CG009.v1 Severe Sepsis

1. Key Recommendations for operational use		
1	Diagnosis	• qSOFA score is a bedside prompt that may identify patients with suspected infection who are at greater risk for a poor outcome. Two or more of: - hypotension: SBP < 100 mmHg - altered mental status (any GCS < 15) - tachypnoea: RR > 22 breaths per minute • Septic shock is defined as sepsis and (despite adequate volume resuscitation) both of: - persistent hypotension requiring vasopressors to maintain MAP > 65 mmHg - lactate > 2 mmol/L
2	Oxygen	• Give oxygen then titrate down to SpO_2 94-98%
3	IV access	• Insert the widest bore cannula feasible • Take venous blood sample: - to measure blood lactate if available - for blood cultures
4	Microbiological sampling	• Take blood cultures • Take any other feasible samples, e.g. respiratory secretions, urine, wound swabs
5	Antimicrobial therapy	• Give antibiotics as soon as possible after recognition of sepsis • Give empiric broad spectrum with one or more antimicrobials to cover all likely pathogens: - including bacterial and potentially fungal and viral coverage • Use local guidelines for empiric antibiotic administration • If in doubt, give 2g IV Ceftriaxone assuming no penicillin allergy
6	Initial Fluids	• Give IV fluid if MAP < 65 mmHg, lactate > 2 or any evidence of end-organ hypoperfusion • Give at least 30 ml/kg of balanced crystalloids or saline within the first 3 hours • Do not give colloids
7	Monitoring	• Insert urinary catheter and monitor urine output hourly • Consider insertion of arterial line if hypotensive at any point • Do not insert central line specifically to measure CVP
8	Vasoactive medication	• Consider inserting a central venous line balanced against: - time required, asepsis, coagulopathy, thrombocytopenia, X-ray availability • Start Noradrenaline infusion in septic shock resistant to initial fluid resuscitation • Target mean arterial pressure (MAP) of 65 mmHg • Consider using Adrenaline (or Noradrenaline plus Dobutamine) with demonstrable or suspected LV systolic dysfunction • If infusing Noradrenaline or Adrenaline through a peripheral vein: - only use 4mg/50ml dilution - monitor the site carefully for signs of extravasation

9	Glucose	• Commence insulin infusion when two consecutive blood glucose levels are >10 mmol/L • Control hyperglycaemia with a variable rate insulin infusion to target 6 - 10 mmol/L • Monitor blood glucose levels every 1 - 2 hours
10	Ongoing fluid therapy	• Use crystalloids for subsequent intravascular volume replacement • Do not use central venous pressure to guide ongoing fluid therapy • Use a fluid challenge technique as long as haemodynamic factors continue to improve • A fluid challenge is 250ml crystalloid solution • In patients in sinus rhythm undergoing mechanical ventilation, visible systolic pressure variation may indicate fluid responsiveness • In spontaneously breathing patients, inferior vena cava collapsibility on ultrasound may indicate fluid responsiveness
11	Steroids	• Do not use steroids routinely for patients on vasoactive medication • Consider Hydrocortisone 100mg IV if shock is refractory to vasoactive medication • Give Hydrocortisone 100mg IV to patients who have had any recent systemic steroid therapy

2. Document History			
Reference Number	CG009		
Version	1		
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		Paediatric	X
		Neonatal	X
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	BASICS Scotland		✓
	Medic 1		X
	Tayside Trauma Team		X
	Rural GPs Association of Scotland		✓
	SAS Air Ambulance Division		for information

3. Scope and purpose

- Overall objectives:

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection which is associated with an in-hospital mortality greater than 10%. Septic shock is a subset of sepsis with circulatory and cellular / metabolic dysfunction associated with a greater risk of mortality than with sepsis alone. Sepsis and septic shock are medical emergencies and treatment and resuscitation should begin immediately. The aim of this guideline is to summarise the early management and resuscitation of adult patients with sepsis or septic shock that can be applied to a remote and rural healthcare setting, mindful of variable resources between these facilities.

- Statement of intent:

This guideline is not intended to be construed or to serve as a standard of care. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. Clinicians using this guideline should work within their skill sets and usual scope of practice.

- Feedback:

Comments on this guideline can be sent to: scotamb.CPG@nhs.net

- Equality Impact Assessment:

Applied to the ScotSTAR Clinical Standards group processes.

- Guideline process endorsed by the Scottish Trauma Network Prehospital, Transfer and Retrieval group.

