R.L.JALAPPA HOSPITAL & RESEARCH CENTRE, TAMAKA, KOLAR – 563103

ANTIBIOTIC POLICY

Prepared by	Dept of Microbiology
Reviewed by	HIC Committee
Issue Number	03
Issue Date	15.03.2017
Validity	15.03.2018
Date of next Review	16.03.2018

Approved by	Medical Superintendent	Seal & Signature
Issued by	Quality Department	Issue date & Seal

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INTRODUCTION

Antimicrobial resistance is a major issue confronting healthcare providers and their patients. Infectious agents in health care settings are under heavy antibiotic pressure which results in the emergence of resistant organisms which consequently spread to patients through cross infection. Antimicrobial resistant organism increases mortality and the length of hospital stay which in turn increases the cost of health care. Changing antibiotic resistance patterns, rising cost of antibiotics has made selecting the optimal antibiotic regimen more difficult now than before.

As a response to these challenges, the antibiotic guidelines for in-house use is developed considering the current microbial data of our hospital and their antibiogram, clinician's opinion and adhering to the national guidelines. In addition to the antibiotic recommendation the guideline also contains the dosage of antibiotics.

Mission of this antibiotic guideline is to ensure that every patient of RL Jalappa Hospital and Research Centre gets optimal antibiotic therapy. As the name emphasizes these are only guidelines and departure from them may be necessary occasionally which should be documented.

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Changes in the in the present issue:

The following are additions and changes made in the present issue:

1. Antibiogram of different samples received in the laboratory in the year 2016 has been revised.
2. Antibiotic policy has been modified according to the hospital antibiogram and referring the national guidelines.
3. Added Antimicrobial guidelines for prophylaxis of Surgery
4. Added Use of Anti-microbial Agents (AMA) in Obstetrics & Gynecology
5. Added Treatment of Muti-Drug Resistant Bacterial Pathogens
6. Added Guidelines for Optimizing Use of Key Antimicrobials
7. Added Restricted Antimicrobial agent order form

Instructions to users of Antimicrobial Guidelines

Anti-microbial Guidelines (AMGL) for empiric management of infections is based on the local pathogenic bacteria isolated and their antimicrobial resistance (AMR) data of our hospital and the national guidelines. The empirical management must be altered in 48-72 hours according to antimicrobial susceptibility test report data on isolation of specific pathogen(s) causing infection.

Empirical or presumptive anti-infective therapy: presumptive treatment is a one-time treatment given for a presumed infection in a person, or group of people, at high risk of infection. Presumptive treatment is prescribed typically while waiting for the culture report. To optimize an accurate microbiological diagnosis, clinicians should ensure that diagnostic specimens are properly obtained and promptly submitted to the microbiology laboratory, before the institution of antimicrobial therapy.

BLOOD STREAM INFECTIONS- ICU ANTIBIOGRAM

Total isolates=24

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
Klebsiella pneumoniae	25	Imipenem 100%, Meropenem 100%, Levofloxacin 92%, Amikacin 77%, Amoxycillin-Clavulanic acid 71%, Piperacillin-Tazobactum 69%, Chloramphenicol 69%.
Acinetobacter	23	Levofloxacin 75%, Cotrimoxazole 75%, Doxycycline 67%, Tetracycline 67%, Piperacillin-Tazobactum 67%, Imipenem/meropenem 60%, ceftazidime 58%, Ciprofloxacin 58%, Piperacillin 58%, Amikacin 50%, Gentamicin 50%
Enterococcus species	13	Linezolid 100%, Vancomycin 100%, Gentamycin 71%, Penicillin 57%, Ampicillin 57%.
Pseudomonas aeruginosa	11	Imipenem 100%, Piperacillin-Tazobactum 100%, Ceftazidime 100%, Cefipime 100%, Levofloxacin 100%, Ciprofloxacin 100%, Amikacin 83%, Piperacillin 83%.

BLOOD STREAM INFECTIONS- IPD ANTIBIOGRAM

Total isolates=9

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
Salmonella typhi	44	Sensitive to all antibiotics Cefotaxime 100%, Ceftriaxone 100%, Chloramphenicol 100%, Ciprofloxacin 100%, Cotrimoxazole 100%,

URINARY TRACT INFECTIONS- ICU ANTIBIOGRAM

Total isolates=25

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
E. coli	60	Imipenem/Meropenem 100%, Amikacin 73%, Nitrofurantoin 60%, Piperacillin-Tazobactum /Amoxycillin-Clavulanic acid 60%, Gentamycin/ Tobramycin 60%.Levofloxacin 39% , Ciprofloxacin 13%, Tetracycline 20%, Cotrimoxazole 13%, Norfloxacin 6%, Ampicillin/Cefotaxime/ Ceftazidime/ Ceftriaxone 0%
Klebsiella pneumoniae	24	Imipenem/Meropenem 83%, Tetracycline 83%, Nitrofurantoin 50%, Norfloxacin 33%, Amikacin 17%, Gentamycin/ Tobramycin 17%.

URINARY TRACT INFECTIONS- IPD ANTIBIOGRAM

Total isolates= 69

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
E. coli	67	Imipenem 100%, Nitrofurantoin 96%, Amikacin 93%, Gentamycin/ Tobramycin 73%, Piperacillin-Tazobactum /Amoxycillin-Clavulanic acid 62%, Tetracycline 33%, Cotrimoxazole 31%, Levofloxacin 35%, Norfloxacin 24%,
Enterococcus	19	Vancomycin 100%, Linezolid 100%, Nitrofurantoin 85%, Penicillin 54%, Ampicillin 54%, Gentamycin 10%
Klebsiella pneumoniae	10	Tetracycline 100%, Imipenem 71%, Amikacin 71%, Gentamycin/ Tobramycin 57%, Piperacillin-Tazobactum /Amoxycillin-Clavulanic acid 57%, Levofloxacin43%, Ciprofloxacin 43%, Norfloxain 43%, Cefotaxime/ Ceftazidime/ Ceftriaxone 29%

URINARY TRACT INFECTIONS- OPD ANTIBIOGRAM

Total isolates= 57

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
E. coli	63	Imipenem 97%, Amikacin 97%, Nitrofurantoin 86%, Gentamycin/ Tobramycin 78%, Piperacillin-Tazobactum /Amoxycillin-Clavulanic acid 72%, Levofloxacin 72%, Norfloxacin 47%, Tetracycline 44%, Cotrimoxazole 42%,
Pseudomonas aeruginosa	23	Imipenem 100%, Piperacillin-Tazobactum 100%, Ceftazidime 100%, Amikacin 100%, Gentamycin/ Tobramycin 100%, Piperacillin 92%, Ciprofloxacin 50%,
Klebsiella pneumoniae	10	Imipenem 100%, Tetracycline 100%, Amikacin 50%, Piperacillin-Tazobactum /Amoxycillin-Clavulanic acid 50%, Gentamycin/ Tobramycin 50%, Levofloxacin 50%, Cefotaxime/Ceftriaxone 50%

SKIN AND SOFT TISSUE INFECTION- ICU ANTIBIOGRAM

Total isolates = 154

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
E coli	31	Imipenem/Meropenem/Ertapenem 100%, Chloramphenicol 96%, Amikacin 89%, Gentamycin/ Tobramycin 66%, Levofloxacin 51%, Piperacillin-Tazobactum /Amoxycillin-Clavulanic acid 47%, Tetracycline 38%, Cotrimoxazole 30%, Ciprofloxacin 28%, Cefotaxime/Ceftriaxone/Ceftazidime 13%, Piperacillin 9% Ampicillin 6%.
Staphylococcus aureus (MRSA=25%)	13	Linezolid 100%, Chloramphenicol 100%, Tetracycline 95%, Doxycycline 95%, Gentamycin 95%, Clindamycin 85%, Erythromycin 80% , Amoxycillin-Clavulanic acid 75%, Cotrimoxazole 60%, Ciprofloxacin 35%, Penicillin 5%
Acinetobacter	12	Imipenem/meropenem 26%,Tetracycline/Doxycycline 26%, Cotrimoxazole 21%, Amikacin 16%, Tobramycin/ Gentamycin 16%, Ciprofloxacin 16%, Levofloxacin 16%, Piperacillin-Tazobactum 6%, Piperacillin 5%, Cefotaxime/Ceftriaxone/Ceftazidime 5%.
Enterococcus species	12	Vancomycin 100%, Linezolid 100%, Penicillin 78%, Ampicillin 78%, Gentamycin 78%

