WAHT-CRI-023

Guidelines for Management of Sepsis and Septic Shock in Adults

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

THIS GUIDELINE IS FOR USE BY THE FOLLOWING STAFF GROUPS :

All Consultants in Intensive Care Medicine employed by Worcestershire Acute Hospitals NHS Trust

Lead Clinician(s)

Proposed by:
Dr M McAlindon
Consultant Anaesthetics/ICM

Seconded by:
ICM Forum 14th February 2022

This guideline should not be used after end of: February 2024

Key amendments to this guideline

Date	Amendment	By:
14/9/16	Guideline updated to reflect new Sepsis definitions, NICE guidance and WAHT 'Suspected Sepsis' screening process.	Dr M McAlindon
18/9/18	Updated with links to V3 of 'Suspected Sepsis' screening tools (Inpatient and ED).	Dr M McAlindon
17/1/22	Updated with links to V4 of 'Sepsis Patient Pathway' (Inpatient and ED) and 'Deteriorating Patient Alert' sticker. Further elements of NICE guidance (NG 51) and Quality Standards (QS161) referenced. ICU Sepsis follow-up process described. WAHT Sepsis training process included. Process for monitoring Sepsis Patient Pathway including audit and outcome data review outlined.	Dr M McAlindon

WAHT-CRI-023

Guidelines for Management of Sepsis and Septic Shock in Adults

GUIDELINES FOR THE PROVISION OF INTENSIVE CARE SERVICES

4.4.1 SEPSIS

Author: Anthony Gordon
Local interpretation: Dr G P Sellors, Dr M McAlindon

INTRODUCTION

Sepsis is the most common reason for admission to general Intensive Care Units. Mortality rates remain high and, although trials of new therapeutics have generally been negative, there is emerging evidence that mortality rates from sepsis are improving. This would appear to be due to improved recognition of sepsis and illness severity by all clinical staff, and timelier, standardised management. There is consensus that early treatment with appropriate antibiotics and fluid resuscitation improves outcomes for patients.

BACKGROUND

There are more than 30,000 admissions to ICU due to sepsis in the UK each year, and the number is rising[1]. Mortality rates remain high and there are more deaths in the UK from sepsis than from either breast or colon cancer. In 2004, a set of internationally agreed guidelines for the management of sepsis (*Surviving Sepsis Campaign*) were published, and these have been updated every few years[2]. Over the last decade there is evidence that mortality rates from sepsis are now beginning to fall[3]. Although there may not be uniform agreement about all aspects of these clinical guidelines, there is some evidence to suggest that improved compliance with the guidelines may be associated with improved outcomes[4].

Both a UK Parliamentary and Health Service Ombudsman enquiry (2013)[5] and a UK National Confidential Enquiry into Patient Outcome and Death (NCEPOD, 2015)[6] highlighted Sepsis as being a leading cause of avoidable death that kills more people than breast, bowel and prostate cancer combined. Subsequently there is an increased focus on Sepsis and NHS England has identified tackling Sepsis as a clinical priority for improving patient outcomes. NICE have recently published guidelines for Sepsis recognition, diagnosis and early management (July, 2016).[7]

The focus of good sepsis management centres on early recognition and prompt treatment. Although there is some debate about the exact components of resuscitation and what targets to aim for[8] [9], the goals of sepsis management should be to restore intravascular volume, and to ensure an adequate blood pressure and cardiac output to perfuse vital organs. Treating early with appropriate antibiotics (with source control when possible) improves outcomes[10], and it is therefore important to take microbiological cultures and have local antibiotic policies that reflect local resistance patterns.[11] It is important that a senior doctor experienced in sepsis management reviews all patients who have sepsis at an early stage.

Recent sepsis trials have demonstrated that synthetic starches lead to a worse outcome compared to crystalloids[12], dopamine leads to more arrhythmias that noradrenaline, and using higher doses of catecholamines to achieve higher blood pressure targets adds no

clear advantage and may lead to more side-effects. Among adults with septic shock, the early use of vasopressin compared with norepinephrine has not been found to improve the number of kidney failure–free days.[13]

RECOMMENDATIONS

1) Early signs of sepsis can easily be missed, especially by inexperienced staff. People with suspected sepsis should be assessed using a structured set of observations to stratify risk of severe illness or death. Details of the NEWS tool which allows staff to recognise acutely ill patients developing sepsis and escalate their care are available within the trust NEWS guideline.

2) Confusion, mental state and cognitive state in suspected sepsis:
    a. Interpret a person's mental state in the context of their normal function and treat changes as being significant.
    b. Be aware that changes in cognitive function may be subtle and assessment should include history from patient and family or carers.
    c. Take into account that changes in cognitive function may present as changes in behaviour or irritability in both children and in adults with dementia.
    d. Take into account that changes in cognitive function in older people may present as acute changes in functional abilities.

