Sepsis Management in Non-Pregnant Adult Patients - Full Clinical Guideline

Reference no.: CG-T/2014/177

1. Introduction

The recorded incidence of sepsis is rising by approximately 11.5% each year in UK according to Hospital Episodes Statistics (HES) data. In the United Kingdom, there are more than 250,000 episodes of sepsis annually, with at least 44,000 patient deaths. Improving recognition, early treatment and resuscitation has been shown to increase survival rates

2. Aim and Purpose

The purpose of this guideline is to provide clear guidance for staff treating adult non-pregnant patients with sepsis or suspected sepsis across the Trust and ensure standardised screening, treatment and follow up is delivered consistently in order to improve sepsis outcomes.

The guideline applies to all nursing and medical staff from University Hospitals of Derby and Burton NHS Foundation Trust treating non pregnant adults with the exception of patients deemed not for active therapy after consultant assessment.

Clinical areas where separate guidelines exist and should be consulted include:

- Paediatric Clinical Guidelines
- Obstetric and Maternity Guidelines
- Early Onset Neonatal Sepsis Guideline
- Late Onset Neonatal Sepsis Guideline
- Sepsis Unknown Origin in Non-Pregnant Adults
- Neutropenic Sepsis Guideline

3. Key Responsibilities/Duties

Trust Board
The Trust Board has a legal responsibility for Trust policies and guidelines and for ensuring that they are carried out effectively.

Patient Safety Group (PSG)
Patient Safety Group meets regularly in accordance with the terms of reference. The Trust Deteriorating Patient Group reports to the Patient Safety Group. Patient Safety Group provides advice, support and escalation of information or concerns as necessary in relation to the reports.

Senior clinical Staff: Ensure that staff are aware of the trust guideline and the process to follow with the sepsis screening tool and the sepsis 6 care bundle. Ensure staff have attended 'Essential to role' sepsis training.

Doctors: Must be aware of the trust guideline and the process to follow with the sepsis screening tool and sepsis 6 care bundle. All grades of doctors to have attended 'Essential to role' training for sepsis.

Matrons and Ward Sisters: are responsible for ensuring this guideline is disseminated to clinical staff in their areas of responsibility and ensure their staff have attended 'Essential to role' training for sepsis. Ensure any incidents where late or no IV antibiotics were given and/or blood cultures were not taken, within 60 minutes of deterioration, an incident form is entered in Datix.

Individual staff: Adhere to and follow the trust guideline. Report any untoward incidents where IV antibiotics were not given within 60 minutes and /or blood cultures were not taken within 60 minutes.

4. Definitions, Keywords

4.1 Sepsis Definitions:

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

Septic Shock is persisting hypotension requiring vasopressors to maintain a mean arterial pressure (MAP) of 65 mmHg or more (BP systolic of 90 mmHg) and having a serum lactate level higher than 2 mmol/l despite adequate volume resuscitation.

Septic shock is a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.

Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mmHg (BP systolic of 90 mmHg) or greater with serum lactate level greater than 2 mmol/L (>18mg/dL) in the absence of hypovolemia. This combination is associated with hospital mortality rates greater than 40%.

5. Management of sepsis

5.1 Recognition

Every patient who has:

- NEWS (National Early Warning Score) of 5 or more or a single score of 3 in one parameter.

  And/or

- Looks sick (acutely unwell)?

  Plus has a

- Suspicion of infection

should be screened for sepsis using the approved sepsis screening tool.

The screening tool uses Red flags (high risk of developing sepsis) and Amber flags (moderate risk of developing sepsis) to initiate the appropriate therapeutic response as indicated in the sepsis screening tool (Appendix 1).

Remember! Many conditions can mimic sepsis (trauma, cerebral haemorrhage, myocardial infarction etc) and a positive screening test is not necessarily a confirmation of diagnosis. If you identify one or more Red Flags, assume the patient has sepsis, start initial management and involve a senior clinician (F2 or above) in patient care early.

5.2 Initial Treatment

Initial management of a suspected sepsis patient includes an immediate assessment of ABCDE, a brief history and examination of the relevant body followed by

Sepsis 6 Pathway / Bundle

The Sepsis 6 should be delivered as quickly as possible, but always within the first hour following recognition of red flags.

