### NEUTROPENIC SEPSIS IN ADULT PATIENTS

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<th>TARGET AUDIENCE</th>
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<td>All staff at LTH, particularly those involved in acute admission of cancer patients namely A &amp;E, medical assessment units, Ribblesdale ward, oncology directorate.</td>
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### CLINICAL GUIDELINE

The governing principles outlined within this document are fully supported in every respect by the Clinical Governance Sub-Committee. All members of staff are required to adhere to the principles involved as outlined within this document, together with any related procedures, which are enabled by this guideline.

This guideline was produced in consultation with:

- All consultant oncologists/haematologists
- Consultant Microbiologists: Dr Cheesbrough, Dr Reddy, Dr Barnes, Dr Orr

GROUP OR COMMITTEE APPROVED BY:

(This will involve local or specialist group review / scrutiny using a body of expertise and knowledge who have confirmed that the document is fit for purpose. Where no such relevant body exists for the approval of a document approval may be obtained from those individuals or groups involved in the consultation process).

DEFINITION OF CLINICAL GUIDELINES

Clinical Guidelines are evidence based systematic statements to assist practitioners and patients in making decisions about appropriate health care for specific clinical circumstances.

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2. Adaptation
Protocol for the Management of Neutropenic Sepsis in Adult Patients with Solid Tumours January 2012

3. Guideline Aim
1. To ensure all patients with suspected neutropenic sepsis receive antibiotics within 1 hour of arrival at the trust.
2. To ensure all patients with neutropenic sepsis receive appropriate investigations and antibiotics.
3. To treat patients with neutropenic sepsis in accordance with NICE guidance.
4. To assess patients with neutropenic sepsis for early discharge on oral antibiotics.
Protocol for the Management of Neutropenic Sepsis in Adult Patients

NEUTROPENIC SEPSIS IS AN ACUTE MEDICAL EMERGENCY. SUSPECTED NEUTROPENIC SEPSIS MUST BE TREATED WITH ANTIBIOTICS WITHIN 1 HOUR OF ARRIVAL IN THE HOSPITAL.

FAILURE TO INITIATE ANTIBIOTICS EARLY MAY RESULT IN OVERWHELMING SEPSIS AND DEATH.

Advice may by obtained from the acute oncology team on bleeps 3353 and 3316 (M-F 9-4pm) or from the consultant or registrar on call for oncology/haematology (via LTH hospital switchboard).

Background:

A report by the National Confidential Enquiry into Patient Outcome and Death (Systemic anti-cancer therapy: for better for worse? [2008]) and a follow-up report by the National Chemotherapy Advisory Group (Chemotherapy services in England: ensuring quality and safety [2010]) highlighted problems in the management of neutropenic sepsis in adults receiving chemotherapy. In response to these concerns the National Institute of Health and Clinical Excellence (NICE) issued clinical guidance 151: Prevention and treatment of Neutropenic Sepsis in cancer patients (September 2012).

This protocol is based on these guidance and proposed NICE pathways and is consistent with guidance on febrile neutropenia from both the European Society of Medical Oncology and The American Society of Clinical Oncology.

Patients with cancer have an increased risk of infection. The degree of risk is dependent on the extent of the disease, as well as the chemotherapy or radiotherapy given to treat the cancer. Reversible bone marrow suppression is a consequence of many chemotherapy regimens.
Neutropenic sepsis is a potentially fatal complication of anticancer treatment (particularly chemotherapy). Mortality rates ranging between 2% and 21% have been reported in adults. Aggressive use of inpatient intravenous antibiotic therapy has reduced morbidity and mortality rates and intensive care management is now needed in fewer than 5% of cases in England.

The risk of infection increases with reducing neutrophil count. Patients with neutrophil count <0.5 are at particularly high risk of developing sepsis. Other patients at increased risk include age >60 years, haematology patients, patients with indwelling central catheters and those with poor general health and/or co-morbidities.