4. Explanatory Statements		
4.1 Diagnosis	**Authors' recommendation**	**Level [Reference]**
• *qSOFA score is a bedside prompt that may identify patients with suspected infection who are at greater risk for a poor outcome. 2 or more oft:* - *hypotension: SBP < 100 mmHg* - *altered mental status (any GCS < 15)* - *tachypnoea: RR > 22 breaths per minute* • *Septic shock is defined as sepsis and (despite adequate volume resuscitation) both of:* - *persistent hypotension requiring vasopressors to maintain MAP > 65 mmHg* - *lactate > 2 mmol/L* Sepsis is life-threatening organ dysfunction due to a dysregulated host response to infection. This is a medical emergency requiring urgent assessment and treatment.	N/A	Guideline [1]

4.2 Oxygen	**Authors' recommendation**	**Level [Reference]**
• *Give oxygen then titrate down to SpO_2 94-98%* Supplemental oxygen should be delivered to all patients with sepsis and oxygenation should be monitored continuously with pulse oximetry. Intubation and mechanical ventilation may be required to support the increased work of breathing or to manage the altered mental status that typically accompanies sepsis.	GPP	

4.3 IV Access	**Authors' recommendation**	**Level [Reference]**
• *Insert the widest bore cannula feasible* • *Take venous blood sample:* - *to measure blood lactate if available* - *for blood cultures*	GPP	

4.4 Microbiological sampling	**Authors' recommendation**	**Level [Reference]**
• *Take blood cultures* • *Take any other feasible samples, e.g. respiratory secretions, urine, wound swabs* Obtain appropriate microbiologic cultures (including blood) before starting antimicrobial therapy in patients with suspected sepsis or septic shock providing this does not delay administration of antimicrobials. Taking all appropriate microbiology samples may not be practical prior to transfer.	Strong	Guideline [2]

4.5 Antimicrobial therapy	Authors' recommendation	Level [Reference]
• *Give antibiotics as soon as possible after recognition of sepsis* • *Give empiric broad spectrum with one or more antimicrobials to cover all likely pathogens:* - *including bacterial and potentially fungal and viral coverage* The rapidity of administration is central to the beneficial effect of appropriate antimicrobials. Risk-benefit ratio favours the rapid administration of antimicrobials even if it is not possible to obtain cultures promptly.	Strong	Guideline [2]
• *Use local guidelines for empiric antibiotic administration* • *If in doubt, give 2g IV ceftriaxone assuming no penicillin allergy* The initial selection of antimicrobial therapy should be broad enough to cover all likely pathogens and choice depends on complex issues related to the patient's medical history and local epidemiological factors. Consider potential drug intolerances and toxicities.	GPP	

4.6 Initial fluids	Authors' recommendation	Level [Reference]
• *Give IV fluid if MAP < 65 mmHg, lactate > 2 or any evidence of end-organ hypoperfusion* • *Give at least 30 ml/kg of balanced crystalloids or saline within the first 3 hours* Sepsis-induced hypoperfusion may manifest as acute organ dysfunction and / or decreased MAP and increased serum lactate. Whilst protocolised fluid resuscitation has not been shown to be of benefit, this fixed volume of fluid enables initiation of resuscitation whilst obtaining more specific information and whilst awaiting more precise measurements of haemodynamic status.	Strong	Guideline [2]
• *Do not give colloids* There is no evidence of any clear benefit of colloids compared to crystalloid solutions in sepsis; there may be harm associated with the use of synthetic starches. Albumin (if available) is the colloid of choice if it is necessary for intravascular volume replacement as it has no association with harm in sepsis.	Strong	Guideline [2]

4.7 Monitoring	Authors' recommendation	Level [Reference]
• *Insert urinary catheter and monitor urine output hourly*	GPP	
• *Consider insertion of arterial line if hypotensive at any point* In shock states, estimation of blood pressure using a cuff may be inaccurate. Use of an arterial cannula provides a more accurate and reproducible measurement of arterial pressure and also allows beat-to-beat analysis.	Conditional	Guideline [2]

• *Do not insert central line specifically to measure CVP* The use of CVP alone to guide fluid resuscitation can no longer be justified because the ability to predict a response to a fluid challenge when the CVP is with normal range is limited. Central line insertion should be reserved for difficult IV access or administration of vasoactive medications.	Strong	Guideline [2]

4.8 Vasoactive medication	**Authors' recommendation**	**Level [Reference]**
• *Consider inserting a central venous line balanced against:* - *time required, asepsis, coagulopathy, thrombocytopenia, X-ray availability* Vasoactive medications should normally be infused through a central line. In certain circumstances, it may be necessary to administer through a cannula in a large peripheral vein. These circumstances include the need for immediate resuscitation or time pressure to move the patient.	GPP	
• *Start noradrenaline infusion in septic shock resistant to initial fluid resuscitation*	Strong	Guideline [2]
• *Target mean arterial pressure (MAP) of 65 mmHg* A target MAP of 65-70 mmHg is suitable for most adult patients, however, a higher MAP can be considered in patients with pre-existing hypertension who may be dependent on a higher MAP for adequate end-organ perfusion.	Strong	Guideline [2]
• *Consider using Adrenaline (or Noradrenaline plus Dobutamine) with demonstrable or suspected LV systolic dysfunction* Both agents are suggested by the SSC although there is a relative absence of evidence that the addition of either to a noradrenaline infusion is beneficial.	Conditional	Guideline [2]
• *If infusing Noradrenaline or Adrenaline through a peripheral vein:* - *only use 4mg/50ml dilution* - *monitor the site carefully for signs of extravasation*	GPP	