3) Although there remains uncertainty about the value of protocolised resuscitation, all patients with sepsis-induced tissue hypoperfusion should be resuscitated promptly. If a patient has a NEWS score of greater than 5, the ‘Sepsis Six’ pathway should be used.

4) Relevant microbiological samples for culture (including blood cultures) should be taken ideally before antibiotics are started. This sampling should not significantly delay antibiotic treatment. In patients with sepsis-induced acute organ failure, hypo perfusion or shock, broad-spectrum intravenous antibiotics to cover likely pathogens should be administered within one hour of diagnosis. In stable patients, in whom the diagnosis of infection is uncertain, it may be appropriate to wait for the results of microbiological testing. Antibiotic therapy should be subject to appropriate clinical review by either: Infection (infectious diseases/ clinical microbiologist) senior doctor (ST3+), Infection pharmacist or a senior member of clinical team (ST3+) within 72 hours.

5) People with suspected sepsis who need treatment to restore cardiovascular stability should have an intravenous fluid bolus within 1 hour of risk being stratified. During the first six hours of resuscitation, the priorities should be to ensure adequate intravenous fluid replacement, administration of vasopressors to maintain a target mean arterial pressure, and consideration of inotropes and red-cell transfusion if oxygen delivery is deemed to be inadequate.

6) Please refer to Trust antibiotic guidelines (MicroGuide) for the empirical treatment of sepsis and targeted antibiotic therapy.

7) Antibiotic prescriptions should be reviewed daily as part of the FASTHUG and FIDDLE and Start Smart Then Focus checklists. This review should consider whether

antibiotics should be continued, changed or stopped. On weekdays there is daily specialist microbiological input. Out of hours and at weekends the on call Consultant microbiologist is readily contactable for clinical advice via the hospital switchboard.

8) Radiological services, including ultrasound and CT scanning, are available 7-days per week to aid sepsis diagnosis and potentially drain infected collections. If applicable, source control (percutaneous drainage/surgery) should be undertaken as soon as practically possible and within 12 hours.

9) If intravascular catheters are a likely source of sepsis, they should be removed promptly (and sent for culture) after other vascular access has been established.

10) Intravascular catheters should be sited with reference to Saving Lives High Impact Intervention 2A.

11) Central vascular catheters should be sited with application of full Matching Michigan standards.

12) Crystalloids should be the initial resuscitation fluid. Hydroxyethyl starches may lead to worse outcomes, including renal dysfunction, and should be avoided.

13) Fluid therapy should be titrated using dynamic measures, e.g. pulse-pressure/stroke-volume variation, focused echocardiography, cardiac output, oxygen delivery, lactate clearance. Repeated fluid challenges and re-assessments will generally be required to ensure adequate fluid resuscitation. Excessive fluid administration should be avoided if there is no improvement in haemodynamics.

14) A target mean arterial pressure should be defined. For most patients 65-70mmHg is appropriate. Occasionally, higher targets may be needed in chronic hypertensive patients, especially if hypoperfusion is evident at lower blood pressures. Similarly in younger, previously healthy patients a lower blood pressure may be adequate if perfusion is adequate.

15) Noradrenaline is the initial vasopressor of choice, and must be administered via a central venous catheter. Dopamine leads to a higher rate of tachycardia and arrhythmias. Patients requiring vasopressor therapy should have an arterial catheter placed to measure invasive blood pressure and for blood sampling.

16) Acute lung injury is common in sepsis. Mechanical ventilation should be readily available for all patients who have sepsis. The ventilation strategy should be lung-protective (i.e. tidal volumes limited to ~6mls/kg of ideal body weight and plateau pressure limited to 30 cmH20).

17) Patients who have sepsis are at high risk of developing acute kidney injury. The ability to offer timely renal replacement therapy must be available. Both intensive care units within Worcestershire are able to offer renal replacement therapy.

18) People with suspected sepsis in acute hospital settings and at least 1 of the criteria indicating high risk of severe illness or death should have an immediate review by a senior clinical decision-maker.

19) People with suspected sepsis in acute hospital settings who receive intravenous antibiotics or fluid bolus should be seen by a Consultant if their condition fails to respond within 1 hour of initial treatment.[14]

REFERENCES

1. Harrison DA, Welch CA, Eddleston JM. 'The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: secondary analysis of a high quality clinical database, the ICNARC Case Mix Programme Database'. *Crit Care* 2006; 10(2):R42.

2. Dellinger RP, Levy MM, Rhodes A, et al. 'Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012'. *Intensive Care Med* 2013; 39(2):165-228.

3. Kaukonen KM, Bailey M, Suzuki S, et al. 'Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012'. *JAMA* 2014; 311(13):1308-16.

4. Levy MM, Dellinger RP, Townsend SR, et al. 'The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis'. *Intensive Care Med* 2010; 36(2):222-31.

5. Parliamentary and Health Service Ombudsman: Time to act: Severe sepsis: rapid diagnosis and treatment saves lives. 12th September, 2013. http://www.ombudsman.org.uk/__data/assets/pdf_file/0004/22666/FINAL_Sepsis_Report_web.pdf

6. NCEPOD: Sepsis: Just Say Sepsis! (2015) http://www.ncepod.org.uk/2015sepsis.html

7. Sepsis: recognition, diagnosis and early management. NICE guidelines [NG51]. Published date: July, 2016. https://www.nice.org.uk/guidance/ng51

8. Rivers E, Nguyen B, Havstad S, et al. 'Early goal directed therapy in the treatment of severe sepsis and septic shock'. *N Engl J Med* 2001; 345(19):1368-77.

9. Yealy DM, Kellum JA, Huang DT, et al. 'A randomized trial of protocol-based care for early septic shock'. *N Engl J Med* 2014; 370(18):1683-93.

10. Kumar A, Roberts D, Wood KE, et al. 'Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock'. *Crit Care Med* 2006; 34(6):1589-96.

11. Public Health England. Start Smart Then Focus: Antimicrobial Stewardship Toolkit for English Hospitals, update March 2015

12. Perner A. et al. 'Hydroxyethyl Starch 130/0.42 versus Ringer's Acetate in Severe Sepsis'. N Engl J Med 2012; 367:124-134July 12, 2012DOI:10.1056/NEJMoa1204242

13. Gordon A. et al. 'Effect of Early Vasopressin vs Norepinephrine on Kidney Failure in Patients With Septic Shock: The VANISH Randomized Clinical Trial'. JAMA. 2016; 316(5):509-518. doi:10.1001/jama.2016.10485.

14. NICE Sepsis: Quality standard [QS161]. Published: 13 September 2017, updated: 18 June 2020. https://www.nice.org.uk/guidance/qs161

LOCAL ASPCECT OF CARE

The terminology around sepsis has changed and new international consensus definitions have been published (JAMA, February, 2016). Previous terminology included terms SIRS (systematic inflammatory response syndrome), severe sepsis and septic shock but new terminology suggests using terms sepsis and septic shock only.

Sepsis is defined as a life-threatening organ dysfunction due to a dysregulated host response to infection (formerly Severe Sepsis).

Septic shock is defined as persisting hypotension requiring vasopressors to maintain a mean arterial pressure (MAP) of 65 mmHg or more and having a serum lactate level of greater than 2 mmol/l despite adequate volume resuscitation in the context of sepsis.

NICE guidelines recommend actions according to clinical parameters that stratify risk of severe illness or death from sepsis.

The Trust has recently updated the 'Suspected Sepsis Screening Tool (Version 4)' into the Sepsis Patient Pathway to reflect the new sepsis definitions, diagnostic criteria and NICE guidelines. The emphasis in the updated Sepsis Patient Pathway is on the 'team approach' to sepsis diagnosis and management. These documents also aim to facilitate effective documentation of a 'face to face' medical review in patients with suspected sepsis. Separate pathways are available for use in ED and inpatient areas.


PC WIS067 Sepsis Screening Tool Inpatie


PC WIS068 Sepsis Screening Tool Emerg

All patients with NEWS score >/= to 5 should be escalated to an appropriate individual with 'acute illness management' skills (as per NEWS escalation policy) and also be screened for Sepsis. Escalation and screening for Sepsis should be documented in the medical notes using the 'Deteriorating Patient Alert' sticker. It may also be used in any patient in whom sepsis is suspected within WAHT. If Sepsis is suspected following elevated NEWS and signs of an infection then the relevant Sepsis Patient Pathway (ED vs Inpatient) should be followed and the Deteriorating Patient Alert sticker completed as @ye' to suspected sepsis. If Sepsis is not suspected based on no signs of infection in the presence of elevated NEWS (i.e. other pathology is clinically suspected) then the box on the Deteriorating Patient Alert sticker can be completed as 'No' to suspected sepsis and sepsis screening is complete at that stage.


Deteriorating Patient Alert Sticker[49] (1).pc

Suspected/confirmed infection and signs of organ dysfunction should be present to diagnose sepsis in accordance with the new International Consensus definitions (see Sepsis Patient Pathway).

The WAHT inpatient Sepsis Patient Pathway can be applied to Critical Care patients and facilitate management of sepsis within HDU/ICU. It is however primarily designed for use outside of the Critical Care environment.

A comprehensive list of systemic manifestations of infection and sepsis-induced organ dysfunction in critically ill patients can be found in Appendix 1. A list of relevant medical history features and signs suggestive of a new infection are included in Appendix 2.

