

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)

Dr M McAlindon Consultant Anaesthetics/ICM Seconded by: ICM Forum 28th March 2025

Approved by

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Key amendments to this guideline

Date	Amendment	By:
14/9/16	Guideline updated to reflect new Sepsis definitions,	Dr M McAlindon
	NICE guidance and WAHT 'Suspected Sepsis'	
	screening process.	
18/9/18	Updated with links to V3 of 'Suspected Sepsis'	Dr M McAlindon
	screening tools (Inpatient and ED).	
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), NICE Quality Standards (QS161) and Surviving Sepsis Campaign Guidelines (2021) are referenced. <u>ReSPECT process</u> signposted_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
<u>1/10/24</u>	Updated to exclude details of Sepsis Patient Pathway pre-ICU; now covered in separate guidance for Sepsis management using Allscripts Sunrise EPR. Updated to include details of sepsis screening within ICCA on ICU. Updated in accordance with updated AoMRC and NICE guidance.	Dr M McAlindon



Guidelines for Management of Sepsis and Septic Shock in Adults

GUIDELINES FOR THE PROVISION OF INTENSIVE CARE SERVICES

4.4.1 SEPSIS

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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 rising¹. 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 years². Over the last decade there is evidence that mortality rates from sepsis are now beginning to fall³. 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 outcomes⁴.

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 for⁸, 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 outcomes¹⁰, 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 crystalloids¹², dopamine leads to more arrhythmias than 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

In 2022, The Academy of Medical Royal Colleges (AoMRC) produced a statement on the initial antimicrobial treatment of sepsis. The aim of this was to balance timely assessment and management of patients with sepsis whilst recognising the importance of anti-microbial stewardship principles.

'Sepsis is a complication of infection in which a dysregulated host response is associated with organ dysfunction and increased risk of death. For twenty years, the care of patients with sepsis has been the subject of national and international quality improvement initiatives. These have included the recommendation that broad spectrum antimicrobials be administered within one hour of presentation. While this degree of urgency may be appropriate for the most severely ill patients with septic shock or where sepsis is the result of a surgical emergency, the mandate was extended to all patients with presumed sepsis, even though supporting evidence is weak and contested, and a significant proportion of patients do not benefit. The evolution of clinical guidelines into performance metrics with penalties for non-compliance inhibit the exercise of clinical judgement and distract from making a non-infective diagnosis. They also hamper antimicrobial stewardship, and likely contribute to increasing antimicrobial resistance. Recent International and American guidelines are cognizant of these issues and have adopted a more measured view.¹¹⁵

This report proposed that urgency of treatment of adult and paediatric patients with suspected sepsis be based on National Early Warning Scores in secondary care (NEWS2 for adults, PEWS for children) combined with clinical and laboratory assessments of severity, urgency and probability of infection. They advocated a structured approach in the form of clinical decision support frameworks linking time frames for initial assessment and treatment to severity bands. (See Appendix 3).

RECOMMENDATIONS

- 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 NEWS2 tool which allows staff to recognise acutely ill patients developing sepsis and escalate their care are available within the trust NEWS2 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.



- 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 (Eolas app) 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 and documented using the Trust 'Peripheral Vascular Device Insertion Record'.
- 11) Central vascular catheters should be sited with application of full Matching Michigan standards and documented utilising the Trust 'Central Line Insertion LocSSIP'. Ongoing management should be supported using the 'Central Venous Access Device' care pathway.
- 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

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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 implemented an electronic 'Sepsis Patient Pathway' within Allscripts Sunrise EPR to aid diagnosis and management of Sepsis.



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

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 ON ICU

NEWS2 and risk stratification using the AoMRC clinical decision support framework (see appendix 3) is not used within ICU for critically ill patients. Data that can be used to aid the diagnosis of sepsis in ICU patients by experienced clinicians is however routinely captured within ICCA, the ICU-based EPR (Philips - IntelliSpace Critical Care and Anaesthesia).

