January 2015

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

Erfan Hussain  
_Aga Khan University, erfan.hussain@aku.edu_

Bushra Jamil  
_Aga Khan University, bushra.jamil@aku.edu_

Naseem Salahuddin  
_Indus Hospital, Karachi, Pakistan_

Follow this and additional works at: [http://ecommons.aku.edu/pakistan_fhs_mc_med_med](http://ecommons.aku.edu/pakistan_fhs_mc_med_med)  
Part of the [Infectious Disease Commons](http://ecommons.aku.edu/pakistan_fhs_mc_med_med)

Recommended Citation  
Available at: [http://ecommons.aku.edu/pakistan_fhs_mc_med_med/526](http://ecommons.aku.edu/pakistan_fhs_mc_med_med/526)
Guidelines for the Initial Management of Adults with Sepsis/Severe Sepsis/Septic Shock: 2015

Erfan Hussain*, Bushra Jamil**, Naseem Salahuddin***

*Section of Pulmonary and Critical Care Medicine, Department of Medicine, **Adult Infectious Diseases, The Aga Khan University, Karachi, Pakistan. ***Indus Hospital, Karachi, Pakistan

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.1,2 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.3

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.4,5,6

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.7,8
- 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.9,10,11,12

It is important to emphasize that the patient who meets the
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.3, 14 This recommendation is made with the following caveats:

  0 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.

  0 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.

  0 Given the varied reasons for an elevated base deficit, it is 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.15

The factors which are clearly associated with sepsis outcomes include the site of infection, the kind of organisms involved and their susceptibility patterns, timeto 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: 3rd generation cephalosporins currently ranges from 50-80%, ciprofloxacin 30-70%, piperacillin-tazobactam 20-30% and carbapenems between 2-15%.16

Of special consideration is the fact that carbapenem resistance enterobacteriaceae (CRE) is associated with a high antibiotic resistance pattern including 3rd generation cephalosporins and ciprofloxacin the mortality approaches 90%.17

Please see Appendix 5 for details.

Intravenous Fluids and Vasopressors:

- Intravenous A ccess:
The following is suggested:

  o Initial IV access for sepsis should be an upper extremity peripheral line

  o 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.19, 20

- Type of fluid for resuscitation:

  o For sepsis there is no recommendation for routine fluid administration.

  o For severe sepsis and septic shock crystalloids (Normal saline or Ringers Lactate) are recommended over colloids.9, 22

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

  o In the 3 Hour bundle fluid is administered to a total dose of 30cc/kg.

  o Crystalloid is administered as a fluid bolus

    250 cc over 10 minutes

    500 cc over 15 minutes

    1000 cc over 30 minutes

  o 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

  o 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.9, 25

    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
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. 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.

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.

2. **Systemic Inflammatory response (SIRS)** 2 or more of the following:
   a. Temp > 38 or < 36
   b. Heart rate > 90 beats/min

3. **Sepsis**: SIRS + Infection (known or suspected source) = Sepsis

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

   - Cardiovascular: 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. Creatinine > 2.0 mg/dL
   - Pulmonary: PaO2/FiO2 ≤ 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 3 days
   - Metabolic: pH ≤ 7.3 and plasma lactate > 4
   - Altered Mental Status
   - Bilirubin > 2mg/dL

5. **Septic Shock**: Persistent arterial hypotension despite adequate volume resuscitation

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

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

(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 ≥ 4 mmol/L
- CV: Systolic BP ≤ 90 mmHg, MAP ≤ 70 mmHg 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: PaO2/FiO2 ≤ 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 3 days
- 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 Antibiogram)

If MAP < 65 mmHg and/or Lactate > 4 mmol/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 5 ml/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?

☐ Pneumonia, empyema  ☐ Bone/joint infection  ☐ Implantable device infection
☐ Urinary tract infection  ☐ Wound infection  ☐ Other infection
☐ Acute abdominal infection  ☐ Blood stream catheter infection
☐ Meningitis  ☐ Endocarditis
☐ 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.

