<td>&gt; 60</td>
<td>40 - 60</td>
</tr>
<tr>
<td>Interval (h)</td>
<td>8 – 12</td>
<td>12 – 24</td>
</tr>
</tbody>
</table>

* Based on dialysis frequency and serum concentrations.

NOTES:

1) IBW (kg): \(50 + 2.3 \times \text{height in inches} – 60\) for males.
\(45 + 2.3 \times \text{height in inches} – 60\) for females

2) For non-obese patients, use actual body weight (ABW) instead of IBW.

3) Note that in obese patients, use of ABW in this equation tends to over-estimate creatinine clearance, while use of IBW tends to under-estimate creatinine clearance.

*Developed in-house by The Ottawa Hospital*
ALGORITHM FOR THE MANAGEMENT OF FEBRILE NEUTROPENIC PATIENTS
WITH NO SITE OF INFECTION OR CAUSATIVE ORGANISMS IDENTIFIED

Antibiotic Therapy Initiated

IV Antibiotics
Reassess on Day 3

Low Risk – Oral Tx
Reassess on Day 3

Afebrile

Febrile

Change to IV Antibiotic Regimen

 ANC ≥ 500

ANC < 500

D/C Abx after afebrile x 48hrs &
ANC ≥ 500 x 2 days

D/C Abx after afebrile x 5 days & remains
clinically well

ANC ≥ 500

ANC < 500

D/C Abx after afebrile x 48 hours and ANC
≥ 500 x 2 days

D/C Abx after afebrile x 5 days and
clinically well

Continue Abx if initially unstable, mucositis or
ANC < 100

D/C Abx once ANC ≥ 500 or after 2 weeks

D/C 5 days after
ANC > 500

ANC ≥ 500

ANC < 500

D/C Abx after afebrile x 5 days & remains
clinically well

Add to (e.g. vanco) or change
Abx regimen; Consider antifungal if remains neutropenic

ANC ≥ 500

ANC < 500

Continue current regimen

D/C Abx after afebrile x 5 days and
clinically well

R/A Day5

Afebrile

Febrile

Clinically Stable

Continue current regimen; R/A
Vanco if cultures negative

Reassess Patient*

Unstable or Deterioration

Reassess Patient*

Developed in-house by The Ottawa Hospital

*Repeat P/E, reculture, R/A vasc catheters, diagnostic imaging.
NOTE: Duration of therapy will be determined by site of infection or organism if any is identified