CLINICAL PROCEDURE

FEBRILE NEUTROPENIA

TARGET AUDIENCE

All clinical staff including medical, nursing and pharmacy.

PURPOSE

This document incorporates the key requirements for a hospital neutropenic fever (NF) guideline/pathway. The document includes evidenced based recommendations for the assessment and management of NF and sepsis.

1. Consensus definitions
2. Investigations
3. Initial antibiotic therapy based on severity
4. Ongoing antibiotic therapy
5. Prophylaxis
6. Antiviral and antifungal therapy
7. Management of the low risk patient with neutropenic fever

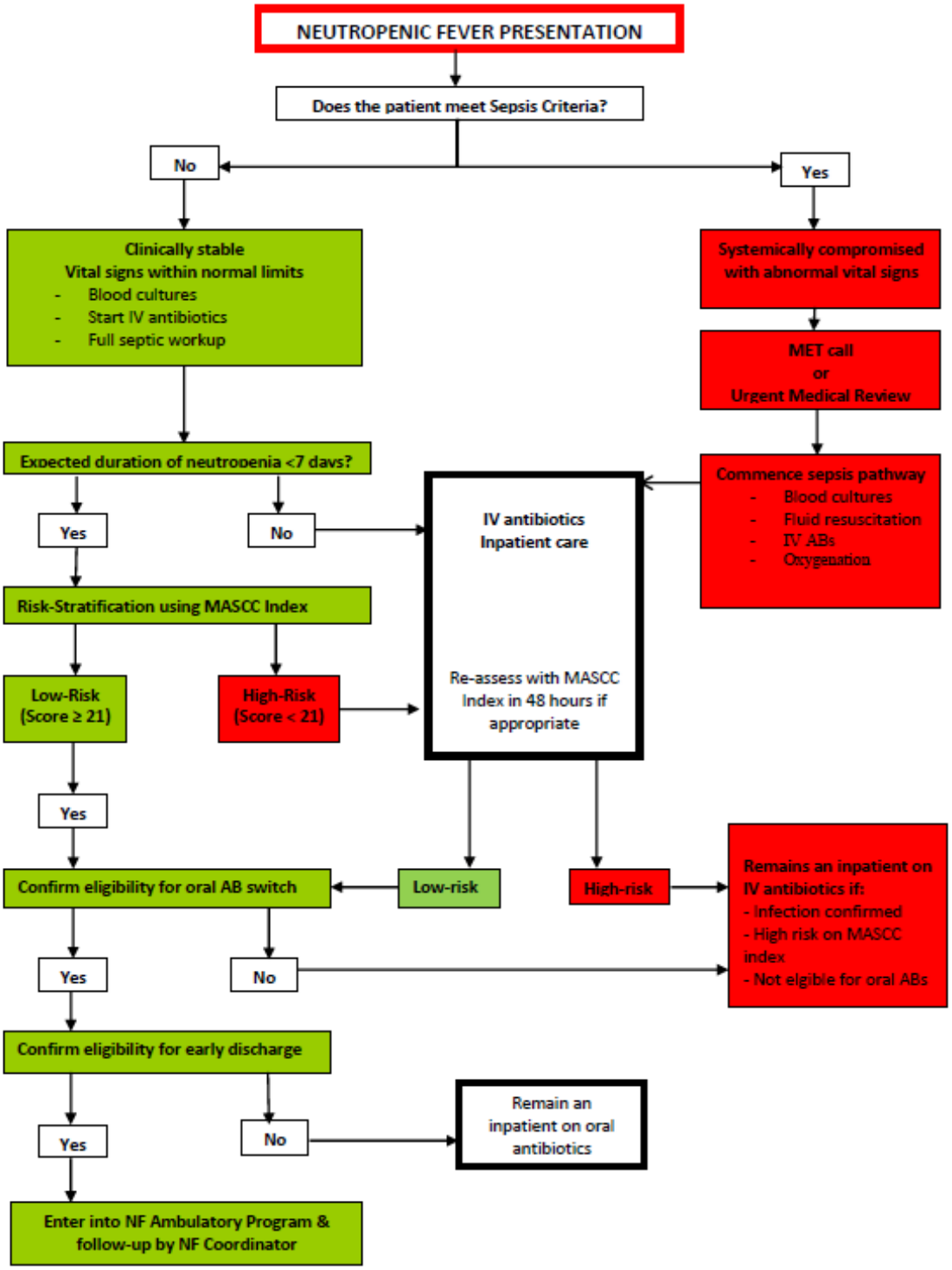
MANAEMENT OF NEEUTROPENIC FEVER

All patients with neutropenic fever as defined above should be initially assessed for the presence of systemic cardiovascular compromise, and whether they are considered high- or low-risk for medical complications. These factors determine the initial choice of antibiotic therapy, time to administration of antibiotics, the likely duration of admission and whether ambulatory care may be considered (see Figure 1). Recently, evidence has demonstrated that prompt administration of antibiotics is associated with a measureable decrease in mortality such that now, time to first dose antibiotic has been included in international sepsis guidelines (Kumar et al., 2006) (Dellinger et al., 2008)

Importantly, neutropenic patients can present septic with haemodynamic compromise without fever (if elderly, or on steroids) in which case there should be no delay in treatment while evaluating for further fever. All patients presenting with fever following chemotherapy should be managed as if they have neutropenic fever and receive empiric antibiotics without waiting for laboratory confirmation of neutrophil count (expert opinion). This management may then be modified if neutrophil count and function are confirmed to be adequate.

Optimal empiric management will be informed by the patient's presenting clinical status. As such, all patients presenting with NF should be evaluated using the Sepsis Pathway (Guideline and Pathway Document MR 63/T).

FIGURE 1: FLOWCHART FOR OP VERSUS IP MANAGEMENT



Empiric Management

Notification lines	Unit registrar notified of patient arrival or onset of fever for neutropenic patients
Review times	Inpatients reviewed within 30 minutes of referral to treating medical team
Emergency department (ED) Triage Category	ED presentation triaged ideally as Cat 2 (medical assessment within 10 minutes)
Investigations	**See Investigations**
Time to first dose antibiotic	Within 30 minutes of fever onset if systemically compromised (grade C recommendation). This should follow the immediate collection of at least one set of blood cultures and administration of intravenous fluids or other support as medically appropriate. Within 60 minutes if clinically stable (from presentation) after blood cultures have been taken according to 6.3.1 (grade C recommendation). The commencement of antibiotics should not be delayed by the competing imperative to conduct further investigations, including CXR and cultures of sites other than blood (grade C recommendation).
Maintain $Sa0_2$ >95%	Apply oxygen to achieve a $Sa0_2$>95%
Fluid Resuscitation	Consider fluid challenge in all patients as venodilation and capillary leak will be present **If SBP < 90mmHg or lactate ≥ 4:** Rapid fluid challenge with 20ml/kg of Hartmann's solution (or other crystalloid fluid) by large bore IV catheter and using rapid infuser (NOT through PICC line) If high risk of pulmonary oedema administer minimum 10ml/kg of Hartmann's solution for initial bolus
Notification of ICU	If initial fluid challenge fails, ie. no increase in SBP (refer above) If medical emergency team (MET) call criteria is reached (via an emergency call)