Currently this dataset is being streamlined into a sepsis module within ICCA for clinician review and aid clinical decision-making regarding sepsis management. A Sequential Organ Failure Assessment (SOFA) Score is also calculated for risk stratification.³ (See Appendix 5)

INITIAL RESUSCITATION AND INFECTION ISSUES

a) INITIAL RESUSCITATION (FIRST 6 HOURS)

- Give oxygen to achieve a target saturation of 94–98% for adult patients or 88–92% for those at risk of hypercapnic respiratory failure. There is insufficient evidence to make a recommendation on the use of conservative oxygen targets in adults with sepsis-induced hypoxemic respiratory failure.¹
- 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 <u>as a guide</u> (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 \geq 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. Inflammatory variables:
 - o low or high white blood cell count or more than 10% immature forms
 - Raised plasma C-reactive protein (CRP)
 - Raised plasma Procalcitonin (PCT)
 - See also WAHT-KD-022: Procalcitonin (PCT) Measurement to Guide Antimicrobial Therapy on ICU.
- 2. Relevant microbiological samples for culture (including blood cultures) should be taken before antibiotics are started.
 - This sampling should not significantly delay antibiotic treatment (more than 45 minutes).
- 3. In patients with sepsis broad-spectrum intravenous antibiotics to cover likely pathogens should be administered within one hour of diagnosis.
 - In stable patients (moderate risk group), in whom the diagnosis of infection is uncertain, it may be appropriate to wait for the results of microbiological testing.
- 4. Obtain two or more blood cultures (during the first hour for <u>severe</u> sepsis) provided this does not significantly delay antimicrobial administration.
 - One or more blood cultures should be collected by percutaneous venepuncture and undertaken according to WAHT guidelines
 - In case of suspected meningo-encephalitis a senior clinical decision maker should perform an initial assessment and ensure that:
 - antibiotics start within 1 hour of the person with suspected bacterial meningitis arriving at hospital, and in line with the section on antibiotics for bacterial meningitis in hospital
 - blood tests and lumbar puncture are performed before starting antibiotics (if it is safe to do so and will not cause a clinically significant delay to starting antibiotics), and in line with the sections on blood tests and lumbar puncture.⁴
- 5. Take one blood culture from each vascular access device in place for more than 48 hrs.
- 6. Take samples for culture from other sites as clinically indicated (e.g. urine, wounds, faeces, CSF).
 - Including atypical pneumonia screen (urinary legionella and pneumococcal antigen testing).
- 7. 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.



- Eolas available on the Trust intranet, provides the full Worcestershire Secondary Care Adult Prescribing Policy. This is available on both the intranet and also smartphones/tablets for ease of access. https://eolasmedical.com/access-link/c87b7a2f-0812-4c63-ad9e-b80c8afa0c57
- 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.
- For adults with sepsis or septic shock, dosing strategies of antimicrobials should be optimised based on accepted pharmacokinetic/pharmacodynamic (PK/PD) principles and specific drug properties.¹ Liaise with Critical Care Pharmacist.
- Consider combination therapy in *Pseudomonas* infections.
- Patients with suspected or proven neutropenia should be managed according to specific guideline (see also WAHT-HAE-003 – Guideline for the management of suspected neutropenic sepsis in Oncology / Haematology patients).
- 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, ideally, 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/I. 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.
- In the initial resuscitation from sepsis-induced hypo-perfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hr.¹
- Target CVP ≥8 mm Hg (≥12 mm Hg if mechanically ventilated) <u>as a guide</u> (central venous pressure may not correlate with left ventricular filling).

b) VASOPRESSORS

- For adults with septic shock on vasopressors an initial target mean arterial pressure (MAP) of 65 mmHg is recommended over higher MAP targets.¹ This should be reviewed in context of patient's baseline physiology and markers of end organ perfusion.
- In patients requiring vasopressors, insert an arterial catheter as soon as practical.
- For adults with septic shock, it is recommended that an appropriate vasopressor be commenced peripherally to restore mean arterial pressure rather than delaying initiation until a central venous access is secured.



- Guidance regarding use of peripheral vasopressors as bridging therapy prior to transfer to a Critical Care setting and establishment of central venous access is covered in 'Administration of Peripheral Vasopressors for Critically III Patients' (WAHT-CRI-033).
- Septic patients requiring vasopressors also require cardiac output monitoring. Cardiac output monitors available within WAHT include LiDCO[™] and Pulmonary Artery Flotation Catheters using Edwards Lifesciences Hemesphere[™].
- Centrally administered 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

2021 surviving sepsis guidelines suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation).¹

• If this is not achievable, IV hydrocortisone is recommended at a dose of 200 mg/day.¹ Evidence shows that a course of low-dose corticosteroids lasting 5 days of longer leads to better outcomes for patients with septic shock.

- An ACTH stimulation test is <u>not recommended</u> to identify the subset of adults with septic shock who should receive hydrocortisone.
- Hydrocortisone is preferred to dexamethasone.
- Fludrocortisone (50<u>-300</u>µg orally od) may be included if an alternative to hydrocortisone is being used that lacks significant mineralocorticoid activity.
- Fludrocortisone 50µg orally od is <u>optional</u> if hydrocortisone is used.



- 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) 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 *Clostridioides difficile*.
- A short duration of IVIG might be appropriate in the following sepsis states:
 - Fulminant *C. difficile* colitis, following discussion with microbiology.
 - Necrotising (PVL-associated) Staphylococcus aureus sepsis
 - Staphylococcal or Streptococcal toxic shock syndrome

f) NUTRITIONAL/VITAMIN SUPPLEMENTS

SSC does not support the use of selenium or IV Vitamin C 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 10⁹/L regardless of bleeding.
 - Platelet count is in the range 5–30 x 10⁹/L and there is significant bleeding risk.
 - Platelet count of more than 50 x 10⁹/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 <u>maximum</u> 6 mL/kg (predicted) body weight in patients with ALI/ARDS.
- Target an initial upper limit plateau pressure ≤30 cm H₂O. Consider chest wall compliance when assessing plateau pressure.
- Allow p_aCO₂ 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_iO₂ or plateau pressure, provided they are not put at risk from positional changes. For adults with sepsis-induced moderate-severe ARDS prone ventilation is recommended for greater than 12 hr daily.¹
- 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. For adults with sepsis-induced hypoxemic respiratory failure, use of high flow nasal oxygen over non-invasive ventilation is recommended.
- 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_iO₂ levels that can be safely delivered with a face mask or nasal cannula.
- Do not use a pulmonary artery catheter for the <u>routine</u> 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-KD-022.
- 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. For adults with sepsis induced moderate-severe ARDS, using intermittent NMBA boluses when required, over NMBA continuous infusion is recommended.¹
- For adults with sepsis-induced severe ARDS, referral to an experienced centre for Veno-venous (VV) ECMO should be considered when conventional mechanical ventilation fails.

NUTRITION AND GLUCOSE CONTROL

- For adult patients with sepsis or septic shock who can be fed enterally, early (within 72 hr) initiation of enteral nutrition is recommended.¹
- Use intravenous insulin to control hyperglycaemia in patients with sepsis following stabilization in the ICU.
- For adults with sepsis or septic shock, we recommend initiating insulin therapy at a glucose level of ≥ 10 mmol/L.¹ Monitor insulin therapy and blood glucose levels 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.
- 'Critical Care Unit Nutrition Guidelines' (WAHT-KD-022) covers insulin and glucose control in the critically ill.

RENAL REPLACEMENT THERAPY (RRT)

- In adults with sepsis or septic shock and AKI, with no definitive indications for renal replacement therapy, renal replacement therapy is not recommended.¹
- 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 for Renal Replacement Therapy within Worcestershire Critical Care Units' (WAHT-KD-022).
- 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.

STRESS ULCER PROPHYLAXIS

- Provide stress ulcer prophylaxis using a 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

For adult survivors of sepsis or septic shock, assessment and follow-up for physical, cognitive, and emotional problems after hospital discharge is recommended.¹

Patients admitted to ICU with sepsis requiring prolonged ICU stay (>/= 72h) and/or mechanical ventilation (>/= 48h) 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 <u>rehabilitation after critical illness in adults</u> 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.

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



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WAHT-KD-022 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 10⁹/l
- Leucopaenia <4 x 10⁹/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



WAHT-KD-022 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-KD-022 APPENDIX 3

Appendix Figure 1: NEWS2

<u>NICE Guideline 51</u> classifies red-band (score of 3) vital signs as high-risk criteria, and orange-band (score of 2) as moderate-to-high risk criteria for adult patients with suspected sepsis

Physiological	Score						
parameter	3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO ₂ Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO ₂ Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (*C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	



Initial antimicrobial treatment of sepsis

Figure 1: Clinical Decision Support framework for initial evaluation of sepsis in adults ≥16 years

Vital signs	Vital signs: NEWS-2 'Physiology first'	0	1-4	5-6	≥7	
sessment	History, examination, lab results	If clinical or carer concern, continuing deterioration, surgically remediable sepsis, neutropaenia, or blood gas / lab evidence of organ dysfunction, including elevated serum lactate, upgrade actions at least to next NEWS-2 level \rightarrow				
Initial ass	Comorbid disease, frailty, patient preferences?	Consider influence of comorbid disease, frailty and ethnicity on NEWS-2, and patient preferences for treatmen intensity, limits, end-of-life care				
Initial (generic) actions	Monitoring and escalation plan	Standard observations	 Registered nurse review <1 h Obs 4-6 hrly if stable. Escalate if no improvement 	 Obs hourly. Review <1 hr by clinician competent in acute illness assessment Escalate if no improvement 	 Obs every 30 mins. Review <30 min by clinician competent in acute illness assessment. Senior doctor review <1 hr if no improvement: refer to Outreach or ICU 	
	Initial treatment of precipitating condition	Standard care	<6 hr	<3 hr	<1 hr	
ictions	Unlikely	Standard care	Review daily and reconsider infection if diagnosis remains uncertain			
Likelihood of infection & specific a	Possible	Review at least daily	 < 6 h Source identification & control plan documented. 	 < 3 h: Microbiology tests Antimicrobials: administer or revise 	< 1 h: • Microbiology tests • Antimicrobials: administer or revise (broad- spectrum if causative organism uncertain).	
	Probable or definite	< 6 h • Diagnostic tests & R plan	< 6 h • Microbiology tests • Antimicrobials: administer or revise • Source identification & control plan. • D/w ID/micro if uncertain, & review	 Source identification & control plan documented. 6h Source control initiated 48 – 72 h Review antimicrobials with ID/micro/senior clinician 	< 3 h • Source identification 3-6 h • Source control initiated according to clinical urgency 48 – 72 h: • Review antimicrobials with ID/micro/senior clinician	

13 Academy of Medical Royal Colleges



Notes on clinical decision support framework for sepsis in adults in Figure 1.

- NEWS2 should be used in conjunction with clinical assessment, and not to replace clinical judgement.
- Time zero = first NEWS2 on presentation to ED, or ward deterioration. Clinicians should take into account lag-time bias (NEWS2 recorded in the community or in the ambulance, potential delays in monitoring) and changes in the patient's condition which might indicate the need to upgrade actions and timelines.
- NEWS2 should be used in secondary care to assess and monitor acutely ill patients.
- NEWS2 may be used in community settings (e.g. primary care, care homes) and particularly at the interfaces of care (e.g. referral and communication from one setting to another) to enable adequate and appropriate prioritisation, planning and placement.
- Additional concerns about a serious infective diagnosis may include the presence of septic shock or conditions in which rapid deterioration to septic shock is especially likely, such as necrotising fasciitis, intestinal perforation or ischaemia and meningitis, or conditions which increase susceptibility to sepsis such as immunocompromise. For these conditions, the severity status and accompanying actions should be upgraded according to patient need, and at least to the next NEWS band. The timelines given above indicate outer time limits; if a decision is made to give antimicrobials or to undertake a source control procedure there should not be avoidable delay.
- Other urgent management to provide organ-system support or analgesia may be necessary.
- Whenever possible promptly obtain appropriate microbiological samples before giving antimicrobials.
- Document rationale for prescription (or not) of antimicrobials and provide rationale for choice
- Reserve broad-spectrum antimicrobials for high illness severity or higher-risk e.g. immunocompromised) patients when the infective agent has yet to be characterised.
- The term 'antimicrobial' includes antibacterial, antifungal and antiviral agents. The time intervals specified refer to antibacterial agents as it may take longer to identify non-bacterial pathogens.
- Review appropriateness of initial broad-spectrum antimicrobials within 48 72 hours.
 Seek senior clinical input, including from microbiology or infectious disease physicians, if the patient is not improving.
- Discontinue antimicrobials at the earliest appropriate opportunity.



WAHT-KD-022 APPENDIX 4

Taxonomy of sepsis

Infection	Invasion of body tissues by disease-causing microorganisms	
Uncomplicated infection	Infection not resulting in new or worsening organ dysfunction i.e. change in SOFA score <2 points	
Sepsis	Life-threatening organ dysfunction caused by a dysregulated host response to infection. Clinically characterised by a change in SOFA score ≥ 2 points	
Septic shock	A subset of sepsis in which particularly circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Clinically identified by a vasopressor requirement to maintain a mean arterial pressure \geq 65 mmHg plus a serum lactate >2 mmol/L that persist despite adequate fluid resuscitation	
NEWS2	National Early Warning Score-2. An aggregate severity of illness score (0-20) for adults with points ascribed to increasing physiological abnormalities (respiratory rate, pulse oximetry- measured oxygen saturation, requirement for supplemental oxygen, systolic blood pressure, heart rate, level of consciousness, temperature).	
SOFA score	Sequential Organ Failure Assessment score. An aggregate point score (1-4) with points ascribed to increasing physiological and biochemical abnormalities representing dysfunction of six organ systems (respiratory, cardiovascular, hepatic, coagulation, renal, neurological).	
SIRS	Systemic Inflammatory Response Syndrome. Characterised by ≥ 2 criteria exceeding thresholds for temperature, heart rate, respiratory rate and white blood count. Formerly used in combination with infection to identify 'sepsis' but now discarded as often represents an appropriate (i.e. non-pathological) host response to any inflammatory (i.e. non-specific for infection) insult.	
Severe sepsis	Outdated terminology combining SIRS + organ dysfunction; now replaced by 'sepsis'	
Bacteraemia / Fungaemia / Viraemia	Presence of these micro-organism in the blood stream	
Septicaemia	Redundant (and meaningless) term formerly used to describe sepsis	
Blood poisoning	Redundant (and meaningless) term formerly used to describe sepsis	
Urosepsis	Should only be used to describe a urinary tract infection (UTI) with new organ dysfunction, not any type of UTI	
Neutropenic sepsis	Should only be used in patients with neutropenia related to an underlying disease or treatment who develop new infection-related organ dysfunction.	
	Neutropenic infection should preferentially be used for neutropenic patients with an uncomplicated infection.	
	n.b. sepsis itself may induce a transient leucopenia but this should not be classified as neutropenic sepsis alongside the above populations.	
Febrile neutropenia	Patient with neutropenia and a pyrexia \geq 38°C which may or may not be due to infection	
Pneumonia	Infection of one or both lungs caused by a pathogen. This term should be reserved for more serious lung infection rather than an uncomplicated lower respiratory tract infection.	



WAHT-KD-022 APPENDIX 5

SOFA SCORE

Score	0	1	2	3	4
Respiratory					
PaO ₂ /FiO ₂ , mmHg	> 400	≤ 400	≤ 300	≤ 200	≤ 100
				with respiratory support	
Coagulation					
Platelets × 10 ³ /mm ³	> 150	≤ 150	≤ 100	≤ 50	≤ 20
Liver					
Bilirubin, mg/dL (µmol/L)	< 1.2 (< 20)	1.2–1.9 (20–32)	2.0–5.9 (33–101)	6.0–11.9 (102–204)	> 12.0 (> 204)
Cardiovascular					
Hypotension	No hypotension	MAP < 70 mmHg	Dopamine ≤ 5 or dobutamine (any dose)*	Dopamine > 5 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1 *	Dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1*
Central nervous system					
Glasgow Coma Scale	15	13–14	10–12	6–9	< 6
Renal					
Creatinine, mg/dL (µmol/L)	< 1.2 (< 110)	1.2–1.9 (110– 170)	2.0–3.4 (171–299)	3.5–4.9 (300–440)	> 5.0 (> 440)
OR urine output				< 500 ml/d	< 200 ml/d

^{*}Adrenergic agents administered for at least one hour (doses given are in mcg/kg/min)

Vincent JL, De Mendonca A, Cantraine F, Moreno R, Takala J, Suter PM et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med. 1998;26:1793–800.



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