HYWEL DDA UNIVERSITY HEALTH BOARD

Suspected Neutropenic Sepsis Procedure

Procedure Number:	392	Supersedes:		Classification	Clinical

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4	19.7.2018	Clinical Written Control Documentation Group	13.8.2018	29.8.2018	13.8.2021

Brief Summary of Document:	Neutropenic sepsis is a potentially fatal complication of anticancer treatment (particularly chemotherapy); it is also seen in a number of haematological diseases. NICE (2012) reports mortality rates ranging between 2% and 21%, however, aggressive use of intravenous antibiotic therapy in inpatients has reduced morbidity and mortality rates and intensive care management is now needed in fewer than 5% of cases in England.
Scope	This procedure applies to all adult patients with suspected or confirmed neutropenic sepsis due to either anti-cancer treatment or secondary to bone marrow disease. This procedure will be followed by all staff involved in the care of patients with suspected or confirmed neutropenic sepsis.

To be read in conjunction with:	351 – Monitoring and recording of adult physiological observations and the response to physical deterioration policy

Owning committee/group	Haematology / Oncology Clinical Advisory Group Chair – Gina Beard, Lead Cancer Nurse

Reviews and updates		
Version no:	Summary of Amendments:	Date Approved:
1-2	New Procedure	25.1.2015
3	Amendment to reflect new All Wales Guidance re temperature and contact changes as appropriate	27.1.2016
4	Updated	13.8.2018

Glossary of terms

Term	Definition
C. Diff	Clostridium difficile also known as C. difficile or C. diff, is a bacterium that can infect the bowel and cause diarrhoea. The infection most commonly affects people who have recently been treated with antibiotics, but can spread easily to others.
GCSF	Granulocyte colony stimulating factor (GCSF) is a type of growth factor that makes the bone marrow produce white blood cells to reduce the risk of infection after some types of cancer treatment. G-CSF also makes some stem cells move from the bone marrow into the blood. Stem cells are the cells in the bone marrow that make red blood cells, white cells and platelets.
LMWH	Low molecular weight heparin (LMWH).
MASCC	Multinational association for Supportive Care in Cancer (MASCC) risk index for identifying low-risk neutropenic sepsis patients.
MRSA	Methicillin-resistant staphylococcus aureus (MRSA) is a type of bacteria that's resistant to several widely used antibiotics.
Neutropenic	A neutrophil count of $<1.0x10^9/l$
Neutropenic Sepsis	A neutrophil count of <1.0 with either: • a temperature ≥37.5°C **or** • a temperature <36.0°C **or** • clinical signs / symptoms of infection
NEWS	National Early Warning Score (NEWS) can assist in the decision for determining whether or not a patient is at risk of sepsis or severe sepsis. NEWS score – 3-5 Could this patient have an acute illness or an unstable chronic disease? **(THREE =Threat)** NEWS Score – 6-8 The patient is likely to deteriorate rapidly **(SIX = Sick)** NEWS Score – ≥9 This patient has an immediately life threatening critical illness **(NINE = Now)**
NICE	The National Institute for Health and Care Excellence (NICE)
SOB	Shortness of Breath
UKONS	United Kingdom Oncology Nursing Society (UKONS)

Keywords	neutropenic, neutropenic sepsis, sepsis, bone marrow disease, febrile, chemotherapy, neutropenia, pyrexia

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1. INTRODUCTION

Neutropenic sepsis is a potentially fatal complication of anti-cancer treatment (particularly chemotherapy); it is also seen in a number of haematological diseases. Mortality rates ranging between 2% and 21% have been reported in adults (NICE 2012).

Chemotherapy is most commonly given in a day-case or outpatient setting therefore most episodes of suspected neutropenic sepsis will present in the community. People receiving chemotherapy and their carers need to be told about the risk of neutropenic sepsis and the warning signs and symptoms. A patient is deemed to be at risk of neutropenic sepsis if they have received anti-cancer treatment (particularly chemotherapy) within the preceding 6 weeks.

Neutropenic sepsis is a medical emergency that requires immediate hospital investigation and treatment. With early recognition and management as outlined within this procedure patient outcome can be improved. Aggressive use of intravenous antibiotic therapy in inpatients has been shown to reduce morbidity and mortality rates, and intensive care management is now needed in fewer than 5% of cases in England (NICE 2012).

This procedure is based on the advice and guidance from the NICE (2012) guideline “Neutropenic sepsis: prevention and management in people with cancer” and the United Kingdom Oncology Nursing Society (UKONS) (2016) “Oncology / Haematology 24 hour triage rapid assessment and access toolkit”.

