The Christie
NHS Foundation Trust

CLINICAL GUIDANCE FOR

THE MANAGEMENT OF SEPSIS (INCLUDING NEUTROPENIC SEPSIS)

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Target audience:	All Clinical Staff		

Key points

- Clinical guidance for the early recognition, management and treatment of a septic patient (including neutropenic sepsis)
- Empirical treatment for patients with high risk neutropenic sepsis and sepsis of unknown origin

CONTENTS

1. ASSOCIATED DOCUMENTS

NICE CG151 - Neutropenic sepsis
NICE NG51 - Sepsis: recognition, diagnosis and early management
Emergency Pathway for patients with suspected sepsis
Adult antimicrobial guide (Microguide)
Antimicrobial Policy
Aseptic Non Touch Technique (ANTT) Policy
Out of hours tool (Infection Control)
Central Venous Access Device Policy (CVAD)
National Early Warning Score 2 (NEWS 2) and observations policy for the management of acutely ill Adult Patients

2. INTRODUCTION

2.1 Statement of intent

This document has been developed using national standards and clinical guidance and is a trust approved document for the recognition, management and treatment of sepsis (including neutropenic sepsis).

2.2 Purpose

These guidelines are aimed at all Christie NHS Foundation Trust staff that need to be aware of the risks of sepsis in a cancer population and to provide a basis for prompt diagnosis and treatment. They are to adhere to NICE guidelines [NG51] and [CG151].

2.3 Scope

These guidelines apply to all clinical staff that record initial patient observations and where can assist in the escalation and early management of suspected sepsis.

3. DEFINITIONS

Term	Meaning
SEPSIS	Sepsis is a life-threatening organ dysfunction due to a deregulated host response to infection. It should be considered whenever there is an acute deterioration, raised NEWS2 score**,** and/or the patient looks clinically unwell.
NEUTROPENIA	Increased susceptibility to infection is likely when the neutrophil count falls below 1000/mm^3 with escalating risk at <500/mm^3 (Significant) and at <100/$mm^{3.}$ (Severe)
NEWS2	National Early Warning Score 2 - V6.0
SACT	Systemic Anti-Cancer Treatment
SEPSIS 6 PATHWAY	IV Antibiotics, IV fluids, Oxygen – Blood Cultures, Lactate, Hourly Urine Output
AKI	Acute Kidney Injury
PGD	Patient Group Direction

4. DUTIES

This section outlines the roles and responsibilities of all staff involved in promoting the highest standard of practice in relation to sepsis.

4.1 Chief Executive

The Chief Executive has overall responsibility for ensuring that the organisation adheres to the standards set out in this clinical guidance. Also ensuring that safe and secure handling of medicines is carried out at all times.

4.2 Senior Managers as applicable

4.2.1 Sepsis Consultant Lead

The Sepsis Consultant Lead and Consultant Microbiologist are responsible for:

- Implementing the Sepsis steering group objectives
- Promoting and providing advice and support to clinical teams on the recognition, diagnosis and management of sepsis
- Promoting and implementing best practice in sepsis
- Providing guidance and advice on relevant procedures
- Contact details available under Department, sepsis page on HIVE

4.2.2 Sepsis Nurse Specialist

The Sepsis nurse specialist is responsible for promoting and monitoring the highest standard of practice by:

- Implementing the Sepsis steering group objectives as outlined in Sepsis Steering Group minutes
- Promoting and providing advice and support to clinical teams on the recognition, diagnosis and management of sepsis
- Promoting and implementing best practice in sepsis
- Providing and monitoring ongoing clinically relevant competency based training to all staff appropriate to their role
- Acting as a liaison for clinical staff and non-clinical departments, reporting into and from the Sepsis steering group
- Engaging in clinical audit activities on behalf of the Sepsis steering group
- Assisting the clinical lead to ensure local and national targets are met.
- Co-coordinating and monitoring new initiatives, projects or recommendations from internal or external sources
- Providing support to clinical departments who investigate and analyse breaches, incidents and errors in clinical practice, providing measures to prevent these in future
- Support link nurses within clinical areas in promoting best practice in relation to the early recognition, management and treatment of sepsis / neutropenic sepsis

4.2.3 Divisions

It is the responsibility of divisions to support all staff to carry out tasks enabling them to recognise and treat sepsis in a timely manner:

- The responsibility of ensuring that the guidelines for the management of sepsis (including neutropenic sepsis) are adhered to rests with the general managers, divisional directors, lead nurses and matrons. They must ensure action is taken in response to deficiencies reported following audit reviews and clinical incidents to the Sepsis steering group to raise areas of concern.