☐ Hyperthermia > 38.3 °C (101.0 °F)  ☐ Tachyphnea > 20 bpm  ☐ Hyperglycemia (plasma glucose >140 mg/dL) or 7.7 mmol/L in the absence of diabetes
☐ Hypothermia < 36 °C (96.8°F)  ☐ Leukocytosis (WBC count >12,000 µL–1)
☐ Altered mental status  ☐ Leukopenia (WBC count < 4000 µL–1) the absence of diabetes
☐ 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 Bili rubin > 2 mg/dl (34.2mmol/L)
☐ Platelet count < 100,000 µL Lactate > 2 mmol/L (18.0 mg/dl)
☐ Coagulopathy (INR >1.5 or aPTT >60 secs)
☐ Acute lung injury with PaO2/FiO2 <250 in the absence of pneumonia as infection source
☐ Acute lung injury with PaO2/FiO2 <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)  Time: _:_ (24 hr. clock)

Version 7.2.13
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 chlorhexidine or povidone iodine (if chlorhexidine 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 chlorhexidine or povidone iodine, cleanse a 5 cm area using circular motion starting at the site and working outward.
   4. Allow to dry for 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
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**

**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**

<table>
<thead>
<tr>
<th>DATE AND TIME</th>
<th>ORDER, SIGNATURE AND TITLE</th>
<th>RN SIGNATURE - TIME</th>
</tr>
</thead>
</table>

- **Allergies:**
- **Attending Physician:**
- **Primary Diagnosis:**
  - [ ] Sepsis
  - [ ] Severe Sepsis
  - [ ] Septic Shock
- **Secondary Diagnosis:**
  - Pneumonia
  - Urinary Tract Infection
  - Abd Infection
  - Other
- **Condition:**
  - [ ] Critical
  - [ ] Stable
- **Admit to:**
- **Oxygen:**
- **Vital Signs every 15 minutes X 1 hour, then per unit policy**
- **Strict Intake and Output**
- **Activity:**
  - [ ] Bed Rest
  - [ ] Other
- **Diet:**
  - [ ] NPO
  - [ ] Other
- **LABS:**
  - [ ] Sepsis Panel (IF CHECKED SEND ENTIRE LABS BELOW)
  - [ ] CBC with Differential and Platelet Count
  - [ ] PT/PTT
  - [ ] BUN/Creatinine
  - [ ] Serum Electrolytes (Na, K, Cl, HCO3, BUN, Creatinine)
  - [ ] Lactic Acid and Repeat every 6 hours for next 24 Hours
  - [ ] Urine DR
  - [ ] Procalcitonin
  - [ ] Blood Cultures X 2
  - [ ] Urine Cultures
  - [ ] Sputum Cultures
  - [ ] Cultures Other

- **Additional Labs:**
- [ ] Chest X-Ray
- [ ] Other Imaging Studies
- [ ] EKG 12 Lead
- [ ] IV Saline Lock with flush of Normal Saline 3ml every 12 hours
<table>
<thead>
<tr>
<th>DATE AND TIME</th>
<th>ORDER, SIGNATURE AND TITLE</th>
<th>RN SIGNATURE - TIME</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT Prophylaxis:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ANTIBIOTICS: ADJUST FOR RENAL and/or HEPATIC DYSFUNCTION**

**SEPSIS SOURCE UNKNOWN:**
- **Piperacillin-Tazobactum 3.375gm Q6 Hours IV**
- **Imipenem Cilastatin 500mg Q8 Hours IV**
- **Cefoperazone Sulbactam 400mg Q12 Hours IV**
- **Clindamycin 600mg Q8 Hours IV**

*IF MRSA SUSPECTED THEN ADD:*
- **Vancomycin: Load 20mg/kg IV**
- **Maintenance 15mg/kg Q12 Hours IV**

**SUSPECTED:**
- **Piperacillin-Tazobactum 3.375gm Q6 Hours IV**
- **And Levofloxacin 500mg Q24 Hours IV**

*OR:*
- **Ceftriaxone 2gm Q24 Hours IV**
- **And Levofloxacin 500mg Q24 Hours IV**

