

# RIGHT DIAGNOSIS - SEPSIS AND SEPTIC SHOCK

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**SEPSIS:** A life-threatening organ dysfunction caused by a dysregulated host response to infection.

## THREE STEP SEPSIS CLASSIFICATION MODEL:

- Step 1 involves the use of the NEWS-2 score to detect dysregulated host responses indicative of sepsis when the score is  $\geq 6$  and prompts further evaluation
- Step 2 evaluates the presence of risk factors that predispose patients to infections.
- Step 3 involves determining evidence of infection

| Interpretation                                   | Outcome          |
|--------------------------------------------------|------------------|
| (i) Step-1 = negative                            | Asepsis          |
| (ii) Step-1= positive with step-2 & 3 = negative |                  |
| Step-1, 2 & 3(a) = positive                      | Possible sepsis  |
| Step-1, 2 & 3(b) = positive                      | Probable sepsis  |
| Step-1, 2 & 3(c) = positive                      | Confirmed sepsis |

**SEPTIC SHOCK:** Suspected (or documented) infection AND vasopressor therapy needed to maintain mean arterial pressure at  $\geq 65$  mmHg and serum lactate  $> 2.0$  mmol/L despite adequate fluid resuscitation

| NEWS 2 Score<br>(Or any score like SOFA/MEWS can be used): |             | Score |        |           |                           |                     |
|------------------------------------------------------------|-------------|-------|--------|-----------|---------------------------|---------------------|
| Physiological parameter                                    |             | 3     | 2      | 1         | 0                         |                     |
| Respiration rate (per minute)                              | $\leq 8$    |       |        | 9–11      | 12–20                     | $\geq 25$           |
| SpO <sub>2</sub> Scale 1 (%)                               | $\leq 91$   |       | 92–93  | 94–95     | $\geq 96$                 |                     |
| SpO <sub>2</sub> Scale 2 (%)                               | $\leq 83$   |       | 84–85  | 86–87     | 88–92<br>$\geq 93$ on air | $\geq 97$ on oxygen |
| Air or oxygen?                                             |             |       | Oxygen |           | Air                       |                     |
| Systolic blood pressure (mmHg)                             | $\leq 90$   |       | 91–100 | 101–110   | 111–219                   | $\geq 220$          |
| Pulse (per minute)                                         | $\leq 40$   |       |        | 41–50     | 51–90                     | $\geq 131$          |
| Consciousness                                              |             |       |        |           | Alert                     | CPU                 |
| Temperature (°C)                                           | $\leq 35.0$ |       |        | 35.1–36.0 | 36.1–38.0                 | $\geq 39.1$         |

Improves the detection and response to clinical deterioration in adult patients.

| STEP                                           | DESCRIPTION                                                                                                                                                                                                                                                    |
|------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Step 1: Evidence of Dysregulated Host Response | Assessed using the National Early Warning Score-2 (NEWS-2) $\geq 6$                                                                                                                                                                                            |
| Step 2: Risk factors for infection             | Evaluated based on the presence of risk factors such as chronic illnesses, malnutrition, unhygienic living conditions, immunosuppressive states, age, trauma, structural diseases, recent surgery, travel history, animal bites, and previous hospitalizations |
| Step 3: Evidence of Infection                  | Determined through -                                                                                                                                                                                                                                           |
| 3a. Clinical Evidence                          | Syndromic diagnosis including pyelonephritis, infective endocarditis, intra-abdominal infections, skin and soft tissue infections, meningitis, cerebrospinal fluid shunt infections, catheter-related infections, osteomyelitis, abscesses, and pneumonia      |
| 3b. Supportive/Suggestive Evidence             | Imaging (X-ray, ultrasound, computed tomography, magnetic resonance imaging, positron emission tomography) and biomarkers (blood, urine, other fluids)                                                                                                         |
| 3c. Confirmatory Evidence                      | Direct visualization, endoscopic evidence, microscopy and culture growth, polymerase chain reaction/gene detection, and immunological methods                                                                                                                  |