4.2.4 Ward/Departmental Managers

The ward/departmental managers are responsible for ensuring:

- Implementation of the clinical guidance for the management of sepsis (including neutropenic sepsis) and monitoring compliance within their area
- Reporting any sepsis related clinical incidents via the trust incident reporting system and taking remedial action where appropriate
- Ensuring all staff for which they have responsibility to undertake essential training appropriate to their role
- Investigate non-compliance with essential sepsis training sessions and ensure compliance is gained and understood
- Support staff in the completion of the IV antibiotic process competency assessment packages

4.2.5 Registrant in charge

The registrant in charge of a ward/department is responsible for ensuring:

- Staff adhere to all trust clinical guidance, policies and procedures for any patient presenting with suspicion or confirmation of sepsis including neutropenic sepsis
- Safe and appropriate management of all patients with sepsis whilst in charge of that ward/department
- Individuals work within their professional scope of registered bodies
- The appropriate action is taken in the event of a clinical incident/event or near miss and is reported via the trust incident reporting system
- Ensure all clinical incidents/ events and/or near misses are escalated via sepsis link nurse for review in sepsis steering group

4.2.6 Ward/Departmental staff

Ward/Departmental staffs have a responsibility to:

- Adhere to all trust clinical guidance for the appropriate management of and patient with suspicion or confirmation of sepsis
- Complete the trust approved Sepsis training relevant to their role in a timely manner and prior to expiry of compliance
- Complete clinical one to one IV antibiotic PGD competencies relevant to their role with their link nurse, clinical practice facilitator or sepsis clinical nurse specialist
- Work within the professional scope of their registered bodies
- Report all clinical incidents/events and near misses to the nurse in charge and ensure these are reported via the trust incident reporting system

4.2.7 Medical Assessors

Medical assessors have the responsibility to:

- Adhere to all trust clinical guidance, policies and procedures for the appropriate management of sepsis including neutropenic sepsis
- Work within the professional scope of their registered bodies
- Ensure documentation adheres to the local and national coding guidelines
- Ensure all sepsis related clinical incidents/events and near misses are reported via the trust incident reporting system

Keep up to date with current trust guidelines ensuring early recognition, management and treatment for sepsis (suspected), including prompt prescribing of antibiotic cover where appropriate

4.3 Committees in level of hierarchy

4.3.1 Sepsis steering group (SSG)

The Steering group lead by consultant, sepsis lead and microbiology consultant is responsible for promoting the highest standard of practice by:

- Identifying the need to develop or review procedural documents
- Clearly document in the committee meetings minutes
- Approve the final draft for factual accuracy, content, omissions and style
- Complete the procedural document development checklist and submission to document ratification committee
- Ongoing review and maintenance
- Making recommendations to all clinical and nursing staff concerning the appropriate early recognition and management of sepsis based on national guidelines and adapted for local conditions as appropriate
- Promoting continuing education in relation to sepsis to all relevant clinical employees
- Monitoring the Trust compliance and performance for the 1 hour door to needle targets
- Reviewing quality assurance measures and critical incident reports/ root cause analysis pertaining to the management of patients with (suspected) sepsis

4.3.2 Resuscitation and Deteriorating Patients Committee (RDPC)

The resuscitation committee has delegated responsibility for setting the highest standard of resuscitation practice by:

- Making recommendations to the organisation concerning appropriate pre, peri and post resuscitation management. This advice is based on national guidelines and adapted for local conditions as appropriate
- Monitoring performance of the resuscitation service
- Reviewing quality assurance measures & critical incident reports
- Promoting continuing education in resuscitation for all relevant members of the hospital staff.

4.3.3 Drugs & Therapeutics Committee (DTC)

The Drugs & Therapeutics committee is responsible for:

- Approval of all new drugs and regimens advising which medicines should be available to prescribe
- Authorisation of guidelines
- Developing policies where appropriate including those required by National Cancer Standards

4.3.4 Nosocomial Infection Performance (NIPR) / Antimicrobial Stewardship Committee

- The Antimicrobial stewardship committee is part of the Trusts NIPR committee and monitors on a monthly basis antimicrobial usage throughout the Trust.

5. INITIAL ADVICE AND MANAGEMENT FOR FEBRILE CANCER PATIENTS

5.1 Hotline

- All Christie-registered patients on Systemic Anti-Cancer Therapy (SACT) will have been issued with an information card which will detail information about their chemotherapy regimen.
  This information card will also provide an immediate contact number which may

be the chemotherapy team (in working hours) or the Christie Acute Oncology Management Service (AOMS) incorporating the Hotline. The latter provides 24 hour advice, 7 days / week to patients and professionals.

5.2 External Hospital Admissions

- For patients under treatment at The Christie seen in other Trusts, the Hotline AOMS should be contacted on **0161 446 3658** for advice on how to manage the patient locally or referral back to the centre.