SKIN AND SOFT TISSUE INFECTION- IPD ANTIBIOGRAM

Total isolates=697

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
E coli	21	Imipenem 100%, Amikacin 88%, Chloramphenicol 87%, Gentamycin/ Tobramycin 71%, Piperacillin-Tazobactum/ Amoxycillin-Clavulanic acid 55%, Cotrimoxazole 40%, Tetracycline 37%, Levofloxacin 31%, Ciprofloxacin 19%, Ceftazidime/Ceftriaxone/Cefotaxime 12%
Staphylococcus aureus	20	Linezolid 100%, Chloramphenicol 95%, Doxycycline 93%, Tetracycline 91%, Gentamycin/ Tobramycin 81%, Clindamycin 76%, Cotrimoxazole 64%, Amoxycillin-Clavulanic acid 58%, Erythromycin 57%, Ciprofloxacin 29%, Penicillin 7%
Pseudomonas aeruginosa	18	Imipenem 72%, Piperacillin-Tazobactum 78%, Ceftazidime 74%, Amikacin 66%, Levofloxacin 63%, Gentamycin/ Tobramycin 63%, Ciprofloxacin 62%, Piperacillin 56%
Enterobacter species	11	Imipenem /Meropenem 96%, Chloramphenicol 76%, Levofloxacin 72%, Amikacin 69%, Tetracycline 69%, Gentamycin/Tobramycin 59%, Ciprofloxacin 56%, Cotrimoxazole 56%, Piperacillin-Tazobactum 66%, Amoxycillin-Clavulanic acid 20%, Cefotaxime/Ceftriaxone 2%

SKIN AND SOFT TISSUE INFECTION- OPD ANTIBIOGRAM

Total isolates=127

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
Staphylococcus aureus (MRSA= 39%)	42	Linezolid 100%, Doxycycline 100%, Chloramphenicol 96%, Tetracycline 89%, Gentamycin 79%, Clindamycin 79%, Cotrimoxazole 75%, Amoxycillin-Clavulanic acid 61%, Erythromycin 54%, Ciprofloxacin 21%, Penicillin 14%.
Pseudomonas aeruginosa	18	Imipenem/Meropenem 100%, Piperacillin-Tazobactum 100%, Ceftazidime 92%, Levofloxacin 83%, Piperacillin 83%, Ciprofloxacin 67%, Amikacin 75%, Gentamycin/ Tobramycin 75%,.
Beta hemolytic Streptococci	15	Penicillin 100%, Levofloxacin 100%, Clindamycin 80%, Erythromycin 80%, Chloramphenicol 70%, Tetracycline 50%,
E coli	13	Imipenem /Meropenem100%, Levofloxacin 100%, Chloramphenicol 88%, Amikacin 88%, Ciprofloxacin 77%, Piperacillin-Tazobactum 66%, Amoxycillin-Clavulanic acid 55%, Gentamycin/Tobramycin 55%, Cotrimoxazole 33%, Cefotaxime/Ceftriaxone 22%

RESPIRATORY INFECTIONS: ICU ANTIBIOGRAM

Total isolates = 109

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
Klebsiella pneumoniae	35	Imipenem/Meropenem/Ertapenem 100%, Amikacin 100%, Tobramycin 82%, Chloramphenicol 79%, Gentamycin 74%, Piperacillin-Tazobactum/ Amoxycillin-Clavulanic acid 74%, **Levofloxacin 92%,**Ciprofloxacin 68%, Tetracycline 68%, Cotrimoxazole 45%, Cefotaxime/Ceftriaxone/Ceftazidime 24%.
Pseudomonas aeruginosa	31	Imipenem/Meropenem 100%, Amikacin 100%, Ceftazidime 97%, Gentamycin/ Tobramycin 97%, Piperacillin-Tazobactum 94%, Levofloxacin 94%, Ciprofloxacin 94%, Piperacillin 71%,
Acinetobacter	29	Tetracycline 87%, Doxycycline 87%, Levofloxacin 61%, Imipenem 58%, Meropenem 54%, Amikacin 51%, Gentamicin/Tobramycin 51%, Piperacillin-Tazobactum 48%, Ciprofloxacin 45%, Cotrimoxazole 41%, ceftazidime 35%, Piperacillin 35%,

RESPIRATORY INFECTIONS: IPD ANTIBIOGRAM

Total isolates = 41

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
Klebsiella pneumoniae	53	Imipenem 100%, Chloramphenicol 86%, Amikacin 77%, Levofloxacin 72%, Piperacillin-Tazobactum/ Amoxycillin-Clavulanic acid 68%, Gentamycin/Tobramycin 50%, Ciprofloxacin 47%, Tetracycline 45%, Cotrimoxazole 27%, Cefotaxime/Ceftriaxone/Ceftazidime 18%.
Acinetobacter	29	Imipenem 88%, Tetracycline 88%, Doxycycline 88%, Levofloxacin 88%, Piperacillin-Tazobactum 77%, Amikacin 77%, Cotrimoxazole 66%, Gentamicin/Tobramycin 55%, Ciprofloxacin 45%, ceftazidime 44%, Piperacillin 44%,
Pseudomonas aeruginosa	20	Imipenem 100%, Ceftazidime 100%, Piperacillin-Tazobactum 100%, Amikacin 100%, Gentamycin/ Tobramycin 100%, Piperacillin 100%, Levofloxacin 100%, Ciprofloxacin 100%,

RESPIRATORY INFECTIONS: OPD ANTIBIOGRAM

Total isolates = 9

Most Common Organism	Prevalence %	Antibiotic Sensitivity (%)
Klebsiella pneumoniae	78	Imipenem 100%, Chloramphenicol 100%, Tetracycline 100%, Amikacin 88%, Gentamycin/Tobramycin 88%, Levofloxacin 63%, Piperacillin-Tazobactum/ Amoxycillin-Clavulanic acid 63%, Ciprofloxacin 62%, Cotrimoxazole 50%, Cefotaxime/Ceftriaxone/Ceftazidime 38%, Ampicillin13%.

ANTIBIOTIC POLICY

Blood Stream Infections				
Location	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
ICU	*Kleb.pneumoniae* *Acinetobacter* *Enterococcus* *Pseudomonas* *E coli*	Meropenem* or Imipenem-cilastatin* +Amikacin		Escalate or Deescalate according to the culture report
IPD	*Salmonella typhi* *Staphylococcus aureus*	Ceftriaxone 2 g IV BD for 2 weeks +/- Azithromycin 500 mg BD for 7 days	Cotrimoxazole 960 mg BD for 2 weeks	
OPD	*Salmonella typhi*	Cefixime 20mg/kg/day for 14 days or Azithromycin 500 mg BD for 7 days.	Cotrimoxazole 960 mg BD for 2 weeks	

URINARY TRACT INFECTIONS				
Location	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
ICU (Complicated Pyelonephritis)	*E coli* *Klebsiella pneumoniae* *Enterococci* *Staphaureus*	Piperacillin-Tazobactam 4.5gm IV 6 hourly or Amikacin 1 g OD IV or Cefoperazone-Sulbactam 3gm IV 12 hourly	Imipenem 1g IV 8 hourly or Meropenem 1gm IV 8 hourly	Get urine cultures before antibiotics & switch to a narrow spectrum agent based on sensitivity. Treat for 10-14 days. De-escalate. Monitor renal function if aminoglycoside is used.
IPD (Uncomplicated Pyelonephritis)	*E coli* *Enterococci* *Klebsiella pneumoniae* *Pseudomonas aeruginosa*	Amikacin 1 g OD IM/IV or Gentamicin 7mg/kg/ day OD (Monitor renal function closely and rationalize according To culture report)Complete total duration of 14 days	Piperacillin-Tazobactam 4.5g IV 6 hourlyor Cefoperazone-Sulbactam 3g IV 12 hourly	Urine culture and susceptibilities need to be collected before starting antimicrobial treatment to guide treatment.
OPD uncomplicated Cystitis	*E coli* *Pseudomonas aeruginosa* *Klebsiella pneumoniae* Proteus spp	Nitrofurantoin 100 mg BD for 7 daysor Cotrimoxazole 960mg BD for 3-5 days or Ciprofloxacin 500 mg BD for 3-5 days	Cefuroxime 250 mg BD for 3-5 days	Get urine cultures before antibiotics & modify therapy based on sensitivities.

Asymptomatic bacteriuria **NOT** to be treated except in pregnant women and immunocompromised patients.

