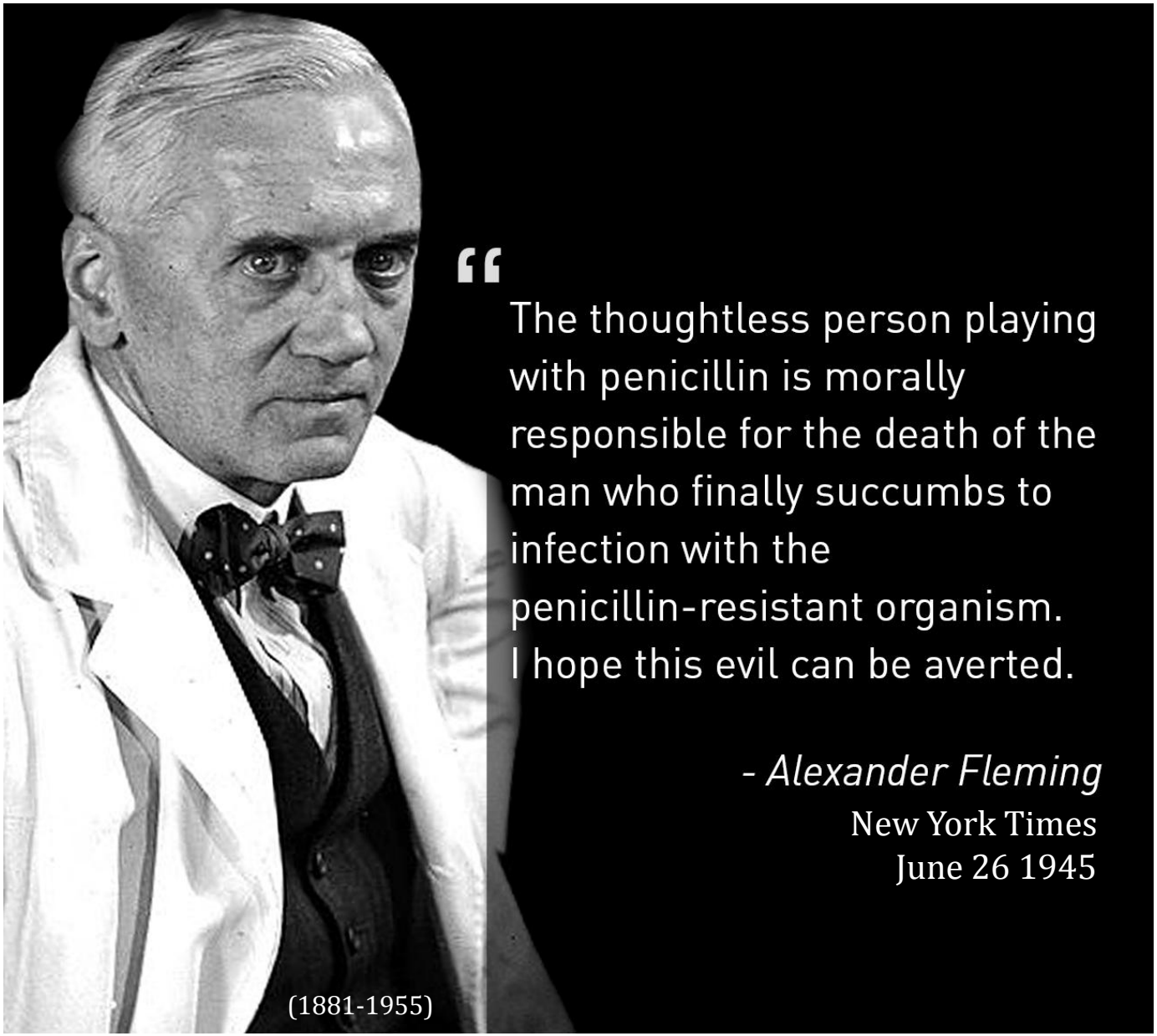
National Treatment Guidelines for Antimicrobial Use in Infectious Diseases

NCDC , GOI, OCT 24, 2016


“
The thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted.
- Alexander Fleming
New York Times
June 26 1945
(1881-1955)

Magic Bullets

- Antimicrobial drugs are the greatest contribution of the 20th century to therapeutics
- Importance is magnified in developing countries where infective diseases predominate
- As a class, they are one of the most frequently used as well as misused drugs