5.3 Microbiology

- Clinicians may also seek advice from the responsible oncology team and additional microbiology advice from the local or Christie microbiologist if needed. Microbiology ward rounds are held every Monday, Wednesday and Friday however if you are not able to get answers from the team or the Christie microbiologist there is on call microbiologists available at Salford Royal Foundation Trust and should be contacted on **0161 206 4570**.
  For virology queries, contact Manchester Royal Infirmary via switch

6. RISK FACTORS STRATIFICATION

6.1 Risk Factors for Sepsis

- Age ≥75yr or ≤1yr
- Recent trauma, surgery or invasive procedure within the last 6 weeks
- Recent SACT in the last 6 weeks
- Impaired immunity due to illness or drugs e.g. neutropenia, long term steroid treatment, haematological malignancies, immunosuppressant
- Autologous stem cell transplants <6 months
- Allograft stem cell transplant <2 years
- Indwelling lines or catheters
- People with any breach of skin integrity
- Intravenous drug misusers
- Diabetes

6.2 Risk Factors for Neutropenic patients

Up to 60% of febrile neutropenic patients prove to have infections and 16-20% of those with a neutrophil count <100/mm^3 has a bacteraemia. Fever is commonly as a result of bacteraemia and usually due to Gram positive cocci (e.g. coagulase negative staphylococci, *Staphylococcus aureus*, viridans streptococci) or Gram negative bacilli (e.g. *Escherichia coli*, Klebsiella spp, *Pseudomonas aeruginosa* etc).

Fungal infections tend to occur after patients have received broad-spectrum antibiotics and have had prolonged periods of neutropenia but may present as primary infections.

Infections in neutropenic patients typically take 2-7 days to respond to antimicrobial therapy. Acute respiratory viral infections e.g. influenza or respiratory syncytial virus may be associated with severe illness in the immunocompromised host.

The risk of infection is greater the faster the rate of decline of the neutrophil count and the longer the duration of neutropenia especially if neutropenia lasts for >10 days.

- **Suspect sepsis if a patient presents with signs or symptoms that indicate possible infection, even if they do not have a high temperature**

- **Please Note: Pyrexia may be absent in some infected patients who are dehydrated, severely 'shocked', taking steroids or NSAIDs**

- **Infection must also be considered in any patient undergoing treatment for cancer and who is unwell and particularly in those who are neutropenic**

- **Take into account that people with sepsis may have non-specific, non-localised presentations, for example "feeling very unwell"**

NB. Conversely pyrexia may be a complication of non-infectious causes e.g. transfusion, drugs such as cytarabine, and malignant disease such as lymphoma and renal carcinoma.

6.3 High risk patients

- Those who are already in-patients when fever and neutropenia develop
- Outpatients who need acute hospital care for problems in addition to the fever and neutropenia
- Outpatients with uncontrolled cancer (e.g. acute leukaemia not in remission, those with tumours progressing during anticancer therapy)
- Patients on immunosuppressive agents e.g. cyclosporin A, steroids
- Patients with chronic GVHD
- Patients with specific foci of infection e.g. intravascular catheter infection, tunnel infection
- New pulmonary infiltrate
- Presence of any of the following features
- abdominal pain, nausea and vomiting, diarrhoea
- neurological or mental changes
- allogeneic stem cell transplants or autologous stem cell transplants
- pregnancy
- HIV
- recent treatment with antibiotics (within previous 72 hours)
- renal failure (creatinine clearance <30ml/min)
- hepatic failure
- respiratory insufficiency
- haemodynamic instability
- inability to take oral medications
- Neutropenia likely to last for >10 days
- Recent fludarabine treatment
- NEWS2 $\geq$ 5 (or scoring 3 in any single parameter)
- Phase I or II clinical trial patients (inform investigator)

6.4 Low risk patients

All those not in the above categories and where NEWS2 <5, If in doubt treat as high risk patient.

7. CLINICAL ASSESSMENT OF THE SEPTIC PATIENT

If the patient is NOT at risk of impaired immunity, they must have a sign of infection and meet the sepsis risk criterion to treat with IV antibiotics.

If infection is suspected a full history and examination should be carried out for consideration of antibiotics. Urgency of assessment and IV antibiotic administration is dependent upon the patient's condition, deterioration and if clinical observations indicate:

- NEWS2 ≥5
- NEWS2 scoring 3 in any single parameter
- "Looks clinically unwell"

The patient should then be assessed following the sepsis risk criterion below for consideration of IV antibiotic cover.

THIS SHOULD BE ACHIEVED WITHIN ONE HOUR FROM SUSPICION OF SEPSIS.
DO NOT DELAY ADMINISTRATION OF ANTIBIOTICS WHILST AWAITING FBC/NEUTROPHIL COUNT RESULTS.