Skin and Soft Tissue Infections				
Location	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
ICU (Necrotizing fasciitis)	*E coli* *Staphylococcusaureus* *Acinetobacter* *Enterococcus species* *Enterobacter species*	Piperacillin-Tazobactam 4.5gm IV 6 hourly or Cefoperazone-Sulbactam 3gm IV 12hourly AND Clindamycin 600-900mg IV 8 hourly.Duration depends on the progress	Imipenem* 1g IV 8hourly or Meropenem 1gm IV 8hourly AND Clindamycin 600-900mg IV TDS/linezolid 600 mg IV BD	Early surgical intervention crucial
IPD (Cellulitis)	*E coli* *Staphylococcus aureus* *Pseudomonas aeruginosa* *Enterobacter species* *Acinetobacter*	Amoxicillin-Clavulanate 1.2gm IV TDS/625 mg oral TDS or Ceftriaxone 2gm IV OD	Clindamycin 600-900mg IV TDS	Treat for 5-7 days.
OPD (Furuncul osis)	*Staphylococcus aureus* *Pseudomonas aeruginosa* *β Streptococci*	Amoxicillin-Clavulanate 1.2gm IV/Oral 625 TDS or Ceftriaxone 2gm IV OD Duration – 5-7 days	Clindamycin 600-900mg IV TDS	Get pus cultures before starting antibiotics

Respiratory tract Infections				
Location	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
ICU (VAP)	*Kleb pneumoniae Pseudomonas aeruginosa Acinetobacter species*	BL-BLI Piperacillin+tazobactam 4.5 gm 6 hrly or Cefoperazone-sulbactam 3 gm 12hrly OR Antipseudomonal Carbapenem PLUS Aminoglycoside eg.amikacin 20 mg/kg/day OrAntipseudomonal fluoroquinolone e.g. Ciprofloxacin 400 mg 8 hrly, levofloxacin 750 mg daily	Carbapenems + doxycycline	De-escalate/ escalate as per the culture report
IPD	*Kleb. pneumoniae Acinetobacter Pseudomonas*	Piperacillin+tazobactam 4.5 gm 6 hrly or Cefoperazone-sulbactam 3 gm 12 hrly	levofloxacin 750 mg daily	
OPD Community acquired Pneumonia	*S. pneumoniae, H.influenzae, Legionella, E.coli, Klebsiella sp., S.aureus*	Mild to moderate cases Amoxycillin- 500mg-1 g TDS oral. If IV indicated, amoxycillin-clavulanate 1.2g IV TDS or Ceftriaxone 2g IV OD.For Severe cases Amoxycillin-clavulanate 1.2 g IV TDS Or Ceftriaxone 2g IV OD Duration 5-8 days	Piperacillin-Tazobactam 4.5gm IV 6 hourly or Imipenem 1g IV 6hourly or Cefoperazone-Sulbactam 3gm IV 12 hourly	If atypical pneumonia suspected, Doxycycline 100mg bd or Azithromycin 500 mg oral/IV OD

Antimicrobial guidelines for prophylaxis of Surgery
Case definitions
Surgical Wound Classification

1. Class I/Clean: uninfected operative wound in which no inflammation is encountered & respiratory, alimentary, genital, or uninfected urinary tract is not entered. Operative incisional wounds following blunt trauma are included here.
2. Class II/ Clean-Contaminated: Operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination.
3. Class III/Contaminated: Open, fresh, accidental wounds. Operations with major breaks in sterile technique or gross spillage from the GIT.
4. Class IV/Dirty-Infected: Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera.

Perioperative prophylaxis

a. Choosing prophylactic antibiotics

- Antibiotics should be chosen on the basis of their effectiveness against the pathogens most likely

to be encountered rather than against every possible pathogen. Skin flora (eg, *Staphylococcus* organisms) are the usual target, so first-generation cephalosporins are recommended (cephalexin, cephalothin) in most studies. Few studies also recommend cefuroxime.

- Patients with a history of anaphylaxis or urticaria after penicillin therapy should not receive prophylaxis with a beta-lactam antibiotic. Vancomycin or clindamycin should be used as alternative.

b. Timing of prophylactic antibiotics

- Give first dose before incision
- Antibiotics should be administered before an incision is made to ensure that antimicrobial levels in the tissue are adequate and maintained for the duration of the procedure.
- Prophylaxis should be started preoperatively in most circumstances, ideally within 30-60 minutes before incision, except for Vancomycin and Fluoroquinolones which need to be given 120 minutes before incision.

c. Route of administration

- Prophylactic antibiotics for surgical procedures should be administered intravenously.

d. Dose selection

- The dose of an antibiotic for prophylaxis is same **as for therapy of infectio**n.

e. Duration

- **Continue no longer than 24 hours postoperatively (Except cardiac surgery where data is conflicting)**
- Most studies have demonstrated efficacy of postoperative antibiotic prophylaxis for only 12 hours or less. Whenever short and long courses are compared, the shorter course has proven equally effective. A single dose is as effective as multiple doses, and antimicrobial prophylaxis after wound closure is unnecessary.
- Prolonged antibiotic prophylaxis beyond 24 hours is not only ineffective in reducing infections but increases antimicrobial resistance and the risk of colitis due to *Clostridium difficile*.

f. Redose for longer surgeries

- Patients undergoing surgery that extends beyond two half-lives of an antibiotic should be re-dosed intraoperatively.
- An additional dose of prophylactic agent is not indicated in adults, unless there is blood loss of upto 1500 ml during surgery or haemodilution of up to 15 ml/kg.

Pathogen-specific antimicrobial therapy according to the pathogen isolated

Surgical Wound Classification	Common Organisms	Antimicrobial prophylaxis
Class I/Clean	Gram Positive cocci (*S. aureus*, CoNS)	None or single perioperative dose of cefuroxime/ cephalexin (Ideally 2grams)
Class II/ Clean-Contaminated	Gram Negative Bacilli, Anaerobes *S. aureus*	**1stLine:** Cefazolin or Ampicillin-sulbactam or Ceftriaxone (in patients of acute cholecystitis or acute biliary tract infections) **Alternative: In case of allergies;** if mixture of GP and GN is suspected: Ceftriaxone only if not ESBL clindamycin or vancomycin with cefazolin, aztreonam, gentamicin, or single-dose fluoroquinolone in ßlactamallergic
Class III/ Contaminated	Gram Negative Bacilli Anaerobes	**1st line:** Cefazolin + Metronidazole **2nd Line:** Metronidazole + Aminoglycoside/ Fluoroquinolone
Class IV/Dirty-Infected	GramNegative bacilli, Anaerobes may be mixed with Gram positive bacteria	**1st Line:** Cefazolin + metronidazole, **Treatment for infected surgical wounds** Ertapenem + Clindamycin + aminoglycoside/aztreonam **Or** fluoroquinolone+ metronidazole + aminoglycoside/fluoroquinolone

Use of Anti-microbial Agents (AMA) in Obstetrics & Gynaecology

Clinical condition / procedure	Common pathogens	Preferred AMA	Alternate AMA	Comments
Vaginal delivery: For GBS (Group B Streptococcus) prophylaxis in women who do not know their GBS status in the following situations: Preterm labour (<37 wks) Prolonged rupture of membranes (>18 hrs) Fever during labour or chorioamnionitis History of previous baby with GBS infection. Bladder or kidney infection due to GBS.	Group B Streptococci	Ampicillin 2gm IVfollowed by 1gm IV 4-6 hrly till delivery	Cefazolin 2 g IV followed by 1 g 8 hrly till delivery If allergic, Vancomycin 1 gm IV 12 hrly till delivery	Not recommended routinely for normal vaginal delivery. Delivery is considered akin to drainage of an abscess as the fetus and placenta is removed which are the nidus of infection

3rd or 4th degree Perineal tear	**Gram positive** *Staph. aureus*, **Gram negative** Enterobacteriaceae, **Anaerobes**	Single dose cefoxitin or cefotetan 1gm IV	Single dose Cefazolin 1 gm IV plus metronidazole 500 mg IV OR single dose IV cefuroxime 1.5 gm plus metronidazole 500 mg IV OR single dose IV 1.2 gm amoxicillin/ clavulanic acid. If allergic, single dose IV clindamycin 600-900 mg	Prophylaxis is considered to prevent adverse outcomes arisingfrom infection eg fistulas
Preterm pre-labour rupture of membranes	**Gram positive** GBS **Gram negative:** Enteric gram	IV Ampicillin 2gm followed by 1 gm 4-6 hourly for 48 hours followed by oral amoxicillin 500 mg 8	If erythromycin 333 mg is not available, use erythromycin stearate 250 mg 6 hourly for 7 days	

	negative bacilli, Ureaplasma, mycoplasma **Anaerobes** (including *G. vaginalis*	hourly for 5days PLUS oral erythromycin 333 mg 8 hourly for 7 days		
Caesarean delivery	**Gram positive aerobes:** GBS, Staphylococci, Enterococci, **Gram egative Aerobes:** *E. coli, Klebsiella, Proteus* **Anaerobic GramPositive cocci** Peptococci, Peptostreptococci **AnaerobicGram negative bacilli**: *Bacteroides,*	Single dose cefazolin 2gm IV Dose is 3gm if patient is >100kg	If allergic, single dose clindamycin 600-900 mg IV + Gentamicin 1.5mg/kg IV	Puerperal endometritis is polymicrobial,(aerobic–anaerobic). These organisms are part of vaginal flora and are introduced into the upper genital tract coincident with vaginal examinations during labour and/or instrumentation during surgery