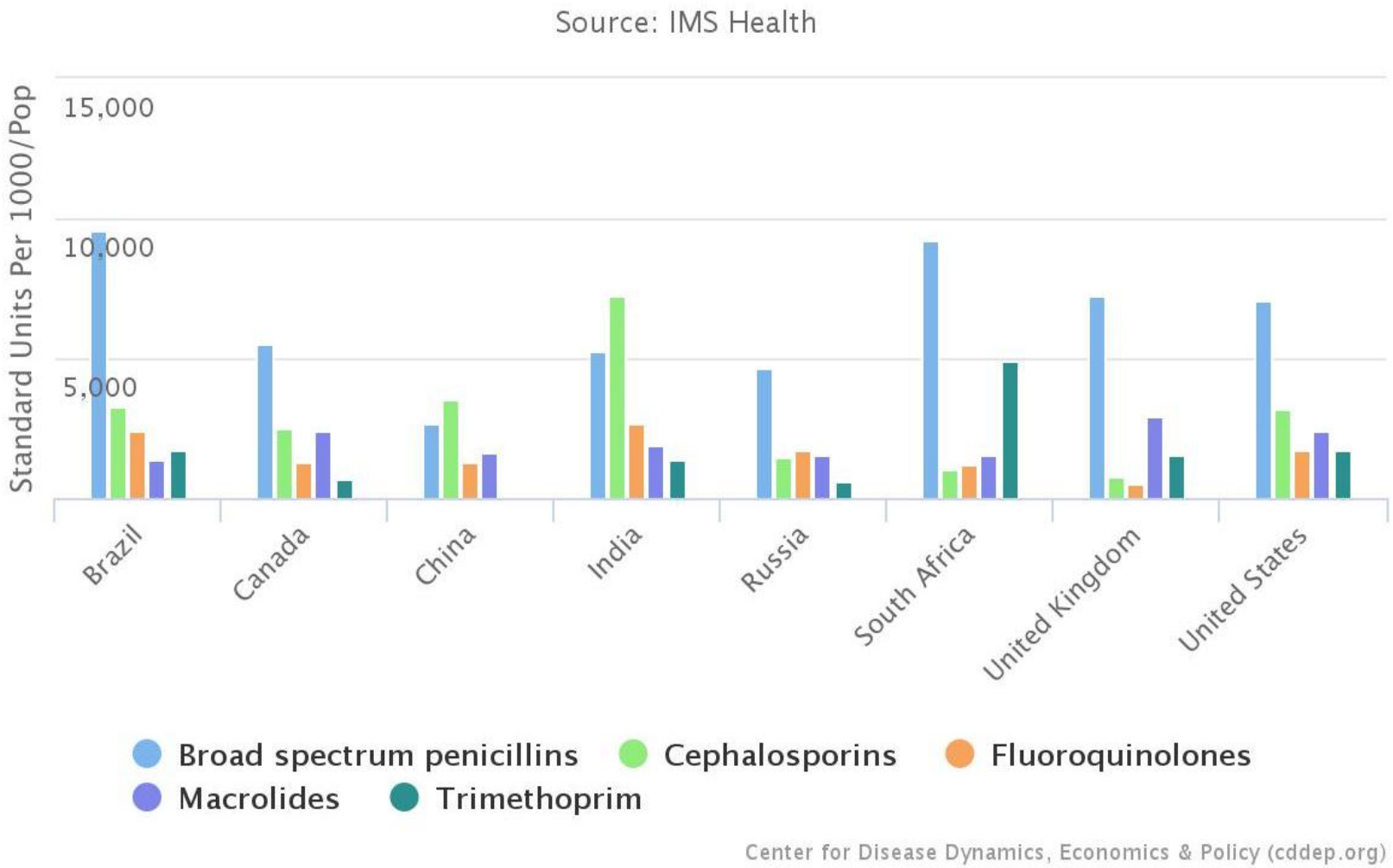
Laxminarayan R et al. PLoS Med. 2016 Mar; 13(3): e1001974

Antibiotic resistance

- Antibiotic resistance is a global public health threat.
- The crude infectious disease mortality rate in India today is 416.75 per 100,000 persons
- India is the world's largest consumer of antibiotics for human health at 12.9×10^9 units (10.7 units per person).
- The next largest consumers:
  - China - 10.0×10^9 units (7.5 units per person)
  - US - 6.8×10^9 units (22.0 units per person)