8. EMERGENCY PATHWAY FOR PATIENTS WITH SUSPECTED SEPSIS (INCLUDING NEUTROPENIC SEPSIS)

EMERGENCY SEPSIS PATHWAY ALGORITHM

Carry out a full history and examination immediately and initiate IV antibiotic treatment **WITHIN ONE HOUR** from diagnosis of suspicion or confirmation of sepsis.

8.1 Sepsis risk criterion

8.1.1 High risk - Red flag

If infection is suspected and there is **one or more high risk criterion**, then the patient may need immediate clinician review by a ST3 or above or ANP give IV antibiotics and commenced on the sepsis 6 pathway. They should be discussed with a consultant.

8.1.2 Moderate risk – Amber flag

If Infection is suspected and there is **two or more moderate risk criterion with a lactate ≥ 2mmol/L and or confirmed AKI**, they should be reviewed by ST3 or above or ANP give IV antibiotics and commenced on the sepsis 6 pathway.

If infection is suspected and there is **two or more moderate risk criterion but the lactate ≤ 2mmol/L and no AKI present**, they should be reviewed by ST3 or above or ANP within three hours for consideration of antibiotics.

If infection is suspected and there is only one moderate risk criterion, the patient should be re-assessed within one hour and blood tests reviewed if indicated.

8.1.3 Low risk

If the patient is low risk, they should be assessed and managed according to clinical judgement.
NB. For further information see appendices 19.2

9. EMPIRICAL TREATMENT FOR PATIENTS WITH HIGH RISK NEUTROPENIC SEPSIS AND SEPSIS OF UNKNOWN ORIGIN

NB. This guidance refers only to neutropenic sepsis and sepsis of unknown origin, for sepsis of known origin refer to Trust Antimicrobial Policy / Microguide ADULT ANTIMICROBIAL GUIDE (MICROGUIDE)

NB. All antimicrobial doses are approximate and may need to be altered according to patient's clinical condition, weight and renal function etc. Refer to the Trust Antimicrobial Policy for details.

NB. In patients with renal impairment dose adjustment is required see BNF and summary of product characteristics (SmPC) for details.

No Penicillin Allergy	**Non severe Penicillin Allergy**	**Severe Penicillin Allergy** Immediate reaction or anaphylaxis or delayed severe skin reaction	**Patient has poor renal function or received reno-toxic SACT in last 7 days e.g.** Cisplatin, Ifosfamide, High dose Methotrexate, Trabectedin
1st Line: **Piperacillin/tazobactam IV 4.5g QDS** **+** **IV Gentamicin** (dose as per antibiotic guideline) A decision to administer Gentamicin to a patient with a known or suspected AKI should be discussed with a senior doctor. The lower dose of 3mg/kg should be considered **NB: Sepsis of unknown origin without neutropenia** **Piperacillin/tazobactam IV 4.5g TDS can be used +**	**1st Line:** **Meropenem IV 1g TDS**	**1st Line:** **IV Vancomycin** (dose as per antibiotic guideline) **+** **IV Gentamicin** (dose as per antibiotic guideline) **+** **IV Metronidazole 500mg TDS** This combination **is not prescribed as a PGD** The patient should be reviewed by a prescriber urgently Patients with such allergies should be discussed with immunology as they may be candidates for formal allergy testing.	**1st Line:** **Meropenem IV 1g TDS** Patients who have received reno-toxic SACT **after 7 days** of initial treatment can still receive: **Piperacillin/Tazobactam 4.5g QDS** **+** **IV Gentamicin** (dose as per antibiotic guideline) However they should have a frequent review and monitoring of renal function.

IV Gentamicin (dose as per antibiotic guideline) (Increased if necessary to 4.5g QDS, increased frequency may be used for severe infections)			
2nd Line: **Meropenem 1g IV TDS** (If Gentamicin cannot be given)	**2nd Line**: Contact Microbiology	**2nd Line**: Contact Microbiology	**2nd Line**: Contact Microbiology
Duration and Oral Step Down Review after **48-72 hours** If patient stable, cultures negative, and neutrophil count >1.0 then consider discharge with a 5 day course of: **PO Co-amoxiclav 625mg TDS + PO Ciprofloxacin 750mg BD**			

Only consider including a glycopeptide (e.g. vancomycin) as first line treatment if:

- IV catheter related infection e.g. signs of inflammation around the catheter insertion point or along catheter track
- MRSA or penicillin resistant pneumococci are likely
- Patient has severe mucositis
- Severe Penicillin Allergy

If the patient is poorly or deteriorating or if there is no improvement within 24 - 48 hours, contact the relevant oncologist, haematologist or microbiologist (for Christie patients via switchboard **0161-446-3000**).

