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## Guidelines for the Initial Management of Adults with Sepsis/Severe Sepsis/Septic Shock: 2015

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### The “3 Hour” Bundle

#### Introduction

Sepsis is the leading cause of morbidity and mortality. It is estimated that 60-80% of deaths in low and in low to middle income countries occurs due to sepsis.<sup>1,2</sup> Data from Pakistan is scanty. Sepsis accounts for about 1.3% of all admissions at the Aga Khan University Hospital, Karachi, Pakistan, and has mortality approaching 37%, which is significantly associated with the presence of septic shock.<sup>3</sup>

With the publication of both the Protocol Based Care for Early Septic Shock (ProCESS) and the Australasian Resuscitation in Sepsis Evaluation (ARISE) trials in 2014, the importance of adherence to the 3 Hour Bundle of initial sepsis management to significantly impact on the morbidity and mortality of patients along the sepsis spectrum, was recognized.<sup>4,5,6</sup>

Severe sepsis and septic shock can be managed effectively using our locally-adapted sepsis guidelines, which delineate simple interventions to be instituted in a timely manner. This is expected to have a significant impact on sepsis outcomes in our patients.

#### The 3 Hour Bundle Management Protocol (Appendix 1)

There are 4 main components to the 3 Hour Bundle. These are:

1. Early recognition of Sepsis/Severe Sepsis/Septic Shock
2. Diagnostic work up
3. Antibiotic administration
4. Fluid and vasopressor management

#### Early Recognition

Early recognition of the patient presenting along the sepsis spectrum remains critical to the effective early implementation of the 3 Hour Bundle. Two main areas to the successful development of early recognition are education and the use of screening tools.

##### 1. Education

Education remains a cornerstone in the successful implementation of guidelines into practice. It is hoped that with the development and acceptance of these guidelines a local, provincial and national dialogue can be started as to how to collect the necessary epidemiological data for sepsis as well as

as well as plan for dissemination of these guidelines to the healthcare professionals and our patients

##### 2. Screening Tools

The use of a screening tool can both help educate and provide rapid identification of the patient with sepsis by first responders such as: ER Triage nurses and physicians, Rapid Response and Cardiac Arrest Teams, and the bedside and/or OPD nurse and physician. An example of a sepsis screening tool is provided in Appendix 2.

#### Diagnostic Work Up

When possible a complete diagnostic panel for patients with sepsis should be sent including:

- Complete blood count and Platelets
- Basic Electrolytes (Sodium, Potassium, Chloride, Bicarbonate, Glucose, Bun and Creatinine)
- PT/PTT and INR
- Urine DR
- Cultures: Blood, Urine and Sputum
- Lactic Acid

Radiological studies (x-rays, ultrasound, CT scans) should be ordered guided by the history and physical exam. If an infective source is identified that is amenable to surgical correction a surgical consult should be called early for appropriate source control.

Special Consideration of the following is recommended:

- **Blood Cultures.** Please see Appendix 3 for proper sampling and handling of blood cultures
- **Biomarkers of Sepsis:** Biomarkers of sepsis such as ESR and CRP have no role in the diagnosis, prognostication and/or therapy guidance of sepsis. At present only Procalcitonin has any significant sensitivity and specificity for diagnosis, prognostication and therapy guidance for sepsis. Having said that the sensitivity and specificity for any of the above tests (including Procalcitonin) remains less than optimal and therefore its routine use in sepsis cannot be recommended.<sup>7,8</sup>
- **Lactate:** The last decade has seen resurgence in the diagnostic, prognostic and therapeutic guidance of lactate for the patient with sepsis, severe sepsis septic shock.<sup>9,10,11,12</sup> It is important to emphasize that the patient who meets the

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definition of sepsis and yet has no other signs, symptoms or laboratory evidence suggestive of severe sepsis can still meet the new operational definition of severe sepsis with an isolated lactate of 4 mmol/L or higher (Glossary of Terms).

- Base Deficit: In view of the resource limitations to healthcare delivery in Pakistan it is understood that a blood lactate test may not be available. It is therefore suggested that the base deficit in an arterial blood gas sample may be used to detect acidosis in the patient with sepsis.<sup>13,14</sup> This recommendation is made with the following caveats:
  - To date there has been no study to evaluate the utility of base deficit in lieu of a serum lactate for the diagnosis of severe sepsis or as a marker for resuscitation in severe sepsis/septic shock.
  - Base deficit cannot be used as a surrogate marker for lactate if there is hyperchloremic acidosis from normal saline administration, renal failure or diabetic ketoacidosis.
  - Given the varied reasons for an elevated base deficit, it has limitations as an endpoint of resuscitation for sepsis.