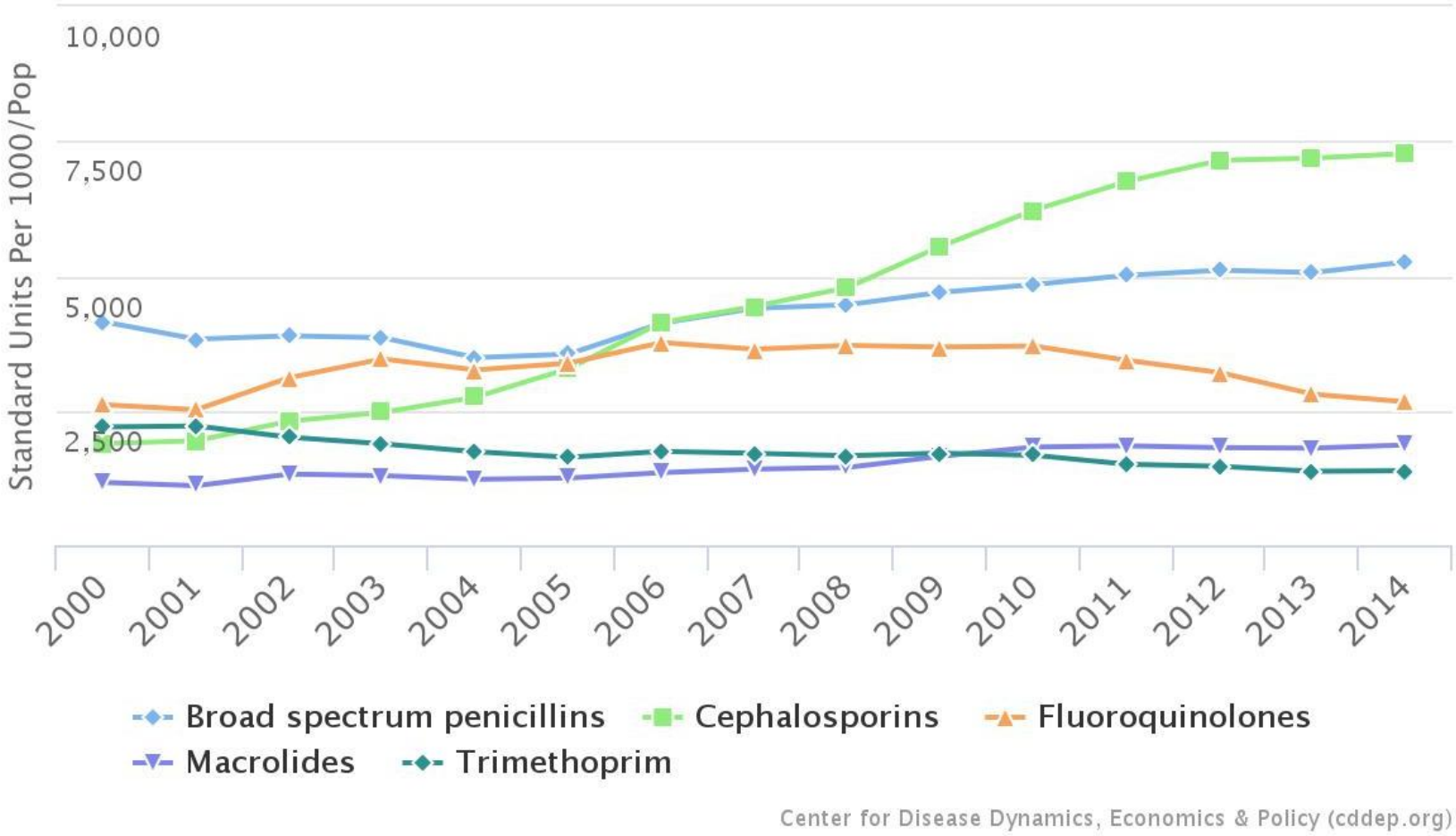
Laxminarayan R et al. PLoS Med. 2016 Mar; 13(3): e1001974

Global Antibiotic Use: Major Countries



Laxminarayan R et al. PLoS Med. 2016 Mar; 13(3): e1001974
Available at http://resistancemap.cddep.org/AntibioticUse.php