9.1 Nursing guidance for IV antibiotic PGD treatment

If the patient triggers for suspected sepsis as either an emergency or established inpatient, PGD IV antibiotics should be given within the hour, taking into consideration the following limitations:

- If the patient has had no infection pathway commenced and no previous antimicrobial treatment (oral or IV), administer IV antibiotics as per PGD within the hour
- If a medical review has not taken place or the patient has not received any oral antibiotics within the previous twelve hours, administer IV antibiotics as per PGD within the hour
- If the patient has had antibiotics stopped or switched to oral antibiotics within the previous twelve hours and re-triggers the patient should receive a senior

Clinical review within the hour prior to considering titrating antibiotics back to IV

- If the patient is already on IV antimicrobial treatment and has not had a senior clinical review within the past twelve hours from time of suspected sepsis, patient requires general medical review with aim to have a senior clinical review within the following twelve hours.

NB. Antibiotic Patient Group Direction (PGD) guidance
PIPERACILLIN/TAZOBACTAM, GENTAMICIN, MEROPENEM

9.2 Treatment of low risk patient – oral antibiotic regimen

PO Ciprofloxacin 750mg BD and PO Co-amoxiclav 625mg TDS
This will normally be informed by culture results and/or clinical findings.

Other oral antibiotic options:
Levofloxacin or equivalent quinolone (NB. this may be less effective in *Pseudomonas* infections)
Clindamycin (if Gram positives and anaerobes are likely to be responsible e.g. cellulitis, fasciitis)
Neutropenic patients with fever should be managed in hospital but may be treated as outpatients at the discretion of the responsible clinician.
If low risk hospitalised patients are stable on antibiotic therapy, consider discharge home to continue oral antibiotics as an option if:

- patient is mentally competent
- lives near the hospital (within an hour)
- has someone at home all the time
- has access to transport and a telephone
- conditions at home are deemed satisfactory

10. INITIAL MANAGEMENT OF THE ACUTELY UNWELL SEPTIC PATIENT

The management plan should include an agreed frequency of physiological observations with a standard trigger (NEWS2) for contacting the parent clinical team or critical care outreach. Communication of clinical cases and handover should follow the SBAR format.

- Immediate priority based assessment of the patient following an ABCDE format
- Obtain a brief patient history
- Commence sepsis 6 pathway
- A limited examination of the relevant systems of the body
- Initiation of appropriate monitoring , observations and bedside investigations
- A secondary assessment after stabilisation of the patient including a more thorough history, detailed examination by system and appropriate investigations
- The formulation and communication of an appropriate plan including when to involve other clinical teams
- Referral to Critical care outreach team bleep 12591

If treating for sepsis or suspicion of sepsis clearly document in the patient's electronic medical notes adhering to the local and national coding guidelines.

10.1 History and examination

Expected onset and anticipated duration of neutropenia may be estimated by establishing day of neutropenia in relationship to first day of the current cycle of chemotherapy.

It is useful to enquire whether:

- Blood products have been administered within the previous 6-24 hours as this may account for a febrile episode.
- Rigors are associated with use or flushing of a central venous line.

Check the patient record (notes and electronic annotations) for alerts such as previous infection with *Clostridium difficile* or multidrug resistant organisms.

When looking for a focus is important to enquire and look for inflammation/infection at the following sites and sample as appropriate:

- Mouth – teeth, gums, pharynx
- ENT problems esp. involving sinuses
- Eyes including fundi
- Gastrointestinal symptoms
- Lung – cough, shortness of breath, sputum
- Perineum especially anal area (defer PR examination until antibiotics started)
- Diarrhoea – if present, isolation precautions are advisable – discuss with the infection prevention and control team
- Skin lesions – (NB think about fungal, *Pseudomonas aeruginosa*, generalized herpes and *Varicella zoster* infections)
- Look for genital-urinary infections or discharges. Consider the possibility of reactivation of genital herpes, fungal infection and necrotising fasciitis.
- Look at vascular access sites especially central venous line insertion sites, stem cell aspiration sites, nail margins, skin tunnels, surgical incision sites
- Renal tract signs and symptoms, especially if previous instrumentation, surgery or catheterisation.

A full systems review should include a thorough history of overseas residence and travel, pets, hobbies, occupation, sexual history and potential environmental exposures to unusual organisms. Important overseas related organisms might include strongyloides and *Salmonella typhi* (Typhoid fever)

10.2 Investigations

- Full blood count (FBC)
- CRP (C-reactive protein)
- Urea and electrolytes (U+Es)
- Liver function tests, including albumin
- Coagulation screen
- Group and save
- ABG / POCT (including lactate)
- ECG if hypotensive, having chest pain, bradycardic, tachycardia or has an arrhythmia
- Chest radiography (if indicated)