	Prevotella spp. **Facultatively anaerobic Gram-ariable rod:** *G.vaginalis*			
Rescue cervical encerclage	Vaginal flora	Inj Ampicillin 2 gm single dose		To prevent ascending infection from vaginal flora to unexposed membranes
Puerperal sepsis / Septic abortion /chorioamnionitis	**Gram positive***:* Streptococci *(A,B,D),Staph.aureus* **Gram negative***: E.coli,*Enterobacteria ceae *including Klebsiella, Enterobacter, Citrobacter, Proteus mirabilis. Pseudomonas aeruginosa,*	Inj. Piperacillin +Tazobactem 4.5 gm IV 8 hrly X 7-14 days	Clindamycin 600-900 mg IV 8 hourly+ Gentamicin 60 mg IV 8 hourly+ metronidazole 500 mg IV 8 hourly or Ampicillin-Sulbactam 3 g IV Q6H	Usually polymicrobial

	Anaerobes *Gardnerella vaginalis, Bacteroides Clostridium perfringes,*			
Hysterectomy (AH, VH, Laparoscopic) and surgeries for pelvic organ prolapse and/or stress urinary incontinence	Polymicrobial: **Gram positive:** Staphylococci, enterococci, **Gram Negative**: aerobic gram negative, **Anaerobes** *Bacteroides* spp,	Cefazolin 2 gm IV single dose Dose is 3 gm if patient is >100kg	Cefuroxime 1.5 g IV single dose OR If allergic to cephalosporin, Clindamycin 600 -900 mg IV + gentamicin 1.5mg/kg IV	In AH & LH, vagina is opened at end of procedure & exposure to vaginal flora is brief.In VH, there is greater colonisation of surgical site. In AH for cancer with resection of upper vagina, there may be colonization with anaerobes. In such cases, metronidazole 500 mg IV may be added. If BV is suspected, oral metronidazole

				500 mg BD for 7 days is given,beginning at least 4 days pre-op
Laparoscopy (uterus and/or vagina not entered) / Hysteroscopy / Ectopic pregnancy	Skin commensals: *Staph. aureus*	Cefazolin 1 gm IV single dose	Cefuroxime 1.5 g IV sinlge dose If allergic, use IV clindamycin 600 mg	
Abortions (medical and surgical)	*Chlamydia, Neisseria gonorrhoeae*	Azithromycin 1 g orally plus metronidazole 800 mg orally at time of abortion	Doxycycline 100 mg orally twice daily for 7 days, starting on day of abortion, plus metronidazole 800 mg orally at time of abortion	No prophylaxis for missed / incomplete abortion
HSG	*Chlamydia, Neisseria gonorrhoeae*	Doxycycline 100 mg orally Before procedure		Doxycycline continued twice daily for 5 days if there is history of PID or fallopian tubes are dilated at procedure

Pelvic Inflammatory Disease (mild to moderate)	*N. gonorrhoeae*, *C. trachomatis* and anaerobes. *E. coli*, *Bacteroides* GBS, GAS, S. aureus, respiratory pathogens (eg, *H. influenzae*, *S. pneumoniae*,	NACO: Tab. Cefixime 400 mg orally STAT **PLUS** Tab. Metronidazole 400 mg BD X 14D **PLUS** Cap. Doxycyline, 100 mg bd X 14 D	CDC: Levofloxacin500mg OD X 14 days OR Ofloxacin 400 mg OD X 14 days With or without Metronidazole 500 mg BD X 14 days OR Ceftriaxone 250 mg IM single dose plus Doxycycline orally 100 mg BD X 14 days with or without Metronidazole 500 mg BD X 14 days	
Pelvic InflammatoryDisease (severe) eg tubo-ovarian abscess, pelvic abscess		Cefotetan 2 g IV BD PLUS doxycycline 100 mg	Cefoxitin 2 g IV every 6 hours PLUS Doxycycline100mg	An attempt should be made to obtain cultures and deescalate

		orally or IV BD	orally or IV every 12 hours OR Clindamycin 900 mg IV every 8 hours PLUS gentamicin loading dose IV or IM (2 mg/kg), followed by maintenance dose (1.5 mg/kg) every 8 hours. Single daily dosing (3–5 mg/kg) can be substituted	based on that. Duration is two weeks, but can be extended dependingupon clinical situation. Antibiotics may be altered after obtaining culture reports of pus/or blood
Vaginal candidiasis	*C. albicans, C. glabrata, C. tropicalis*	Tab Fluconazole 150 mg orally single dose **OR** local Clotrimazole 500 mg vaginal tablet once only	Miconazole, nystatin vaginal tablets/creams	Treat for 7 days in pregnancy, diabetes Recurrent infections: 150 mg Fluconazole on day 1,4,7 then weekly for 6months
Vaginal trichomoniasis	*T. vaginalis*	Tab.Secnidazole 2 gm oral, single dose **OR**		Alcohol avoided during treatment and 24 hours after

		Tab. Tinidazole 500 mg orally,twice daily for 5 days **OR** Tab.Metronidazole 400 mg, twice daily for 7 days		metronidazole or 72 hours after completion of tinidazole to reduce possibilityof disulfiram-like reaction. Partner treatment essential
Bacterial vaginosis	Overgrowth of anaerobes *(Gardnerella vaginalis)*	**Metronidazole** 400 mg orally BD X 7 days OR **Metronidazole** gel 0.75%,one applicator (5 g) intravaginal x 5 days OR **clindamycin** cream 2%,one applicator (5 g) intravaginal x 7 days	**Secnidazole** 2 g orally OD X one day OR **Tinidazole** 2 g orally OD X 2 days OR **Tinidazole** 1 g orally OD X 5 days OR c**lindamycin** orally 300 mg BD X 7 days OR c**lindamycin** ovules 100 mg intravaginally OD HS for 3 days*	Refrain from sexual activity or use condoms during the treatment. Clindamycin cream is oil-based and might weaken latex condoms

Dosage Guide for Commonly Used Antimicrobial Agents

ANTIBIOTICS	ADVERSE REACTION	ROUTE	PAEDIATRIC DOSE	ADULT DOSE
Amikacin	Nephrotoxicity, Ototoxicity	Intravenous	15-22.5 mg/Kg/day in 2-3 doses	15mg/Kg/day q 8-12 hours, max doses 1.5mg/Kg
Amoxycillin	Fever, rash, diarrhea, abdominal cramps, AST ALT elevation.	Oral	20-50mg/Kg/day, 3-4 doses	250-500mg q 8 hourly
Amoxycillin-clavunate (co-amoxyclav)	Rash, diarrhea, abdominal, AST ALT elevation	Oral, Intravenous	40mg/kg/day (amoxicillin) in 2 doses 90mg/kg/day if penicillin resistant *S. pneumoniae*suspected in otitis media 100mg/kg/day	375mg 8hourly 625-1000mg 12 hourly
Ampicillin	Hypersensitivity reaction, nausea,	Intravenous or	100-400 mg/kg/day in 4 doses (IV)	500 mg-1gm q 6 hourly

	diarrhea, exfoliative dermatitis, seizures, precipitates infectious mononucleosis rash, interstitial nephritis.	Oral		
Azithromycin	Leukopenia, transient elevation of liver enzymes, renal toxicity.	Oral	10 mg/kg/day once daily Enteric fever 20 mg/kg/day once daily	500mg daily
Azetronam	Rash, Diarrhoea , vomiting, AST, ALT elevation	Intravenous	30 - 120mg/kg/day Q 6-8 hourly In cystic fibrosis max dose 200 mg/kg/day	1-2g q 8 hourly, Max dose 8gm in 24 hours
Benzathine penicillin	Hypersensitivity and Jarisch Herxheimer reaction, haemolytic anemia, seizures with high doses in renal	Intramuscular	1,200,000 units(>30 Kg) 600,000 units (<30 Kg)	1.2-2.4 million units/dose

	failure			
Cefadroxil	Rash eosinophilla	Oral	30 mg/kg/day in 2 doses	500mg bid or 1 g bid
Cefazolin	Leukopenia, eosinophilia, rash, transient elevation of liver enzymes renal toxicity	Intravenous	100 mg/kg/day 3-4 divided doses	0.52gm q 6-8 hourly
Cefepime	Same as third generation cephalosporins. Adjust dose in renal failure.	Intravenous		1-4gm/day 2-3 doses
Cefixime	Diarrhoea, Leukopenia, renal toxicity, transient elevation of liver enzymes.	Oral	15mg/kg/day in 2 divided doses, 20mg/kg/day in 2 divided doses for enteric fever.	400mg/day in 1-2 divided doses.