#### Antibiotics

The importance of early and appropriate antibiotic administration cannot be overemphasized in managing sepsis. The study by Kumar et al demonstrated that for every hour delay in administration of antibiotics to the patient with sepsis induced hypotension or shock resulted in 12% decreased probability of survival.<sup>15</sup>

The factors which are clearly associated with sepsis outcomes include the site of infection, the kind of organisms involved and their susceptibility patterns, time to diagnosis and institution of fluid resuscitation and the types of antibiotics selected for empiric and definitive treatment.

Our local data shows that among enterobacteriaceae (E.coli, klebsiella, enterobacter) resistance patterns are as follows: 3<sup>rd</sup> generation cephalosporins currently ranges from 50-80%, ciprofloxacin 30-70%, piperacillin-tazobactam 20-30% and carbapenems between 2-15%.<sup>16</sup>

Of special consideration is the fact that carbapenem resistance enterobacteriaceae (CRE) is associated with a high sepsis-related mortality of up to 80%.<sup>17</sup> The numbers of deaths are 2-fold higher among patients with bacteremia caused by CRE as compared with carbapenem-sensitive enterobacteriaceae (CSE).<sup>18</sup>

In our context, mortality secondary to bacteremia caused by carbapenem-resistant gram negatives (including CRE, acinetobacter and pseudomonas) has been 54% vs 36% due to sensitive organisms. With additional resistance to 3<sup>rd</sup> generation cephalosporins and ciprofloxacin the mortality approaches 90%.<sup>19</sup>

Please see Appendix 5 for details.

#### Intravenous Fluids and Vasopressors:

- Intravenous Access:

The following is suggested:

- Initial IV access for sepsis should be an upper extremity peripheral line
- Initial IV access for severe sepsis and septic shock should be either single or two upper extremity peripheral lines of 18 gauge or larger when possible.

Pedal peripheral IV access (foot IVs) should be avoided because of the increase in transit time from the foot to the central circulation that can result from vasoconstriction from hypotension, shock, and/ or the administration of vasopressors.<sup>20,21</sup>

- Type of fluid for resuscitation:

- For sepsis there is no recommendation for routine fluid administration.
- For severe sepsis and septic shock crystalloids (Normal saline or Ringers Lactate) are recommended over colloids.<sup>9,22</sup>

- Dose and method of fluid administration for severe sepsis and septic shock.<sup>10,23,24</sup>

- In the 3 Hour bundle fluid is administered to a total dose of 30cc/kg.
- Crystalloid is administered as a fluid bolus
  - 250 cc over 10 minutes
  - 500 cc over 15 minutes
  - 1000 cc over 30 minutes
- Administer as follows:
  - 10 ml/kg over 15-30 minutes
  - If a systolic blood pressure of 90mmHg or greater or a Mean Arterial Pressure of 65 mmHg or greater is not reached after the above bolus then repeat 5ml/kg over 15 minutes and repeat every 15 minutes until the above blood pressure goal is reached or a total of 30 cc/kg administered.

- Vasopressors

- If vasopressors are used to support the blood pressure while the fluid boluses are given or after the 30ml/kg total dose is given and the patient is still in shock the following is recommended.<sup>9,25</sup>
  - Norepinephrine is the first line vasopressor for use in septic shock
  - Dopamine may be used in place of Norepinephrine if Norepinephrine is not available
  - If the maximum dose of Norepinephrine or Dopamine is reached, and the patient is still in shock, then Epinephrine can be added.
  - Vasopressin in doses of 0.03-0.04 units/min can be added to norepinephrine to help attain the above blood pressure

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targets or to reduce the dose of norepinephrine being given.