A validated Risk Stratification Tool (MASCC) can be used to identify those at low risk of developing septic complications to allow consideration of early discharge.

All patients presenting with suspected neutropenic sepsis should be assessed by a healthcare professional with competence in managing complications of anticancer treatment within 24 hours of presentation to secondary care.

Patients having anticancer treatment and their carers are provided with written and oral information, both before starting and throughout their anticancer treatment, on:
- neutropenic sepsis
- how and when to contact 24-hour specialist oncology advice
- how and when to seek emergency care.

For adult patients (aged 18 years and older) with acute leukaemias, stem cell transplants or solid tumours in whom significant neutropenia and/or septic complications is anticipated to be of a higher than usual risk as consequence of chemotherapy, prophylaxis with a fluoroquinolone can be offered during the expected period of neutropenia only.
Definition of neutropenic sepsis:

Diagnose neutropenic sepsis in patients having anticancer treatment whose neutrophil count is \(0.5 \times 10^9\) per litre or lower and who have either:

- a temperature higher than 38°C **or**
- other signs or symptoms consistent with clinically significant sepsis.

**NOTE:** The absence of a fever does **NOT** rule out neutropenic sepsis especially if the patient is unwell and has recently received chemotherapy. Neutropenic sepsis could present with non specific symptoms such as confusion in the elderly or rigors without pyrexia. Patients may have taken medication which could mask the fever, i.e. paracetamol or steroids.

Symptoms and signs of sepsis in adults may include –

- Temperature >38°C or <36 °C
- Respiratory rate > 20 breaths/minute
- Heart rate >90 beats/minute
- Acutely altered mental state
- Hyperglycaemia (BM>7.7 mmol/L) in the absence of diabetes

The presentation of sepsis is variable and all of these signs do **NOT** need to be present to diagnosis sepsis. You might also expect specific signs to be absent in certain patient groups (patients on beta-blockers, for example, may not be tachycardia).

However, neutropenia alone is not an indication for antibiotics in a stable patient with no new symptoms suggestive of sepsis.
Suspected Neutropenic Sepsis
Neutropenic sepsis is a medical emergency and can be fatal.

**HISTORY**

Is the patient on chemotherapy?
Date of last treatment? IF WITHIN 28 DAYS THEN FOLLOW NEUTROPENIC SEPSIS TRIAGE PATHWAY.

- Check underlying diagnosis, disease status, date/type of recent chemotherapy
- Note symptoms of infection: rigors, cough, sore throat, diarrhoea, dysuria, skin lesions.
- Check for presence of central venous access device.
- List all drugs and allergies

**EXAMINATION**

Remember basic ABC and refer to sepsis care pathway.

- Temperature, BP, heart rate, oxygen saturation, respiratory rate, peripheral perfusion, altered mental state.
- Search for source of infection i.e. chest examination, check central line devices, any wounds or skin lesions, mouth and throat.
- Record any SIRS criteria or signs of severe sepsis (temp >38 or <36, respiratory rate >20/min, HR>90bpm, altered mental state, SBP<90mmHg, SpO2<90%)

**ACTION**

- **URGENT FULL BLOOD COUNT** (Suspected neutropenic sepsis DO NOT wait for results before IV antibiotics)
- U&E, LFT, CRP, lactate, glucose
- CULTURES: Blood cultures-peripheral and central line, MRSA screen, MSSU/CSU if symptomatic, sputum if available, stool culture if diarrhoea, wound swabs.
- CXR only if clinically indicated eg if hypoxic or clinical signs in chest.
- Arterial blood gases if hypoxic.
- **Do not access central lines unless trained to do so. Insert peripheral cannula if not trained to use central line.**
- All patients should be reviewed by a member of the oncology team within 24 hours of presentation (this can be the following day if patient stable)
  - Bleep acute oncology on 3353 or 3316(M-F 9-4pm) or on call oncology registrar (at weekends or if urgent review is required)
- Determine MASCC Score (multinational association for supportive care in cancer)
First line antibiotics should be given within 1 hour of arrival. It is Vital that time of admission and time of first dose of antibiotics is accurately recorded.