Cefotaxime	Arrythmia, transient elevation of liver enzymes, renal toxicity.	Intravenous	100mg/kg/day in 3-4 divided doses, 200mg/kg/day in 4 divided doses for meningitis	1-2gm 6-8 hourly
Ceftazidime	Hypersensitivity reaction, dizziness, rash, diarrhea, colitis, exfoliative dermatitis, thrombocytopenia	Intravenous Intramuscular	75-100mg/kg/day in 3 divided doses 100mg/kg/day in meningitis (IV)	1-2g q 8-12 hourly (IV)
Ceftriaxone	Gall bladder sludging , transient elevation of liver enzymes, renal toxicity	Intravenous	50-100 mg/kg/day in 2 divided doses Meningitis 100mg/kg/day in 2 divided doses	1-2gm q 12-24 hourly
Cefuroxime	Leukopenia, eosinophilia, allergic reaction, transient	Intravenous	75-100mg/kg/day in 3 divided doses	750mg- 1.5g q 8 hourly

	elevation of liver enzymes , renal toxicity			
Cefuroxime	Leukopenia, eosinophilia, allergic reaction, transient elevation of liver enzymes , renal toxicity	Oral	20-30mg/kg/day in 2 divided doses	250-500md bid
Cephalexin	Transient neutropenia, AST and ALT elevation, arthralgia, rash, eosinophilia.	Oral	30-40mg/kg/day in 3 divided doses	250-500mg q 8 hourly
Chloramphenicol	Bone marrow suppression, aplastic anaemia, grey baby syndrome, hemolysis in G6PD deficiency	Oral Intravenous	75-100mg/kg/day in 4 divided doses Avoid in infants less than 3 months	50mg/kg/day in 4 divided doses

Ciprofloxacin	Nausea, vomiting, abdominal discomfort, arthralgia, photosensitivity transient elevation of liver enzymes	Oral Intravenous	20-30mg/kg/day in 2 divided doses	250-750mg q 12 hourly
Clarithromycin	Transient elevation of liver enzymes, renal toxicity, nausea, abdominal cramps	Intravenous Oral	15mg/kg/day in 2 divided doses	250-500mg bid
Clindamycin	Diarrhea, nausea, pseudomembranous colitis, skin rash, Erythema multiforme , raised ALT AST, thrombocytopenia, leucopenia	Oral Intravenous	40-60mg/kg/day in 3-4 divided doses	150-300 mg q 6-8 hourly (oral, iv) Severe infections 300-600 mg 8 hourly IV

Cloxacillin	Dose related neutropenia, elevated AST, ALT, Cholecystitis interstitial nephritis.	Oral Intravenous	50-100mg/kg/day in 3-4 divided doses. 100-200mg/kg/day divides q 6 hourly	250-500mg/kg/day in 3-4 divided doses 1-2 gram q 6 hourly
Cotrimoxazole	Megaloblastic anaemia, distrurbance, rash, erythema mutliforme major/minor	Oral	5-10mg/kg/day in 2 divided doses (5-0 mg trimethoprim) 20mg/kg/day in 4 divided doses in Pneumocystis jirovecii pneumonia	160mg (Trimethoprim) bid
Ertapenem	Diarrhoea, nausea, vomiting, headache, hallucination, seizures, arrhythmia, pseudomembranous colitis, dose reduction in renal	Intravenous Intramuscular	3-12 years: 15mg/kg/day twice daily. (not to exceed 1gm/day)	13 years and above 1gm IV infusion/ IM once daily in 3-5 ml of lidocain CI if hypersensitivity to lidocaine/β lactam

	failure			
Erythromycin	Arrhythmia Jaundice	Oral	40on 4 divided doses	250-500mg q 6 hourly
Furazolidine	Avoid alcohol, tyramine containing food, Mao inhibitors, Nausea headache, dizziness, fall in BP, urticarial, safety in pregnancy unknown	Oral	100mg 3-4 times a day 5mg/kg in 3-4 divides doses (not below one year)	100mg 3-4 times a day
Gentamicin	Nephrotoxicity ototoxicity and optic neuritis	Intravenous Intramuscular	5-7.5 mg/kg/day in 2-3 divided doses	1.3-6 mg/kg/day in 3 divided doses
Imipenemcilastin	Nausea, diarrhea, rash	Oral	Intravenous	500mg once daily
Linezolid	Peripheral and optic neuropathy, thrombocytopenia, hypertension,	Oral Intravenous	10mg/kg/dose 6-8 hourly (oral, IV)	400-600 mg q 12 hourly

	myelosuppression, colitis.			
Meropenem	Hypotension, transient elevation of liver enzymes, renal modification in renal failure	Intravenous Oral	7.5 mg/kg/day/dose (IV) divided doses in meningitis	1.5-3gm/day in 3 divided doses 6gm/day in meningitis
Metronidazole	Nausea, metallic taste, disulfuran like reaction with alcohol, peripheral neuropathy	Intravenous Oral	7.5 mg/kg/day dose 3 times/day 30-50mg/kg/day in 3 divided doses for liver abscess	500-700 q 8 hourly
Nalidixic acid	Hepatotoxicity, myalgia, leukopenia, vertigo, rash, dizziness, pseudotumor cerebri, seizure, avoid in G6PD deficiency	Oral	8 mg/kg/day in 2 divided doses	1gm 4 times/day

Nitofurantoin	Discoloration of urine, vertigo, rash, methemoglobinemia, cholestatic jaundice, hepatocellular damage and neuropathy. Avoid at term and labour.	Oral	8 mg/kg/day in 2 divided doses	50-100 mg q 6 hourly (5-7mg/kg/day in 4 divided doses max dose 400mg)
Norfloxacin	Sam as quinolones	Oral	20-30 mg/kg/day in 2 divided doses	200-400 mg twice daily
Ofloxacin	Leukopenia, transient of liver enzymes, renal toxicity. May precipitate psychosis/seizures,photosensitivity.	Oral Intravenous	20 mg/kg/day in 2 divided doses	200-400 q 12 hourly
Penicillin G	Hypersensitivity reaction like anaphylaxis rare.	Oral Intravenous	50,000units/kg/ dose 6 hourly (Oral) 200,000-400,000	2-24 million units day in divided doses q 4-6 hours (IV)

	nonfatal reactions are like serum sickness, rash contact dermatitis seen in 1 in 1000 adults. Jarisch Herxheimer reaction, haemolytic anaemia with high doses		units/kg/day in 4 divided doses (IV)	
Penicillin V	Rash, haemolytic anaemia interstitial nephritis, seizure with high doses.	Oral	20-50 mg/kg/day in 4 divided doses	250-500 mg every 6-8 hourly.
Piperacillin – Tazobactum	Leukopenia, transient elevation of liver enzymes, renal toxicity.	Intravenous	200-400mg/kg/day in 3-4 divided doses	4.5 gm q 8hourly
Teicoplanin	Hypersensitivity reactions, rash, less	Intravenous Intramuscular	10mg/kg/day /dose every 12 hours for 3	400mg once daily (6-30mg/kg/day)

	nephrotoxic as compares to Vancomycin		doses the 10mg/kg/day once daily	
Tigecycline	Nausea, vomiting, allergic reactions, photosensitivity, pseudo tumor cerebri, pancreatitis. No dose adjustment to renal failure	Intravenous	Above 10 years	100mg followed by 50mg every 12 hurly infusion over 30-60 minutes.
Vancomycin	Red man syndrome, oto-toxicity, nephrotoxicity	Intravenous	40-60 mg/kg/day in 3-4 divided doses	0.5gm q 6 hourly or 1gm q 12 hourly