#### Recommendations for implementation and monitoring of the 3 Hour Bundle

- Order sets provide a method of funneling the decision matrix of the bedside provider along best practice recommendations.<sup>26</sup> An example of an order set modified and developed at the Aga Khan University Hospital (AKUH) Karachi Pakistan is presented in the appendix section of this document (Appendix 4). The addition of a carbon back to the order set allows easy storage and later abstraction of data for monitoring of compliance with the bundle elements.
- When following compliance of the 3 hour bundle in an emergency room, time zero is when the patient presents to triage.
- An algorithm for the 3 hour bundle, modified and developed at the AKUH Karachi Pakistan is presented in Appendix 1.
- Following an institution's lactate test volume and volume of norepinephrine units used can help an organization follow the penetration of the sepsis bundle in that institution.<sup>12</sup>

#### Glossary of Terms:

##### 1. Bundle:

A set of evidence based diagnostic and therapeutic interventions (usually 3-5 elements) that together can help improve patient outcomes.<sup>27</sup>

##### 2. Systemic Inflammatory response (SIRS)<sup>28</sup> 2 or more of the following:

- a. Temp >38 or <36
- b. Heart rate >90 beats/min

- c. Resp rate >20 breaths/min
- d. WBC >12,000 or <4,000 or 10% bands

##### 3. Sepsis<sup>28</sup>

SIRS + Infection (known or suspected source) = Sepsis

##### 4. Severe Sepsis<sup>28</sup>

Sepsis criteria + evidence of organ dysfunction or *Sepsis criteria + Lactate >/ 4mmol/L*

- Cardiovascular: Systolic BP  $\leq$ 90 mmHg, MAP  $\leq$ 70 mm Hg for at least 1 hour despite volume resuscitation, or the use of vasopressors.
- Renal: Urine output < 0.5 ml/kg body weight/hr for 1 hour despite volume resuscitation. Creatinine > 2.0 mg/dL
- Pulmonary: PaO<sub>2</sub>/FiO<sub>2</sub>  $\leq$ 250 if other organ dysfunction present or  $\leq$  200 if the lung is the only dysfunctional organ.
- Hematologic: Platelet count  $\leq$ 100K or decreased by 50% in 3 days
- Metabolic: pH  $\leq$  7.3 and plasma lactate > 4
- Altered Mental Status
- Bilirubin > 2mg/dL

##### 5. Septic Shock<sup>10</sup>

Persistent arterial hypotension despite adequate volume resuscitation

##### 6. Hypotension<sup>10</sup>

Systolic blood pressure of <90 mmHg, or a mean arterial pressure (MAP) < 65 mmHg, or a decrease of >/ 40mmHg in the systolic blood pressure from baseline

##### 7. Shock<sup>10</sup>

Life threatening, generalized form of circulatory failure associated with inadequate oxygen utilization by the cells resulting in cellular dysoxia

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( See appendix 1 to 5 from next page.)

# Appendix 1

- SIRS criteria
- Temp >38°C or <36°C
  - Heart rate >90 beats/min
  - Resp rate >20 breaths/min
  - WBC >12,000 or <4,000 or 10% bands
- SIRS + Infection = SEPSIS

- SEVERE SEPSIS**  
Sepsis criteria + evidence of organ dysfunction or *Sepsis criteria + Lactate ≥ 4mmol/L*
- CV: Systolic BP ≤90 mmHg, MAP ≤70 mm Hg for at least 1 hour despite volume resuscitation, or the use of vasopressors.
  - Renal: Urine output < 0.5 ml/kg body weight/hr for 1 hour despite volume resuscitation
  - Pulmonary: PaO<sub>2</sub>/FiO<sub>2</sub> ≤250 if other organ dysfunction present or ≤200 if the lung is the only dysfunctional organ.
  - Hematologic: Platelet count ≤100K or decreased by 50% in 3days
  - Metabolic: pH ≤7.3 and plasma lactate > 4 mmol/L
  - Altered Mental Status

Recognize Severe Sepsis. FILL OUT SEPSIS ORDER SET



Cultures + Lactate, CBC, Basic Metabolic panel PT/PTT INR, LFTs, Urine DR  
Radiology: CxR and others  
Early Surgical Consultation is recommended if the above work up suggests a surgical amenable focus of infection



Start Antibiotics (Refer to Hospital Antibigram)



If MAP <65 mmHg and/or Lactate > 4mmol/L and/or signs/labs of organ dysfunction START IVF Crystalloid (10 ml/kg) over 15-30 minutes THEN If BP goal not attained give 5ml/kg every 15 minutes up to 30 ml/kg



PATIENT REMAINS WITH MAP < 65 mmHg AFTER 1 L of FLUID START NOREPINEPHRINE AT 0.01 µg/kg/min and titrate to MAP ≥65 mmHg. CONTINUE FLUID RESUSCITATION UNTIL TOTAL 30cc/kg/ given



Insert Central Venous Access at 3 hours if patient still in shock and titrate Norepinephrine to obtain a MAP > 65 mmHg. IF PATIENT IN SHOCK AFTER 3 HOURS OR REPEAT LACTATE ≥4 mmol/L at 3 HOURS THEN:



ADVANCE RESUSCITATION : CALL EXPERT CONSULTATION

## Appendix 2

### Evaluation for Severe Sepsis Screening Tool

Instructions: Use this optional tool to screen patients for severe sepsis in the emergency department, on the medical/surgical floors, or in the ICU.