Trends in antibiotic consumption in India



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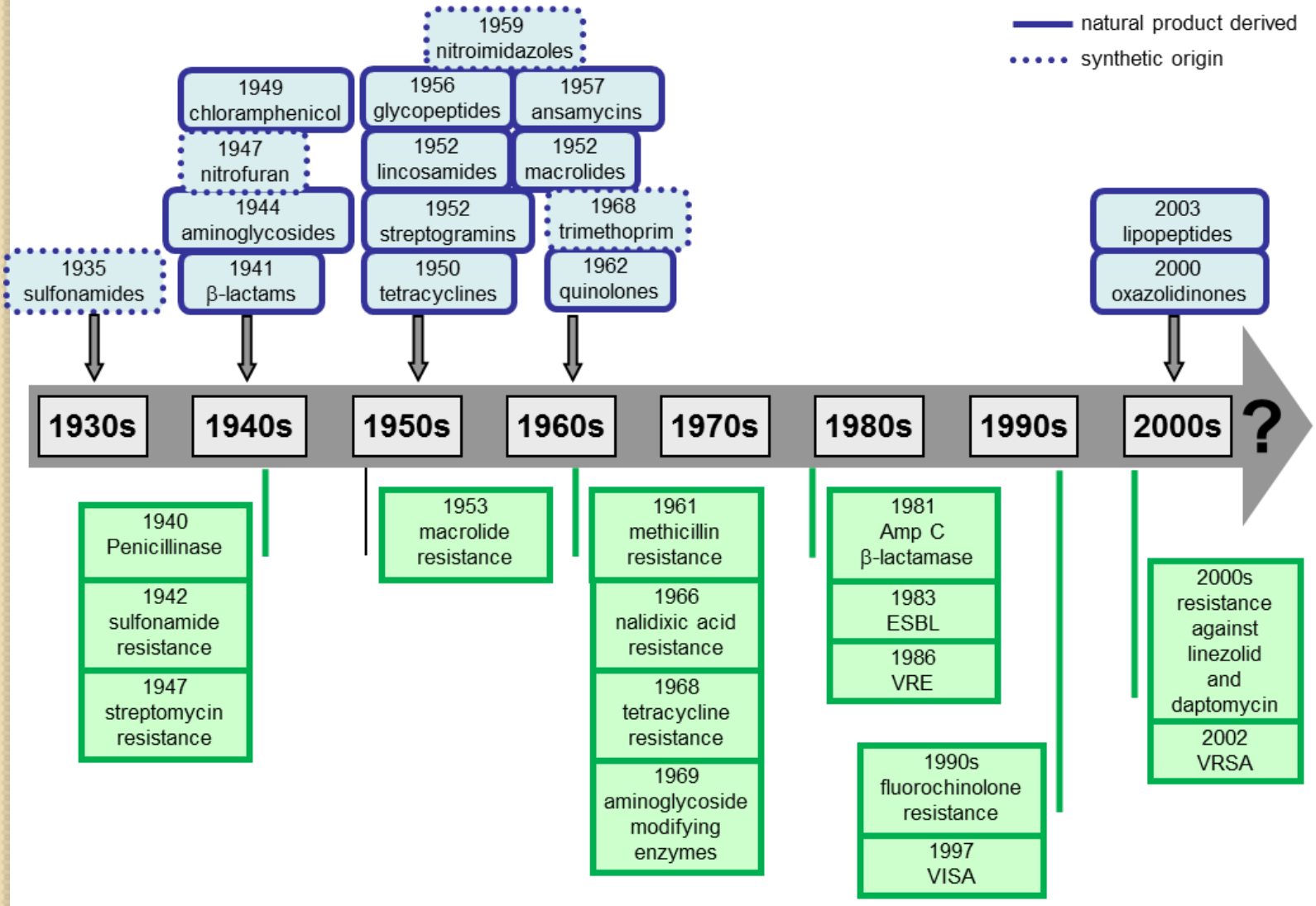
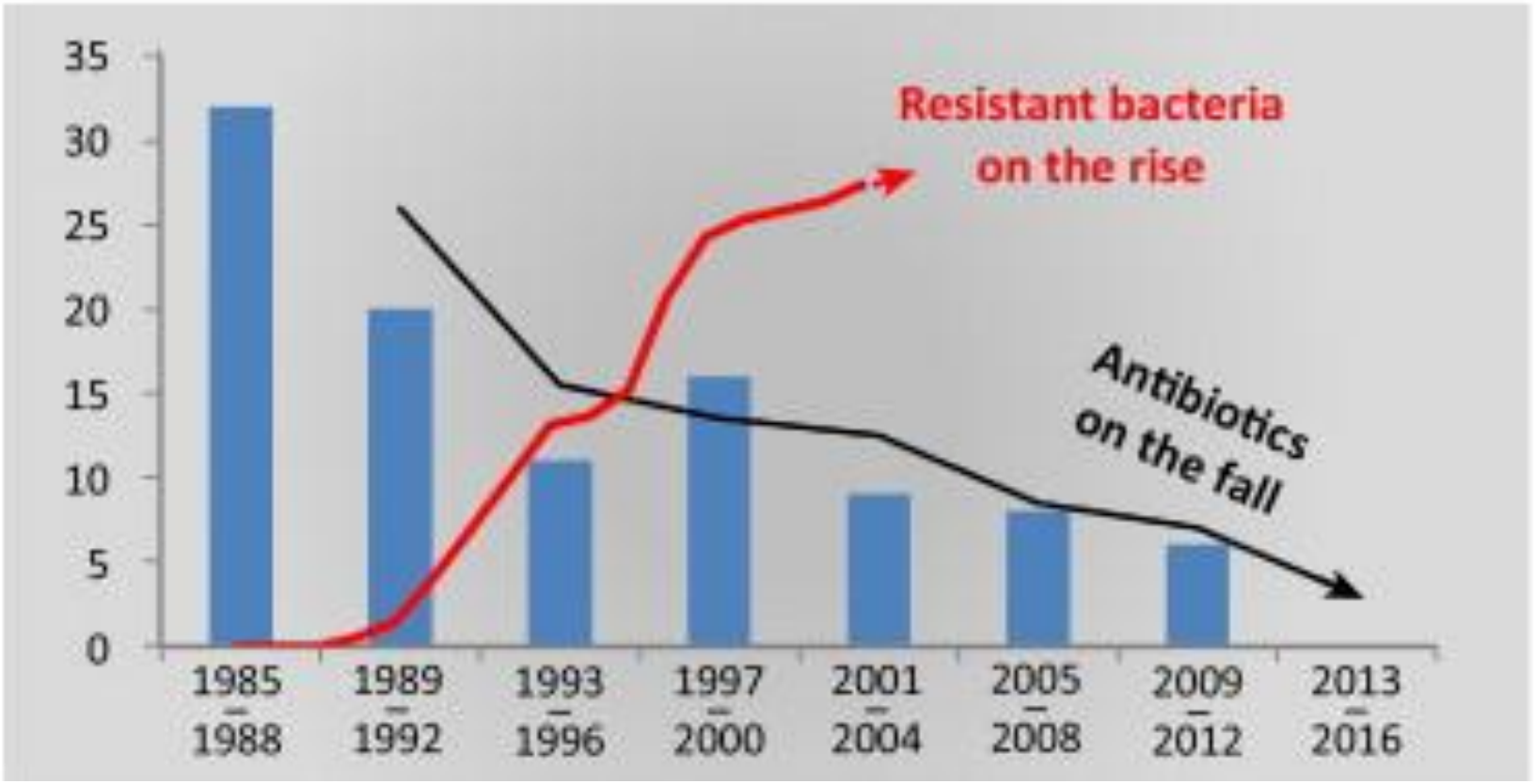
Introduction of new antibiotic classes