Drug doses in Pediatric Age group

Drug name	Dose	Frequency	Maximum dose	Comments
Cefepime Infants >14 days of age and Children >40 kg in weight	50 mg/kg	q 12 h		
Ceftazidime Infants and children <12 years	100–15 mg/kg/d	Divided q 8 h	6 g	
Cefotaxime Infants and children a) < 50 kg b) >12 years and >50 kg	100–200 mg/kg/d 1–2 g	Divided q6-8 h q 8 h	2 g	
Ceftriaxone Infants and children	50-75 mg/kg/d	Divided q 12 h	2 g	
Vancomycin Infants and children	40 mg/kg/d	Divided q 6-8 h	2 g	

Linezolid Infants and children <12 years Children >12 years of age and adolescents	10 mg/kg 10 mg/kg	q 8 h q 12 h		
Piperacillin	100-300 mg/kg/d	q 8 h	4 g	
Ciprofloxacin	20–30 mg/kg/d	divided every 12 h	800 mg	
Levofloxacin Children 6 months to 5 years of age Children >5 years of age	10 mg/kg 10 mg/kg	q12 h q 24 h	500 mg	
Amikacin Infants and children	15–22.5 mg/kg/d	q 24 h		

Gentamicin	5-7.5 mg/kg/d	q 24 h		If normal renal function
Meropenem Infants ≥3 months of age and children	20 mg/kg	q 8 h	1 g	
Imepenem-cilastin Infants < 3 months of age Infants > 3 months of age and children	100 mg/kg/d 60-100 mg/kg/d	Divided q 6 h Divided q 6 h	4 g	
Fluconazole	12 mg/kg/d	q 24 h		
Anidulafungin Children 2– 17 years of age	1.5 mg/kg/day			Limited experience
Micafungin Children >2 years of age	1–4 mg/kg/day		150 mg	Limited experience

Caspofungin Children 3months-17 years	loading dose of 70 mg/m2/day on day 1 followed by 50 mg/m2/		70 mg; may increase to 70 mg/m2/day if clinical response is inadequate.	
Clindamycin	10 mg/kg/dose	q 6-8 h	900 mg Q 8	

Treatment of Muti-Drug Resistant Bacterial Pathogens

1. Methicillin- Resistant *S. aureus* (MRSA)

a. These organisms are considered resistant to all penicillins, cephalosporins and macrolides.

b. Though MRSA strains may be reported as susceptible to fluoroquinolones, aminogycogides, chloramphenicol and doxycycline in-vitro, these drugs are NOT to be used alone or as initial treatment for serious MRSA infections.

c. Rifampicin use should be avoided in diseases other than Mycobacterial diseases.

d. The drug of choice for treatment of infections due to MRSA is the glycopeptides i.e Vancomycin and Teicoplanin.

e. Linezolid can be used to treat skin and soft tissue infections caused by MRSA.

f. Mupirocin local application (intranasally bid x 5 days) for eradicating nasal carriage.

g. Daptomycin: Daptomycin is an intravenous antibiotic approved to be used for the treatment of complicated skin infections and *Staphylococcus aureus* bacteraemia. Daptomycin should NOT be used for treatment of pneumonia due to its inactivation by surfactant.

2. Vancomycin Resistant Enterococcus (VRE)

a. Enterococci are a therapeutic challenge because of their intrinsic resistance to many antibiotics. The acquisition of resistance to vancomycin by enterococci has seriously affected the treatment and infection control of these organisms.

b. The treatment for VRE should be based on infection severity and in-vitro susceptibility of the strain to other antibiotics.
c. Linezolid: Linezolid is the only drug specifically approved for the treatment of VRE-blood stream infections. Linezolid may be particularly useful in patients who require oral or outpatient therapy (when intravenous therapy is undesirable), who are intolerant to glycopeptides, or who have impaired renal function. Linezolid is a bacteriostatic agent; furthermore, linezolid toxicity when administered for prolonged courses may limit its use in VRE endocarditis.
d. Ampicillin: Isolates that remain relatively susceptible to penicillin or ampicillin may be treated with high doses of these agents.
e. Daptomycin: Not approved for treatment of VRE infection. Not approved for treatment of endocarditis. Limited clinical information for VRE, but bactericidal activity makes consideration of this agent as sole therapy in serious infections. However, emergence of resistance during therapy has been reported.
f. Doxycycline: Not a first line therapy. For susceptible isolates, not for bacteremia or endocarditis. It should not be used as monotherapy.
g. Nitrofurantoin: Uncomplicated UTIs have been treated successfully with nitrofurantoin.
h. Fosfomycin: For urinary tract infections (cystitis) with isolates susceptible to fosfomycin.
i. Chloramphenicol: For chloramphenicol-susceptible isolates of *E faecium* and *E. faecalis*. Not a first-line therapy and it should not be used as monotherapy.
j. Gentamicin or streptomycin: To be used in combination with ampicillin for the treatment of enterococcal endocarditis caused by organisms susceptible in vitro to either agent; streptomycin is used when gentamicin cannot be used because of resistance.

k. Tigecycline: Tigecycline has *in vitro* activity against a broad spectrum of Gram-positive and -negative bacteria, anaerobes as well as multidrug-resistant pathogens such as MRSA and VRE. However, there is not much clinical data regarding its use for treatment of VRE infections.

3. **Extended Spectrum Beta-Lactamases (ESBL) Producing Enterobacteriaceae.**

a. ESBLs are plasmid mediated β-lactamases that confer resistance to broad spectrum β- lactum antibiotics including third and fourth generation cepahlosporins, azetronam, and extended spectrum penicillins. These plasmids often encode mutations which confer resistance to other broad spectrum agents including aminoglycosides, co-trimoxazole and fluoroquinolones, resulting in organism resistant to most broad-spectrum antibiotics.

b. A major problem with ESBLs is their capacity to cause therapeutic failure with cephalosporins and azetreonam when host organism appears to be susceptible to these agents in laboratory tests. Hence, CLSI recommends that laboratories should report ESBL producing isolates as resistant to all penicillins, cephalosporins (including cefepime and cefpirome), and azetreonam irrespective of *in-vitro* test results.

c. The emergence of ESBL producing enterobacteriaceae is related to indiscriminate use of third generation cephalosporins.

d. The carbapenems (Ertapenem, Meropenem and Imipenem) are currently considered the drug of choice for serious infections caused by these pathogens. Piperacillin Tazobactam and Cefoperazone-Sulbactam may be considered options in mild infections and when ESBL producers are demonstrably susceptible *in -vitro*.

Carbapenem- Resistant Enterobacteriaceae (CRE)

a. Mechanism of resistance :
   i. Combinations of ESBL or AmpC and porin loss: Porin loss is often unstable and may impose a fitness cost, meaning that these strains rarely spread. Ertapenem is particularly affected.
   ii. Acquired carbapenemases

b. Treatment :
   i. Most carbapenemase producers are extremely drug resistant: being resistant to β-lactam antibiotics, aminogycosides, and β-lactam–βlactam inhibitor combinations.
   ii. Polymyxins, tigecycline & fosfomycin are the agents with most frequent *in vitro activity*, but all have limitations. Dosage will vary with the patient and infection site, but should be on the principle of 'highest safe' rather than 'minimum potentially effective; durations should be as standard for the infection type.
   iii. Colistin - Case reports of successful use in a range of infections due to carbapenemase producers.
   iv. Tigecycline: Active *in-vitro* vs. most carbapenem-resistant *E. coli*. Licensed for complicated skin and soft-tissue Infections and complicated intraabdominal infections. Case reports of success in various infections with carbapenemase producers. Low blood concentrations; off-label use should be cautious for blood stream infections, unsuitable in urinary infections as only 22% excreted in urine. Excess deaths in some trials, especially ventilator associated pneumonia (not a licensed indication).

v. Others: a few isolates are susceptible to other antibiotics including e.g. chloramphenicol, ciprofloxacin and cotrimoxazole. Most producers, however, are resistant to these drugs.