If patient meets severe sepsis criteria-follow severe sepsis guidelines and consider referral to critical care.

**Antibiotic Guidance**

(NB: Consult Product Information literature for dose reductions in liver and renal impairment and LTH antibiotic guidance available on intranet)

**First Line Antibiotic Therapy**

**Patients NOT Allergic to Penicillin**

Give iv **TAZOCIN 4.5g tds** (DO NOT prescribe empiric aminoglycoside unless specific clinical indication as per NICE guidance 2012)

Signs of SEVERE Sepsis (refer to LTH sepsis care pathway):
- Add iv Gentamicin 5mg/kg od.
- In patients with impaired renal function (EGFR <50), recent platinum based chemotherapy, urological malignancies (at risk of urinary obstruction) –Give iv Meropenem 1g tds instead of iv Tazocin and iv Gentamicin. (see antibiotic guidance for doses in renal impairment)

**Patients Allergic to Penicillin**

If there is a history of an anaphylactic reaction, or an accelerated allergic reaction DO NOT prescribe Tazocin or Meropenem (see note below).

**Note:** GI symptoms do not, by themselves, constitute an allergic reaction and are not therefore a contraindication to use of penicillins. Symptoms of a significant allergic reactions may include erythema, pruritis, angioedema, hypertension or shock, urticaria, wheezing, rhinitis.

Allergic to Penicillin (NOT ANAPHYLAXIS)- Give iv Meropenem 1g tds

Allergic to Penicillin (ANAPHYLAXIS/significant allergic reaction)- CIPROFLOXACIN 400mg IV infusion, twice daily. **AND** TEICOPOLANIN 400mg IV bolus 12 hourly for first 3 doses and then 400mg 24 hourly thereafter. (Increase dose of Teicoplanin to 600mg if patient weight >70kg)

NB if patient has received prophylactic Ciprofloxacin prior to admission substitute Gentamicin for Ciprofloxacin (dose will depend on renal function).

For patients with a high probability of line infection (rigors on flushing line or red and tender exit site) or known MRSA consider adding TEICOPOLANIN 600mg IV 12 hourly for first 3 doses and 24 hourly thereafter if the patient is not already receiving it.

Consider addition of iv Metronidazole 500mg tds or oral Metronidazole 400 mg tds if Clostridium difficile infection suspected or in presence of perianal infection.

**IF IN DOUBT PLEASE CONTACT MICROBIOLOGY FOR ADVICE**
Low Risk Patients
MASCC Score ≥ 21

Fulfils criteria for oral antibiotics?

YES

Oral Antibiotic treatment:
Co-amoxiclav 625mg po tds + Ciprofloxacin 750mg po bd for 5 days (check doses if renal impairment)

Fulfils criteria for oral antibiotics and early discharge?

YES

Discharge home following early discharge procedure

NO

Continue oral antibiotics as an inpatient

High Risk Patients
MASCC Score < 21

Admit patient and continue iv antibiotics (see antibiotic guidance above)
Daily review by member of the oncology or haematology team
Reassess MASCC after 48 hours if still neutropenic
See guidance below on ongoing management of inpatients with neutropenic sepsis

Continue IV antibiotics and following guidance on management of inpatient with neutropenic sepsis.
Management of In-Patients withConfirmed Neutropenic Sepsis

- All patients with confirmed neutropenic sepsis should be reviewed by a member of the oncology or haematology team within 24 hours of admission.
  - For patients admitted Monday to Friday (before 4pm) this will usually be by a member of the acute oncology service (Bleeps 3316 and 3353).
  - For patients admitted between 4pm on Friday and Sunday (or Bank Holiday) this will be by the on call oncology registrar (contact via switch board).

- Ensure any oral chemotherapy drugs are discontinued.