1. Give O2 to maintain SpO2 94% -98% in acutely ill patients with no signs of type 2 respiratory failure

In sepsis, a critical imbalance exists between oxygen demand by the tissues and its supply. Oxygen delivery is compromised due to a combination of reduced blood pressure and possibly flow, tissue oedema and abnormal flow of blood through capillary beds. Demand of the cells for oxygen is increased as the hypermetabolic state means cells have increased oxygen requirement. Patients with known COPD/hypercapnia will need a different target range prescribing, according to their personal care plan (typically 88-92%). As per Oxygen guideline.

Remember! Patients being treated for a suspected or known covid pneumonia will need to remain on the covid target saturation range of 92-94%. As per Oxygen Guideline.

2. Take Cultures

Blood cultures should be taken percutaneous, and from all intravenous access devices that have been in for more than 24 hours. Please refer to the UHDB guideline Blood Cultures and Bloodstream Infections in Adults on Koha (Net-i).

Cultures should be taken before antibiotics are started unless this creates a considerable delay in antibiotic administration (eg purpura fulminans). If a patient is already on antibiotics but has deteriorated, blood cultures will need to be taken as part of the sepsis 6 care bundle regardless of the patient's temperature.

If the source of sepsis is suspected/known send other cultures too, for example sputum, urine, CSF, or any overt pus.

3. Antibiotics

IV Antibiotics should be administered within one hour following deterioration (NEWS score of 5 or above, or 3 in one domain).

Please refer to local antibiotic guidelines to treat specific infection by identified focus. In sepsis of unknown origin, the dedicated guideline should be followed while all efforts are made to identify the source of infection.

4. Intravenous fluid resuscitation

Aims of fluid resuscitation: To bring the patient's pulse, blood pressure, mental state, lactate, and urine output within usual baseline for that patient.

Give intravenous fluid boluses as quickly as possible with lower volumes in patient at risk of overload. Fluid of choice is crystalloid (Hartmann's or 0.9% Sodium Chloride). Start patient on a fluid balance chart.

Monitor response to each fluid challenge and repeat if the systolic blood pressure remains <90 mmHg (MAP< 65mmHg), patient's mental state is not back to baseline and lactate is still higher than 2mmol/l.

Stop iv fluid resuscitation if there are signs of fluid overload and consider the need for diuresis to offload fluids.

If 30ml/kg have been administered and the patient remains poorly perfused (low BP, altered mental state, high lactate, reduced urinary output) consider inotrope therapy, involve Critical Care Outreach Team and senior clinician immediately.

5. Measure serum lactate- see guidance below on ABG and VBG sampling.

Lactate level higher than 2.5mmol/L is associated with an increase in mortality. The higher the serum lactate, the worse the degree of shock and the higher the mortality. Lactate levels higher than 4mmol/L in patients with suspected infection, have been shown to yield a 5-fold increase in the risk of death and are associated with a mortality approaching 30%.

Normally, the body metabolises glucose to produce adenosine triphosphate, known as ATP. The end product of this process (glycolysis) produces another substance called pyruvate. Glycolysis does not require oxygen. The pyruvate is then metabolised with oxygen in the cellular mitochondria to produce more ATP.

In the absence of oxygen, pyruvate is converted to lactate producing other substances that allow further glycolysis to happen. In sepsis and in other pathological conditions, lactate is a marker of anaerobic respiration.

The development of metabolic acidosis in septic patients reflects inadequate tissue perfusion, increased glycolysis in peripheral tissues and impaired hepatic clearance of lactate and pyruvate. As perfusion worsens and continues, tissue hypoxia generates more lactic acid and metabolic acidosis worsens.

6. Measure accurate urine output and fluid balance

Consider catheterisation and start a fluid balance chart if not done before. Urine output correlated with BP measurement provides a better way of assessing circulatory status in a septic unwell patient.

5.3 Secondary review and monitoring

After the initial assessment and resuscitation, the patient should have a patent airway, adequate ventilation and cardiovascular resuscitation should have commenced. These need to be rechecked regularly.

Perform investigations to confirm or clarify problems that are clinically evident, or to look for complications that are likely in each particular clinical setting. Investigations will be governed by the availability of these tests and the time available. (See Appendix 2 for more details).

Monitoring should be generally guided by the Trust's Observations and Escalation for Adult Inpatients Clinical Guideline.