1. Is the patient's history suggestive of a new infection?

- |   |  |   |
|---|--|---|
| <input type="checkbox"/> Pneumonia, empyema         | <input type="checkbox"/> Bone/joint infection            | <input type="checkbox"/> Implantable device infection |
| <input type="checkbox"/> Urinary tract infection    | <input type="checkbox"/> Wound infection                 | <input type="checkbox"/> Other infection              |
| <input type="checkbox"/> Acute abdominal infection  | <input type="checkbox"/> Blood stream catheter infection | _____   |
| <input type="checkbox"/> Meningitis                 | <input type="checkbox"/> Endocarditis                    |   |
| <input type="checkbox"/> Skin/soft tissue infection |  | _____ Yes      _____ No                               |

2. Are any two of following signs & symptoms of infection both present and new to the patient? Note: laboratory values may have been obtained for inpatients but may not be available for outpatients.

- |  |   |   |
|--|---|---|
| <input type="checkbox"/> Hyperthermia > 38.3 °C (101.0 °F) | <input type="checkbox"/> Tachypnea > 20 bpm                                   | <input type="checkbox"/> Hyperglycemia (plasma glucose >140 mg/dL) or 7.7 mmol/L in the absence of diabetes |
| <input type="checkbox"/> Hypothermia < 36 °C (96.8 °F)     | <input type="checkbox"/> Leukocytosis (WBC count >12,000 $\mu\text{L}^{-1}$ ) |   |
| <input type="checkbox"/> Altered mental status             | <input type="checkbox"/> Leukopenia (WBC count < 4000 $\mu\text{L}^{-1}$ )    |   |
| <input type="checkbox"/> Tachycardia > 90 bpm              |   |   |

If the answer is yes, to both questions 1 and 2, *suspicion of infection* is present:

- ✓ Obtain: lactic acid, blood cultures, CBC with differential, basic chemistry labs, bilirubin.
- ✓ At the physician's discretion obtain: UA, chest x-ray, amylase, lipase, ABG, CT scan.

\_\_\_\_\_ Yes      \_\_\_\_\_ No

3. Are any of the following organ dysfunction criteria present at a site remote from the site of the infection that are NOT considered to be chronic conditions? Note: in the case of bilateral pulmonary infiltrates the remote site stipulation is waived.

- SBP < 90 mmHg or MAP < 65 mmHg
- SBP decrease > 40 mm Hg from baseline
- Creatinine > 2.0 mg/dl (176.8 mmol/L) or urine output < 0.5 ml/kg/hour for 2 hours Bilirubin > 2 mg/dl (34.2 mmol/L)
- Platelet count < 100,000  $\mu\text{L}$  Lactate > 2 mmol/L (18.0 mg/dl)
- Coagulopathy (INR > 1.5 or aPTT > 60 secs)
- Acute lung injury with PaO<sub>2</sub>/FiO<sub>2</sub> < 250 in the absence of pneumonia as infection source
- Acute lung injury with PaO<sub>2</sub>/FiO<sub>2</sub> < 200 in the presence of pneumonia as infection source

\_\_\_\_\_ Yes      \_\_\_\_\_ No

If *suspicion of infection* is present AND *organ dysfunction* is present, the patient meets the criteria for SEVERE SEPSIS and should be entered into the severe sepsis protocol.

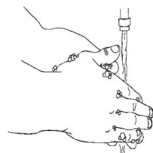
Date: \_\_\_ / \_\_\_ / \_\_\_ (circle: dd/mm/yy or mm/dd/yy)  
Version 7.2.13

Time: \_\_\_:\_\_\_ (24 hr. clock)

## Appendix 3

### Technique for Proper Blood Culture Sampling

1. Gather necessary equipment: 20 ml syringe, 2 aerobic and 2 anaerobic bottles for 2 sets of blood cultures, skin prep swabs, tourniquet, sharps disposal box, gloves.