investigations

Blood Cultures (BC)	For optimal sensitivity and specificity, ideally **at least two separate blood culture sets** should be collected from **separate venepuncture sites** prior to commencement of antibiotics. For optimal sensitivity and specificity, ideally **at least two separate blood culture sets** should be collected from **separate venepuncture sites** prior to commencement of antibiotics. Blood cultures (BC) should be avoided from central venous access devices (CVAD). If there is collection of a blood culture from CVAD lumen, then peripheral blood cultures should also be performed. This may assist in the diagnosis of clinically relevant blood stream infections by allowing the time necessary for blood culture from the peripheral vein to become positive to be compared to the time until blood culture from a central venous catheter becomes positive. (Raad et al., 2004) A differential time to positivity of ≥ 120 minutes has been shown to be predictive of clinically relevant catheter-related blood stream infections. (Abdelkefi et al., 2005; Towns, Jarvis, & Hsueh) This approach is particularly useful in patients in whom catheter retention is desirable. At least 20mls of blood should be drawn from each site and 10mls inoculated into one aerobic and anaerobic bottle. Two sets of blood cultures in a 24 hour period will detect approximately 90-95% of blood stream infections in adults. (Lee, Mirrett, Reller, & Weinstein, 2007; Towns et al.) In some cases this number of blood cultures may not be possible within the recommended time constraints for antibiotic administration. In such cases, the highest priority is the prompt administration of antibiotics (see 6.2.1). To minimise the risk of contamination during blood culture collection, appropriate sterile collection should be used including: hand hygiene with alcohol rub/gel prior to procedure; Skin disinfection with chlorhex/alcohol swab, isopropyl alcohol for BC bottle caps and CVAD caps,use of sterile gloves and no-touch technique for venepuncture; avoidance of needle exchange prior to inoculation of bottle(s) (Towns et al.) As per peter Mac procedures Collection of Peripheral Blood Cultures Repeat blood cultures prior to Day 3 are not recommended for the majority of patients with neutropenic fever unless clinically unstable and/or suspected new infectious foci are present. For patients with initially positive blood cultures, repeat peripheral cultures should be performed to document clearance of bacteraemia (expert opinion).
Measurement of Lactate*	A serum lactate ≥2 mmol/L is related to illness severity and poorer patient outcomes. Patients with a lactate ≥4mmol/L, regardless of hypotension **must** receive fluid resuscitation (refer above) Lactate must be measured within minutes via an arterial blood gas

	(ABG) or venous blood gas (VBG) using a blood gas analyser (send on ice) * Hyperlactatemia is typically present in patients with severe sepsis or septic shock and may be secondary to anaerobic metabolism due to hypoperfusion
Haematology	Full blood examination (FBE), Coagulation profile
Biochemistry	Electrolytes, Creatinine (Cr), liver function tests (LFTS)
Sepsis workup	Chest x-ray (CXR) Urine – mid stream urine (MSU) for microscopy culture sensitivity (MCS)
	If indicated: Sputum specimen for MCS Viral studies if presence of upper respiratory symptoms (sore throat, cough): respiratory multiplex for viral PCR Stool specimen for MCS (must be stipulated) and *C.difficile* Wound swabs for MCS if bacterial infection suspected or HSV/VZV PCR if herpes simplex or varicella infection suspected. Urinary legionella antigen and streptococcal antigen (if pneumonia)
If high risk for fungal infection and/or presence of lung infiltrates or lesions	High resolution CT scan (chest +/- abdomen / liver / spleen +/-sinus) PET/CT scan (if available) Bronchoscopy Non culture based tests (NCBT) for IFI including - Aspergillus PCR (on serum and BAL) - Galactomannan from BAL (NOT indicated in serum) - PJP PCR
Persistent fever despite intensive investigation as above	- Referral to infectious diseases (ID) - Ix for wider systemic infection based on risk (eg. CMV in allograft transplant) - Consider PET as high negative predictive value for bacterial or fungal infection

Symptomatic Management Of The Febrile Patient

Indications for MET call

A sudden or acute deterioration in a patient's vital signs OR in patients who present unwell at onset should prompt a MET call.

Management of hypotension

Commence IV fluids as outlined in the sepsis pathway (MR/63T) and commence a fluid record

Management of rigor

Warm patient if experiencing chills or rigor with space blanket (if available) and request an order for IV pethidine 12.5 - 25mg (if not already prescribed). Administer IV pethidine up to 25mg to ameliorate rigor. Repeat IV pethidine injection can be used if rigor is not subsiding.

Initial antibiotic choice (for normal renal function or CrCl >50 ml/min)

In view of emerging evidence regarding efficacy and toxicity differences between empiric treatment regimens, and strong evidence of heterogeneity in clinical practice, the following recommendations were developed to provide clinicians with initial guidance for selecting an appropriate empiric strategy in the setting of neutropenic fever (see Table 1 for summary).