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5.4 Treatment of underlying problem

Consider need of surgical intervention – drainage of pus-filled cavities (intra- abdominal collection, pseudo cysts, abscess, empyema), debridement of necrotic devitalised tissue, infected tissue, or gross tissue contamination (open chronic wounds), removal of infected prosthesis or foreign body which can't be treated by antibiotics alone and must be treated surgically at the earliest opportunity. Remove peripheral or central lines if they are considered to be infected.

5.5. Further care

If the patient's condition fails to improve or worsens then referral to the critical care team is mandatory, except in cases where aggressive treatment is considered inappropriate. A senior doctor should be contacted to discuss any limitations of therapy.

A referral to critical care should be considered for:

- Hypoxia despite high concentrations of inspired oxygen (FiO2 – 90%-100%)
- Persistent hypotension systolic BP <90mmHg or MAP <65mmHg despite an adequate fluid challenge as per guidance above
- Persistent altered mental state (if this is new for patient)
- Urine output <0.5ml/kg/h

Sepsis Therapy On Critical Care

Sepsis and complications of sepsis is a common reason for admission to critical care. Approximately 25% admissions are for sepsis/septic shock with the mortality rate for this condition is 40-50%. Prompt admission, stabilisation and review of the diagnosis is important.

These tasks (if applicable) should be completed within 24 hours:

1. Review the diagnosis.
2. Has the Sepsis 6 Pathway/bundle been completed? If not, complete it.

3. Review the antibiotic prescription:
    a. If agents have been used for more than 3 days, seek help from microbiology
    b. Is a wider spectrum antibiotic required?
    c. Has the likely organism changed to 'Hospital Acquired'?
    d. Consider a fungal infection?
    e. Is combination therapy required? – Pseudomonas? – Neutropenia?
    f. Contact the duty microbiologist if further help is required.
4. Has source control been achieved?
    a. Involve surgical or radiological teams
    b. Replace/Remove any causative medical devices –catheters/tubes
5. Fluid Therapy:
    a. Use a fluid challenge technique while it is associated with a haemodynamic improvement
    b. Give fluid challenges of 1000 ml of crystalloids or 300–500 ml of colloids over 30 minutes. More rapid and larger volumes may be required in sepsis-induced tissue hypoperfusion
6. Maintain MAP >65mmHg:
    a. Norepinephrine, centrally administered, is the first line agent. Metaraminol can be used while central venous access is obtained
    b. Use Epinephrine if BP is poorly responsive
    c. Insert an arterial line as soon as practical
    d. Dobutamine can be used where there is poor cardiac contractility
    e. The use of a cardiac output monitor in difficult cases or where the diagnosis is uncertain is valuable. Use Trans-Oesophageal Doppler, Arterial line analysis algorithms or serial echocardiography. The pursuit of supra-normal levels of cardiac index or oxygen delivery is not recommended
7. Steroids:
    a. Consider intravenous hydrocortisone for adult septic shock when hypotension remains poorly responsive to adequate fluid resuscitation and high dose vasopressors
    b. A short synacthin test is not recommended
    c. Hydrocortisone is preferred against all other steroids
    d. Steroid therapy may be weaned once vasopressors are no longer required
    e. Hydrocortisone dose should be <300mg/day
8. Blood product administration:
    a. Give red blood cells when haemoglobin decreases to <7.0 g/dl to target a haemoglobin of 7.0 – 9.0 g/dl in adults
    b. A higher haemoglobin level may be required in special circumstances (eg:myocardial ischaemia, severe hypoxaemia, acute haemorrhage, cyanotic heart disease or lactic acidosis)
    c. Do not use fresh frozen plasma to correct laboratory clotting abnormalities unless there is bleeding or planned invasive procedures
    d. Administer platelets only after discussion with a haematologist
9. Mechanical ventilation of sepsis induced acute lung injury:
    a. Target a tidal volume of 6ml/kg (predicted) body weight in patients with acute lung injury (ALI)
    b. Target upper limit plateau pressure ≤30cmH2O
    c. Allow the arterial carbon dioxide level to increase above normal, if needed to minimise plateau pressures and tidal volumes
    d. Set optimal Peak End Expiratory Pressure.
    e. Maintain patients in a semi recumbent position

f. Do not routinely use a pulmonary artery catheter in patients with ALI
g. Consider a conservative fluid strategy in patients with ALI who do not have evidence of tissue hypoperfusion