2. Verify the patient's identification and explain procedure
3. Wash or sanitize hands before and after removing gloves. Follow Standard Precautions for all patients. Wear clean gloves.



Masks with face shields may be worn for drawing blood cultures depending on the clinical situation.

4. Assemble necessary equipment before preparation of the patient's skin.
  1. Remove dust caps from culture bottles.
  2. Clean surface with alcohol wipe.
  3. Leave the alcohol wipe on the bottle top during skin preparation.
5. Remove alcohol wipe just prior to inoculating the bottles - do not use iodine.
6. Apply tourniquet to the extremity and identify the phlebotomy site.
7. Preparation of the phlebotomy site: *clean site with chloraprep or 70% isopropyl alcohol for 30 seconds prior to chlorhexidene or povidone iodine (if chlorhexidene is not available, inferior)*



1. Using chloraprep, use a firm scrubbing motion for

- 30 seconds over a 5 cm area of the skin using circular motion starting at the site and working outward.
2. Allow 30 seconds for drying before venipuncture.
3. Using sequential chlorhexidene or povidone iodine, cleanse a 5 cm area using circular motion starting at the site and working outward.
4. Allow to dry for a at least 30 seconds to allow antiseptic effect
5. Clean patient's skin with alcohol to remove excess iodine (to prevent iodine burns).

If unable to use either of the above

- a) Use alcohol to cleanse the patient's skin, using a circular motion starting at the site and moving outward.
  - b) Repeat times two.
  - c) Allow to dry.
6. Do not touch the venipuncture site after skin preparation. If palpation is absolutely necessary, sterile gloves must be applied immediately prior to palpation.
  7. Insert needle into vein and withdraw 20 ml of blood. *Do not collect blood through IV cannula even it is freshly inserted.*

8. Inject 10 ml of blood into each culture bottle. Needles should not be changed before inoculating culture medium.
9. If an inadequate amount of blood was obtained (less than 5 ml), and repeat phlebotomy cannot be performed; all blood should be preferentially inoculated in the aerobic culture bottle.
10. Label culture bottles with patient's name and MR number.
11. Fill out Microbiology lab slip.
  1. Indicate site from which blood was collected using comment section. If using a Vascular Access Device (VAD) to draw culture, you must indicate type and site of VAD in the comments section (i.e., left subclavian triple lumen).
  2. Indicate suspected diagnosis, if necessary (required for R/O endocarditis).
  3. Include date and time of collection.
  4. Document that cultures were obtained on appropriate form
12. Send specimens to the laboratory as soon as possible. Do not refrigerate blood culture specimens.

Contd. on next page

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13. Send second set of blood cultures using the same procedure as above. If a different peripheral site is possible, the second set may be drawn immediately. If using the same site, wait at least 10 minutes for the second set, and if possible (i.e. not waiting to give antibiotics) draw second set 1-3 hours later.

*Biosafety Considerations:*

*Discard used syringes in the sharps bin; used gloves and swabs should be discarded as controlled medical waste.*

14. In order to rule out diagnoses, more specific blood culture procedures may be necessary.

1. Suspected catheter sepsis
  1. Draw two culture sets, *using a fresh syringe for every venipuncture/draw*
  2. One set is obtained from a suspected site.
  3. Second set must be from a separate peripheral site.
  4. If catheter is removed, send tip (3 cm) using

sterile procedure for cultures. Do not send catheter tip without sending concomitant blood cultures.

2. Acute endocarditis
  1. Draw two culture sets from two separate sites during the first 1-2 hours of evaluation.
  2. Begin therapy.
3. Subacute endocarditis
  1. Draw 2-3 blood culture sets on day 1.
  2. If all are negative additional sets can be drawn on days 2 and 3 (no more than 4 sets in a 24 hour period).
  3. Immediate antibiotics are less important than establishing a specific microbial diagnosis.
4. Endocarditis patients on anti-microbial therapy
  1. Draw resin blood culture sets on each of three successive days.
  2. Indicate "R/O endocarditis" in special instructions on lab requisition.



Appendix 4

PHYSICIANS' ORDERS

Patient Identification & Location

ADULT SEPSIS ORDER SET PAGE 1 of 3

Note:  Check Box Where Appropriate

PLEASE WRITE ALL 'MEDICATION AND IV FLUID' ORDERS ON THE SEPARATE SHEET, DESIGNED FOR THE PURPOSE

DATE AND TIME	ORDER, SIGNATURE AND TITLE	RN SIGNATURE - TIME
	Allergies:	
	Attending Physician:	
	Primary Diagnosis:	
	<input type="checkbox"/> Sepsis <input type="checkbox"/> Severe Sepsis <input type="checkbox"/> Septic Shock	
	Secondary Diagnosis: <input type="checkbox"/> Pneumonia <input type="checkbox"/> Urinary Tract Infection	
	<input type="checkbox"/> Abd Infection <input type="checkbox"/> Other	
	Condition: <input type="checkbox"/> Critical <input type="checkbox"/> Stable	
	Admit to:	
	Oxygen:	
	Vital Signs every 15 minutes X 1 hour, then per unit policy	
	Strict Intake and Output	
	Activity: <input type="checkbox"/> Bed Rest <input type="checkbox"/> Other	
	Diet: <input type="checkbox"/> NPO <input type="checkbox"/> Other	
	LABS:	
	<input type="checkbox"/> Sepsis Panel (IF CHECKED SEND ENTIRE LABS BELOW)	
	<input type="checkbox"/> : CBC with Differential and Platelet Count	
	<input type="checkbox"/> : PT/PTT	
	<input type="checkbox"/> : BUN/Creatinine	
	<input type="checkbox"/> : Serum Electrolytes (Na, K, Cl, HCO <sub>3</sub> , BUN, Creatinine)	
	<input type="checkbox"/> : Lactic Acid and Repeat every 6 hours for next 24 Hours	
	<input type="checkbox"/> : Urine DR	
	<input type="checkbox"/> : Procalcitonin	
	<input type="checkbox"/> : Blood Cultures X2	
	<input type="checkbox"/> : Urine Cultures	
	<input type="checkbox"/> : Sputum Cultures	
	<input type="checkbox"/> : Cultures Other	
	<input type="checkbox"/> Additional Labs:	
	<input type="checkbox"/> Chest X-Ray	
	<input type="checkbox"/> Other Imaging Studies	
	<input type="checkbox"/> EKG 12 Lead	
	<input type="checkbox"/> IV Saline Lock with flush of Normal Saline 3ml every 12 hours	

## PHYSICIANS' ORDERS

Patient Identification & Location

ADULT SEPSIS ORDER SET PAGE 2 of 3

Note:  Check Box Where Appropriate

PLEASE WRITE ALL 'MEDICATION AND IV FLUID' ORDERS ON THE SEPARATE SHEET, DESIGNED FOR THE PURPOSE

DATE AND TIME	ORDER, SIGNATURE AND TITLE	RN SIGNATURE - TIME
	<input type="checkbox"/> DVT Prophylaxis:	
	ANTIBIOTICS: ADJUST FOR RENAL and/or HEPATIC DYSFUNCTION	
	SEPSIS SOURCE UNKNOWN:	
	<input type="checkbox"/> Piperacillin-Tazobactum 3.375gm Q6 Hours IV	
	OR	
	<input type="checkbox"/> Imipenem Cilastatin 500mg Q8 Hours IV	
	OR	
	Cefoperazone Sulbactam 400mg Q12 Hours IV	
	And Clindamycin 600mg Q8 Hours IV	
	IF MRSA SUSPECTED THEN ADD	
	<input type="checkbox"/> Vancomycin: Load 20mg/kg IV	
	Maintenance 15mg/kg Q 12 Hours IV	
	SUSPECTED	
	<input type="checkbox"/> Piperacillin-Tazobactum 3.375gm Q6 Hours IV	
	And Levofloxacin 500mg Q24 Hours IV	
	OR	
	<input type="checkbox"/> Ceftriaxone 2gm Q24 Hours IV	
	And Levofloxacin 500mg Q24 Hours IV	
	SUSPECTED SKIN & SOFT TISSUE INFECTION:	
	<input type="checkbox"/> Cefazolin 2gm Q8 Hours IV	
	IF Penicillin Allergic	
	Clindamycin 600mg Q8 Hours IV	
	And	
	Ciprofloxacin 400mg Q12 Hours IV	
	IF MRSA SUSPECTED THEN ADD	
	<input type="checkbox"/> Vancomycin: Load 20mg/kg IV	
	Maintenance 15mg/kg Q 12 Hours IV	
	SUSPECTED ABDOMINAL INFECTION:	
	<input type="checkbox"/> Piperacillin-Tazobactum 3.375gm Q6 Hours IV	
	OR	
	<input type="checkbox"/> Imipenem Cilastatin 1 gm Q8 Hours IV	
	OR	
	<input type="checkbox"/> Ceftriaxone 2gm Q24 Hours IV	
	And Amikacin 15mg/kg Q24 Hours IV	
	And Metronidazole 500mg Q8 Hours IV	

## PHYSICIANS' ORDERS

Patient Identification & Location

ADULT SEPSIS ORDER SET PAGE 3 of 3

Note:  Check Box Where Appropriate

PLEASE WRITE ALL 'MEDICATION AND IV FLUID' ORDERS ON THE SEPARATE SHEET, DESIGNED FOR THE PURPOSE

DATE AND TIME	ORDER, SIGNATURE AND TITLE	RN SIGNATURE - TIME
	SUSPECTED UROSEPSIS	
	<input type="checkbox"/> Piperacillin-Tazobactum 3.375gm Q6 Hours IV	
	OR	
	<input type="checkbox"/> Imipenem Cilastatin 500mg Q8 Hours IV	
	IF RISK OF ENTEROCOCCUS	
	Vancomycin: Load 20mg/kg IV	
	Maintenance 15mg/kg Q 12 Hours IV	
	SUSPECTED CNS INFECTION	
	<input type="checkbox"/> Ceftriaxone 2gm Q24 Hours IV	
	AND	
	Vancomycin: Load 20mg/kg IV	
	Maintenance 15mg/kg Q 12 Hours IV	
	OR	
	<input type="checkbox"/> Meropenem 2gm Q8 Hours IV	
	SUSPECTED HOSPITAL ACQUIRED INFECTION	
	Piperacillin-Tazobactum 3.375gm Q6 Hours IV	
	AND Vancomycin: Load 20mg/kg IV	
	Maintenance 15mg/kg Q 12 Hours IV	
	OR	
	Imipenem Cilastatin 500mg Q8 Hours IV	
	AND Vancomycin: Load 20mg/kg IV	
	Maintenance 15mg/kg Q 12 Hours IV	
	AND Colistin 9MU stat and 3MU Q 8hours IV	
	See appendix 5 for details	
	FOR PATIENTS WITH SYSTOLIC BLOOD PRESSURE LESS THAN 90 mmHg	
	Initial intravenous fluids per kg estimated <i>idea</i> /body weight	
	Target BP greater than 90 mmHg systolic and Mean Arterial Pressure (MAP) greater than 65 mmHg	
	<input type="checkbox"/> Normal saline (10 ml/kg) _____ ml over 15-30 minutes THEN	
	If BP goal not attained 5ml/kg every 15 minutes up to 30 ml/kg	
	<input type="checkbox"/> Ringers Lactate (10 ml/kg) _____ ml over 13-30 minutes THEN	
	If BP goal not attained 5ml/kg every 15 minutes up to 30 ml/kg	
	VASOPRESSOR (Titrate to systolic BP greater than 90 mmHg and MAP greater than 65 mmHg)	
	<input type="checkbox"/> Norepinephrine _____ mg in _____ ml D5W at _____ micrograms/min	
	Continuous Infusion	
	IF AFTER RECEIVING FLUID BOLUS 30ml/kg PATIENT STILL	
	IN SHOCK AND/OR REPEAT LACTATE 4 OR GREATER OBTAIN	
	URGENT EXPERT CONSULTATION	

## Appendix 5

### Antibiotics in Sepsis

#### Before Selecting Empirical therapy

- Selection of antibiotic must be based on clinical assessment of site of infection
- Viremia, severe malaria or fungemia must be considered as possible causes of sepsis
- Antibiotics must be administered as soon as possible, within 2 hours of admission to ER or ICU
- Two sets of blood cultures, urine analysis and urine culture must be drawn *prior to* institution of antibiotic
- Obtain history of previous use of antibiotics in past 3 months. Avoid same antibiotic if possible
- Dose must be prescribed on weight basis
- Dose must be adjusted for renal or hepatic insufficiency, diabetes
- Hematologic malignancy or febrile neutropenia must be considered
- Combination therapy and use of colistin may be considered for suspected highly resistant pathogens, e.g sepsis in patients with pro-longed hospital or ICU stay, transfer from another healthcare facility, immunocompromised status.
- Only intravenous antibiotic should be used until there is clinical improvement
- Empiric antifungal therapy should be considered initially in specific circumstances, e.g. perforated viscus or prolonged antibacterial therapy in immunocompromised patients

#### During antibiotic therapy

- *Once culture and sensitivity reports are available, de-escalate to a narrower spectrum antibiotic*
- Once patient shows clinical improvement and is stable, de-escalate to oral preparation, if an equally effective oral preparation is available
- Antibiotic should be given for no longer than 7-10 days
- Source control is essential, i.e. drainage of abscess, repair or resection of perforated viscus, removal of cannula, catheter, devices, debridement of infected tissue.