Development of bacterial resistance



- Imperative to have standardized national treatment guidelines:
  - To contain the further development of antimicrobial resistance with no new drug on the horizon and
  - Reduce the existing levels of reported resistance in the country

Emerging Resistance

- More than 50% of Escherichia coli strains causing urinary tract infections are reported worldwide to be resistant to fluoroquinolones.
- Similarly, patients suffering from gonorrhea are reported to be resistant to the last resort of antibiotics - third generation cephalosporins.
- High mortality (64%) was seen among patients infected with Methicillin resistant Staphylococcus aureus (MRSA).
- Over all, the antimicrobial resistance is associated with higher mortality rate, longer hospital stay, delayed recuperation and long term disability.
- Similar observations on the emergence of antimicrobial resistance

CAUSES OF ANTIBIOTIC RESISTANCE

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

Over-prescribing of antibiotics

Patients not finishing their treatment

Over-use of antibiotics in livestock and fish farming

Poor infection control in hospitals and clinics

Lack of hygiene and poor sanitation

Lack of new antibiotics being developed

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www.who.int/drugresistance

#AntibioticResistance

World Health Organization

Large-scale selection and dissemination of resistance genes in India

Factors

- Poor public health indicators,
- rising incomes, and the
- availability of inexpensive antibiotics over the counter without a prescription

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Current Policies/Guidelines

- There are definite policies/guidelines for appropriate use of antimicrobials at national level in specific national health programmes (e.g. RNTCP, National AIDS Control Programme, National Malaria Control Programme) etc

- For other pathogens of public health importance like enteric fever, diarrhoeal disease, respiratory infections etc., the individual hospitals are following their own antimicrobial policies and hospital infection control guidelines.

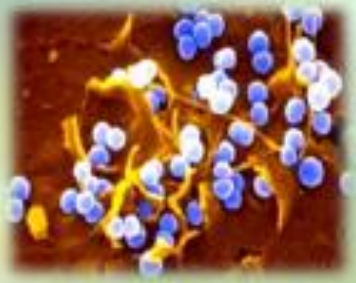
- Reliable Indian data on antimicrobial resistance (AMR)for important pathogens of public health importance is an essential pre requisite for developing/modifying appropriate guidelines for use of antimicrobials.

Currently, there is no accepted national database of antimicrobial resistance in different pathogens except for those where there is a specific national health programme.

सत्यमेव जयते

National Treatment Guidelines

for Antimicrobial Use in Infectious Diseases



Version 1.0 (2016)

NATIONAL CENTRE FOR DISEASE CONTROL
Directorate General of Health Services
Ministry of Health & Family Welfare
Government of India

National Treatment Guidelines for Antimicrobial Use in Infectious Diseases

- The 2016 National guideline includes:
  - Empiric treatment choices for different syndromes, infections of specific body sites, and in certain special settings
  - Antimicrobial choices for multi-drug resistant bacterial pathogens
  - Optimizing and monitoring use of antimicrobials
  - Preventive strategies for healthcare associated infections, case definitions and diagnosis of common infections.

Available at www.ncdc.gov.in/writereaddata/linkimages/AMR_guideline7001495889.pdf

How to use these guidelines?

- These guidelines list the recommended treatments for common infectious diseases that are based on scientific evidence, literature review and are consistent with the already existing international guidelines and formulated with the collective opinion of a wide group of recognised national experts.

Empirical or presumptive anti-infective therapy

SYNDROMIC APPROACH FOR EMPIRICAL THERAPY OF COMMON INFECTIONS

The syndromic approach is based on the presence of consistent groups of symptoms and easily recognized signs caused by a single pathogen or a mixture of pathogens.

SYNDROMIC APPROACH FOR EMPIRICAL THERAPY OF COMMON INFECTIONS

- Before starting **presumptive therapy** the following to be ensured

1. Standard investigations for all suspected infections for correct and accurate diagnosis and prognosis.

2. Antibiotics SHOULD be started only after sending appropriate cultures if facilities are available.

   Similarly any change in antibiotic MUST be guided by sensitivity profile.

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SYNDROMIC APPROACH FOR EMPIRICAL THERAPY OF COMMON INFECTIONS…

3. Assessment of factors affecting activity of antimicrobilas viz., renal excretion, interactions and allergy before prescribing antibiotics.

4. Review of antibiotic therapy MUST be done daily and the therapy escalated or deescalated accordingly espacially after the culture reports are available.

- **Empirical Therapy** is justified in patients with life threatening infections, in ICU settings and while awaiting results of culture

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Common approach

- To use broad spectrum antimicrobial agents as initial empiric therapy with the intent to cover multiple possible pathogens commonly associated with the specific clinical syndrome.

- However, once laboratory results of microbiology tests are available with identification of pathogen along with antimicrobial susceptibility data, **every attempt should be made to narrow the antibiotic spectrum**.

- This is a critically helpful and integral component of antimicrobial therapy because it can **reduce cost and toxicity and significantly delay the emergence of antimicrobial resistance in the community**.

- Antimicrobial agents with a narrower spectrum should be directed at the most likely pathogens for the duration of therapy for infections such as community-acquired pneumonia, urinary tract infections, soft tissue infections etc. in an OPD setting because specific microbiological tests are not routinely performed or available or affordable.

Ear Infections

Ear infection	Likely Etiology/	Suggested Regimen	Alternate	Remarks
Malignant otitis externa	*P. aeruginosa* (in >90% cases)	Piperacilin+Tazobactam 4.5gm IV 6h Or Imipenem/Meropenem Ciprofloxacin	Ceftazidime	Debridement usually required. Rule out osteomyelitis; Do CT or MRI, If bone involved , treat for 4-6 wks.
Acute otitis media	S. *pneumoniae* *H. influenzae* *Morexella catarrahalis*	Amoxicillin+clavulanate 90/6.4mg /kg/day bid or cefpodoxim /cefuroxime axetil 250mg BD	Ceftriaxone 50mg/kg I/M for 3 days	Treat children <2 years If >2 years, afebrile and no ear pain- consider analgesics and defer antibiotics Duration of treatment If age <2 years: 10 days If age >2 years : 5-7 days
Mastoiditis				
Acute	S.*pneumoniae* *S.aureus* *H.infiuenzae* *P.aeruginosa*	Cefotaxime 1-2 gm iv 4-8 hourly Ceftriaxone 2 gm iv OD		Modify as per culture Unusual causes- Nocardia, TB, Actinomyces.
Chronic	Polymicrobial	Piperacillin- tazobactam 4.5g IV 8h Meropenem 1 gm iv 8h		

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Ear Infections

Acute Pharyngitis/tonsillitis				
Exudative/Diffuse Erythema	Mostly viral Group A, C, G Streptococcus, Infectious mononucleosis,	Penicillin V oral x10 days or Benzathine Penicillin 1.2 MU IM x 1 dose or Cefdinir or cefpodoxime x 5 days		Penicillin allergic, Clindamycin 300-450 mg orally 6-8 hourly x 5 days. Azithromycin clarithromycin are alternatives.
Membranous pharyngitis	*C.diptheriae*,	Erythromycin 500 mg IV QID or Penicillin G 50,000 units/kg IV 12 hourly. Diptheria antitoxin: Horse serum. <48 hrs:20,000-40,000 units, Nasopharyngeal membranes:40,000-60,000 units >3 days & bull neck : 80,000-1,20,000 units		
Epiglotitis(Supraglotis)	Children: *H.influenzae* , *S.pyogenes, S.pneumoniae, S.aureus*.	Cefotaxime 50 mg/kg IV 8 hourly or ceftriaxone 50 mg/kg IV 24 hourly	Levofloxacin 10 mg/kg IV 24 hourly + clindamycin 7.5 mg/kg IV 6 hourly.	
	Adult: Group A Streptococcus , *H.influenzae*			
Laryngitis(hoarseness)	Viral (90%)	No antibiotic indicated		

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Respiratory Tract Infections

Condition	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
Community acquired Pneumonia	*S. pneumoniae*, *H.influenza*e, Legionella, *E.coli*, *Klebsiella sp.*, *S.aureus*	<u>Mild to moderate cases</u> Amoxycillin-500mg-1 g TDS oral. If IV indicated, amoxycillin-clavulanate 1.2 g IV TDS or Ceftriaxone 2g IV OD For <u>Severe cases</u> Amoxycillin-clavulanate 1.2 g IV TDS OrCeftriaxone 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 MRSA is a concern, add Linezolid 600mg IV/Oral BD If atypical pneumonia suspected, Doxycycline 100mg bd or Azithromycin 500 mg oral/IV OD

Respiratory Tract Infections

Condition	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
Acute pharyngitis	Viral	None required		As most cases are viral no antimicrobial therapy required
	Group A ß-hemolytic Streptococci (GABHS), Group C, G Streptococcus,	*Oral Penicillin v 500mg BD or Amoxicillin 500 mg Oral TDS for 10 days*	*In case of penicillin allergy: Azithromycin 500mg OD for 5 days or Benzathine penicillin 12 lac units IM stat*	*Antibiotics are recommended to reduce transmission rates and prevention of long term sequaelae such as rheumatic fever*
Ludwig's angina Vincent's angina	Polymicrobial (Cover oral anaerobes)	Clindamycin 600 mg IV 8 hourly or Amoxicillin-Clavulanate 1.2gm IV	Piperacillin-Tazobactam 4.5gm IV 6 hourly	Duration based on improvement
Acute bacterial rhinosinusitis	Viral, *S. pneumoniae, H.influenzae, M. catarrhalis*	Amoxicillin-clavulanate 1gm oral BD for 7 days	Moxifloxacin 400mg OD for 5-7days	
Acute bronchitis	Viral	Antibiotics not required	-	-
Acute bacterial exacerbation of COPD	*S. pneumoniae H. influenzae M. catarrhalis*	Amoxicillin-clavulanate 1gm oral BD for 7 days	Azithromycin 500 mg oral OD × 3 days	

UPPER RESPIRATORY TRACT INFECTIONS in Children

(a) **Bacterial Pharyngotonsillitis (Group A Streptococcus) –**

Any of the following Antibiotic (route)	Children (<30kg) (days)	Children (>30kg) (days)
Penicillin V (Oral)	250 mg BID x 10 days	500 mg BID x 10 days
Amoxycillin (Oral)	40 mg/kg/day x 10 days	250 mg TID, can be given BID
Benzathine Pencillin G (IM)	6 Lakh units (Single Dose)	12 Lakh units (Single Dose)

While Penicillin is the drug of choice Amoxycillin is good alternative and used widely.

If the patient is **Pencillin allergic, the alternative drugs are Antibiotic (route) Dose and duration**

Antibiotic (route)	Dose and duration
Erythromycin (oral)	40-50 mg/kg/day BID or TID x 10 days
Azithromycin (oral)	12 mg/kg OD x 5 days
First Generation Cephalosporin (oral) (10 days) (if only, it is non Type 1 allergy to penicillin)	Cefaclor (20-40 mg/kg/d in 3 divided doses) / Cephalexin (50 mg/kg/d in 3 divided doses)

UPPER RESPIRATORY TRACT INFECTIONS

- **Mastoiditis And Other Acute Ear Infection**

  Inj. Amoxicillin-clavulanate OR 3rd Gen Cephalosporin (Ceftriaxone/ cefotaxime).

- **Acute Sinusitis with URI-**

  Oral Amoxycillin (45 mg/kg/day TDS) for 7-10 days is recommended. For severe cases, Amoxycillin Clavulanate (45 mg/kg/day oral BD) or Inj.Ceftriaxone 75 mg/kg/day OD can be used.

- **Ludwig's Angina**

  1st line : Clindamycin IV 8 hourly **or Amoxicillin-Clavulanate IV**

  2nd line : Piperacillin-Tazobactam IV 6 hourly

Acute Otitis media (AOM) –

- Oral Amoxicillin (45mg/kg/day TDS/50-60mg/kg/day in two divided doses) for 7 to 10 days is recommended.
- For severe cases (Severe Otalgia and/ or Temp >390C), Co-Amoxycillin Clavulanate (45 mg/kg/day po BD) or Inj. Ceftriaxone 75 mg/kg/day OD can be used.
- In case of penicillin allergy, Cefidinir (14 mg/kg/d in 2 divided doses) can be used
- Total duration of treatment is recommended for 7 to 10 days.

LOWER RESPIRATORY TRACT INFECTION

For **pneumonia (OPD)**

- Oral Amoxicillin (45mg/kg/day TDS) for a period of 5 days is recommended as the first choice. In case of non availability, one may use oral Co-trimoxazole (8mg/kg/day of TMP component BD).

For S**evere Pneumonia (Children with respiratory distress requiring indoor care)-**

Under 2 months of age:

- Inj Cefotaxime / Ceftriaxone and Gentamicin for 10 days

LOWER RESPIRATORY TRACT INFECTION

For S**evere Pneumonia (Children with respiratory distress requiring indoor care)-**

Over 2 months of age:

- Inj. Ampicillin (50mg/kg/dose 6h) + Gentamicin (7.5mg/kg/day OD i.m or i.v) is used.
- Inj Ampicillin can be switched to Oral Amoxycillin (45mg/kg/day TDS) for 7-10 days once child is stable and able to take oral feeds
- In case of no response in 2 days the patient is assessed for complications like empyema, or infection at any other site.
- In the absence of any complication, Cefotaxime 50mg/kg/dose 6h or Ceftriaxone 75- 100mg/kg/day in two divided doses, IV) is used.
- In case the patient has severe sepsis/ septic shock, Inj. Piperacillin + Tazobactam (90mg/kg/dose 6h) + MRSA cover with IV Vancomycin (15mg/kg/dose 6h) is recommended.