4.9 Glucose	**Authors' recommendation**	**Level [Reference]**
• *Commence insulin infusion when two consecutive blood glucose levels are >10 mmol/L* • *Control hyperglycaemia with a variable rate insulin infusion to target 6 - 10 mmol/L* • *Monitor blood glucose levels every 1 - 2 hours* Intensive insulin therapy is not associated with a mortality benefit in sepsis but is associated with a higher incidence of hypoglycaemia. Treatment should avoid hyperglycaemia, hypoglycaemia and wide swings in glucose levels. The continuation of insulin infusions, especially with the cessation of nutrition, has been identified as a risk factor for hypoglycaemia.	Strong	Guideline [2]

4.10 Ongoing fluid therapy	Authors' recommendation	Level [Reference]
• *Use crystalloids for subsequent intravascular volume replacement* As with the initial resuscitation, there is an absence of any clear benefit of colloid compared to crystalloid solutions in sepsis. There is a suggestion of increased acute kidney injury and renal replacement therapy in patients managed with a chloride-liberal strategy compared to a chloride-restrictive strategy.	Strong	Guideline [2]
• *Do not use central venous pressure to guide ongoing fluid therapy* CVP, is a static measure of filing is no longer recommended; preference is for dynamic measures outlined below.	Strong	Guideline [2] 1++ [3]
• *Use a fluid challenge technique as long as haemodynamic factors continue to improve* • *A fluid challenge is 250ml crystalloid solution.* Following initial fluid resuscitation, additional fluids should be guided by frequent reassessment of haemodynamic status through clinical examination and assessment of physiological parameters such as heart rate, blood pressure, capillary refill time and urine output. The volume can be reduced if there is concern regarding pulmonary oedema or cardiac failure. The response to all fluid challenges should be noted.	Strong	Guideline [2]
• *In patients in sinus rhythm undergoing mechanical ventilation, visible systolic pressure variation may indicate fluid responsiveness* The evidence base for fluid responsiveness is difficult to implement in the remote / retrieval environment since it depends on directly measuring cardiac output. The most useful indicator of potential fluid responsiveness is a pulse pressure variation (PPV) of > 12% in patients in sinus rhythm who are mechanically ventilated with tidal volumes > 6 ml/kg. It is unlikely that the monitor allows appraisal of PPV but if systolic pressure variation is apparent on the arterial line trace, then it is likely to indicate a PPV > 12% [GPP]. Although the Passive Leg Raise technique holds appeal, there are many conditions that must be met [4] and it is unlikely to be suitable in the remote / retrieval setting.	GPP	Guideline [2] 4 [4]
• *In spontaneously breathing patients, inferior vena cava collapsibility on ultrasound may indicate fluid responsiveness* The evidence base for fluid responsiveness in spontaneously breathing patients is much more limited and accordingly even more difficult to apply. Significant variation (> 40%) in the inferior vena cava diameter with inspiration is a *fair* predictor of fluid responsiveness. It is reasonably specific but not very sensitive. Whilst other methods have been investigated and reviewed [7], we do not consider them to be workable in this setting.	Conditional	1+ [5,6] 4 [7]

4.11 Steroids	Authors' recommendation	Level [Reference]
• *Do not use steroids routinely* • *Consider Hydrocortisone 100mg IV if shock is refractory to vasopressors* Two major trials published after the current surviving sepsis campaign (SSC) guidelines have given contradictory results with respect to mortality with the use of steroids. In context of the remote / retrieval environment, steroids are not required routinely for patients on vasopressors but can be considered in patients with escalating vasopressor requirements. Neither trial reported relevant significant harm with the use of steroids.	Conditional	1++ [8] 1+ [9]
• *Give Hydrocortisone 100mg IV to patients who have had any recent systemic steroid therapy*	GPP	Guideline [2]

5. References

1. Singer M et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis – 3). *JAMA*. 2016; 315(8):801-810.

2. Rhodes A et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Intensive Care Medicine*. 2017; 43:304-377

3. Marik P, Cavallazzi R. Does the central venous pressure predict fluid responsiveness? An updated meta-analysis and a plea for some common sense. Crit Care Med 2013; 41: 1774-1181.

4. Monnet X, Redoul J-L. Passive leg raising: five rules, not a drop of fluid! Critical Care 2015;19: 18

5. Airapetian N et al. Does inferior vena cave respiratory variability predict fluid responsiveness in spontaneously breathing patients? Critical Care 2015; 19: 400

6. Muller L et al. Respiratory variations of inferior vena cava diameter to predict fluid responsiveness in spontaneously breathing patients with acute circulatory failure: need for a cautious use. Critical Care 2012; 16: R188.

7. Chaves R et al. Assessment of fluid responsiveness in spontaneously breathing patients: a systematic review of the literature. Ann Intensive Care 2018; 8: 21.

8. Venkatesh B et al. Adjunctive glucocorticoid therapy in patients with septic shock. NEJM 2018; 378: 797-808.

9. Annane D et al. Hydrocortisone plus fludrocortisone for adults with septic shock. NEJM 2018; 378: 809-818.