10. Glucose control:
    a. Use IV insulin to control hyperglycaemia in patients with septic shock following stabilisation in the ICU
    b. Aim to keep blood glucose <10 mmol/L using a validated protocol for insulin dose adjustment
    c. Provide a glucose calorie source (feed ideally) and monitor blood glucose values every 1-2hrs (4 hrs when stable) in patients receiving intravenous insulin
11. Bicarbonate therapy:
    a. Do not use bicarbonate therapy for the purpose of improving haemodymanics or reducing vasopressors when treating hypoperfusion induced lactic acidaemia with pH ≥ 7.15
12. Deep Vein Thrombosis prophylaxis:
    a. Consider the use of compression stockings or an intermittent compression device
    b. All sepsis patients are high risk and should be treated with subcutaneous Heparin unless there is a significant contra-indication
13. Stress Ulcer Prophylaxis:
    a. Provide stress ulcer prophylaxis with Ranitidine or Lansoprazole. The benefit of this should be weighed against the development of ventilator associated pneumonia

6. Post sepsis follow up and advice

It is every practitioners responsibility to familiarise themselves with local follow up arrangements. This can be either: Sepsis support groups, GP clinics, ITU follow up sessions. Patient needs to be informed of post sepsis syndrome symptoms and the fact that sometimes there is a long recovery period and an increased susceptibility to infections.

Symptoms of post-sepsis syndrome:

- Difficulty sleeping, either difficulty getting to sleep or staying asleep
- Nightmares
- Hallucinations
- Panic attacks
- Disabling muscle or joint pain
- Difficulty concentrating
- Decreased cognitive (mental) functioning
- Loss of self-esteem
- Depression
- Extreme fatigue

7. Monitoring compliance and effectiveness

Monitoring Requirement:	Compliance with sepsis screening and sepsis 6 care bundle.
Monitoring Method:	Sepsis training compliance Monthly sepsis audit of those patients who have red flags for sepsis.
Report prepared by:	Patient Safety Nurse/Patient Safety Team
Monitoring report presented to:	Deteriorating Patient Group Patient Safety Group ICB as part of the Trust Contract
Frequency of report	Deteriorating Patient Group - monthly Patient Safety Group - quarterly ICB as part of the Trust Contract - quarterly

8. References and further reading:

NICE Guideline 51 Sepsis: recognition, assessment, and early management, July 2016

UK Sepsis Trust: Adult (Age 12+) Sepsis Screening Tool & Sepsis 6 Care Bundle (UKST 2020 1.3 May 2020 tool)

UHDB Blood Cultures and Bloodstream Infections in Adults - Microbiology Full Guideline (on Koha)

Which lactate levels are associated with increased mortality in sepsis/septic shock? Author: Andre Kalil, MD, MPH; Michael R Pinsky, MD, CM, Dr(HC), FCCP, MCCM, Critical Care Medicine., Jan 2019

Dellinger, R.P. & Schorr, C.A. A Users' Guide to the 2016 Surviving Sepsis Guidelines. Critical Care Medicine, March 2017:45(3):381-385

Rhodes, A et al Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Critical Care Medicine, March 2017:45(3) DOI: 10.1097/CCM.0000000000002255

Judith E Tintinalli, Gabor D Kelen – Emergency Medicine- a comprehensive study guide 8th edition

Emergency oxygen use in adult patients, BTS https://www.brit-thoracic.org.uk/document-library/clinical-information/oxygen/emergency-oxygen-use-in-adult-patients-guideline/emergency-oxygen-use-in-adult-patients-guideline

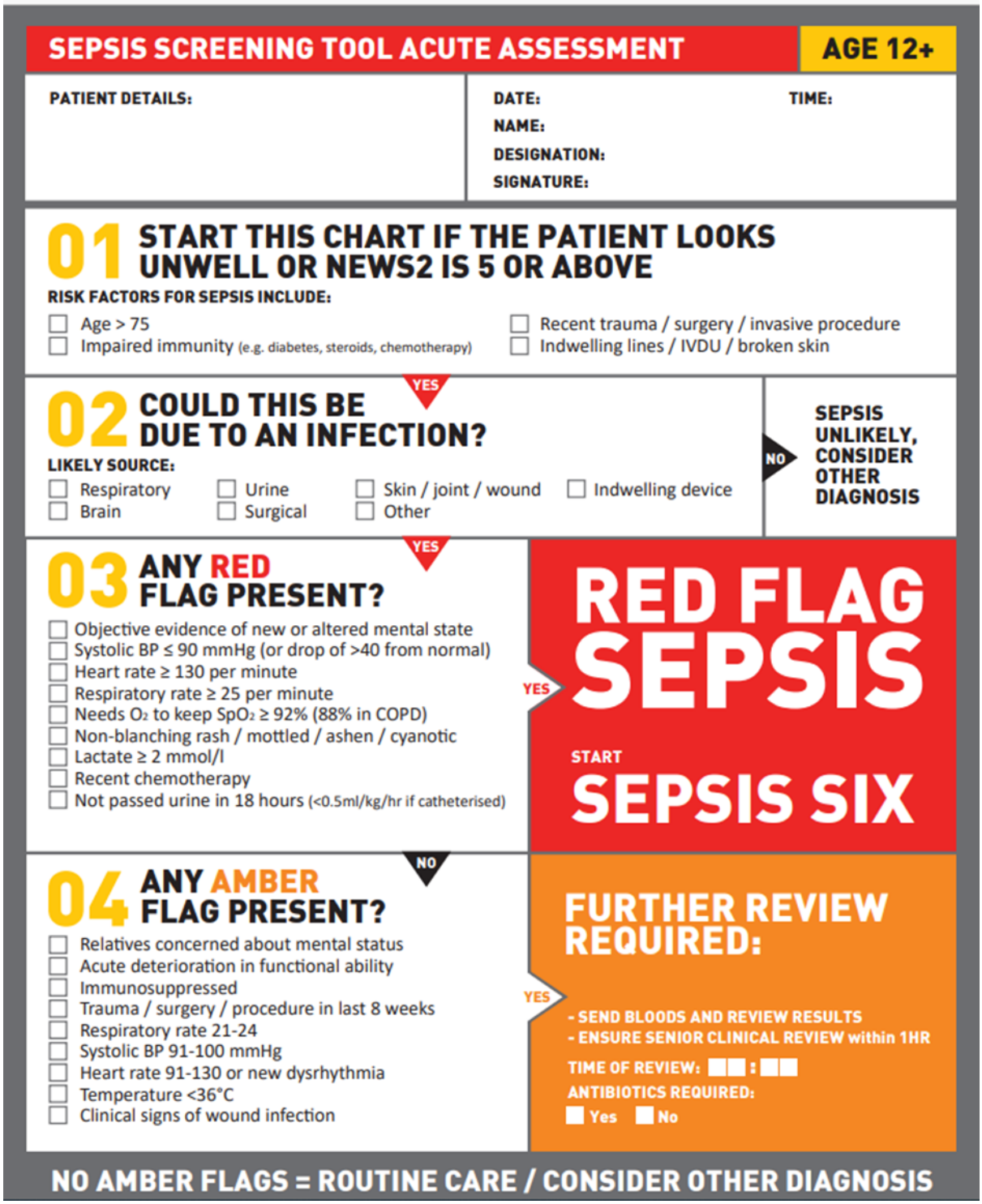
The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) Singer et al. JAMA. 2016; 315 (8):801-810. doi:10.1001/jama.2016.0287

Documentation Controls

Development of Guideline:	**Reviewed in May 2023, with:** Clinical Lead for Sepsis - Dr Adilah Miraj Patient Safety Team - Karen Wiley Sepsis Steering Group Interim review of guideline prior to the planned release of NICE sepsis guidance in 2023 ?28 June 2023. The UHDB sepsis guideline will then be reviewed and updated to align with the latest NICE sepsis guidance.
Consultation with:	**Review of the guideline** 2023 Approved at the Sepsis Steering Group in May 2023. Approved at the Clinical Guidelines Group July 2023 Dr Adilah Miraj - Lead Consultant for Critical Care, Burton
Approved By:	UHDB Sepsis Steering Group - 15 May 2023
Review Date:	December 2023 - following the release of the updated NICE Sepsis Guidance (that is expected from June 2023 onwards) - Extended to June 2024
Key Contact:	adilah.miraj@nhs.net

Appendices

Appendix 1: Adult Sepsis Screening tool



SEPSIS SCREENING TOOL - THE SEPSIS SIX

AGE 12+

PATIENT DETAILS:	DATE: TIME: NAME: DESIGNATION: SIGNATURE:

COMPLETE ALL ACTIONS WITHIN ONE HOUR

01 ENSURE SENIOR CLINICIAN ATTENDS

NOT ALL PATIENTS WITH RED FLAGS WILL NEED THE 'SEPSIS 6' URGENTLY. A SENIOR DECISION MAKER MAY SEEK ALTERNATIVE DIAGNOSES/ DE-ESCALATE CARE. RECORD DECISIONS BELOW

NAME: GRADE:

TIME ☐☐:☐☐

02 OXYGEN IF REQUIRED

START IF O_2 SATURATIONS LESS THAN 92% - AIM FOR O_2 SATURATIONS OF 94-98%
IF AT RISK OF HYPERCARBIA AIM FOR SATURATIONS OF 88-92%

TIME ☐☐:☐☐

03 OBTAIN IV ACCESS, TAKE BLOODS

BLOOD CULTURES, BLOOD GLUCOSE, LACTATE, FBC, U&Es, CRP AND CLOTTING
LUMBAR PUNCTURE IF INDICATED

TIME ☐☐:☐☐

04 GIVE IV ANTIBIOTICS

MAXIMUM DOSE BROAD SPECTRUM THERAPY
CONSIDER: LOCAL POLICY / ALLERGY STATUS / ANTIVIRALS

TIME ☐☐:☐☐

05 GIVE IV FLUIDS

GIVE FLUID BOLUS OF 20 ml/kg if age <16, 500ml if 16+
NICE RECOMMENDS USING LACTATE TO GUIDE FURTHER FLUID THERAPY

TIME ☐☐:☐☐

06 MONITOR

USE NEWS2. MEASURE URINARY OUTPUT: THIS MAY REQUIRE A URINARY CATHETER REPEAT LACTATE AT LEAST ONCE PER HOUR IF INITIAL LACTATE ELEVATED OR IF CLINICAL CONDITION CHANGES

TIME ☐☐:☐☐

RED FLAGS AFTER ONE HOUR – ESCALATE TO CONSULTANT NOW

RECORD ADDITIONAL NOTES HERE:

e.g. allergy status, arrival of specialist teams, de-escalation of care, delayed antimicrobial decision making, variance from Sepsis Six

THE UK SEPSIS TRUST

UKST 2020 1.3 PAGE 1 OF 2 / UKST, REGISTERED CHARITY 1158843

Appendix 2: Common initial investigations

Haematological	FBC (Full Blood Count), raised WCC (White Cell Count) common, may be reduced in overwhelming sepsis, Coagulation screen, Malaria blood film (malarial parasites) if history of travel abroad, Confirm sickle cell/thalassaemia status if relevant family history or specific abnormalities on the FBC to suggest haemoglobinopathy.
Biochemistry	Sodium, potassium, urea, creatinine, Glucose, Amylase (raised in pancreatitis, ischaemic bowel, perforated bowel) CRP (C-reactive protein), Liver function tests, Troponin if infarct likely, CK (creatinine kinase) in crush injuries
Arterial Blood Gas (ABG) contraindicated if platelets <80	Respiratory function, Acid-base balance Lactate
Venous Blood Gas **(VBG)**	**pH** – Good correlation (difference: +0.035 pH units) **pCO2** - Good correlation in normocapnia, ***Non-correlative in severe hypotension*** (difference +/- 1.5 kPa; but varies greatly with blood flow) **HCO 3**- Good correlation (difference +/- 5.5mmol/l) **Lactate** - Dissociation above 2 mmol/L – if greater than 2 do ARTERIAL SAMPLE (difference +/- 0.3) **PO2** - values compare poorly
ECG	To exclude cardiac causes of hypotension or to differentiate sinus tachycardia from arrhythmia
Chest X-ray	To confirm clinical findings in chest (e.g. acute pneumonia), to investigate underlying lung disease
Microbiological	To confirm the presence of infection - samples depend on history and examination. A 'septic screen' may be required in difficult cases • Blood cultures • Sputum (protected catheter specimens or broncho-alveolar lavage may be available for intubated, ventilated patients)

	• Mid-stream urine (MSU) or catheter specimen of urine (CSU) • CSF (cerebrospinal fluid) where indicated via lumbar puncture. • Wound swabs from any suspected sites (including old cannula sites) • High vaginal swab • Stool for ova, cysts and parasites • Deeper infection may be clinically or radiologically evident. Samples may be amenable to percutaneous aspiration or sent after surgical drainage or debridement