- Abdominal ultrasound (if suspicion of biliary obstruction, hydronephrosis or renal failure)
- Cultures of lesions including culture for fungi
  (Biopsy specimens for fungal or bacterial culture MUST NOT be sent in formalin. Histology should also be considered and send in formalin or other fixative as after discussion with Pathology)
- Stool microscopy for types 5-7, culture and *Clostridium difficile* toxin detection, cryptosporidium if diarrhoea also considers whether virology would be useful- send faeces in clean plain container for electron microscopy. For gastroenteritis send samples for EM and Virology PCR.
- Urinalysis and culture (if urinary symptoms present or patient catheterised)
- Blood cultures (peripheral and also through each lumen of IV line catheter lumens)
- Mycobacterial blood culture should be sent in special MBBact bottles if MAI is suspected
- Respiratory secretions for rapid testing by PCR, e.g. nasal wash, NPA, BAL. Direct viral detection by PCR is the preferred method for diagnosing respiratory viral infections and can be done using NPA, BAL or if not available by nose and throat swab.
- A clotted blood sample (7-10ml, plain tube) should be sent for viral serology and a convalescent sample sent 10-14 days later if appropriate)

If *Varicella zoster* or *Herpes simplex* is being considered:

- Send a glass slide touched against an opened lesion and allowed to air dry, and transported in a slide carrier (vesicular skin lesion kit)
- swabs and blood for viral PCR
- Serum (clotted blood) for IgG and IgM

Also in VZ - remember infection control precautions are needed to protect both staff and other patients – discuss with a member of the infection prevention and control team.

- Patients who are not getting better or are at high risk of a fungal infection should be discussed with the radiologists regarding appropriateness of additional imaging e.g. HRCT (especially useful for diagnosis of pulmonary aspergillosis), MRI, radionuclide imaging or ultrasonography

If invasive fungal infection is being considered:

- Send EDTA blood for Aspergillus PCR
- Aspergillus galactomannan may be useful on clotted blood , CSF and BAL fluid
- Culture and PCR on sputum, BAL and other material e.g. CSF, skin biopsy

If CMV is being considered e.g. after stem cell transplantation:

- Send EDTA blood for CMV PCR.
- Consider CMV PCR on BAL and GI biopsy

If Pneumocystis pneumonia is being considered:

Send bronchial washings (or if these are unobtainable then sputum or serum for *Pneumocystis jirovecii* (PCP) PCR

- Bronchial washings should be routinely microscopically examined and cultured for bacteria, fungi, and mycobacteria

10.3 Follow up assessment / investigations

- FBC daily
- U&Es, LFTs and coagulation at regular intervals depending on clinical features
- Serial CRPs or other acute phase reactants
- If fever persists, repeat blood cultures based on clinical assessment
- Repeat chest radiology as clinically indicated
- If lactate ≥ 2 mmol/L, repeat the lactate sample two hours later

11. REASSESS AT 48 HOURS

11.1 Afebrile at 48 hours

No cause found

- Low risk – consider change to oral antibiotics if not already on them

Cause found

- Continue on appropriate antibiotics based on susceptibility test results

11.2 Persistent fever at 48 hours

Reassess daily with repeat of history taking and clinical examination and repeat laboratory investigations (including repeat cultures) and consider fungal infection and order radiology as clinically appropriate.

11.3 No change - remains febrile "but well"

Continue antibiotics; consider stopping aminoglycoside at 48 hours if cultures negative and no focus evident.

11.4 Deterioration

- Rotate antibiotics e.g. piperacillin/tazobactam to meropenem
- Consider adding in a glycopeptide e.g. vancomycin if there is evidence of a line infection or mucositis.

12. STILL FEBRILE AT DAY 4-6

Request investigations for fungal infection including urgent HRCT Chest depending on availability other investigations such as Aspergillus PCR, PCP PCR, Galactomannan or Beta Glucan may be useful. Consider bronchoscopy if patient is stable enough.

If radiology is suggestive of fungal infection start appropriate antifungals.
If radiology is negative review patient and look for other sources of on-going fever.

If possibility of fungal infections is suggested start antifungal therapy (drug interactions with azoles may be an issue). Discuss with Microbiology Consultant for specific advice.

If positive BAL for fungi, or Aspergillus PCR or galactomannan assay is positive, review with clinical condition and radiology findings.

13. DURATION OF ANTIBIOTICS

13.1 Patients with neutrophil count ≥500/mm3

After review may stop antibiotics if patient has been apyrexial for 3 days if:

- Cultures indicate organism eradicated
- All sites of infection have resolved
- Patient free of signs and symptoms
- Falling acute phase reactants e.g. CRP

13.2 Patients with neutrophil count <500/mm3

- Low risk and above factors a) to d) met, stop antibiotics when patient has been afebrile for 5 days
- High risk (e.g. if patient has mucositis, ulcers, bleeding points, iv-catheter site infection present or if invasive procedures or ablative chemotherapy pending) continue antibiotics so that patient receives at least 10 days treatment in total or until neutrophils >500/mm^3

Patients who have antibiotics stopped while they are still neutropenic should be monitored closely for signs of recurrent infection and fever and if these occur intravenous antibiotics should be started again.