The patient's history, allergies, symptoms, signs, recent antibiotic use and culture data, as well as local antimicrobial flora and infection patterns, should guide the initial choice of antibiotic therapy. Patients with impaired renal function (creatinine clearance less than 50 mL/min) will require adjustments to the suggested doses based on calculated creatinine clearance (grade A recommendation).

Table 1. Initial antibiotic therapy based on severity of presentation

Order of antibiotic administration	Stable NF / SIRS	Sepsis	Severe Sepsis	Septic Shock
1	**All patients:** - <u>*No penicillin allergy*</u>: Piperacillin/tazobactam 4.5g IV 6-hourly OR - <u>*Non-life threatening penicillin allergy (rash):*</u> Cefepime 2g IV 8-hourly OR - <u>*Life-threatening (immediate) penicillin or beta-lactam allergy:*</u> Ciprofloxacin 400mg IV 12-hourly PLUS Vancomycin			
	Patients with proven previous multi-resistant gram negative infection or ESBL colonised Meropenem 1g IV 8-hourly			
2			**Severe Sepsis to Septic Shock:** **Add** Gentamicin 5-7mg/kg ideal body weight IV once daily, adjusted to levels (2 doses max without ID referral) **Add** Vancomycin 1-1.5g IV 12hourly (dependent on creatinine clearance [CrCl]*) as per vancomycin protocol.	

*Creatinine Clearance

Ongoing Antibiotic Therapy

Uncomplicated neutropenic fever

- The antimicrobial regimen should always be reassessed after 48 to 72 hours on the basis of microbiological and clinical data.
- In the absence of positive cultures for resistant organisms;
    - gentamicin should be discontinued after 24–48 hours
    - vancomycin should be discontinued after 48–72 hours
- Monotherapy is as effective as combination therapy for uncomplicated NF
- If patient in low risk group (See Low Risk NF), assess MASCC score at 24-48 hours and consider early IV-Oral Switch
- Antibiotics can be ceased in the following situations;
    1. the cause of apparent sepsis is found to be non-infectious
    2. if mucous membranes and integument are intact, and there is no impending invasive procedure or ablative chemotherapy planned
    3. when patients become afebrile within 72-96hours, no causative organism is isolated and the neutrophil count is at least 0.5 x 10^9 cells/L
- If the neutrophil count is less than 0.5 x 10^9 cells/L and neutropenia is expected to be prolonged, the decision to discontinue or continue antibiotic therapy should be based upon clinical criteria and individual clinicians' judgement.
- For patients who become afebrile after commencement of on oral antibiotics, the total minimum duration of antibiotic therapy should be 7 days.

Modification of initial regimen

Use of vancomycin

Empiric vancomycin is considered unnecessary in most clinically stable patients receiving monotherapy with an anti-pseudomonal beta-lactam who have no definite sites of gram-positive infection (Grade A recommendation). Routine addition of vancomycin to the initial empiric antibiotic regimen within 72 hours does not reduce mortality and is associated with an increased risk of adverse events, mainly nephrotoxicity (level I evidence, grade A recommendation).(Paul, Borok, Fraser, Vidal, & Leibovici, 2005; Vardakas, Samonis, Chrysanthopoulou, Bliziotis, & Falagas, 2005) There is now good evidence to show that empiric (non-targeted) first-line use of vancomycin is unnecessary and potentially harmful. (Paul et al., 2005)

The following situation may be deemed appropriate:

- Patients with **microbiologically documented Gram-positive infection** should receive vancomycin until identification and susceptibility results are available, at which time therapy should be modified appropriately (expert opinion).
- **Systemic compromise.** Evidence regarding glycopeptide use in patients presenting with neutropenic fever and systemic compromise is lacking. There is currently no consensus opinion. Vancomycin may be given appropriate consideration.

- **Patients at risk of resistant gram-positive infection.** For these patients presenting with shock, addition of vancomycin to empiric therapy *is* recommended (expert opinion).
- **Patients with cellulitis, obviously infected vascular devices or MRSA carriers <u>with</u> extensive skin breaks/desquamation**: Vancomycin, according to a validated protocol, should be added to the beta-lactam antibiotic regimen described for clinically stable patients in Table 3, for 48–72 hours then reviewed according to culture results (expert opinion)

Multi-drug resistant infections

Patients with multi-drug resistant (MDR) infections are increasingly seen and should be considered if they have key risk factors. Risk factors for acquiring a multi-drug resistant organism include overseas travel (within last 6 months), prolonged hospital stay and antibiotic exposure.

It is highly recommended patients with MDR infections should be discussed and managed in conjunction with the Infectious Diseases service

Broadening of antibiotic coverage

Any subsequent modifications to the initial choice of antibiotic should be guided by repeat clinical assessment (e.g. emergence of focal sites of infection) and microbiological culture results (expert opinion).

As the median time to resolution of fever in patients successfully treated with frontline antibiotics is 3–5 days, escalation of antibiotic coverage should **<u>not</u>** occur prior to this period in the absence of clinical instability, isolation of a resistant organism or emergence of new infective foci (expert opinion).

Duration of antibiotic therapy

The duration of therapy should typically be 7 to 10 days and guided by clinical response. Longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteraemia with S. aureus, some fungal and viral infections, or prolonged neutropenia.

Duration of antibiotic therapy including oral antibiotic switch regimens

The treatment course for FN may be parenteral with/without an oral switch.

Patients with a MASCC score of **≥21** at presentation (see risk stratification below) may be commenced on oral antibiotics at onset or after 24 hours according to physician preference.

Oral antibiotic regimen;

No beta-lactam allergy	Amoxicillin-clavulanate 875/125mg BD Ciprofloxacin 750 mg BD*
Beta-lactam allergy	Clindamycin 450 mg TDS Ciprofloxacin 750 mg BD*
* dose reduction required with renal impairment, consult ID fellow	
Fluoroquinolone allergy	Amoxicillin-clavulanate 875/125mg BD

When patients become afebrile within 3–5 days while on parenteral therapy and no causative organism is isolated, it is preferable to stop antibiotic treatment when the neutrophil count recovers to at least 0.5 x 10^9 cells/L (expert opinion). This may include oral switch while counts recover.

If the neutrophil count is less than 0.5 x 10^9 cells/L and neutropenia is expected to be prolonged, the decision to discontinue or continue antibiotic therapy should be based upon clinical criteria and individual clinicians' judgment. Antibiotic therapy may be ceased if the mucous membranes and integument are intact, and there is no impending invasive procedure or ablative chemotherapy planned (expert opinion).(Hughes et al., 2002)

For patients who become afebrile whilst **on oral antibiotics**, the total minimum duration of antibiotic therapy should be 7 days (expert opinion). This treatment duration has been used safely in clinical studies of oral antibiotic therapy (Rolston et al., 2006) and is supported by previous consensus opinion. (Hughes et al., 2002; Tamura et al., 2004) (Worth LJ, 2010)

Removal of vascular catheters

Venous catheters (including PICCs) should be routinely removed in the setting of *Staphylococcus aureus* and Candida spp. bloodstream infection. For other isolates, infectious diseases consultation should be sought.

Refer to the Infectious Diseases Society of America (IDSA) 2009 Guidelines for the diagnosis and management of intravascular catheter-related infections (Clin Infect Dis 2009:49).

Antibiotic Prophylaxis

The use of oral prophylactic antibiotics in patients with neutropenia is not universally recommended due to a lack of evidence showing a reduction in mortality and concerns that such practice promotes antimicrobial resistance.

Key practice points:

- There is currently insufficient evidence to recommend routine use of fluoroquinolone (FQ) prophylaxis in patients at low risk of developing neutropenic fever (Slavin MA, 2010)
- FQ prophylaxis should also not be routinely used in high-risk haematology patients
- FQ prophylaxis could be considered in outpatient SCT and palliative patients with bone marrow failure
- Support is given to use of FQ prophylaxis during the first cycle of TPF protocol (docetaxel 75mg/m2 IV D1 cisplatin and fluorouracil) for head and neck cancer, when G-CSF prophylaxis is not used. Two RCTs mandated the use of ciprofloxacin as primary prophylaxis. (Vermorken et al., 2007); (Posner et al., 2007)

Addition of antiviral therapy

Antivirals should not be added to the empiric regimen without clinical or serological evidence of viral infection. The exception may be the treatment for influenza, in which the patient has an influenza-like illness during the influenza season and has a history of contact.

The drug of choice is **oseltamivir 75 mg oral BD** to be continued for 5 days.

Addition of antifungal therapy

Addition of empiric antifungal therapy depends on whether the patient has been receiving yeast or mould prophylaxis. It should be considered in all high risk haematology patients who continue to be febrile after 96 hours. Further investigation includes a HRCT chest (+/- CT sinuses) and non-culture based tests (aspergillus PCR and galactomannan).

Persistent fever

- In the case of persistent or ongoing fever 72- 96hrs **after** IV antibiotic commencement further investigations are warranted.
- Review all microbiology and radiology
- Antibiotics should not be altered if patient is clinically stable while investigations are being undertaken.
- If patient is clinically unstable (worsening sepsis) then consider antibiotics with increased spectrum:
    - Addition of vancomycin and/or gentamicin
    - Escalation to meropenem
    - Discussion with ID service
- A high resolution CT (chest +/- abdomen / liver / spleen / sinus) or PET (if available) should be considered if a patient is high risk for invasive fungal infection (IFI)

Management of the LOW RISK patient with neutropenic fever and Ambulatory Program

Related Documentation:

- MR63U Neutropenic Fever Risk Stratification Tool
- MR63V Neutropenic Fever Home Assessment Chart
- Re-admission - Emergency Department Letter
- Patient Information for Early Discharge on Oral Antibiotics

Risk stratification

The risk of a patient with NF experiencing medical complications may be assessed using the Multinational Association for Supportive Care in Cancer (MASCC) risk index developed by Klastersky et al. (2000). The MASCC is a well validated tool that is supported by Peter Mac, national and international guidelines for the management of NF. This tool may be used to guide the subsequent approach to treatment.

The criteria below need to be fulfilled to be suitable for assessment with the MASCC risk index.

Criteria	**Eligible**	**Not Eligible**
Patient is neutropenic (ANC) of < 1.0 x 10^9 cells/L	☐ Yes	☐ No
Fever of ≥38.3^{o}C OR ≥38.0^{o}C on two occasions	☐ Yes	☐ No
Expected duration of neutropenia < 7 days	☐ Yes	☐ No
All criteria needs to be fulfilled to continue with MASCC index		

MASCC index

Is patient less than 60 years old?	☐ Yes	2	☐ No	0
Does the patient have a solid tumour OR Does the patient have a haematology malignancy with no previous fungal infection?	☐ Yes	4	☐ No	0
Does the patient have COPD?	☐ Yes	0	☐ No	4
Was patient an outpatient at time of fever onset?	☐ Outpatient	3	☐ Inpatient	0
Was patient dehydrated at first presentation of NF? (in the absence of clinical markers of dehydration - assess recent history of oral intake and /or excess fluid losses)	☐ Yes	0	☐ No	3
Was patient hypotensive at first presentation of NF (SBP < 90mmHg)?	☐ Yes	0	☐ No	5
What was the patient's burden of illness? (Subjective assessment of symptom severity and physiologic reserve – how sick is the patient now?) Note: If severe symptoms or moribund, score 0	☐ None or mild symptoms	5	☐ Moderate symptoms	3
Tallied score for checked boxes (MASCC score) _____				
☐ High-Risk (less than 21)	☐ Low-Risk (greater or equal to 21)			

The maximum value in this system is 26. A score of ≥21 suggests low risk and predicts a <5% risk for severe complications and a very low mortality (<1%) in NF patients.

Oral Antibiotic switch

Low risk patients (MASCC ≥21) may be commenced on oral antibiotics at onset or after 24hours if the following criterion is fulfilled and it is the physicians' preference.

At least one dose of oral antibiotics should be given prior to hospital discharge in order to monitor for side effects.

No beta-lactam allergy	Amoxicillin-clavulanate 875/125mg BD Ciprofloxacin 750 mg BD*
Beta-lactam allergy	Clindamycin 450 mg TDS Ciprofloxacin 750 mg BD*
* dose reduction required with renal impairment, consult ID fellow	
Fluoroquinolone allergy	Amoxicillin-clavulanate 875/125mg BD

Eligibility criteria for oral antibiotics;

Criteria	**Eligible**	**Not Eligible**
Stable disease	☐ Yes	☐ No
No active infection with multi-resistant organism infection (MRSA, VRE, MDRGN)	☐ Yes	☐ No
Patient not on antibiotic prophylaxis (excluding PJP prophylaxis) prior to this admission	☐ Yes	☐ No
Able to swallow / tolerate oral antibiotics (≤ Grade 2 mucositis and maintaining >50% of dietary intake)	☐ Yes	☐ No
Stable mental state^	☐ Yes	☐ No
Normal findings on chest x-ray (if applicable)^	☐ Yes	☐ No
Haemodynamically stable (SBP ≥100mmHg, HR 60-100 bpm regular)^	☐ Yes	☐ No
Minimal diarrhoea, vomiting, electrolyte imbalance^	☐ Yes	☐ No
^ reversible elements. If only reversible criteria are not fulfilled, re-assess in 48hours. - If non reversible elements present continue with IV antibiotics If all criteria present and the physician's preference is for oral antibiotics continue to following section		

Early discharge

Low risk patients who are eligible for oral antibiotics may be discharged to an ambulatory program or with close outpatient monitoring. The patient will require outpatient monitoring until neutrophil count has recovered to ≥1.0 x 10^9 cells/L.

Eligibility criteria for early discharge:

Criteria	**Eligible**	**Not Eligible**
Availability of a 24hour caregiver	☐ Yes	☐ No
Good education of patient and carer on reportable symptoms	☐ Yes	☐ No
No confirmed focus of infection requiring IV antibiotics	☐ Yes	☐ No
Availability of a telephone	☐ Yes	☐ No
Availability of 24hour phone advice from Peter Mac	☐ Yes	☐ No
Within 1-hour of an emergency department or treating hospital	☐ Yes	☐ No
Suitably resourced follow-up - PM@H visits / NF co-ordinator	☐ Yes	☐ No
Treating teams preference	☐ Yes	☐ No
No documented allergy to the required oral antibiotics	☐ Yes	☐ No
No history of non-compliance with medical care or physical or verbal aggression	☐ Yes	☐ No
No previous history of non-compliance or absconding from medical care	☐ Yes	☐ No

Ambulatory / Outpatient setting

Once eligibility for early discharge is completed the patient is included in the ambulatory program with hospital in the home visits organised and follow-up in the Neutropenic Fever Clinic as an outpatient.

Discharge from hospital is likely to be either 24 – 48hrs after admission or discharge without admission (ie. from the Emergency department).

Discharge resources should include;

- hospital in the home appointments through PM@H
- Pathology slips
- educational material;
    - home observation and assessment chart with instructions for use, (hyperlink here to document)
    - reasons for re-admission with hospital personnel contact numbers
    - letter for presentation to an emergency department including description of medical history, recent treatment received and current situation (hyperlink here to document)
- ensure patient has a thermometer

PeterMac@Home

The following is a recommended schedule for hospital in the home visits and interventions.

- visits organised for Day 1 and 2 (Day 0 is day of discharge) followed by alternate days until ANC ≥ 1.0 x 109 cells/L (expected that 2 visits will be sufficient)
- interventions to be undertaken during home visit;
  - blood specimens taken (FBE, U&E, CRP & LFT's)
  - home assessment chart reviewed / discussed (refer to home assessment chart), including temperature, oral intake / hydration, bowel patterns
- patients' blood results monitored daily by Neutropenic Fever (NF) Coordinator who will liaise with treating team
- patient contacted by telephone by NF Coordinator / treating medical officer on Day 3 to do a phone review , discuss results and appointment finalised
- patient to return to hospital for a review in Neutropenic Fever Clinic between Day 5 and 7