RISK STRATIFICATION IN ADULTS WITH SUSPECTED SEPSIS

Table 1 Risk stratification tool for adults, children and young people aged 12 years and over with suspected sepsis

Category	High risk criteria	Moderate to high risk criteria	Low risk criteria
History	Objective evidence of new altered mental state	History from patient, friend or relative of new onset of altered behaviour or mental state History of acute deterioration of functional ability Impaired immune system (illness or drugs including oral steroids) Trauma, surgery or invasive procedures in the last 6 weeks	Normal behaviour
Respiratory	Raised respiratory rate: 25 breaths per minute or more New need for oxygen (40% FiO_2 or more) to maintain saturation more than 92% (or more than 88% in known chronic obstructive pulmonary disease)	Raised respiratory rate: 21–24 breaths per minute	No high risk or moderate to high risk criteria met
Blood pressure	Systolic blood pressure 90 mmHg or less or systolic blood pressure more than 40 mmHg below normal	Systolic blood pressure 91–100 mmHg	No high risk or moderate to high risk criteria met
Circulation and hydration	Raised heart rate: more than 130 beats per minute Not passed urine in previous 18 hours For catheterised patients, passed less than 0.5 ml/kg of urine per hour	Raised heart rate: 91–130 beats per minute (for pregnant women 100–130 beats per minute) or new onset arrhythmia Not passed urine in the past 12–18 hours For catheterised patients, passed 0.5–1 ml/kg of urine per hour	No high risk or moderate to high risk criteria met
Temperature		Tympanic temperature less than 36°C	
Skin	Mottled or ashen appearance Cyanosis of skin, lips or tongue Non-blanching rash of skin	Signs of potential infection, including redness, swelling or discharge at surgical site or breakdown of wound	No non-blanching rash

Sepsis: recognition, diagnosis and early management NICE guideline NG51 https://www.nice.org.uk/guidance/ng51

INITIAL RESUSCITATION AND INFECTION ISSUES

a) INITIAL RESUSCITATION (FIRST 6 HOURS)

1. Give oxygen to achieve a target saturation of 94−98% for adult patients or 88−92% for those at risk of hypercapnic respiratory failure.

2. Take into account that if peripheral oxygen saturation is difficult to measure in a person with suspected sepsis, this may indicate poor peripheral circulation because of shock.

3. Begin resuscitation immediately in patients with hypotension or elevated serum lactate ≥2mmol/l; do not delay pending admission to the Intensive Care Unit.

4. Early Goal Directed Resuscitation Goals

    a. CVP 8–12 mmHg as a guide (central venous pressure does not necessarily correlate with left ventricular filling)

    b. Mean arterial pressure in range 65 to 70 mm Hg

    c. Urine output ≥0.5 ml/kg/hr

d. Central venous (superior vena cava) oxygen saturation ≥70% or mixed venous ≥65%

e. If venous oxygen saturation target is not achieved
   i. Consider further fluid
   ii. Consider transfusion packed red blood cells to haematocrit of ≥30%
   iii. Consider starting dobutamine infusion, maximum 20µg/kg/min

5. Central venous access is specifically mentioned in the early goal directed resuscitation goals. All central venous catheters must be placed and cared for in accordance with the requirements of both the NPSA "Matching Michigan" Campaign and the Department of Health High Impact Intervention No1 "Central venous catheter care bundle".

b) DIAGNOSIS

1. Obtain appropriate samples for culture before starting antibiotics provided this does not significantly delay antimicrobial administration.

2. Obtain two or more blood cultures (during the first hour for sepsis) provided this does not significantly delay antimicrobial administration.

3. One or more blood cultures should be collected by percutaneous venepuncture and undertaken according to WAHT guidelines (see Pathology A-Z webpage on intranet).

4. Take one blood culture from each vascular access device in place for more than 48 hrs.

5. Take samples for culture from other sites as clinically indicated (e.g. urine, wounds, faeces, CSF).

6. Perform imaging studies promptly to confirm source of infection.

c) ANTIBIOTIC THERAPY

- Close liaison with the Consultant Microbiologist and Infectious Disease Consultants represents the gold standard.

- WAHT-PHA-001 provides the detail of the Worcestershire Secondary Care Adult Prescribing Policy.

- Review results of previous microbiological investigations as this may inform the choice of empirical antimicrobial therapy (e.g. previous infection/colonisation with MRSA or other resistant organisms).

- Begin intravenous antibiotics as early as possible and always within the first hour of recognising sepsis and septic shock.

- Broad-spectrum: one or more agents active against likely bacterial/fungal pathogens and with good penetration into presumed source.

- Reassess antimicrobial regimen daily to optimize efficacy, prevent resistance, avoid toxicity, and minimise costs.

- Consider combination therapy in *Pseudomonas* infections.

- Consider combination empiric therapy in neutropaenic patients (see also WAHT-HAE-003).

- Review microbiology culture and other results daily and amend antibiotic therapy as dictated by antibiotic sensitivities and/or clinical progress.

- Duration of therapy: review after 5 days along with clinical progress and microbiology results. A longer course may be indicated if response is slow or there are inaccessible foci of infection or immunologic deficiencies.