Patients who remain febrile after their neutrophil counts have returned to 500/mm^3 should be assessed for the presence of fungal infections (consider evaluation of liver and spleen by ultrasonography for hepatosplenic candidiasis, CT or MRI scans, serum for galactomannan, EDTA blood for candida and aspergillus PCR, and PCR for viral infections).

14. USE OF ANTIVIRAL DRUGS IN PATIENTS WITH HEAMATOLOGICAL MALIGNANCIES

Patients with lesions due to herpes simplex virus (HSV) or varicella zoster virus (VZV) should be treated with aciclovir if they are neutropenic and febrile, even if it is thought the lesions are not contributing to the sepsis.

Consideration should be given to the possibility of CMV if patients have pneumonitis, gastrointestinal or CNS symptoms especially if they have had a stem cell transplant.

These patients should have an EDTA blood sample collected together with bronchoalveolar lavage, faeces, and biopsy (as appropriate clinically) sent for CMV PCR.

Discuss the appropriate use of ganciclovir or foscarnet with a virologist and haematologist.

If CMV infection is proven monitor response to therapy with twice weekly PCR on EDTA bloods, If CMV viral load does not appear to be reducing with ganciclovir discuss resistance testing with a consultant virologist.

In patients with recurrent CMV, long term ganciclovir or other maintenance antiviral therapy may be indicated for example cidofovir, valganciclovir. In CMV pneumonitis, hyperimmune globulin should be used in addition to ganciclovir or foscarnet.

NB. Please refer to the haematology team and CMV SOP (Q-Pulse reference: SCT/MEDICAL/SOP/ (11.8) "Prevention, diagnosis and management of CMV in stem cell transplant patients") for more information.

If a lower respiratory tract infection is suspected send nasal washings or nasopharyngeal aspirate for rapid virus antigen detection, respiratory secretions or nose and throat swab for respiratory virus PCR and blood for antibody testing. Respiratory syncytial virus and parainfluenza virus may require nebulised ribavirin. For treatment of influenza refer to Trust Influenza Policy.

15. CONSULTATION, APPROVAL & RATIFICATION PROCESS

Sepsis Steering Group, Resus and deterioration Committee and Patient safety committee.

16. PROCESS FOR MONITORING EFFECTIVE IMPLEMENTATION

The effectiveness of this guidance will be monitored via an ongoing weekly and monthly audit measuring performance of the "One hour door to needle target (D2N)". This audit will be undertaken by the Sepsis nurse specialist and results will be sent and reviewed within the Executive performance review and discussed further within the Sepsis steering group.

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25. NICE guidelines [NG51] Sepsis: recognition, diagnosis and early management. July 2016