Recommended measures to control spread of Multi-drug resistant organisms (MDRO) :

i. Improved laboratory detection and reporting of MDRO
ii. Enhanced infection surveillance and control in ICUs
iii. Prevent spread by barrier precautions: Gowns and gloves
iv. Hand Washing
v. Restricted use of 3rd generation cephalosporin

Guidelines for Optimizing Use of Key Antimicrobials

A. Antimicrobial Prescribing: Good Practice

1. Send for the appropriate investigations in all suspected infections as recommended. These are the minimum required for diagnosis, prognosis and follow up of these infections.
2. All attempts shall be made to send microbiological samples prior to initiating antimicrobial therapy. Rapid tests, such as Gram stain, can help determine therapeutic choices when decision on empiric therapy is required.
3. Differentiation between contamination, colonization and infection is important to prevent overuse of antimicrobials. Use hospital guidelines based on local antibiograms when choosing antimicrobial therapy whenever possible. If alternatives to those recommended as used, reasons in the case records should be documented.
4. Prescribing antibiotics just in case an infection is present is rarely justified. Where patients are in hospital close observation is usually a better option till the diagnosis is made.
5. Choice of antibiotics: This depends on antibiotic susceptibility of the causative organism. There are some infections, which can be treated by one of several drugs. The choice can be based on Toxicity, Efficacy, Rapidity of action, Pharmacokinetics and Cost. *Use the most effective, least toxic and least expensive antibiotic for the precise duration of time needed to cure or prevent infection.* Pathogens specific guidance in hospital policy is encouraged. Before prescribing consider the following:
    a. Which organism is likely to cause the disease?
    b. What is the clinical diagnosis and what other steps should be taken to reach diagnostic precision?

c. Which antimicrobial agents are available and active against the presumed cause of the illness? Is their range of antimicrobial activity appropriate and what information is available about the likelihood of drug resistance?
d. Check for factors, which will affect choice of drug and dose, e.g., renal function, interactions, allergy, pregnancy and lactation.
e. Check that the appropriate dose is prescribed. If uncertain, contact Infectious Diseases Physician or clinical microbiologist. Alternatively, check in the formulary.
f. What is the duration of treatment?
g. Is treatment working?

6. Clinical Diagnosis: The antibiotic treatment chosen must be based on presumptive diagnosis made on some assumption regarding the nature of disease. The treating doctor may not have difficulty in choosing the appropriate antibiotic to treat a disease caused by a single microorganisms e.g. scarlet fever, typhoid, anthrax, as microbiological diagnosis is implicit in clinical diagnosis. However, diseases such as pneumonia, meningitis and urinary tract infection can be caused by spectrum of bacterial species and doctor may be wrong if he has to guess which antimicrobial agent to use. In such instances one should seek a bacteriological diagnosis.
7. Empiric Therapy – If the causative agent is not known and where delay in initiating therapy would be life threatening or risk serious morbidity, antimicrobial therapy based on a clinically defined infection is justified and the following points should be taken into consideration :
    a. Do not rush to treat.
    b. Collect the necessary specimens before commencing therapy.

c. Cover all possible microbial causes.
d. Try to attain synergy.
e. Consider possible interaction with other drugs.
f. Accuracy of diagnosis should be reviewed regularly and treatment altered/stopped when microbiological results become available.
g. Use less costly drugs where possible.

8. The need for antimicrobial therapy should be reviewed on a daily basis. For most infections 5 – 7 days of antimicrobial therapy is sufficient (simple UTI can be adequately treated with 3 days of antibiotic).
9. All IV antibiotics may only be given for 48 – 72 hours without review and consideration of oral alternatives. New microbiological or other information (e.g. fever defervescence for at least 24h, marked clinical improvement; low CRP) should at this stage often permit a switch to oral antibiotic(s), or switch to an IV narrow spectrum alternative, or cessation of antibiotics (no infection present).
10. Once culture reports are available, the physician should step down to the narrowest spectrum, most efficacious and most cost effective option. If there is no step down availed, the reason shall be documented and is subjected to clinical audit.
11. Some guiding principles for de-escalation /Escalation:
    a. If ESBL +ve: drug choice is monotherapy with carbepenems. Preferably choose group I carbepenem. Piperacillin –Tazobactum and Cefoperazone –Sulbactam can be used if in-vitro sensitive and for mild infections.
    b. Vancomycin should be used only for confirmed MRSA infections and not in MSSA infections.

c. In case of Pan drug resistant Pseudomonas /Acinetobacter spp. combination therapy using colistin along with beta-lactams (using PK/PD principles) should be discussed with microbiologist / physician.

12. Treatment with antibiotic combinations: In order to avoid antagonism between drugs and undesirable side effects of several antibiotics it is advisable to use a single drug where ever possible. There are situations however, when the use of antibiotic combination is desirable. The situations are:
    a. A temporary expedient during the investigation of an obscure illness.
    b. To prevent the development of bacterial resistance in long term therapy e.g treatment of tuberculosis.
    c. To achieve synergistic effect, e.g. in treating infective endocarditis.
    d. Mixed infection, when one drug is not effective against the pathogen.
    e. To permit a reduction of the dose of potentially toxic drug.

The choice of the drug should be that they act synergistically. The following combinations are synergistic

1. Aminoglycoside and beta–lactam antibiotic.
2. Beta –lactam antibiotic and beta–lactamase inhibitor.
3. Beta –lactam antibiotic and Glycopeptide (vancomycin/teicoplanin)
4. Sulphamethoxazole and Trimethoprim.

13. Is Treatment working? Where treatment is apparently failing, advice from an ID physician/clinical microbiologist should normally be sought rather than blindly changing to an alternative of

antimicrobial agent. Antimicrobial drug therapy cannot be considered in isolation and other aspects of therapy must be taken into account in judging the effect of treatment. Even an appropriate antibiotic may be ineffective unless pus is drained, septic shock treated and hypoxia and anemia corrected. There are several conditions in which chemotherapy alone cannot eliminate an infection. Obstructive lesions can cause infection to recur, unless they can be dealt with surgically. Also, chemotherapy cannot obviate the necessity for draining an abscess or removing sequestra or calculi. Failure of treatment can also be due to a super-added infection, e.g. phlebitis, development of resistance during therapy or poor tissue penetration.

14. Laboratory control of the effects of treatment: Whether treatment has been successful or not is best judged by clinical criteria, but it is useful to know whether the infecting organism has been eliminated. Repeated cultures are, therefore sometimes indicated.

B. Reserve Antimicrobials

These reserve antimicrobials will be made available following a recommendation from the Microbiology Department as per culture report or if included in an antimicrobial policy for a clinical specialty that has been agreed with antibiotic management team. They are held in reserve to maintain their effectiveness in treating certain difficult infections by reducing the spread of microbial resistance and to encourage cost effective prescribing. Before a reserve antibiotic is issued to the ward, the pharmacist is instructed to ascertain the indication and if this falls outside the approved policy, to request that the prescriber consult the ID Physician/clinical microbiologist.

The following criteria has been proposed to protect the Carbapenems and Linezolid from overuse –

1. Severe sepsis as defined by more than one organ failure of new onset and/or elevated serum lactate.
2. Clinical failure of other classes of antibiotics over 48 hours in terms of worsening inflammatory markers, unresolving fever and new/worsening hemodynamic instability.
3. Underlying severe immuno-suppression – Neutropeniea, immuno-suppressive therapy, Diabetic Ketoacidosis (DKA) etc.
4. The organism is susceptible to only carbapenems / linezolid, as per culture report.

The following criteria has been proposed for initiating Colistin –

1. Pan-resistant organism as per culture report with evidence of invasive disease – fever/ leucocytosis/elevated procalcitonin (PCT) or culture from a sterile site.
2. Clinical failure of all other classes of antibiotics over 72 hours.

The following criteria has been proposed for initiating Rifampicin –

1. Empiric or proven TB as a part of ATT (4 drug regimen).

Rifampicin should not be prescribed in our country for any treatment other than for Mycobacteria and for chemoprophylaxis of meningoccal meningitis in clinically indicated population.

Rifampicin should not be prescribed alone as an anti-bacterial.

The following criteria has been proposed for initiating Aminoglycosides –

1. The focus of infection is not lung or an anaerobic abscess.

2. Only as a part of initial empiric regimen of a combination therapy – shall step down to single drug after culture report.
3. Other safer drug options have been ruled out in a culture report.

C. Hypersensitivity

All patients should be asked about drug allergies. This is the responsibility of the doctor caring the patient. If a patient reports a drug allergy clarify whether this is an allergy or drug intolerance. In some cases there will be an overlap between drug allergy and drug intolerance.

- Clinical features suggestive of drug allergy:
  One or more symptoms developed during or following drug administration including difficulty breathing, swelling, itching, rash, and anaphylaxis, swelling of the lips, loss of consciousness, seizures or congestion involving mucous membranes of eyes, nose and mouth.
- Clinical features suggestive of drug intolerance:
  One or more symptoms developed during or following drug administration including gastrointestinal symptoms e.g. nausea, vomiting, diarrhoea, abdominal pain and feeling faint.