Ambulatory model

Day	Appointments / interventions	Responsibility
0 (day of discharge)	Bloods taken prior to hospital discharge Follow up Hospital in the home appointments Educational material / self-assessments (temp / oral intake) Readmission letter	Treating medical team
1	Home visit Blood tests Wellbeing check, etc.	Hospital in the home
2	Home visit Blood tests Wellbeing check, etc.	Hospital in the home
3	Telephone follow up Blood results discussed	Treating medical team / Nurse co-ordinator
4	Home visit if ANC <1.0	Hospital in the Home
5-7	Attend NF ambulatory care clinic	Treating medical team / Nurse co-ordinator

Re-admission

The following re-admission criteria need to be reported to the appropriate hospital personnel immediately;

- Feeling unwell / new signs and symptoms
- New, recurrent or persistent fever (> 48hrs after discharge)
- Decline in ability to self-care or carer no longer available
- Inability to continue with antibiotics (ie. allergy, vomiting, severe diarrhoea)
- Significant decrease in oral intake (ie. < 50% baseline)
- Positive blood culture result (reported after patient hospital discharge)

Prior to discharge all patients will be educated on reportable symptoms and reason for re-admission (as outlined above).

DEFINITIONS

Fever	≥ 38.3ºC once or ≥ 38.0ºC on two occasions
Neutropenia	< 1.0 x 10^9 cells/L
Stable Neutropenic fever (NF)	Neutropenia plus fever with other vital signs (Respiratory rate [RR], Heart rate [HR], blood pressure [BP], oxygen saturation [$Sa0_2$]) within normal limits
Systemic inflammatory response syndrome (SIRS)	2 or more of the following: Temp < 36ºC or > 38ºC HR > 90b/min RR > 20/min or $PaC0_2$<32 mmHg WCC < 4 x 10^9/L or > 12 x 10^9/L
Sepsis	SIRS / uncomplicated sepsis triggered by an infection
Hypoperfusion	Systolic blood pressure (SBP) ≤ 90 mmHg Lactate ≥4 mmol/L Altered conscious state Urine output ≤0.5ml/kg/hr
Severe sepsis	Sepsis with evidence of hypo-perfusion or end-organ dysfunction
Septic shock	Severe sepsis with refractory hypo-perfusion or hypotension
Clinically stable	RR, HR, BP and $Sa0_2$ within normal limits with no evidence of hypo-perfusion
Systemically compromised	Signs of hypo-perfusion and hypotension

Features of Systemic Compromise:

Systolic blood pressure ≤90 mmHg,or ≥30 mmHg below that patient's usual blood pressure, or requirement for vasopressor support
While breathing room air, an arterial pO2 of ≤60 mmHg, or arterial oxygen saturation ≤90%, or requirement for mechanical ventilation
Confusion or altered mental state
Disseminated intravascular coagulation or abnormal PT/APTT
Cardiac failure or arrhythmia, renal failure, liver failure, or any major organ dysfunction*

*Organ failure only if new or significantly worsening. Disregard stable pre-existing congestive heart failure or chronic pre-existing arrhythmias (such as AF).

RESPONSIBILITIES

Nursing Staff	Initial patient assessment and identification of systemic cardiovascular compromise Timely notification of patient status to medical staff Collection of blood cultures and performance of septic screen Timely administration of first and subsequent doses of prescribed antibiotic therapy
Medical Staff	Prompt patient assessment and identification of systemic cardiovascular compromise Timely prescription of appropriate antibiotics as per these guidelines Provide other directed therapy as the clinical setting dictates

KEY PERFORMANCE INDICATORS

Time to first dose antibiotic

Re-admission rates

LEGISLATION/REFERENCES/SUPPORTING DOCUMENTS

- Sepsis Pathway (Guideline and Pathway Document MR 63/T)
- PeterMac@Home Neutropenic Fever Assessment Form
- Australian Commission on Safety and Quality in Health Care, 2017, *National Safety and Quality Health Service Standards*, Sydney.

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FURTHER INFORMATION

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