**SUSPECTED SKIN & SOFT TISSUE INFECTION:**
- **Cefazolin 2gm Q8 Hours IV**

*IF Penicillin Allergic:*
- **Clindamycin 600mg Q8 Hours IV**
- **And Ciprofloxacin 400mg Q12 Hours IV**

*IF MRSA SUSPECTED THEN ADD:*
- **Vancomycin: Load 20mg/kg IV**
- **Maintenance 15mg/kg Q12 Hours IV**

**SUSPECTED ABDOMINAL INFECTION:**
- **Piperacillin-Tazobactum 3.375gm Q6 Hours IV**

*OR:*
- **Imipenem Cilastatin 1gm Q8 Hours IV**

*OR:*
- **Ceftriaxone 2gm Q24 Hours IV**
- **And Amikacin 15mg/kg Q24 Hours IV**
- **And Metronidazole 500mg Q8 Hours IV**
### SUSPECTED UROSEPSIS

- **Piperacillin-Tazobactum**: 3.375gm Q6 Hours IV

- **Imipenem Cilastatin**: 500mg Q8 Hours IV

**IF RISK OF ENTEROCCOCUS**

- **Vancomycin**: Load 20mg/kg IV
  - Maintenance 15mg/kg Q 12 Hours IV

### SUSPECTED CNS INFECTION

- **Ceftriaxone**: 2gm Q24 Hours IV
  - **AND**
  - **Vancomycin**: Load 20mg/kg IV
  - Maintenance 15mg/kg Q 12 Hours IV

- **Meropenem**: 2gm Q8 Hours IV

**OR**

- **Piperacillin-Tazobactum**: 3.375gm Q6 Hours IV
  - **AND**
  - **Vancomycin**: Load 20mg/kg IV
  - Maintenance 15mg/kg Q 12 Hours IV
  - **AND**
  - **Colistin**: 9MU stat and 3MU Q 8hours IV

**FOR PATIENTS WITH SYSTOLIC BLOOD PRESSURE LESS THAN 90 mmHg**

- **Initial intravenous fluids per kg estimated ideal body weight**
  - **Target BP greater than 90 mmHg systolic and Mean Arterial Pressure (MAP) greater than 65 mmHg**

- **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**

- **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)**
  - **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 prolonged 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 may 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

<table>
<thead>
<tr>
<th>Source of infection</th>
<th>Likely pathogen</th>
<th>Best empirical antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract</td>
<td>E. coli</td>
<td>Carbapenem or Piperacillin -tazobactam or Cefaperazone-sulbactam</td>
</tr>
<tr>
<td>Genital tract</td>
<td>E. coli, Enterococcus, S hemolyticus, A aerobes</td>
<td>Carbapenem or Piperacillin -tazobactam or Cefaperazone-sulbactam + vancomycin</td>
</tr>
<tr>
<td>Respiratory tract (CAP)</td>
<td>S. pneumoniae, atypical</td>
<td>Ceftriaxone + levofloxacin or clarithromycin</td>
</tr>
<tr>
<td>Respiratory tract (HAP)</td>
<td>GPC, GNR, atypical</td>
<td>Carbapenem or Piperacillin -tazobactam or Cefaperazone-sulbactam + levofloxacin or clarithromycin</td>
</tr>
<tr>
<td>Respiratory tract (VAP)</td>
<td>GNR, M RSA</td>
<td>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</td>
</tr>
<tr>
<td>Intra-abdominal</td>
<td>Gram negatives, anerobes</td>
<td>Carbapenem or Piperacillin -tazobactam or Cefaperazone-sulbactam + vancomycin</td>
</tr>
<tr>
<td>SSTI (necrotizing fasciitis)</td>
<td>S. aureus, Streptococi anerobes</td>
<td>A moxicillin/clavulanate or clindamycin + vancomycin</td>
</tr>
<tr>
<td>Burn sepsis</td>
<td>S. aureus, Streptococi, Pseudomonas, Candida</td>
<td>Carbapenem or Piperacillin -tazobactam or Cefaperazone-sulbactam + vancomycin</td>
</tr>
<tr>
<td>Line sepsis</td>
<td>S. aureus, (M SSA, M RSA), Pseudomonas</td>
<td>Ceftazidime or amikacin+ vancomycin</td>
</tr>
<tr>
<td>Infected device</td>
<td>S. aureus, (M SSA, M RSA), Pseudomonas</td>
<td>Ceftazidime or amikacin+ vancomycin</td>
</tr>
<tr>
<td>Bacterial meningitis</td>
<td>S pneumoniae, M eningococcus</td>
<td>Ceftriaxone + vancomycin + steroid</td>
</tr>
</tbody>
</table>
Table 2