If patients are unable to give an allergy history, the doctor caring in the patient should take reasonable steps to contact someone who can provide a reliable allergy history. It is the prime responsibility of the prescribing doctor to ensure that:

i. The allergy box on the patient's drug chart is completed, when a new prescription chart is written or transcribed. If no allergy - specify "No known allergy". The box should be signed and dated. If allergy history cannot be obtained, then specify "history not available." Under no circumstances should the allergy box be left blank. A pharmacist or nurse may complete the allergy box if the allergy status is documented in the clerking in notes.

ii. The allergy box is completed before prescribing a new drug, except in exceptional circumstances. If patients have a suspected drug allergy then the drug and suspected reaction. Should be documented in the clerking-in notes and the drug chart.

D. Alert Antimicrobials

To Prevent and Control the Emergence and Spread of Antimicrobial-Resistant Micro-organisms in Hospitals" one major strategic goal is to "define guidelines for use of key antibiotics", ("Alert" antibiotics) targeted in these guidelines are ciprofloxacin, ceftazidime, cefotaxime, ceftriaxone, vancomycin (or teicoplanin), imipenem, levofloxacin, meropenem, moxifloxacin,piperacillin-tazobactam, linezolid (oral/IV), voriconazole, caspofungin, valganciclovir, ertapenem and newer preparations of amphotericin.

Collectively, these are among the drugs most frequently prescribed irrationally which is largely responsible for the current escalation of antibiotic costs. They also account for a significant proportion of serious antibiotic toxicity including *Clostridium difficile*diarrhoea and CNS toxicity/seizures as well as the emergence of major antimicrobial resistance. Safer, cheaper and equally effective alternatives are often available which allow such agents to be kept in reserve for occasions when there are clear cut microbiological indications. It is critical, therefore, that these Alert antibiotics be prescribed only on the

recommendation of senior medical staff or after discussion with the on-call Clinical Microbiologist or ID physician.

E. Alert antibiotics and their indications

1. CIPROFLOXACIN, INTRAVENOUS

Oral ciprofloxacin is well absorbed and this is therefore the preferred route of administration. Intravenous therapy is only indicated in the following situations:

- When the patient is unable to swallow or the oral route is otherwise compromised.
- In serious sepsis (e.g. nosocomial pneumonia in ITU) when the recommended dose is 400mg 8 hourly.

Common indications for ciprofloxacin in the Antibiotic Policy, either alone or in combination, are as follows:

- second line therapy in exacerbation of chronic bronchitis
- pyelonephritis
- acute inflammatory infective diarrhoeas
- serious infected diabetic ulcers infected burn wounds with coliforms or Pseudomonas infection present

- treatment of documented or presumed gram-ve bacilli resistant to penicillins or cephalosporins or when the patient is allergic (history of anaphylactic reaction or rash) to these agents
- selected haematology patients requiring prophylaxis
- severe acute pelvic inflammatory disease

2. CEFTAZIDIME

Limited use only. Main indication is documented or suspected *Pseudomonas aeruginosa* infection. Other indications currently listed in the Antibiotic Policy are as follows:

- Second line agent in neutropenic patients with septicaemia or pneumonia
- Empiric therapy of CAPD associated peritonitis (not children), 1g IV stat then 125mg/litre in each bag
- Empiric therapy of post operative, post traumatic or shunt associated meningitis
- Empiric therapy of infective exacerbation of cystic fibrosis

3. PIPERACILLIN - TAZOBACTAM

- Currently listed in the antibiotic policy for the following:
- Pneumonia or septicaemia in neutropenic patients (+ Gentamicin)
- As a single agent (or in combination with Gentamicin) for treatment of sepsis which has not responded to first line treatment or if it is not appropriate for gentamicin to be added to first-line therapy.

4. CEFTRIAXONE

- IV Ceftriaxone is currently listed in the antibiotic policy for the following:
- Epiglottitis,
- Brain abscess,
- Bacterial meningitis,
- Pyelonephritis in children,
- Empiric therapy of septicaemia in children,
- In ascites for treatment of sub-acute bacterial peritonitis,
- Skin and soft tissue infections managed via out-patients or the home IV antibiotic programme,
- Acute septic monoarthritis if penicillin allergic,
- Spontaneous bacterial peritonitis.

5. APPROPRIATE USE OF CARBEPENEMS

- Very high rates (60-75%) of resistance to 3rd and 4th generation cephalosporins {due to extended spectrum beta-lactamases (ESBL) production} observed in *E. coli* and *Klebsiella* species..
- This pattern of resistance although seen primarily among nosocomially acquired infections, is also seen isolates of *E coli* and *Klebsiella* species isolated from community acquired infections.

- These strains of bacteria are frequently resistant to other major classes of antibiotics (fluoroquinolones, β-lactam + β-lactamase inhibitor(BL + BLI) combinations and aminoglycosides)
- Carbapenems (imipenem, meropenem and ertapenem), beta-lactam antibiotics with exceptionally broad spectrum of activity, are *the only class* of antimicrobials which remain effective against ESBL-producing isolates of *E coli* and *Klebsiella* species
- Imipenem is susceptible to degradation by the enzyme dehydropeptidase-1 (DHP-1) located in renal tubules and requires coadministrationwith a DHP-1 inhibitor cilastatin. Meropenem and ertapenem are administered without a DHP-1 inhibitor.

Indications for carbapenem use:

1. Infections [e.g., bacteremia, pyelonephritis, intra-abdominal infections (peritonitis, cholangitis, abscesses), nosocomial pneumonia etc.] confirmed (by appropriate culture and susceptibility studies) to be caused by Gram-negative bacteria (*E coli*, *Klebsiella* spp., *Enterobacter* spp., *Pseudomonas aeruginosa*, other non-fermenting Gram-negative bacilli) *resistant to other classes* of antimicrobials and *susceptible only to carbapenemsin-vitro*
2. Initial empiric treatment for severe, life-threatening infections (associated with multi-organ dysfunction, septic shock) caused by Gram-negative bacteria.
    - Febrile neutropenia
    - Ventilator associated / nosocomial pneumonia
    - Pyelonephritis / complicated urinary tract infections

- Complicated intra-abdominal infections

Once the culture and susceptibility reports are available, choose the most appropriate antibiotic based on spectrum of activity, toxicity and cost ('de-escalation').

Indications for Ertapenem use:

Ertapenem has excellent in-vitro and in-vivo activity against ESBL producing Enterobacteriaceae, but lacks activity against *Pseudomonas aeruginosa*, and is therefore not considered appropriate for the treatment of conditions like febrile neutropenia and serious nosocomial infections. Ertapenem does not select Carbapenem-resistant *Pseudomonas aeruginosa* (at least in the short-term). Its use should be restricted to severe Gram-negative or polymicrobial community acquired infections confirmed to be caused by susceptible bacterial pathogens. Hence, this drug may be recommended as the initial choice for ESBL producing strains of *E coli* and *Klebsiella spp.*.

Indication of Meropenem and Imipenem

Meropenem and Imipenem regarded as third line agents and are reserved for:

- serious infections due to multiple resistant strains (e.g. ESBL)
- empiric use in the seriously ill patient in either ITU or Haematology
- the treatment of infective exacerbations in Cystic fibrosis (CF)
- severe acute narcotising pancreatitis
- Outside these clinical settings it should only be used after consultation with a Clinical Microbiologist or ID physician.

Unlike imipenem , meropenem has not been associated with CNS toxicity. Also, it is administered by convenient IV bolus injection. Clinicians must be aware that mechanism of resistance to meropenem and imipenem are different and hence in-vitro test for one carbapenem cannot be used to interpret the other.

Dose

Imipenem*: 500 mg i.v. Q6H

Meropenem: 1 gmi.v.Q8H

Ertapenem: 1gm i.v. /i.m.Q 24H

*Note Anti-infective sub-committee recommends use at a more frequent dosing interval. They believe that optimum plasma concentrations are more reliably maintained with 6-hourly dosing.

R.L.JALAPPA HOSPITAL

RESTRICTED ANTIMICROBIAL AGENT ORDER FORM

Date & Time: _____

Name of the patient: _____ Pt. Wt.: _____

Age/Sex: _____ Ward: _____

UHID /IP No.:

Treating consultant: _____

Diagnosis: _____

RESTRICTED ANTIMICROBIAL AGENTS

Antibacterial	Antifungal
Intravenous Ciprofloxacin	Amphotericin B
Ceftazidime	Voriconazole
Ertapenem	Caspofungin
Meropenem	Posaconazole
Imipenem – Cilastatin	
Rifampicin (other than for *Mycobacterium tuberculosis*)	
Polymyxin B	
Linezolid	
Vancomycin	
Teicoplanin	
Quinupristin - Dalfopristin	
Daptomycin	
Tigecycline	

Prescribed dosage:

Justification for use:

Microbiologist opinion: