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Medical college and Hospital

ANTIBIOTIC POLICY

VERSION 1.0

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Contents

Introduction

AIMS OF ANTIMICROBIAL POLICY

1. To provide a simple, best empirical/specific treatment of common infections
2. To promote the safe, effective, economic and rational use of antibiotics
3. To minimise the emergence of bacterial resistance in the community

PRINCIPLES OF TREATMENT

1. These guidelines are based on the best available evidence.
2. Drug, dose and duration of treatment are suggested but can be modified by consultants based on clinical scenarios
3. Prescribe antibiotic one and only when there is likely to be a clear clinical benefit.
4. Do not prescribe an antibiotic for infections like URTI and diarrhea which are most often caused by viruses and are self-limited.
5. Use simple generic antibiotics first whenever possible. Avoid broad spectrum antibiotics (e.g. Amoxycillin+Clavulanate, Quinolones and Cephalosporins) when standard and less expensive antibiotics remain effective, as they increase the risk of Clostridium difficile colitis, MRSA and drug resistant UTIs.
6. Avoid widespread use of topical antibiotics (especially those agents also available as systemic preparations).
7. Clarithromycin is an acceptable alternative in those who are unable to tolerate Erythromycin because of side effects.
8. Test dose to be given for all antibiotics especially beta-lactam antibiotics.

STEPS TO FOLLOW THE PROTOCOLS

1. Identify the type of infection viz. bloodstream, respiratory, intra-abdominal or urinary tract
2. Define the location — OPD, ICU or In- patient
3. Wait for at least 48hrs of antimicrobial therapy before labeling the patient as non-responding to the therapy and to switch to the next higher line of therapy. Also consider escalation if patient's condition deteriorates.
4. Send samples for cultures and or primary set of investigations before starting antibiotic therapy
5. Once culture / sensitivity report is available initiate specific antimicrobial therapy. Antimicrobial may require being changed/de-escalated.

Principles of Judicious Antimicrobial Prescribing

The appropriate use of antimicrobials is mandatory for the effective delivery of care for patients and is a key factor in the management of antimicrobial resistance.

Antimicrobial stewardship is defined as processes to assist and support clinicians with decisions regarding the optimal selection, dose and duration of an antimicrobial agent.

The objective of AMS is to ensure the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent development of resistance.

1. Send the appropriate investigations for all the infections as recommended. These are the minimum required for diagnosis, prognosis and follow up of these infections.
2. All antibiotic initiations should be done after sending appropriate specimens for culture and sensitivity test.
3. Change in antibiotic should be done after receiving the culture and sensitivity report.
4. Follow the Hospital policy when choosing antimicrobial therapy whenever possible. If alternatives are chosen, document the reason in the case records.
5. Check for factors which will affect drug choice & dose, eg, renal function, drug interactions and allergy.
6. Ensure that the appropriate dose is prescribed.
7. The need for antimicrobial therapy should be reviewed on a daily basis. For most infections 5-7 days of antimicrobial therapy is sufficient (simple UTIs can be adequately treated with 3 days of antibiotic).
8. All IV antibiotics may only be given for 48 – 72 hours without review and then consideration of oral alternatives. New microbiological or other information (eg. 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 a narrow spectrum antibiotic, or cessation of antibiotics (no infection present).
9. Once culture reports are available, the physician shall deescalate 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.
10. Empirical Therapy - Where delay in initiating therapy pending microbiological results would be life threatening or caries risk of serious morbidity. Antimicrobial therapy based on a clinically defined infection is justified. Where empiric therapy is used the accuracy

of diagnosis should be reviewed regularly and treatment altered/stopped when microbiological results become available.

11. Microbiological samples must always be sent prior to initiating antimicrobial therapy. Rapid tests, such as Gram smears, can help determine therapeutic choices when empiric therapy is required.
12. Prescribing antibiotics just in case an infection is present is rarely justified. Where patients are in hospital close observation is usually a better option.

Surgical prophylaxis

Prophylaxis should only be considered in the following scenarios, when either there is a significant risk of infection or when the consequences of infection would be disastrous (e.g. joint replacement surgery):

1. **Contaminated surgery** – Surgical antimicrobial prophylaxis is strongly recommended when there is a risk of macroscopic soiling of the operative field. Examples include: large bowel resection, biliary or genitourinary tract surgery with infective bile or urine.

2. **Clean-contaminated surgery** – surgical antimicrobial prophylaxis is recommended where the mucosa is penetrated under controlled conditions without unusual contamination. Examples include laryngectomy, uncomplicated appendicectomy, cholecystectomy, transurethral resection of prostate gland.

3. **Clean surgery** – surgical antimicrobial prophylaxis is only recommended for insertion of a prosthesis or artificial device or for high risk areas such as the central nervous system, eye, aorta or sternum.

- Antimicrobial prophylaxis cannot be relied upon to overcome poor surgical technique (e.g. inadequate haemostasis, excessive damage to tissues, inadequate debridement).
- The first dose(s) of surgical prophylaxis should be given at a time that ensures adequate plasma and tissue drug levels are achieved at the start of the procedure (i.e. administration of prophylaxis one hour prior to commencement of the operation).
- Repeat intra-operative doses are recommended for prolonged procedures of more than three hours or if there is excessive blood loss. “Prophylaxis” continuing for more than twenty four hours postoperatively is unnecessary and potentially dangerous.

CATEGORIZATION OF ANTIBIOTICS

Restricted use antibiotics:

A written documentation to be maintained which captures the request along with justification for use by the clinician and also captures the approval for use by the authority in charge

Limited access antibiotics:

Unrestricted use of these antibiotics may be allowed for empirical use for first 48-72hrs but after that a clinical justification by clinician and approval from authority in charge needs to be documented as to why these antibiotics cannot be de-escalated and need to be continued further.

Under Surveillance antibiotics:

A close monitoring to check their usage (indication, quantity and pattern) in OPD / Type 1 Patients/ Surgical prophylaxis. Audits to be done at regular intervals to assess their consumption

RESTRICTED USE ANTIBIOTICS

1. **Colistin:** It is the last resort for managing multidrug resistant (MDR) gram negative organisms and its use, dose and duration need to be rationalised. Use should be restricted
2. **Doripenem:** It is the last carbapenem (at least in near future). If Imipenem and Meropenem are effective, we need to conserve the use of Doripenem
3. **Rifampicin:** (For Non-TB use) This is a valuable drug for TB. The use of rifampicin in MDR Pseudomonas, Acinetobacter or MRSA should be restricted
4. **Linezolid:** Alternatives available eg. Vancomycin/Teicoplanin.
5. **Daptomycin:** Alternatives are available for MRSA eg. Vancomycin, Teicoplanin.
6. **Tigecycline:** Bacteriostatic, one of the most Broad spectrum drug, has limited role in MDR infections like SSTI, IAI where ESBL/MRSA and or Acinetobacter are feared.
7. **Sulbactam:** Recently introduced in market. Reserved for pan drug resistant (PDR) Acinetobacter. Dose has to be correct (4-12gm/day for PDR Acinetobacter)

LIMITED ACCESS ANTIBIOTICS

1. **Imipenem/Meropenem :** Use as an empirical drug in sick patients is allowed looking at the antibiograms in most hospitals showing better sensitivity of these antibiotics over other classes, however after culture and sensitivity report is available, if the pathogen is susceptible to other classes of antibiotics or if patient's condition improves – then de-escalation should be advised.
2. **Piperacillin-Tazobactam/Cefoperazone-Sulbactam:** These are as broad spectrum as carbapenems (this fact is not appreciated generally). Use as empirical in sick patients is allowed looking at the antibiograms in most hospitals showing good sensitivity of these antibiotics over other classes, however after culture and sensitivity report is available, if the pathogen is susceptible to other classes of antibiotics or if patient's condition improves - then de-escalation should be advised.
3. **Vancomycin/Teicoplanin:** Use as empirical in sick patients may be allowed specially in BSI, SSTI where MRSA is suspected but if after 48-72hrs culture and sensitivity report shows no staph aureus or MSSA then Vancomycin/Teicoplanin have absolutely no role and should be discontinued.

UNDER SURVEILLANCE ANTIBIOTICS: WHAT AND WHY?

- 3rd generation cephalosporins (both oral and IV) and Flouroquinolones:

One of the main reasons for widespread Extended Spectrum Beta- Lactamase producing organisma (ESBLs) in India in the community is due to overuse of 3rd generation cephalosporins and flouroquinolones at OPD level-Type 1 patients, pediatric patients and surgical prophylaxis.

It is must to remind the clinicians about these antibiotics and the collateral damage they cause. Also it is imperative to exercise control on liberal usage of these antibiotics in a phased manner and perform regular audits on the rate of consumption of these antibiotics. This could be the single most valuable intervention to curb resistance in community in India.

Dosage guide for commonly used antimicrobial agents

ANTIBIOTICS	ROUTE	PAEDIATRIC DOSE	ADULT DOSE
Amikacin	Intravenous	15-22.5 mg/Kg/day in 2-3 doses	15mg/Kg/day q 8-12 h, max doses 1.5mg / kg
Amoxycillin	Oral	20-50mg/Kg/day, 3-4 doses	250-500mg q 8 hourly
Amoxycillin- clavunate (co-amoxyclav)	Oral Intravenous	40mg/kg/day (amoxicillin) in 2 doses 90mg/kg/day if penicillin resistant S.pneumonia suspected 100mg/kg/day in otitis media	375mg q 8 hourly 625 – 1000mg 12 hrly
Ampicillin	Intravenous or Oral	100-400 mg/kg/day in 4 doses (IV)	500mg- 1gm q 6 hrly
Azithromycin	Oral	10mg/kg/day once daily Enteric fever 20 mg/kg once daily	500mg daily
Azetronam	Intravenous	30-120 mg/kg/day q 6-8hrly In Cystic fibrosis max dose 200mg / kg/day	1- 2gm q 8 hrly, max dose 8gm in 24 hours
Benzathine penicillin	Intramuscular	1,200,000 units(>30 kg) 600,000 units(<30 kg)	1.2 – 2.4 million units / dose
Cefadroxil	Oral	30 mg/kg/day in 2 doses	500 mg bid or 1 gm bid
Cefazolin	Intravenous	100 mg/kg/day in 3-4 divided doses	0.52 gm q 6-8 hourly
Cefepime	Intravenous		1-4gm/day in 2-3 doses
Cefixime	Oral	15 mg/kg/day in 2 divided doses, 20 mg/kg/day in 2 divided doses for enteric fever	400 gm /day in 1-2 divided doses
Cefotaxime	Intravenous	100 mg/kg/day in 3-4 divided doses, 200 mg/kg/day in 4 divided doses for meningitis	1 -2 gm 6-8 hourly
Ceftazidime	Intravenous Intramuscular	100mg/kg/day in meningitis (IV) 75-100mg/kg/day in 3 divided doses	1 -2 gm q 12-24 hourly (IV)
Ceftriaxone	Intravenous	50-100mg/kg/day in 2 divided doses Meningitis 100mg/kg/day in 2 divided doses	1 -2 gm q 12-24 hourly
Cefuroxime	Intravenous Oral	75-100mg/kg/day in 3 divided doses 20-30mg/kg/day in 2 divide doses	750mg -1.5gm q 8 hrly 250-500mg bid

Cephalexin	Oral	30-40mg/kg/day in 3 divided doses	250-500mg q 8 hourly
Chloramphenicol	Oral Intravenous	75-100mg/kg/day in 4 divided doses **Avoid in infants less than 3 months**	50 mg/kg/day in 4 divided doses
Ciprofloxacin	Oral Intravenous	20-30mg/kg/day in 2 divided doses	250-750mg q 12 hourly
Clarithromycin	Oral Intravenous	15mg/kg/day in 2 divided doses	250-500mg bid
Clindamycin	Oral Intravenous	40-60mg/kg/day in 3-4 divided doses	150-300mg q 6-8 hourly (oral, iv) severe infections 300-600mg 8 hrly IV
Cloxacillin	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	Oral	5-10mg/kg/day in 2 divided doses (5mg trimethoprim) 20mg/kg/day in 4 divided doses in *Pneumocystis jirovecii* pneumonia	160mg bid
Ertapenem	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 3-5ml lidocaine **CI if hypersensitivity to lidocaine/β lactum**
Erythromycin	Oral		250-500mg q 6 hourly
Furazolidine	Oral	5mg /kg in 3-4 divided doses (not below 1 year)	100mg 3-4 times a day
Gentamicin	Intravenous Intramuscular	5-7.5mg/kg/day in 2-3 divided doses	1.3-6 mg/kg/day in 3 divided doses
Imipenem cilastin	Oral / Intravenous		500mg once daily
Linezolid	Oral Intravenous	10mg/kg/dose in 6-8 hourly (oral, IV)	400-600mg q 12 hourly
Meropenem	Oral Intravenous	7.5mg/kg/day /dose in meningitis	1.5 – 3 gm/day in 3 divided doses 6gm/day in meningitis
Metronidazole	Intravenous Oral	7.5mg/kg/day in 3 divided doses 30-50mg/kg/day in 3 divided doses for liver abscess	500 -700mg q 8 hourly

Nalidixic acid	Oral	8 mg/kg/day in 2 divided doses	1gm 4 times/day
Nitofurantoin	Oral	8 mg/kg/day in 2 divided doses	50 - 100mg/kg/day q 6 hourly (5-7mg/kg/day in 4 divided doses max dose 400mg)
Norfloxacin	Oral	20-30 mg/kg/day in 2 divided doses	200 -400mg twice daily
Ofloxacin	Oral Intravenous	20 mg/kg/day in 2 divided doses	200 -400mg q 12 hourly
Penicillin G	Oral Intravenous	50,000units /kg /dose 6 hourly 200,000 – 400,000units /kg /day in 4 divided doses	 2- 24 million units /day in divided doses q 4-6 hours (IV)
Penicillin V	Oral	20-50 mg/kg/day in 4 divided doses	250 -500mg every 6-8 hourly
Piperacillin – Tazobactum	Intravenous	200-400 mg/kg/day in 3-4 divided doses	4.5gm q 8 hourly
	Intravenous Intramuscular	10 mg/kg/day/dose every 12 hours for 3 doses 10 mg/kg/day once daily	400mg once daily (6-30 mg /kg/day)
Tigecycline	Intravenous	**Above 10 years**	100mg followed by 50mg every 12 hrly infusion over 30-60 minutes.
Vancomycin	Intravenous	40-60 mg/kg/day in 3-4 divided doses	0.5gm q 6 hrly or 1 gm q 12 hrly

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 6-8h	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/day	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 q24 h	500mg	
Amikacin Infants andchildren	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	1–4 mg/kg/day		150mg	Limited experience
Caspofungin Children 3months-17 years	Loading dose of 70 mg / m2 /day on day 1 followed by 50 mg/m2/day thereafter		70 mg; may increase to 70mg/m2/day if clinical response is inadequate	
Clindamycin	10 mg/kg/dose	q 6-8 h	900 mg Q 8	

Surgical antimicrobial prophylaxis

- To be administered within 1 hr before the surgical incision.
- Single dose is recommended. Consider for second intra-operative dose in prolonged surgery based on the choice of antibiotic used for prophylaxis.
- Prophylaxis should **not** be given beyond the duration of surgery (except for cardiothoracic surgery, up to 48 hours permissible)