<table>
<thead>
<tr>
<th>Class</th>
<th>Spectrum</th>
<th>Available preparations</th>
<th>Route of administration</th>
<th>Effective against administration</th>
<th>Not effective against</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbenem</td>
<td>Broad</td>
<td>Meropenem / imipenem / ertapenem</td>
<td>Intravenous</td>
<td>GPC, GNB, anaerobes</td>
<td>M RSA, VRE, Ertapenem ineffective against pseudomonas</td>
</tr>
<tr>
<td>B lactamase inhibitor</td>
<td>Broad</td>
<td>Piperacillin - tazobactam</td>
<td>Intravenous</td>
<td>GPC, GNB, anaerobes</td>
<td>M RSA, VRE, Ertapenem ineffective against pseudomonas</td>
</tr>
<tr>
<td>3rd gen Cephalosporin</td>
<td>Broad</td>
<td>Cefaparazone- sulbactam</td>
<td>Intravenous</td>
<td>GPC, GNB, anaerobes</td>
<td>M RSA, VRE, Ertapenem ineffective against pseudomonas</td>
</tr>
<tr>
<td>1st gen cephalosporin</td>
<td>Narrow</td>
<td>Cefazolin, Cephradine</td>
<td>Intravenous</td>
<td>Strept, GNR</td>
<td>M RSA, VRE, anaerobes</td>
</tr>
<tr>
<td>3rd gen Cephalosporin</td>
<td>Broad</td>
<td>Ceftriaxone</td>
<td>Intravenous</td>
<td>Strept, GNR</td>
<td>M RSA, VRE, anaerobes</td>
</tr>
<tr>
<td>3rd gen Glycopeptide</td>
<td>Narrow</td>
<td>Ceftazidime</td>
<td>Intravenous</td>
<td>GN R, esp pseudom</td>
<td>M RSA, VRE, anaerobes</td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>Narrow</td>
<td>Vancomycin</td>
<td>Intravenous</td>
<td>M RSA, enterococcos</td>
<td>M RSA, VRE, anaerobes</td>
</tr>
<tr>
<td>B lactamase inhibitor</td>
<td>Broad</td>
<td>Aminocillin- clavulanate</td>
<td>Intravenous and oral</td>
<td>GPC, some GNR, anaerobes</td>
<td>E coli, enterobacteriae</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Broad</td>
<td>Levofloxacin</td>
<td>Intravenous and oral</td>
<td>GPC, atypical resp pathogens</td>
<td>A naerobes</td>
</tr>
<tr>
<td>Macrolides</td>
<td>Narrow</td>
<td>Azithromycin, clarithromycin</td>
<td>Oral</td>
<td>Atypical resp pathogens</td>
<td>GN R, anaerobes</td>
</tr>
<tr>
<td>Lincosamide</td>
<td>Narrow</td>
<td>Clindamycin</td>
<td>Intravenous and oral</td>
<td>Strept, Staph (M SSA)</td>
<td></td>
</tr>
</tbody>
</table>

GPC = gram positive cocci, GNR = gram negative rods  
M SSA = meticillin sensitive Staph aureus  
M RSA = meticillin resistant Staph aureus  

Submitted by: Dr. Naseem Salahuddin  
Endorsed by: Members of Medical Microbiologists and Infectious Disease Society of Pakistan (MMIDSP)  

References  
8. Riedel S. Procalcitonin and the role of biomarkers in the diagnosis and management of sepsis Diagnostic Microbiology and Infectious Disease 2012; 73: 221-227  
17. Falagas ME, Lourida P, Poulikakos P, Rafailidis PI, Tansari GS. Antibiotic