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| Suspected site                    | Symptoms /signs                                                                                                                         | Initial microbiologic evaluation                                                                                                                                                                        | RISK FACTORS FOR MULTI-DRUG RESISTANT ORGANISMS                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Upper respiratory tract           | Pharyngeal inflammation + exudate ± swelling/ lymphadenopathy                                                                           | Throat swab for aerobic culture                                                                                                                                                                         | <b>MRSA</b><br>Previous infection/colonization by MRSA in the last 12 months<br>Hemodialysis/peritoneal dialysis/central venous catheters<br>Administration of multiple antibiotics in the last 30 days<br>Immunosuppression/IV Drug addiction<br>Rheumatoid arthritis<br>Patients coming from long-term care facilities or who have undergone hospital stay in the last 12 months                    | <b>ESBL</b><br>Previous infection/colonization with ESBL in the last 12 months<br>Prolonged hospitalization (>10 days, in particular in ICU/hospice/long-term care facilities)<br>Presence of permanent urinary catheter<br>Patients with percutaneous endoscopic gastrostomy<br>Administration of multiple antibiotics in the last 30 days |
| Lower respiratory tract           | Productive cough, pleuritic chest pain, consolidative auscultatory findings                                                             | Sputum of good quality, rapid influenza testing, urinary antigen testing (eg, pneumococcus, legionella; not recommended in children), quantitative culture of protected brush or bronchoalveolar lavage |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
| Urinary tract                     | Urgency, dysuria, loin, or back pain                                                                                                    | Urine culture and microscopy showing pyuria                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
| Vascular catheters: arterial, CVC | Redness or drainage at insertion site                                                                                                   | Culture of blood (from the catheter and a peripheral site), culture catheter tip (if removed)                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
| Pleural catheter                  | Redness or drainage at insertion site                                                                                                   | Culture of pleural fluid (through catheter)                                                                                                                                                             | <b>Pseudomonas aeruginosa</b><br>Previous infection/colonization with P. aeruginosa in the last 12 months, Cystic fibrosis/Poorly controlled Diabetes<br>Administration of multiple antibiotics in the last 30 days<br>Pulmonary anatomic abnormalities with recurrent infections<br>Elderly (>80 years), Presence of permanent urinary catheter, Prolonged steroid use (>6 weeks), Neutropenic fever | <b>ESBL</b><br>Previous infection/colonization with ESBL in the last 12 months<br>Prolonged hospitalization (>10 days, in particular in ICU/hospice/long-term care facilities)<br>Presence of permanent urinary catheter<br>Patients with percutaneous endoscopic gastrostomy<br>Administration of multiple antibiotics in the last 30 days |
| Skin/soft tissue                  | Erythema, oedema, lymphangitis                                                                                                          | Culture blister fluid or draining pus; role of tissue aspirates not proven                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
| CNS                               | Signs of meningeal irritation                                                                                                           | CSF cell count, protein, glucose, Gram stain, and culture                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
| Gastrointestinal                  | Abdominal pain, distension, diarrhoea, and vomiting                                                                                     | Stool culture for Salmonella, Shigella, or Campylobacter; detection of Clostridium difficile toxin                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
| Intra-abdominal                   | Specific abdominal symptoms/signs                                                                                                       | Aerobic and anaerobic culture of percutaneously or surgically drained abdominal fluid collections                                                                                                       | <b>Candida</b><br>Immunosuppression<br>Presence of central venous catheters or intravascular devices/TPN<br>Prolonged hospitalization (>10 days, particularly in an ICU)<br>Recent surgery (particularly abdominal surgery), Prolonged wide-range antibiotic administration, Previous necrotizing pancreatitis<br>Recent fungal infection/colonization                                                | <b>ESBL</b><br>Previous infection/colonization with ESBL in the last 12 months<br>Prolonged hospitalization (>10 days, in particular in ICU/hospice/long-term care facilities)<br>Presence of permanent urinary catheter<br>Patients with percutaneous endoscopic gastrostomy<br>Administration of multiple antibiotics in the last 30 days |
| PD catheter                       | Cloudy PD fluid, abdominal pain                                                                                                         | Cell count and culture of PD fluid                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
| Genital tract                     | Women: Low abdominal pain, vaginal discharge<br>Men: Dysuria, frequency, urgency, urge incontinence, cloudy urine, prostatic tenderness | Women: Endocervical and high vaginal swabs onto selective media<br>Men: Urine Gram stain and culture                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
| Bone                              | Pain, warmth, swelling, decreased use                                                                                                   | Blood cultures, MRI, bone cultures at surgery or by interventional radiology                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |
| Joint                             | Pain, warmth, swelling, decreased range of motion                                                                                       | Arthrocentesis with cell counts, Gram stain, and culture                                                                                                                                                | <b>Candida</b><br>Immunosuppression<br>Presence of central venous catheters or intravascular devices/TPN<br>Prolonged hospitalization (>10 days, particularly in an ICU)<br>Recent surgery (particularly abdominal surgery), Prolonged wide-range antibiotic administration, Previous necrotizing pancreatitis<br>Recent fungal infection/colonization                                                | <b>ESBL</b><br>Previous infection/colonization with ESBL in the last 12 months<br>Prolonged hospitalization (>10 days, in particular in ICU/hospice/long-term care facilities)<br>Presence of permanent urinary catheter<br>Patients with percutaneous endoscopic gastrostomy<br>Administration of multiple antibiotics in the last 30 days |
| Wound or burn                     | Inflammation, edema, erythema, discharge of pus                                                                                         | Gram stain and culture of draining pus, wound culture not reliable                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                             |

## RIGHT TREATMENT - SEPSIS AND SEPTIC SHOCK

| Category                                    | Best practice statement                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|---------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Possible sepsis/<br>septic shock            | <b>Continuously re-evaluate</b><br>Discontinue empiric antimicrobials if alternative cause of illness is demonstrated                                                                                                                                                                                                                                                                                                                                                                                                 |
| Possible/Probable<br>sepsis without shock   | Rapid assessment of the <b>likelihood</b> of infectious vs non-infectious causes                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| High risk of infection<br>with MDR Organism | Empiric antimicrobials with MDR coverage (as per chapter on MDR organisms)                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Sepsis with septic<br>shock                 | <b>Hour - 1 Bundle of Care</b><br>Optimising dosing strategies of antimicrobials based on <b>PK/PD principles</b><br>Rapidly identifying or excluding a specific anatomical diagnosis of infection that requires emergent <b>source control</b><br>Prompt removal of IV access devices that are a possible source of sepsis after other vascular access has been established<br>Use of pharmacologic venous thromboembolism ( <b>VTE prophylaxis</b> (LMWH over UFH) unless a contraindication to such therapy exists |

### Hour-1 Bundle of Care: Initial Resuscitation for Sepsis/Septic Shock

1. Measure lactate level\*
  2. Obtain blood cultures before administering antibiotics
  3. Administer broad-spectrum antibiotics
  4. Begin rapid administration of 30mL/kg **crystalloid** over **3 hours** for hypotension or lactate level  $\geq 4$  mmol/L
  5. Apply vasopressors if hypotensive during or after fluid resuscitation to maintain MAP  $\geq 65$  mm Hg
- Remeasure lactate if initial lactate is elevated ( $> 2$  mmol/L).

| Antibiotic Timing              |                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                   |
|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                | Shock is present                                                                                                                                                       | Shock is absent                                                                                                                                                                                                                                                                                                                                                   |
| Sepsis is definite or probable |  Administer antimicrobials <b>immediately</b> , ideally within 1 hour of recognition. |  Administer antimicrobials <b>immediately</b> , ideally within 1 hour of recognition.                                                                                                                                                                                            |
| Sepsis is possible             |  Administer antimicrobials <b>immediately</b> , ideally within 1 hour of recognition. | <div>  Rapid assessment* of infectious vs noninfectious causes of acute illness.            Administer antimicrobials <b>within 3 hours</b> if concern for infection persists.         </div> |

# RIGHT TREATMENT - SEPSIS AND SEPTIC SHOCK

## IN IMMUNOCOMPETENT PATIENT

- **Piperacillin – Tazobactam** 4.5g q6h/ **Cefepime** 2g q8h/ **Meropenem** 1g q8h/
- If the patient is allergic to beta lactam-**Aztreonam** (2 Gm q8h)/ **Levofloxacin** (750 Mg q24h)
- Add **Vancomycin** (loading dose of 25–30 mg/kg, then 15–20 mg/kg q8–12h) if MRSA suspected
- High risk for MDR; two antimicrobials with gram-negative coverage for empiric treatment over one gram-negative agent

## NEUTROPENIC PATIENT (ANC <500)

- **Cefepime** (2 Gm 8qh) or **Meropenem** (1 Gm 8qh) or **Piperacillin-tazobactam** (3.375 Gm 4qh)
- Add **vancomycin** - if suspected CRBSI, severe mucositis, skin/soft tissue infection, or hypotension

## POST SPLENECTOMY PATIENTS

- **Ceftriaxone** (2 g q24h or 2gm 12h in meningitis)
- Add **Vancomycin** - if local prevalence of Cephalosporin-resistant pneumococci is high
- If the patient is allergic to  $\beta$ -lactam antibiotics: **Levofloxacin** (750 mg q24h) plus **Vancomycin**

|                                                                                                                                                                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ❖ All antimicrobials are administered through IV route (Beta lactam by continuous infusion)                                                                      |
| ❖ Modify antimicrobial regimen in 48-72 hours based on results of culture & susceptibility reports, the site of infection and the clinical status of the patient |
| ❖ In case of deterioration in spite of hiking of antibiotics consider multidrug resistance or sepsis by other organisms (MRSA) - Add Vancomycin if not before    |
| ❖ With high risk of fungal infection (e.g.: immunocompromised patients or patients with febrile neutropenia), add empiric antifungal therapy                     |
| ❖ No recommendation on the use of antiviral agents.                                                                                                              |

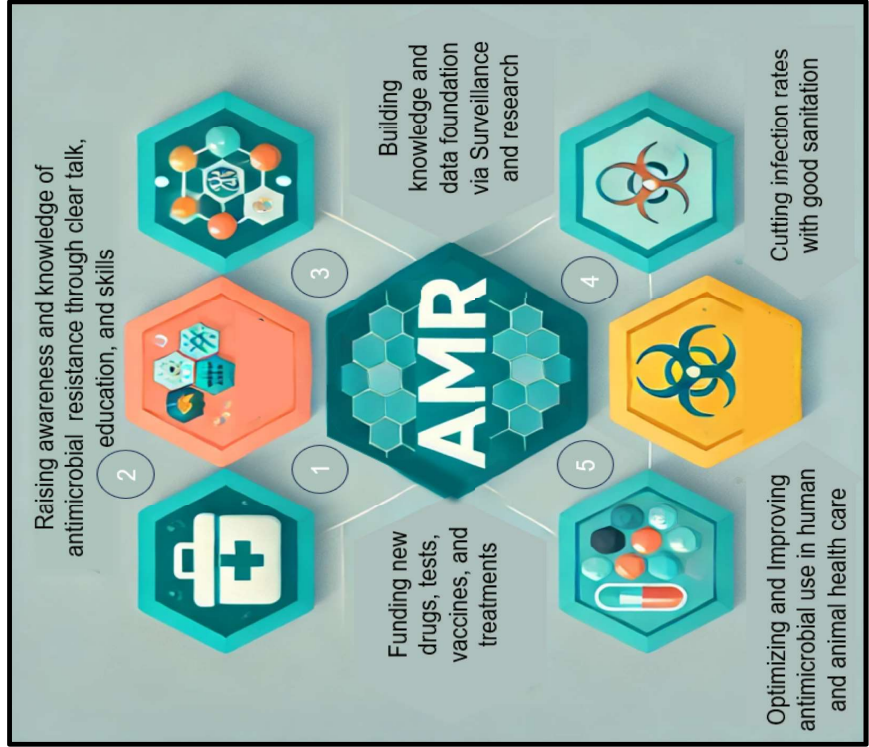
| SOURCE CONTROL METHODS IF SOURCE IDENTIFIED |                                                                                                                            |
|---------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Source                                      | Interventions                                                                                                              |
| Pneumonia                                   | Chest physiotherapy, suctioning                                                                                            |
| Urinary tract                               | Drainage of abscesses, relief of obstruction, removal or changing of infected catheters                                    |
| Catheter-related bacteraemia                | Removal of catheter                                                                                                        |
| Peritonitis                                 | Resection, repair, or diversion of ongoing sources of contamination, drainage of abscesses, debridement of necrotic tissue |
| Pancreatic infection                        | Drainage or debridement                                                                                                    |
| Soft tissue infection                       | Debridement of necrotic tissue and drainage of discrete abscesses                                                          |
| Septic arthritis                            | Joint drainage and debridement                                                                                             |
| Endocarditis                                | Valve replacement                                                                                                          |
| Prosthetic device infection                 | Device removal                                                                                                             |
| Empyema                                     | Drainage, decortication                                                                                                    |
| Sinusitis                                   | Surgical decompression of the sinuses                                                                                      |
| Cholangitis                                 | Bile duct decompression                                                                                                    |

1. Evans et al. *Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. Critical Care Medicine: November 2021 - Volume 49 - Issue 11 - p e1063-e1143*
2. Fauci AS et al., editors. *Harrison's principles of internal medicine. 21st ed. New York: McGraw Hill; 2022.*

# ANTIMICROBIAL RESISTANCE (AMR)

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| BACTERIA POSING A MAJOR THREAT OF AMR |                                                                           |
|---------------------------------------|---------------------------------------------------------------------------|
| 1.                                    | ESBL-E(Extended-spectrum $\beta$ -lactamase-producing Enterobacteriales ) |
| 2.                                    | AmpC-E(AmpC $\beta$ -lactamase-producing Enterobacteriales )              |
| 3.                                    | CRE(Carbapenem-resistant Enterobacteriales)                               |
| 4.                                    | DTR P. aeruginosa (difficult-to-treat resistance)                         |
| 5.                                    | CRAB(carbapenem-resistant Acinetobacter baumannii)                        |
| 6.                                    | Stenotrophomonas maltophilia.                                             |



Strategic Objectives of the Global Action Plan on Antimicrobial Resistance

**Understanding Antimicrobial Resistance (AMR)**  
Antimicrobial resistance (AMR) is one of the top global public health and development threats in 2021, it has been estimated that 4.71 million (95% UI 4.23–5.19) deaths were associated with bacterial AMR, including 1.14 million deaths attributable to bacterial AMR (1). Super-regions with the highest all-age AMR mortality rate in 2050 are forecasted to be South Asia, Latin America, and the Caribbean(1).  
India, in particular, faces alarming rates of ABR, both in community and healthcare settings, and has reported resistance rates of up to 70% to first-line antibiotics like cephalosporins and carbapenems in Gram-negative bacteria.(2).  
Under the better care scenario, across all age groups, 92.0 million deaths (82.8–102.0) could be cumulatively averted between 2025 and 2050, through better care of severe infections and improved access to antibiotics, and under the gram-negative drug scenario, 11.1 million AMR deaths (9.08–13.2) could be averted through the development of a gram-negative drug pipeline to prevent AMR deaths.(1)

**Role of Vaccines in Combating AMR**  
Vaccination strategies are essential in combating antimicrobial resistance (AMR) by preventing infections, limiting transmission, and reducing antibiotic misuse. Implementing these measures has the potential to save millions of antibiotic doses and cut healthcare costs by up to \$30 billion. Vaccines should be integrated into AMR strategies, existing vaccine use should be accelerated, new vaccine development supported, and global regulatory frameworks strengthened (4)

1.Christopher J L Murray, Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050, Lancet 2024; 404: 1199–226/[doi.org/10.1016/S0140-6736\(24\)01867-1](https://doi.org/10.1016/S0140-6736(24)01867-1)  
2.Gandra S, Joshi J, Trett A, Lamkang AS, Laxminarayan R. Scoping report on antimicrobial resistance in India. Center for Disease Dynamics, Economics & Policy: Washington, DC, USA. 2017 Nov;2017:1–46.  
3.Vekemans J, ET AL. Leveraging vaccines to reduce antibiotic use and prevent antimicrobial resistance: a World Health Organization action framework. Clinical Infectious Diseases. [doi.org/10.1093/cid/ciab062](https://doi.org/10.1093/cid/ciab062).  
4.Mendelson M, Matsoso MP. Guest Editorial: The World Health Organization Global Action Plan for antimicrobial resistance. South African medical journal DOI:10.7196/SAMJ.9644

# APPROACH TO MULTIDRUG RESISTANT ORGANISMS

| GROUP            | ORGANISM                                                                                                                                            | INFECTIONS           |                         | RECOMMENDATION REGARDING TREATMENT                                                                                                                                                                                                                              |                                                                                                                                                                                                  |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                  |                                                                                                                                                     |                      |                         | PREFERRED                                                                                                                                                                                                                                                       | ALTERNATIVE                                                                                                                                                                                      |
| ENTERO BACTERIAE | Extended-spectrum $\beta$ -lactamase-producing Enterobacteriales (ESBL-E)<br>(CTX-M-1 mainly<br>Others- TEM and SHV , PER-1, VEB-1, VEB-2, GES-1/2) | UTI                  | Cystitis                | Nitrofurantoin(100 mg BD) and TMP-SMX (160 mg TMP BD)                                                                                                                                                                                                           | Oral Fosfomycin(3 gm PO)                                                                                                                                                                         |
|                  |                                                                                                                                                     |                      | Pyelonephritis and cUTI | TMP-SMX , FQs –levofloxacin(750 mg iv od) when resistance or toxicities of TMP-SMX or fluoroquinolones – Carbapenems can be given                                                                                                                               | Aminoglycosides (amikacin – 15 mg/kg iv od)                                                                                                                                                      |
|                  |                                                                                                                                                     | Non UTI              |                         | Carbapenems(Meropenem- 1 gm iv TDS)<br>After clinical response- <b>Switching</b> to oral fluoroquinolones or TMP-SMX (8-12 mg/kg/day TMP)<br><b>(PIPTAZ- Not suggested for infections outside of the urinary tract, even if susceptibility is demonstrated)</b> |                                                                                                                                                                                                  |
|                  | AMPC $\beta$ -Lactamase-producing Enterobacteriales<br>(K. aerogenes, and C. freundii - most common )                                               | UTI                  | Cystitis                | Nitrofurantoin, TMP-SMX                                                                                                                                                                                                                                         | Aminoglycoside (amikacin – 15 mg/kg iv od)                                                                                                                                                       |
|                  |                                                                                                                                                     |                      | Pyelonephritis and cUTI | TMP-SMX or FQs (levofloxacin)                                                                                                                                                                                                                                   | Aminoglycoside (amikacin – 15 mg/kg iv od)                                                                                                                                                       |
|                  |                                                                                                                                                     | Non UTI              |                         | Cefepime(2 gm iv tds) (weak inducer of ampC and withstands hydrolysis)                                                                                                                                                                                          | <ul style="list-style-type: none"> <li>Carbapenem (when the cefepime MIC is <math>\geq 4</math> <math>\mu\text{g/mL}</math>)</li> <li>If carbapenem resistance- Ceftazidime-avibactam</li> </ul> |
|                  |                                                                                                                                                     |                      |                         | Nitrofurantoin, TMP-SMX, FQs (levofloxacin)                                                                                                                                                                                                                     | <ul style="list-style-type: none"> <li>Single dose aminoglycoside</li> <li>Oral fosfomycin</li> </ul>                                                                                            |
|                  | Carbapenem Resistance Enterobacteriales (CRE)<br><br>Resistant to at least 1 carbapenem antibiotic or producing a carbapenemase enzyme              | UTI                  | Cystitis                | Ceftazidime-avibactam (2.5 gm iv tds)                                                                                                                                                                                                                           | Aminoglycosides                                                                                                                                                                                  |
|                  |                                                                                                                                                     | Non-UTI (if KPC +nt) |                         | Ceftazidime-avibactam(2.5 gm iv tds) + Aztreonam(2 gm iv tds)                                                                                                                                                                                                   | Cefiderocol (If carbapenem resistance)                                                                                                                                                           |
|                  |                                                                                                                                                     |                      |                         | Same as KPC                                                                                                                                                                                                                                                     | Same as KPC                                                                                                                                                                                      |
|                  |                                                                                                                                                     |                      |                         | Ceftazidime-avibactam                                                                                                                                                                                                                                           | Cefiderocol                                                                                                                                                                                      |
|                  |                                                                                                                                                     | Non UTI              |                         | Ceftazidime-avibactam(2.5 gm iv tds) + Aztreonam(2 gm iv tds)                                                                                                                                                                                                   | <ul style="list-style-type: none"> <li>Ceftazidime- avibactam</li> <li>Meropenem-vaborbactam (if available )</li> </ul>                                                                          |
|                  | <b>Polymyxin B and colistin are not suggested for the treatment of infections caused by CRE</b>                                                     |                      |                         |                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                  |

# APPROACH TO MULTIDRUG RESISTANT ORGANISMS

| ORGANISM                                                                                                    | INFECTIONS                                                                                                                              | RECOMMENDATION REGARDING TREATMENT                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                 | Routinely tested for <i>Pseudomonas aeruginosa</i> :                                                                                                                                                                          |
|-------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                             |                                                                                                                                         | PREFERRED                                                                                                                                                                                                                                                                    | ALTERNATIVE                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                               |
| <b>Pseudomonas</b><br>(GES, VES, PER,KPC, PDC, MexAB-OprM)                                                  | Resistant to routine sensitivity pattern *                                                                                              | Meropenem (1 gm iv tds)                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>• Piperacillin-tazobactam</li> <li>• Cefoperazone-sulbactam, Ceftazidime, cefepime</li> <li>• Aztreonam</li> <li>• Fluroquinolones (i.e levofloxacin)</li> <li>• Fosfomycin</li> </ul> |
|                                                                                                             | DTR or CRPA- Resistant to all of the above and carbapenems                                                                              | Ceftazidime-avibactam (2.5 gm iv tds)<br><br>Cefiderocol (2 gm iv tds) is preferred for MBL.                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>• Tobramycin or amikacin(15 mg/kg od) (for complicated UTI*)</li> <li>• Cefotolazane-tazobactam(3 gm iv tds), or Cefiderocol (2 gm iv tds)</li> <li>• <b>Newer drugs- Cefepime-Zidebactam</b> (2+1 gm iv tds)</li> </ul> |                                                                                                                                                                                                                               |
|                                                                                                             | Carbapenem resistant A. baumannii – CRAB **                                                                                             | At least one subbactam-based agent is preferred<br>Nebulized antibiotics are not indicated.<br><b>Sulbactam-durlobactam (1+1 gm iv qid) + either imipenem-cilastatin or meropenem (if available)</b>                                                                         | High dose Ampicillin-sulbactam (6+3 gm iv tds)                                                                                                                                                                                                                  |                                                                                                                                                                                                                               |
| <b>A. baumannii</b><br><br>OXA-23, OXA-24/40,                                                               | Difficult-to-treat resistance (DTR) or Carbapenem-resistant <i>P. aeruginosa</i> (CRPA) (Resistant to all of the above and carbapenems) | Ceftazidime-avibactam(2.5 gm iv tds)<br>imipenem-cilastatin-relebactam, ceftolozane-tazobactam, or cefiderocol (if available)<br>Tobramycin(7 mg/kg iv od) or amikacin in DTR pseudomonas for complicated UTI                                                                |                                                                                                                                                                                                                                                                 | <b>Routinely tested for Acinetobacter baumannii:</b> <ul style="list-style-type: none"> <li>• Meropenem</li> <li>• Cefepime</li> <li>• Minocyclin</li> <li>• Ampicillin-sulbactam</li> </ul>                                  |
|                                                                                                             | <b>S. maltophilia</b> (L1 B- Lactamase ,L2 serine B- Lactamase)                                                                         | Any two of - minocycline, TMP-SMX, or levofloxacin, cefiderocol, ceftazidime-avibactam + aztreonam                                                                                                                                                                           |                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                               |
| <b>Methicillin-resistant Staphylococcus aureus</b><br><br>Vancomycin-resistant staphylococcus aureus (VRSA) |                                                                                                                                         | Vancomycin (15-20 mg/kg TDS)                                                                                                                                                                                                                                                 | TMP-SMX, clindamycin                                                                                                                                                                                                                                            |                                                                                                                                                                                                                               |
|                                                                                                             |                                                                                                                                         | <ul style="list-style-type: none"> <li>• Daptomycin (4 mg/kg iv od) (<b>Except in Pneumonia</b>)</li> <li>• Teicoplanin (400 mg iv od)</li> <li>• Linezolid (600 mg iv bd)</li> </ul>                                                                                        | <ul style="list-style-type: none"> <li>• Rifampin (600 mg iv/po od)</li> <li>• Tigecycline,</li> <li>• Ceftaroline</li> </ul>                                                                                                                                   |                                                                                                                                                                                                                               |
|                                                                                                             | <b>Enterococcus and Enterococcus faecalis</b><br>Vancomycin resistant Enterococcus (VRE)                                                | <b>Synergistic therapy (one cell wall active and one protein synthesis inhibitor) is more effective</b> <ul style="list-style-type: none"> <li>• Ceftriaxone/Ampicillin + Gentamicin(1 mg/kg iv tds)</li> <li>• Daptomycin + Ampicillin (12 gm/dav iv)/Linezolid.</li> </ul> | <ul style="list-style-type: none"> <li>• Tigecycline</li> <li>• Ceftaroline</li> </ul>                                                                                                                                                                          |                                                                                                                                                                                                                               |