SURGERY	MEDICATION
Breast	Inj.Cefazolin 2gm or Inj.Cefuroxime 1.5gm IV stat
Gastroduodenal & biliary	Inj.Cefaperazone- Sulbactam 2gm IV stat & BD for 24hrs(maximum)
ERCP	Inj.Piperacillin-Tazobactum 4.5gm or Inj.Cefaperazone- Sulbactam 2gm IV stat
Cardiothoracic	Inj.Cefuroxime 1.5gm IV stat & BD for 48hrs
Colonic surgery	Inj.Cefaperazone- Sulbactam 2gm IV stat & BD for 24hrs(maximum)
Abdominal surgery (hernia)	Inj.Cefazolin 2gm or Inj.Cefuroxime 1.5gm IV stat
Head & Neck/ ENT	Inj.Cefazolin 2gm IV stat
Neurosurgery	Inj.Cefazolin 2gm or Inj.Cefuroxime 1.5gm IV stat
Obstetrics& Gynecology	Inj.Cefuroxime 1.5gm IV stat
Orthopaedic	Inj.Cefuroxime 1.5gm IV stat & BD for 24 hrs(maximum) or Inj.Cefazolin 2gm IV stat Open reduction of closed fracture with internal fixation- Inj.Cefuroxime 1.5gm IV stat and q 12h or Inj.Cefazolin 2gm IV stat and q 12h for 24 hrs
Trauma	Inj.Cefuroxime 1.5gm IV stat and q 12h (for 24 hrs) or Inj.Ceftriaxone 2gm IV OD
Urologic procedures	Antibiotics only to patients with documented bacteriuria
Trans- rectal prostatic surgery	Inj.Cefaperazone- Sulbactam 2gm IV stat

*Reference:

National Treatment Guidelines for Antimicrobial use in Infectious diseases. Ministry of Health & Family Welfare, Govt of India.Ver 1.0 (2016)

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.

   ***The marker used in our laboratory to assess potential MRSA is the resistance of S.aureus to Cefoxitin.**

2. **Vancomycin Resistant Enterococcus (VRE)**

   The treatment for VRE should be based on infection severity and in-vitro susceptibility of the strain to other antibiotics.

   - **Linezolid**: Linezolid is the only drug specifically approved for the treatment of VRE-blood stream infections.
   - **Ampicillin:** Isolates that remain relatively susceptible to penicillin or ampicillin may be treated with high doses of these agents.
   - **Daptomycin**: Not approved for treatment of VRE infection.
   - **Doxycycline:** Not a first line therapy. For susceptible isolates, not for bacteremia or endocarditis. It should not be used as monotherapy.
   - **Nitrofurantoin:** Uncomplicated UTIs have been treated successfully with nitrofurantoin.
   - **Fosfomycin**: For urinary tract infections (cystitis) with isolates susceptible to fosfomycin.
   - **Chloramphenicol:** For chloramphenicol-susceptible isolates of *E faecium* and *E. faecalis*. Not a first-line therapy and it should not be used as monotherapy.

- **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.

3. Extended Spectrum β-Lactamases (ESBL) Producing Enterobacteriaceae.

- CLSI (Clinical and Laboratory Standards Institute) 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.**
- 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*.

***The marker used in our laboratory to assess potential ESBL production among Enterobactericeae is the resistance to Cefotaxime and Ceftazidime.**

4. Carbapenem- Resistant Enterobacteriaceae (CRE)

- Most carbapenemase producers are extremely drug resistant: being resistant to β-lactam antibiotics, aminogycosides, and β-lactam–βlactam inhibitor combinations.
- **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.
- **Colistin -** Case reports of successful use in a range of infections due to carbapenemase producers**.**
- **Tigecycline:** Licensed for complicated skin and soft-tissue Infections and complicated intra-abdominal infections.
- **Others:** a few isolates are susceptible to other antibiotics including e.g. chloramphenicol, ciprofloxacin and cotrimoxazole. Most producers, however, are resistant to these drugs.

<u>Recommended measures to control spread of Multi-drug resistant organisms (MDRO)</u>

- Improved laboratory detection and reporting of MDRO
- Enhanced infection surveillance and control in ICUs
- Prevent spread by barrier precautions : Gowns and gloves
- Hand Washing
- Restricted use of 3rd generation cephalosporins

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7 STEPS FOR HAND HYGIENE

Duration of entire Procedure**: 60 Seconds**