Hywel Dda University Health Board Haematologists, Oncologists, and Acute Oncology Service have agreed a definition of neutropenia as neutrophils <1.0 $x10^9$/l for this patient group.

Neutropenic sepsis is suspected in all patients at risk of neutropenia with either a temperature ≥37.5°C or <36.0°C or clinical signs / symptoms of infection (UKONS 2016).

It is recognised that the above definitions of what constitutes potential neutropenic sepsis i.e. temperature threshold and neutrophil count deviate from NICE guidance and the All Wales Chemotherapy Alert Card (Appendix one). The decision has been made within the Multi Disciplinary Team reviewing this procedure to adhere to the UKONS “oncology / haematology 24 hour triage rapid assessment and access toolkit” guidance which is deemed to be a more cautious approach especially given the rurality of Hywel Dda University Health Board and potential patient travel time to hospital.

2. SCOPE

This procedure applies to all adult patients with suspected or confirmed neutropenic sepsis due to anti-cancer treatment or with neutropenia secondary to bone marrow disease. This procedure should be followed by all staff involved in the care of patients with suspected and confirmed neutropenic sepsis.

3. AIMS

The aim of this procedure is to reduce the morbidity and mortality related to neutropenic sepsis and to ensure that patients who are at risk of neutropenic sepsis and their families understand what they should expect from Hywel Dda University Health Board.

4. OBJECTIVES

The aim of this procedure will be achieved by:

- The education of patients and provision of All Wales Chemotherapy Alert Card
- Timely initial management of patients with suspected neutropenic sepsis

- Appropriate management of patients with confirmed neutropenic sepsis

5. PRE-PROCEDURE

Chemotherapy patients

All patients receiving chemotherapy will be educated regarding the potential risk of neutropenic sepsis, as part of this education they will be given an All Wales Chemotherapy Alert Card (Appendix one) which outlines when and how to contact the oncology triage line for advice. As previously outlined the All Wales Chemotherapy Alert Card has differing guidance for temperature to this procedure – for this reason the Chemotherapy Day Unit teams in each site across Hywel Dda University Health Board will ensure that the incorrect information is crossed out with permanent marker pen so the alert card reflects the guidance within this procedure (as in Appendix one) – this will be done when a new batch of alert cards are delivered to the unit and double checked by the nurse giving the alert card to the patient.

The oncology triage line is a joint partnership between Hywel Dda University Health Board and Abertawe Bro Morgannwg University Health Board. It provides 24/7 advice to patients receiving chemotherapy. Patients are assessed using the UKONS Oncology / Haematology 24 hour triage rapid assessment and access toolkit which triages oncological emergencies. If a patient is deemed to be at risk of suspected neutropenic sepsis urgent admission to the patient's local hospital is arranged by the oncology triage line nurse. The contact details of the triage line are given in Appendix two.

Bone marrow suppression patients

Patients who are identified by the Haematology Team as at risk of developing neutropenic sepsis due to bone marrow suppression are provided with the All Wales Chemotherapy Alert Card as above. Information detailing the patient's diagnosis is entered into Chemocare to provide those taking triage line phone calls with information.

6. INITIAL MANAGEMENT OF PATIENTS WITH SUSPECTED NEUTROPENIC SEPSIS FLOWCHART – TO BE COMPLETED WITHIN ONE HOUR

Patient has received chemotherapy in the last 6 weeks or is known to be at risk of neutropenia and:
Temperature ≥37.5°C*
OR
Temperature <36.0°C*
OR
Clinical signs / symptoms of infection

↓

Take Blood Cultures peripherally **AND** if central line present from each lumen of line
Check FBC, U&E, LFT, CRP, Lactate
History and examination including NEWS
Complete Sepsis Six
Withhold oral chemotherapy
Chest x-ray (only if clinically indicated)

↓

Administer IV antibiotics (do not wait for blood results)

No penicillin allergy – Piperacillin / tazobactam (Tazocin®) 4.5 g IV QDS

Non-severe penicillin allergy - Meropenem 1g IV TDS

Severe penicillin allergy / suspected central line infection / history of MRSA or C. DIFF – See section 8 for further information

↓

Neutrophils <1.0x10^9/l

YES ↓

Confirmed neutropenic sepsis
See overleaf for ongoing management
Isolation / barrier nursing not routinely required
Patient not to be considered for discharge unless agreed with Acute Oncology Service, Haematology or Oncology (as appropriate)

NO ↓

Treat as antimicrobial
https://webview.rx-guidelines.com/viewing/index/180#dYHaHWqajq

Oncology Patients
Inform Acute Oncology Service (AOS) of all admissions with suspected neutropenic sepsis
AcuteOncology.CancerServices.HDD@Wales.nhs.uk
Glangwili General Hospital – 07814793544 / 07966131423
Withybush General Hospital - 07772532497
Prince Philip Hospital – 07815704200
Bronglais General Hospital – Inform Dr Elin Jones (Locum Consultant in Oncology)

Out of hours advice is available from the on-call Oncology SpR in Singleton Hospital – via switchboard 01792 205666

Haematology Patients
Inform the on-call Haematology Consultant within 24 hours via switchboard

*A history of temperature ≥37.5°C or <36.0°C even if resolved on presentation to hospital must be managed as per this procedure

7. MANAGEMENT OF PATIENTS WITH CONFIRMED NEUTROPENIC SEPSIS FLOWCHART

Repeat blood cultures daily if temperature ≥37.5°C — Samples for microbiology as clinically indicated
IVI if clinically indicated — Fluid balance — Regular NEWS monitoring
Consider transfusion if Hb <80g/l — If platelets <20x10^9/l discuss with haematology, if <50x10^9/l withhold LMWH

Significant isolates in cultures?

YES → Commence targeted treatment as advised by microbiology; if patient deteriorates or fails to respond to treatment re-discuss with microbiology

NO → Is the patient clinically stable?

YES → MASCC scoring by Acute Oncology Service, Haematologist or Oncologist

NO →

- Add Gentamicin IV after 24 hours (see Gentamicin once daily dosing) if not already part of antibiotic regime
- Consider central line as potential site of infection (section 8)
- Consider the need for antifungal treatment – discuss with microbiology
- If does not respond to treatment / acutely unwell discuss with microbiology

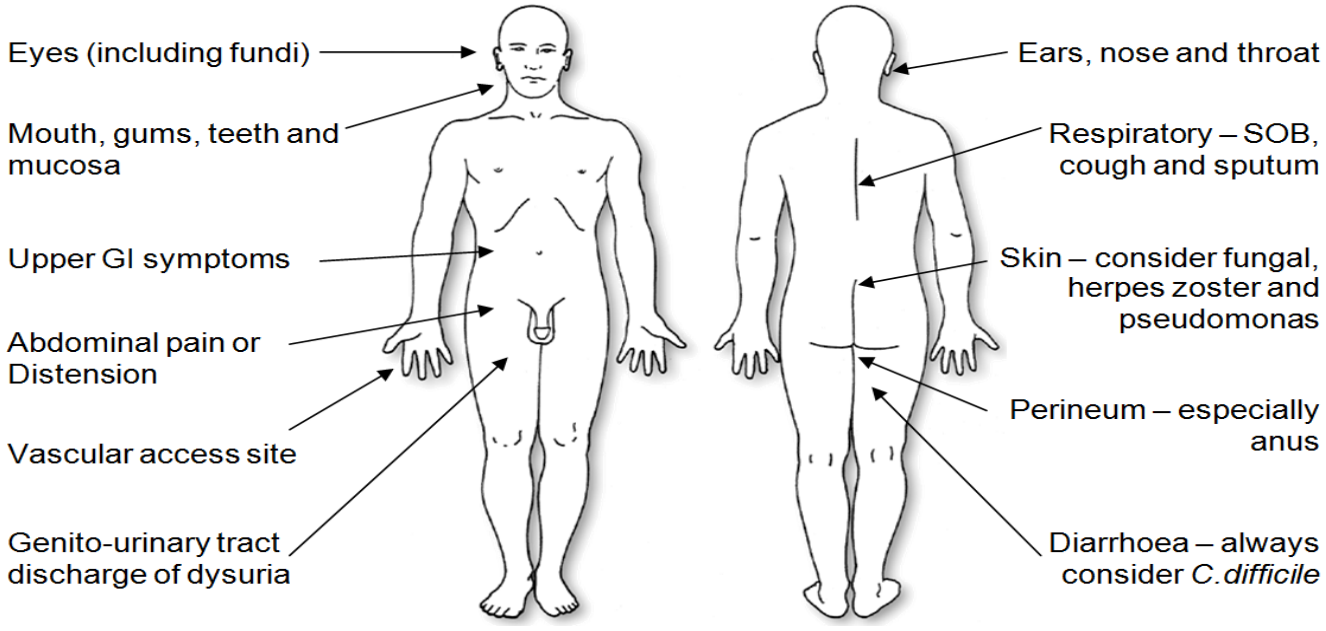
Low Risk MASCC score ≥21

- Consider changing to oral antibiotic therapy – Ciprofloxacin 500mg BD
- Discuss with microbiology if patient has received quinolone prophylaxis or previous MRSA / C.diff

High Risk MASCC score <21

- Continue IV antibiotics
- Reassess MASCC score in 24-48 hours

Check for signs of infection as some infections may not be covered by empirical antibiotics chosen for treating neutropenic sepsis – send samples for culture as indicated:



8. ANTIBIOTICS TO BE USED IN NEUTROPENIC SEPSIS

Allergy status	Initial antibiotic therapy
No known penicillin allergy	Piperacillin / tazobactam (Tazocin®) 4.5g IV QDS See * and ** below
Non-severe penicillin allergy	Meropenem 1g IV TDS See * and ** below
Severe penicillin allergy (e.g. anaphylactic reaction, severe skin reaction)	Ciprofloxacin 400mg IV BD **AND** Teicoplanin 6mg/kg 12 hourly for three doses then daily **AND** Gentamicin IV (see Gentamicin once daily dosing)

*If negative microbiology, an unresponsive fever after 24 hours, and clinical deterioration
Add Gentamicin IV (see Gentamicin once daily dosing)

**If suspected line infection / history of MRSA add Teicoplanin 6mg/kg 12 hourly for 3 doses then daily

Contact microbiology when patients have previous MRSA, C. diff, MDR e.g. ESBL Gram negatives, or if the patient has received quinolone prophylaxis as these cases may require a change of antibiotic.

Unresponsive neutropenic sepsis
Do not switch initial empiric antibiotics in patients with unresponsive fever unless there is clinical deterioration or a microbiological indication.
Consider the need to cover for other aetiology e.g. antifungal cover – discuss with microbiology.

Resolved neutropenic sepsis
Discontinue empiric antibiotic therapy in patients whose neutropenic sepsis has responded to treatment, irrespective of neutrophil count.

In cases of ongoing sepsis where neutropenia has resolved manage as per antimicrobial guidance https://webview.rx-guidelines.com/viewing/index/180#dYHaHWqajq

9. MASCC RISK INDEX SCORE (MULTI-NATIONAL ASSOCIATION OF SUPPORTIVE CARE IN CANCER)

Patients with confirmed neutropenic sepsis should be assessed after 24 hours for the risk of septic complications using MASCC scoring (Appendix three); this must only be carried out by a clinician experienced in the management of neutropenic sepsis i.e. Acute Oncology Service, Oncologist, or Haematologist. A MASCC score of ≥21 is deemed to indicate a low risk of septic complications, a score of <21 is deemed to indicate a high risk of septic complications.

Patients assessed as having a low risk of septic complications using MASCC:
Consider oral therapy: Ciprofloxacin 500mg BD
Contact microbiology if patient has received quinolone prophylaxis or a history of previous MRSA / C. diff as Ciprofloxacin may not be appropriate.

Patients assessed as having a high risk of septic complications using MASCC:
If patient clinically stable or showing improvement continue current IV antibiotic regime, if deteriorating despite management with above IV antibiotics discuss with Microbiology.

Reassess MASCC score after 48 hours of treatment. If low risk see oral option above, if remains high risk continue IV antibiotic therapy – if patient not responding to management discuss with Microbiology.

10. BARRIER NURSING

Isolation / barrier nursing of neutropenic sepsis patients is not routinely required. Follow infection control advice if required based on individual patient symptoms e.g. diarrhoea.

11. GRANULOCYTE-COLONY STIMULATING FACTOR (GCSF)

GCSF should only be considered in cases of neutropenic sepsis unresponsive to the above management and must be discussed with a Haematologist (Haematological patients) or Acute Oncology Service / Oncologist (Oncology patients) prior to initiating.

12. REFERENCES

All Wales Chemotherapy Alert Card.
Available at: http://nww.swcanet.wales.nhs.uk/all-wales-chemotherapy-alert-card

Antibiotic guidelines. 2018.
Available at: https://webview.rx-guidelines.com/viewing/index/180#dYHaHWqajq

MASCC. 2017. *MASCC Risk Index Score*
Available at: http://www.mascc.org/mascc-fn-risk-index-score

National Institute for Health and Clinical Excellence (NICE). 2012. *Neutropenic sepsis: prevention and management of neutropenic sepsis in people with cancer*
Available at: https://www.nice.org.uk/guidance/cg151

NEWS (National Early Warning Score). 2013.
Available at: http://www.1000livesplus.wales.nhs.uk/acute-deterioration-news

United Kingdom Oncology Nursing Society (UKONS). 2016. *Oncology / Haematology 24 hour triage rapid assessment and access toolkit*
Available at: http://www.ukons.org/acute-oncology-forum

13. APPENDIX ONE – ALL WALES CHEMOTHERAPY ALERT CARD

CERDYN RHYBUDD CEMOTHERAPI

CHEMOTHERAPY ALERT CARD

Information For Patients

ALWAYS carry this card & show to staff.
Phone now if you have ANY of the following:

- Temperature above 37.5°C [redacted]
- [redacted]
- A temperature of below [redacted] 36°C
- Shaking/shivering episodes
- Unusual bruising, bleeding or rashes
- Flu like symptoms, chesty cough, or any other signs of infection
- Persistent feeling of sickness or vomiting
- Diarrhoea—more than 4 episodes in 24 hours
- Mouth ulcers or a sore mouth that stops you eating or drinking

Advice for Health Care Professionals

This patient is at risk of severe chemotherapy complications including **Sepsis**

If neutropenic sepsis is suspected:

- Treat as an acute medical emergency
- Start empiric IV antibiotics within 1 hour
  DO NOT wait for FBC result
  See local protocol

For any acutely unwell chemotherapy patient:

- Contact the Acute Oncology Service if available , or use the number below to contact the specialist team
- STOP any chemotherapy drugs until specialist advice obtained

24 Awr / Hour

GLANGWILI HOSPITAL

9am-5pm Monday to Friday call

01267 227134

Outside these hours please call

01792 618829

V.2

Gwybodaeth i gleifion

Cariwch y cerdyn yma BOB AMSER a'i ddangos i staff.
Ffoniwch yn syth os oes gennych UNRHYW UN o'r canlynol:

- Tymheredd dros 37.5°C [redacted]
- [redacted]
- Tymhereddo dan [redacted] 36°C
- Pyliau o ysgwyd neu grynu
- Cleisio, gwaedu neu frechau anarferol
- Symptomau tebyg i ffliw, peswch, neu unrhyw arwydd arall o haint
- Teimlad cyson o salwch neu chwydu
- Dolur rhydd - mwy na 4 o byliau mewn 24 awr
- Wlserau yn y geg neu geg ddolurus sy'n eich atal rhag bwyta neu yfed

Cyngor i Weithwyr Gofal Iechyd Proffesiynol

Mae yna berygl i'r person yma ddioddef o gymhlethdodau cemotherapi difrifol gan gynnwys **Madredd**

Os amheuir madredd neutropenig:

- **Dylech ei drin fel argyfwng meddygol aciwt**
- Dechreuwch wrthfiotigau empirig iv o fewn 1 awr

PEIDIWCH AG AROS am ganlyniadau cyfrif gwaed llawn (FBC)
Dilynwch y protocol lleol

Os yw unrhyw glaf cemotherapi yn ddifrifol sâl:

- Cysylltwch â'r gwasanaeth oncoleg aciwt os yw ar gael, neu defnyddiwch y rhif ar y daflen i gysylltu â thîm arbenigol
- STOPIWCH unrhyw gyffuriau cemotherapi hyd nes y cewch gyngor arbenigol

Patient addressograph

Triniaeth/Treatment

14. APPENDIX TWO – ONCOLOGY TRIAGE LINE CONTACT NUMBERS

Hospital site administering treatment	In-hours (Mon-Fri 9am-5pm)	Out of hours (Mon-Fri 5pm-9am, weekends, and public holidays)
Glangwili General Hospital	01267 227134	01792 618829
Withybush General Hospital	01437 773585	01792 618829
Prince Philip Hospital	01554 783390	01792 618829
Bronglais General Hospital	01970 635459 / 635980	01792 618829
Singleton Hospital	01792 618829	01792 618829

15. APPENDIX THREE – MASCC RISK INDEX SCORE

Characteristic		**Score**
Age	≥60 years	0
	<60 years	2
Patient dehydrated, requiring IV fluids	Yes	0
	No	3
Patient systolic blood pressure	<90 mmHg	0
	≥90 mmHg	5
Does the patient have COPD	Yes	0
	No	4
Does the patient have a solid tumour or no previous fungal infection in a haematological malignancy	Solid tumour or no previous fungal infection in haematological malignancy	4
	Haematological malignancy with previous fungal infection	0
Symptom burden related to neutropenic sepsis	None or mild symptoms	5
	Moderate symptoms	3
	Severe symptoms	0
Was the patient already an inpatient prior to this episode of neutropenic sepsis	Admitted with this episode	3
	Already an inpatient	0
	Total MASCC Score	

MASCC score of ≥21 low risk of septic complications
MASCC score of <21 high risk of septic complications

Table adapted from MASCC Risk Index Score