Table 1

Source of infection	Likely pathogen	Best empirical antibiotic
Urinary tract	E. coli	Carbapenem or Piperacillin –tazobactam or Cefaperazone-sulbactam
Genital tract	E. coli, Enterococcus, S hemolyticus, Anaerobes	Carbapenem or Piperacillin –tazobactam or Cefaperazone-sulbactam + vancomycin
Respiratory tract (CAP)	S. pneumoniae, atypical	Ceftriaxone +levofloxacin or clarithromycin
Respiratory tract (HAP)	GPC, GNR, atypical	Carbapenem or Piperacillin –tazobactam or Cefaperazone-sulbactam + levofloxacin or clarithromycin
Respiratory tract (VAP)	GNR, MRSA	Carbapenem or Piperacillin –tazobactam + Colistin (colistimethate sodium)9MU stat and 3MU Q 8hours IV or Cefaperazone-sulbactam + vancomycin+ Colistin 9MU stat and 3MU Q 8hours IV
Intra-abdominal	Gram negatives, anerobes	Carbapenem or Piperacillin –tazobactam or Cefaperazone-sulbactam + vancomycin
SSTI (necrotizing fasciitis)	S. aureus, Streptococci anerobes	Amoxicilin/clavulanate or clindamycin +vancomycin
Burn sepsis	S. aureus, Streptococci, Pseudomonas, Candida	Carbapenem or Piperacillin –tazobactam or Cefaperazone-sulbactam + vancomycin
Line sepsis	S. aureus, (MSSA, MRSA), Pseudomonas	Ceftazidime or amikacin+ vancomycin
Infected device	S. aureus, (MSSA, MRSA), Pseudomonas	Ceftazidime or amikacin+ vancomycin
Bacterial meningitis	S pneumoniae, Meningococcus	Ceftriaxone + vancomycin + steroid

Table 2

Class	Spectrum	Available preparations	Route of	Effective against administration	Not effective against
Carbapenem	Broad	Meroponem/imepenem / ertapenem	Intravenous	GPC, GNB, anaerobes	MRSA, VRE. Ertapenem ineffective against pseudomonas
B lactamase inhibitor	Broad	Piperacillin – tazobactam	Intravenous	GPC, GNB, anaerobes.	MRSA, VRE
3 <sup>rd</sup> gen Cephalosporin	Broad	Cefaperazone- sulbactam	Intravenous	GPC, GNB, anaerobes.	MRSA, VRE
1 <sup>st</sup> gen cephalosporin	Narrow	Cefazolin, Cephadrine	Intravenous	Strept	MRSA, VRE, anaerobes
3 <sup>rd</sup> gen Cephalosporin	Broad	Ceftriaxone	Intravenous	Strept, GNR	MRSA, VRE, anaerobes
3 <sup>rd</sup> gen Cephalosporin	Broad	Ceftazidime	Intravenous	GNR, esp pseudom	MRSA, VRE, anaerobes
Glycopeptide	Narrow	Vancomycin	Intravenous	MRSA, enterococcus	GNR, anaerobes
Aminoglycoside	Narrow	Amikacin, Tobramycin, Gentamicin	Intravenous	GNR Strept and Entero., anaerobes	
B lactamase inhibitor	Broad	Amoxicillin- clavulanate	Intravenous and oral	GPC, some GNR, anaerobes	E coli, enterobacteriaceae
Fluoroquinolones	Broad	Levofloxacin	Intravenous and oral	GPC, atypical resp pathogens	Anaerobes
Macrolides	Narrow	Azithromycin, clarithromycin	Oral	Atypical resp pathogens	GNR, anaerobes
Lincosamide	Narrow	Clindamycin	Intravenous and oral	Strep, Staph (MSSA)	GNR

GPC= gram positive cocci, GNR= gram negative rods

MSSA= methicillin sensitive Staph *aureus*

MRSA= methicillin resistant Staph *aureus*

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