- Daily FBC and U &Es

- Monitor temperature, BP, pulse, respiratory rate, Oxygen saturation 4 hourly (or more frequently if required)

- Patients should be reviewed at least daily and prompt action taken if the clinical picture deteriorates

- Specific antibiotics should be guided by sensitivities on any positive microbiology cultures

- Discuss all patients with an unresponsive fever after 48 hours with microbiology before switching empiric antibiotics.

- Central venous access can be used to administer antibiotics if staff are trained to use the line. If central line is thought to be the source of infection it may need to be removed especially if signs of severe sepsis. Please discuss with oncology first.

- Consider commencing GCSF in cases of severe sepsis, fungal infections or prolonged neutropenia (discuss with oncology/haematology)

- Assessment for early discharge should be made within 24 hours of admission by a consultant oncologist or haematologist or by the on call oncology registrar (who should only allow discharge following discussion with the consultant oncologist on call) (see criteria for early discharge)

- For inpatients reassess MASSC after 48 hours and consider switch to oral antibiotics and discharge if reassessed as low risk (refer to criteria)

- Discontinue empiric antibiotic therapy in patients whose neutropenic sepsis has responded to treatment after 5 days, irrespective of neutrophil count.

- Antibiotics may need to be continued for longer duration if complicated sepsis, high risk patient or positive blood cultures.

- If patient well with no positive microbiological cultures or clinical/radiological focus of infection discontinue antibiotics if neutrophil count >0.5 and patient afebrile >24 hours.

- Oral antibiotic choice should be based on microbiology sensitivities if available.

- If a patient admitted with suspected neutropenic sepsis is found to have initial neutrophil count >0.5 they should be treated according to clinical, pathological and radiological findings.
MASCC Risk assessment and criteria for use of oral antibiotics in neutropenic sepsis.

The Multinational Association for Supportive Care in Cancer (MASCC) scoring index is a risk assessment tool which has been validated for use in cancer patients. The MASCC scoring index is used to allocate patient a risk category of either high risk or low risk, which will then consequently dictate whether a patient is suitable for treatment with oral antibiotics rather than intravenous. Patients with a MASCC score greater than or equal to 21 can be prescribed oral antibiotics on confirmation of neutropenic sepsis providing the following criteria are fulfilled:

- MASCC score $\geq 21$
- And no evidence of focal infection such as cellulitis, abscess, pneumonia, line infection
- And no diarrhoea or recent C.difficile infection
- And no allergy or contraindication to penicillin or ciprofloxacin
- And no recent positive microbiology culture results suggesting that co-amoxiclav/ciprofloxacin combination would be inappropriate
- And patient has not received prophylaxis with ciprofloxacin within last 28 days
- And able to swallow tablets
- And no vomiting within the previous 24 hours.

Patients not fitting above criteria should receive iv antibiotics as per the protocol for neutropenic sepsis.

If there is any doubt as to the suitability of the patient for oral antibiotic therapy they should be treated with iv antibiotics. This can also be discussed with a haematologist, oncologist or microbiologist

If a patient fulfils suitability criteria for oral antibiotics they can be considered for early discharge.

**Oral antibiotics:**

Co-amoxiclav 625mg po tds + Ciprofloxacin 750mg po bd for 5 days
Assessment and Criteria for Early Discharge

NICE guidance states ‘Consider outpatient antibiotic therapy for patients with confirmed neutropenic sepsis and a low risk of developing septic complications, taking into account the patient’s social and clinical circumstances and discussing with them the need to return to hospital promptly if a problem develops.’

Patients assessed as ‘low risk’ for septic complications can be considered for early discharge on oral antibiotics.

Assessment for early discharge should be made within 24 hours of admission by a consultant oncologist or haematologist or by the on call oncology registrar (who should only allow discharge following discussion with the consultant on call).

Patients who have been admitted for treatment of neutropenic sepsis and are reassessed as low risk following 48 hours of iv antibiotics can also be considered for discharge providing they fulfil criteria for oral antibiotics.

Criteria for early discharge

Low risk (MASSC ≥ 21) patients who are clinically stable with managed other symptoms and suitable for oral antibiotics can be considered for discharge.

Taking into account the patients social and clinical circumstances consider early discharge.

The following criteria should be considered:

- Does the patient have someone at home to support them?
- Does the patient have access to a telephone?
- Does the patient have access to transport if required?
- Would the patient be able to return to hospital within 1 hour if required?
- Is the patient able to understand the information sheet and willing to return to hospital promptly if a problem develops?
Procedure for Discharge of Patients with Low Risk Febrile Neutropenia

Decision for early discharge should be made by a consultant oncologist or haematologist or by the on call oncology registrar (who should only allow discharge following discussion with the consultant on call).

Patients should be discharged home with a copy of the patient information sheet.

It is the discharging doctor’s responsibility to assess the patient’s understanding of the information and that they fulfill criteria for early discharge on oral antibiotics.

The discharging doctor should ensure that the patient’s telephone details are recorded accurately on the quadramed system.

Following discharge the doctor should complete the neutropenic sepsis Varian questionnaire and forward this to the chemotherapy support team.

The chemotherapy support team will call the patient within 24 hours of discharge to reassess symptoms and answer any questions.

The chemotherapy support team is responsible for checking all culture results and arranging review or change of antibiotics if appropriate.

Patients, in whom there has been any deterioration, should be re-admitted.
References


Implementation Strategy
All Oncology areas, acute assessment wards and emergency departments have a copy of the protocol. The protocol is available on the intranet, the acute oncology intranet site and on the network website.
All band 6 and above nurses working in these areas are trained in the acute oncology service and treatment of neutropenic sepsis. All consultants on the oncall medical rota and in the emergency department are trained in the acute oncology service and treatment of neutropenic sepsis. All oncology registrars receive departmental induction in acute oncology including neutropenic sepsis.
There is a continuous audit programme to document the 1 hour door to needle time for patient with suspected neutropenic sepsis.

Patient resources
Patients all receive information about their chemotherapy at the time of consent (Bacup information leaflet) and a booklet detailing their chemotherapy treatments and recent blood counts. Patients are given 24 hour contact numbers to alert the chemotherapy service if they develop signs or symptoms suggestive of potential neutropenic sepsis and told what symptoms to be aware of.
Patients discharged on oral antibiotics are given the Patient Information Leaflet as approved by the LTH Patient Information Group.

Appendix 1 Patient Information Leaflet
Patient Discharge Information

Discharge information for patients with an infection and low white blood count following chemotherapy

Oncology Department
Specialist Services Directorate
Discharge information

You have developed an infection as a result of a low white blood cell count during your chemotherapy treatment. You are going home with tablet antibiotics to treat your infection. We know this is safe practice and of benefit to patients.

However, If you experience any of the following symptoms, please phone the chemotherapy helpline immediately on 01772 523205:

- Vomiting
- Rash
- Diarrhoea
- Temperature - more than 38C
- If you feel unwell and are concerned

Patients occasionally need to return to hospital for antibiotics through a drip.

Following discharge:

- You will receive a telephone call from the chemotherapy support team within 24hrs of discharge.
- Please do not wait for this call if you have any of the above symptoms, ring the 24hour helpline - 01772 523205.
- Please phone for advice if you have any other concerns or worries.
- Please ensure your family members are aware of this information.
- You can drive and continue normal activities following discharge.

Instructions for antibiotics
You have been prescribed:
Co-amoxiclav 625mg tablets to take three times a day for 5 days
Ciprofloxacin 750mg twice a day for 5 days (Including your hospital stay)

Chemotherapy 24 hr helpline 01772 523205
Between 12pm and 4pm Monday – Friday (excluding bank holidays) please ring the pager on 07659 536 133. Type in your telephone number on the keypad of your phone - this pager is not a voice recorder.