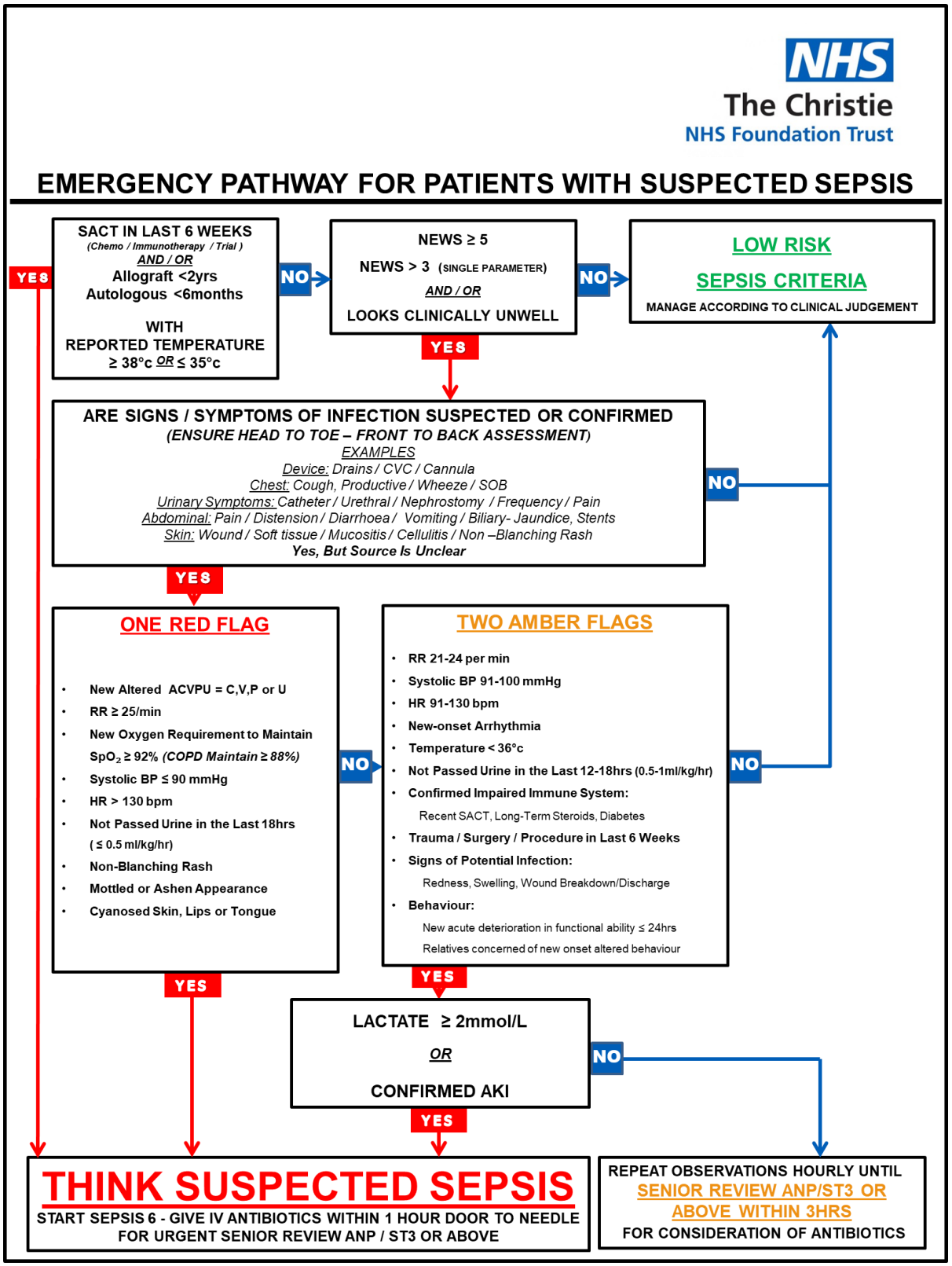
18. VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
1.4	Aug 2007	Dr P.Haji-Michael, Dr K.Dodgson Dr E.Kaczmarski, Dr K.Mutton	Closed	Equality Impact Assessment - 17th August 2010
1.5	Sep 2010	June So on behalf of the DTC, the Christie	Closed	Clinical and research governance committee - October 2010
1.6	Jan 2013	Dr P Haji-Michael	Closed	Acute Oncology Group and NICE Guidance review request
1.7	Feb 2013	Dr P Haji-Michael	Closed	Reviewed with M Leahy recommendations
1.8	28 Feb 2013	Dr P Haji-Michael	Closed	By LLawrence to fit procedural template required format.
1.9	15 May 2013	Dr P Haji-Michael	Closed	To add input from radiology team on the management of renal and hepatic obstruction
2.0	24 Feb 2015	Ruth Clout, P Hall, L Lawrence	Closed	Updating pathway for suspected sepsis to achieve one hour to antibiotics.
2.1	19/8/15	Ruth Clout, C Fitzpatrick, L Lawrence	Closed	Temperature 38°C or above or <36°C
2.2	08/02/16	Dr P Haji-Michael, L Lawrence	Closed	Nice Guidance review of; Neutrophil - severe and significant updated. Updates due to NICE QS90 Urinary and CG191 Pneumonia. Updated ANTIMICROBIAL GUIDELINES FOR COMMON INFECTIONS
2.3	15/10/16	Dr P haji-Michael	Closed	Updated in keeping with NICE NG51 – Identification of sepsis
2.4	20/02/18	Leah Morgan Dr.Ewa Zasada	Closed	Updated to reflect the amalgamation between NICE guidelines NG51 and CG151 within the Trust taking into consideration the cancer patient group.

2.5	16/12/19	Dr P Haji-Michael Katie Mantinieks	Closed	Updated to be in compliance with current Microbiology advice and Antimicrobial Policy Updated to reflect current NICE guidelines NG51 and CG151 Updated to NEWS2 Document format changed to new Clinical Guidance template
3.0	24/09/2020	Dr P Haji-Michael Katie Mantinieks Alex Peel	Closed	Updated empirical IV antibiotic treatment table to follow current Microbiology advice and current resistance patterns.
3.1	24/05/2023	Katie Mantinieks Alex Peel	Closed	Reviewed with no changes currently required.
3.1	30/06/2023	Wiktoria Popieluch	Final	Review date extension has been approved.

19. APPENDICES

19.1 Emergency pathway for patients with suspected sepsis



19.2 Risk stratification tool for adults and young people with suspected sepsis (NICE NG51) 2017