- Stop antimicrobial therapy if cause is found to be non-infectious.

d) SOURCE IDENTIFICATION AND CONTROL

- A specific anatomic site of infection should be established as rapidly as possible and within first 6 hrs of presentation.

- Formally evaluate patient for a focus of infection amenable to source control measures (e.g. abscess drainage, tissue debridement).

- Implement source control measures as soon as possible following successful initial resuscitation (exception: infected pancreatic necrosis, where surgical intervention is best delayed).

- Choose source control measure with maximum efficacy and minimal physiologic upset.

- Remove intravascular access devices if potentially infected. Pay attention to the “Matching Michigan” campaign in this regard.

HAEMODYNAMIC SUPPORT AND ADJUNCTIVE THERAPY

a) FLUID THERAPY

- NICE CG174 recommends fluid-resuscitation using crystalloid solution with a sodium concentration in the range 130-154mmol/l. Within WAHT critical care directorate the favoured crystalloid is Hartmann’s solution.

- NICE CG 174 states that there is no role for tetrastach products in fluid resuscitation. The Surviving Sepsis Campaign (SSC) is against the use of hydroxyethyl starches (grade 1B evidence).

- NICE CG174 states that human albumin solution 4-5% may be considered for fluid resuscitation only in patients with sepsis (formerly severe sepsis). The SSC advocates the use of human albumin solution when patients require substantial amounts of crystalloid resuscitation. Systematic review however suggests that human albumin solutions do not reduce all-cause mortality in adults with sepsis of any severity.

- On the 6th May 2015 the ICM Forum agreed to the use of 20% human albumin as a substitute for 4.5% human albumin solution.

- Use a fluid challenge technique while associated with a haemodynamic improvement either based on dynamic (cardiac output, pulse pressure, stroke volume variation, and focused echocardiography) or static (ABP, heart rate). NICE CG174 recommends that a bolus of 500ml of crystalloid is administered over less than 15 minutes. More rapid and larger volumes may be required in sepsis-induced tissue hypoperfusion. Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent haemodynamic improvement.

- Target CVP ≥8 mm Hg (≥12 mm Hg if mechanically ventilated) as a guide (central venous pressure may not correlate with left ventricular filling).

b) VASOPRESSORS

- Maintain MAP in range 65 to 70 mmHg.

- In patients requiring vasopressors, insert an arterial catheter as soon as practical.

- Septic patients requiring vasopressors also require cardiac output monitoring. Cardiac output monitors available within WAHT include Oesophageal Doppler (CardioQ™), Vigileo™ and Pulmonary Artery Flotation Catheters.

- Centrally administered norepinephrine (noradrenaline) is the initial vasopressor of choice.

- There is no indication for low-dose dopamine for “renal protection”.

- Epinephrine (adrenaline), phenylephrine, or vasopressin should not be administered as the initial vasopressors in septic shock.

- Use epinephrine as the first alternative agent in septic shock when blood pressure is poorly responsive to norepinephrine.

- Vasopressin 0.03 units/min may be subsequently added to norepinephrine with the intent of either raising the MAP or decreasing the dose of noradrenaline.

- Low dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension and vasopressin doses higher than 0.03-0.04 units/minute should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents).

c) INOTROPIC THERAPY

- Use dobutamine in patients with myocardial dysfunction as supported by elevated cardiac filling pressures and low cardiac output.

- Do not increase cardiac index to predetermined supra-normal levels.

d) STEROIDS

Evidence shows that a course of low-dose corticosteroids lasting 5 days or longer leads to better outcomes for patients with septic shock.

- NICE recommend that intravenous corticosteroid should be prescribed for adult patients with vasopressor-dependent septic shock.
- An ACTH stimulation test is not recommended to identify the subset of adults with septic shock who should receive hydrocortisone.
- Hydrocortisone is preferred to dexamethasone.
- Fludrocortisone (50µg orally od) may be included if an alternative to hydrocortisone is being used that lacks significant mineralocorticoid activity.
- Fludrocortisone 50µg orally od is optional if hydrocortisone is used.
- Hydrocortisone dose should be in the range 200 to 300 mg/day
- The duration of treatment should be at least 100 hours at full dose.
- Do not use corticosteroids to treat sepsis in the absence of shock unless the patient's endocrine or corticosteroid history warrants it.

e) DROTROCOGIN ALFA (ACTIVATED)

- On 25th October 2011, Eli Lilly and Company announced the withdrawal of its Xigris drotrecogin alfa (activated) product in all markets following the results of the PROWESS-SHOCK study. NICE has withdrawn its guidance on the use of drotrecogin alfa (activated).

f) INTRAVENOUS IMMUNOGLOBULINS (IVIG)

- SSC does not support the use of IVIG in adult patients with sepsis or septic shock.
- Department of Health Clinical Guidelines for immunoglobulin use do not recommend IVIG for sepsis in the intensive care unit not related to specific toxins or to *Clostridium difficile*.
- A short duration of IVIG might be appropriate in the following sepsis states:
    - Severe or recurrent *Clostridium difficile* colitis.
    - Necrotising (PVL-associated) Staphylococcal sepsis
    - Staphylococcal or Streptococcal toxic shock syndrome

g) SELENIUM

- SSC does not support the use of selenium for the treatment of sepsis.

OTHER SUPPORTIVE THERAPY OF SEPSIS

BLOOD PRODUCT ADMINISTRATION

- Target a haemoglobin concentration of 70–90 g/L in adults.
- A higher haemoglobin level may be required in special circumstances (e.g., myocardial ischemia, severe hypoxemia, acute haemorrhage, cyanotic heart disease, or lactic acidosis)
- Do not use erythropoietin to treat sepsis-related anaemia. Erythropoietin may be used for other accepted reasons.
- Do not use fresh frozen plasma to correct laboratory clotting abnormalities unless there is bleeding or planned invasive procedures.
- Do not use anti-thrombin therapy.
- Administer platelets when:
    - Platelet count <5 x 10^9/L regardless of bleeding.
    - Platelet count is in the range 5–30 x 10^9/L and there is significant bleeding risk.
    - Platelet count of more than 50 x 10^9/L is required for surgery or invasive procedures.

MECHANICAL VENTILATION OF SEPSIS-INDUCED ALI/ARDS

- The Department of Health High Impact Intervention No.5 “Care bundle for ventilated patients (or tracheostomy where appropriate)” must be applied to all patients.
- Elevate the head of the bed to 30°-45°.
- Target a tidal volume of at maximum 6 mL/kg (predicted) body weight in patients with ALI/ARDS.
- Target an initial upper limit plateau pressure ≤30 cm H_2O. Consider chest wall compliance when assessing plateau pressure.
- Allow p_aCO_2 to increase above normal, if needed, to minimize plateau pressures and tidal volumes.
- Novalung™ is presently used within the Worcestershire critical care units. This technology is subject to separate guidelines.
- Set PEEP to avoid extensive lung collapse at end-expiration.
- Consider using the prone position for ALI/ARDS patients requiring potentially injurious levels of f_iO_2 or plateau pressure, provided they are not put at risk from positional changes.

- Non-invasive ventilation may be considered in the minority of ALI/ARDS patients with mild to moderate hypoxemic respiratory failure. The patients need to be haemodynamically stable, comfortable, easily rousable, able to protect/clear their airway, and expected to recover rapidly.

- Consider the use of APRV.

- Consider the use a weaning protocol and SBT regularly to evaluate the potential for discontinuation of mechanical ventilation.

- SBT options include a low level of pressure support with continuous positive airway pressure 5 cm H2O or a T piece.

- Before the SBT, patients should be rousable and haemodynamically stable without vasopressors. They should have no new potentially serious conditions and a low ventilatory and end-expiratory pressure requirement. They should require f_iO_2 levels that can be safely delivered with a face mask or nasal cannula.

- Do not use a pulmonary artery catheter for the routine monitoring of patients with ALI/ARDS.

- Use a conservative fluid strategy for patients with established ALI/ARDS who do not have evidence of tissue hypoperfusion.

SEDATION, ANALGESIA AND NEUROMUSCULAR BLOCKADE IN SEPSIS

- Use sedation protocols with a sedation goal for critically ill mechanically ventilated patients.

- “Analgesia, sedation and management of delirium in critically ill adult patients” is presented in WAHT-CRI-008.

- Use either intermittent bolus sedation or continuous infusion sedation to predetermined end points (sedation scales).

- Daily sedation hold is a requirement of High Impact Intervention No.5.

- Avoid neuromuscular antagonists where possible. Consider monitoring depth of neuromuscular blockade with train-of-four stimulator when using continuous infusions.

GLUCOSE CONTROL

- Use intravenous insulin to control hyperglycaemia in patients with sepsis following stabilization in the ICU.

- Aim to keep blood glucose ≤8.3 mmol/L using a validated protocol for insulin dose adjustment.

- Provide a glucose calorie source and monitor blood glucose values every 1–2 hrs (4 hrs when stable) in patients receiving intravenous insulin.

- Interpret with caution low glucose levels obtained with point of care testing, as these techniques may overestimate arterial blood or plasma glucose values.

- WAHT-CRI-004a and WAHT-CRI-004b covers insulin and glucose control in the critically ill. This guidelines incorporates “tight glycaemic control”.

RENAL REPLACEMENT THERAPY (RRT)

- Intermittent haemodialysis and continuous veno-venous haemofiltration (CVVH) are considered equivalent.

- CVVH offers easier management in haemodynamically unstable patients.

- Intermittent haemodialysis is not available within WAHT.

- RRT modalities offered by WAHT are CVVH and continuous veno-venous haemodiafiltration (CVVHDF). Both modalities are covered by guideline WAHT-CRI-003.

- High Impact Intervention No.3 “Renal dialysis catheter care bundle” applies to all patients undergoing RRT.

BICARBONATE THERAPY

- Do not use bicarbonate therapy for the purpose of improving haemodynamics or reducing vasopressor requirements when treating hypoperfusion-induced lactic acidaemia with pH≥7.15.

DEEP VEIN THROMBOSIS PROPHYLAXIS

- Use either low-dose UFH or LMWH, unless contraindicated.

- Use a mechanical prophylactic device, such as compression stockings or an intermittent compression device, when heparin is contraindicated.

- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for deep vein thrombosis.

- In patients at very high risk, LMWH should be used rather than UFH.

STRESS ULCER PROPHYLAXIS

- Provide stress ulcer prophylaxis using H2 antagonist or proton pump inhibitor.

- Benefits of prevention of upper gastrointestinal bleed must be weighed against the potential for development of ventilator-acquired pneumonia.

CONSIDERATION FOR LIMITATION OF SUPPORT

- Discuss advance care planning with patients and families. Describe likely outcomes and set realistic expectations.

- An assessment of frailty using the Rockwood Clinical Frailty Score (1-9) should be made when considering suitability for escalation to Critical Care. Patients with scores greater than 5 are likely to have poorer functional outcome following critical illness.

- Ensure ReSPECT forms are completed to document discussions regarding the patient's wishes relating to end of life care as well as family involvement.

- ReSPECT forms should also document escalation recommendations, treatment limitations and CPR status.

INFORMATION AND SUPPORT FOR PATIENTS WITH SEPSIS AND THEIR FAMILIES AND CARERS

PEOPLE WHO HAVE SEPSIS AND THEIR FAMILIES AND CARERS

Ensure a care team member is nominated to give information to families and carers, particularly in emergency situations such as in the emergency department. This should include:

- An explanation that the person has sepsis, and what this means
- An explanation of any investigations and the management plan
- Regular and timely updates on treatment, care and progress.
- Ensure information is given without using medical jargon. Check regularly that people understand the information and explanations they are given.
- Give people with sepsis and their family members and carers opportunities to ask questions about diagnosis, treatment options, prognosis and complications. Be willing to repeat any information as needed.
- Give people with sepsis and their families and carers information about national charities and support groups that provide information about sepsis and the causes of sepsis.

INFORMATION AT DISCHARGE FOR PEOPLE WHO HAVE HAD SEPSIS

Ensure people and their families and carers if appropriate have been informed that they have had sepsis.

Ensure discharge notifications to GPs include the diagnosis of sepsis.

Give people who have had sepsis (and their families and carers, when appropriate) opportunities to discuss their concerns. These may include:

- Why they developed sepsis
- Whether they are likely to develop sepsis again
- If more investigations are necessary
- Details of any community care needed, for example, related to peripherally inserted central venous catheters (PICC) lines or other intravenous catheters
- What they should expect during recovery

- Arrangements for follow-up, including specific critical care follow up if relevant
- Possible short-term and long-term problems.

Give people who have had sepsis and their families and carers information about national charities and support groups that provide information about sepsis and causes of sepsis.

Advise carers they have a legal right to have a carer's assessment of their needs, and give them information on how they can get this

ICU FOLLOW-UP

Patients admitted to ICU with sepsis requiring prolonged ICU stay and/or mechanical ventilation should be given follow-up in the WHAT ICU Follow-up Clinic. Requirement for this should be documented on the ICU discharge summary.

See also NICE's guideline on rehabilitation after critical illness in adults for recommendations on rehabilitation and follow up after critical illness.

TRAINING AND EDUCATION

All healthcare staff and students involved in assessing people's clinical condition are required to undertake regular, appropriate training in identifying people who might have sepsis.

Training includes;

- Triage and early identification of patients with suspected sepsis
- Risk stratification strategies
- Local protocol for early treatments, including antibiotics and intravenous fluids
- Criteria and pathways for escalation

MONITORING TOOL

This represents a complex care package. Several monitoring tools, not specific to sepsis, are relevant. These tools include audit of compliance with the high impact interventions and Matching Michigan. All patients with septic shock are recorded by ICNARC.

Audit data is collected by WAHT Sepsis Quality Improvement Project Team regarding compliance with the Sepsis Patient Pathway in all (non-Critical Care) clinical areas.

Outcome data and HSMR-Sepsis for WAHT is monitored via the Healthcare Evaluation Data system (HED).

REFERENCES

1. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008* R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Bion, MD; Margaret M. Parker, MD; Roman Jaeschke, MD; Konrad Reinhart, MD; Derek C. Angus, MD, MPH; Christian Brun-Buisson, MD; Richard Beale, MD; Thierry Calandra, MD, PhD; Crit Care Med 2008; 1-33 Jean-Francois Dhainaut, MD; Herwig Gerlach, MD; Maurene Harvey, RN; John J. Marini, MD; John Marshall, MD; Marco Ranieri, MD; Graham Ramsay, MD; Jonathan Sevransky, MD; B. Taylor Thompson, MD; Sean Townsend, MD; Jeffrey S. Vender, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; for the International Surviving Sepsis Campaign Guidelines Committee Crit Care Med 2008;1-33

2. Sepsis: recognition, diagnosis and early management. NICE guidelines [NG51]. Published date: July, 2016. https://www.nice.org.uk/guidance/ng51

APPENDIX 1

SYSTEMIC MANIFESTATIONS OF INFECTION AND ORGAN DYSFUNCTION

History

- Chemotherapy within 6 weeks
- Recent trauma/surgery/pregnancy
- Relatives concerned about acutely altered mental state
- Acute deterioration in functional ability

General variables

- Fever (>38°C)
- Hypothermia (core temperature <36°C)
- Acutely altered mental status (ACVPU score C or less)
- Significant oedema or positive fluid balance (>20 mL/kg over 24 hrs)
- Hyperglycaemia (plasma glucose >7.7 mmol/L) in the absence of diabetes

Inflammatory variables

- Leucocytosis >12 x 10^9/l
- Leucopaenia <4 x 10^9/l
- Normal WBC count with >10% immature forms
- Significantly elevated plasma C-reactive protein (CRP)
- Significantly elevated plasma pro-calcitonin

Haemodynamic variables

- Arterial hypotension (SBP <90 mmHg; MAP <65 mmHg; or an SBP decrease >40 mmHg)
- Heart rate >130 min^{-1}

Organ dysfunction variables

- ALI with paO2/fiO2 <250 in the absence of pneumonia as infection source
- ALI with paO2/fiO2 <200 in the presence of pneumonia as infection source
- New need for oxygen to keep SpO2 over 92%
- Raised respiratory rate greater than 25 breaths min^{-1}
- Acute oliguria (urine output <0.5 mL/Kg hr for at least 2 hrs, despite adequate fluid resuscitation)
- Creatinine increase > 44.2 µmol/L or Creatinine >176.8 µmol/L

- Coagulation abnormalities (INR >1.5 or PTT >60 secs)
- Ileus (absent bowel sounds)
- Thrombocytopenia (Platelet count<100x109)
- Hyperbilirubinaemia (Bilirubin >34.2 µmol/L)

Tissue perfusion variables

- Elevated plasma lactate > 2mmol/l
- Decreased capillary refill or skin mottling
- Non-blanching rash

APPENDIX 2

HISTORY OR SIGNS SUGGESTIVE OF A NEW INFECTION

- Fever
- Dysuria/loin pain
- Cough / sputum / chest pain
- Headache with neck stiffness
- Abdo pain / distension / diarrhoea
- Cellulitis / wound infection / septic arthritis
- Device-related infection
- Neutropenia
- Endocarditis
- Immunosuppression
- Other infection

WAHT-CRI-023

CONTRIBUTION LIST

Key individuals involved in developing the document

Name	Designation
Dr Gareth Sellors	Consultant, Intensive Care Medicine
Dr Anthony Gordon	Faculty of Intensive Care Medicine
Dr Mike McAlindon	Consultant, Intensive Care Medicine

Circulated to the following individuals for comments

Name	Designation
Dr Steve Digby	Consultant, Intensive Care Medicine
Dr Andrew Burtenshaw	Consultant, Intensive Care Medicine
Dr Steve Haynes	Consultant, Intensive Care Medicine
Dr Laura Kocierz	Consultant, Intensive Care Medicine
Dr Edwin Mitchell	Consultant, Intensive Care Medicine
Dr Jeremy Thomas	Consultant, Intensive Care Medicine
Dr Gavin Nicol	Consultant, Intensive Care Medicine
Dr Tracey Leach	Consultant, Intensive Care Medicine
Dr Olivia Kelsall	Consultant, Intensive Care Medicine
Dr Andy Burtenshaw	Consultant, Intensive Care Medicine
Dr Laura Tulloch	Consultant, Intensive Care Medicine
Dr Philip Pemberton	Consultant, Intensive Care Medicine
Dr Shiju Mathew	Consultant, Intensive Care Medicine
Dr Nick Fitton	Consultant, Intensive Care Medicine
Dr Nick Cowley	Consultant, Intensive Care Medicine
Dr Gareth Sellors	Consultant, Intensive Care Medicine
Dr Hugh Morton	Consultant Microbiologist
Circulated to the following CD's/Heads of dept. for comments from their directorates / departments	
Name	
Dr Sian Bhardwaj	Consultant, Intensive Care Medicine, Clinical Director ICU
ICM Forum	Governance Meeting for ICM