GASTRO-INTESTINAL DISEASES

(1) Dysentery

(a) For inpatients- Inj Ceftriaxone (100mg/kg) for 5-7 days.

(b) For OPD cases

- Cefixime (8mg/kg/day BD) or
- Azithromycin 10-20 mg/ kg (ceiling dose of 1 gm) for 5 days.

  In case of non response after 2 antibiotics, investigate for appropriate therapy.
- Fluoroquinolones are not preferred due to high level of resistance in many parts of the country.

(2) **Cholera**

- Single dose oral azithromycin 10 mg/ kg (ceiling dose of 1 gm) or Doxycycline (50mg for less than 3 years and 100 mg for those above).

Enteric Fever

(a) For OPD cases-

- Oral Cefixime 20 mg/kg/day (max dose of 1200) for 14 days or azithromycin 10-20 mg/kg (ceiling dose of 1 gm) for 7-10 days. Antibiotic therapy should be continued till one week post-fever defervescence.

(b) For inpatients

- Inj Ceftriaxone 100 mg/ kg/day and shift to oral cefixime once fever resolves. Antibiotic therapy should be continued till one week post-fever defervescence.

Second line:

a) Ofloxacin 15mg/kg/d in two divided doses for 10-14 days. Antibiotic therapy should be continued till one week post-fever defervescence.

b) Chloramphenicol (50- 75mg/kg/day PO) x 14 days

c). TMP-SMX (8 mg/kg/day of TMP PO) x 14 days

URINARY TRACT INFECTION (UTI)

Uncomplicated UTI (age> 2 months with lower UTI, without any urinary tract obstruction) –

- Oral Cotrimoxazole (8-10mg of TMP component) /kg/day oral BD or
- Cefixime (8-10 mg/kg/day BD) to be given for 7-10 days or
- Co Amoxycillin+Clavulanic Acid (30-50 mg of Amoxicillin) for 7-10 days.

b) Complicated / Severe UTI (Febrile UTI, Systemic toxicity, renal angle tenderness or with any urinary structural abnormality) and all UTI in children less than 2 months should be treated with parenteral antibiotics.

- Inj. Cefotaxime (150-200mg/kg/day 8h OR
- Inj. Ceftriaxone (100mg/kg/day OD OR
- Inj. Amikacin 15mg/kg OD
- To be given for 10-14 days

c) In Immunocompromised host/ severe systemic sepsis or as second line for complicated UTI-

- Inj. Piperacillin Tazobactum 90mg/kg/dose IV 6h) or Inj. Meropenem (20-40mg/kg/dose 8h) To be given for 10-14 days

FEBRILE NEUTROPENIA

1st Line	2nd Line	3rd Line
Ceftazidime (150 mg/kg/day in 3div doses)+ Amikacin (15-20mg/kg/day in 2 or 3 div doses)	Piperacillin + Tazobactam (200-300 mg/kg/day IV in 3-4 div doses)+ Vancomycin (40 mg/kg/day IV in 4 divided doses)	Meropenem (60 mg/kg/day in 3 div doses) + Amphotericin B (1 mg/kg/day IV for 2 weeks) or liposomal Amphotericin B 1-5 mg kg/day, usually 3 mg/kg/day

OBSTETRICS AND GYNAECOLOGICAL INFECTIONS

Infections	Likely organism	Primary treatment (presumptive antibiotics)	Alternate treatment	Remarks
Asymptomatic Bacteriuria > 1,00,000 cfu/ ml of bacteria of same species in 2 urine cultures obtained 2-7 days apart. Treat as per sensitivity result for 7 days.		Nitrofurantoin 100 mg Oral, BD for 7 days or Amoxicillin 500 mg Oral BD x 7-10 days .	Oral cephalosporins, TMP-SMX or TMP alone	Screen in 1st trimester. Can cause pylonephritis in upto 25% of all pregnant women. 30 % Chance of recurrence after empirical therapy 1. Few direct effects, uterine hypo perfusion due to maternal anemia dehydration, may cause fetal cerebral hypo perfusion. 2. LBW, prematurity,premature labour, hypertension, preeclampsia, maternal anemia, and amnionitis. Need to document pyuria (Pus cells > 10/HPF)
Group B streptococcal Disease, Prophylaxis and Treatment	Group B Streptococci	IV Penicillin G 5 million units. (Loading dose) then 2.5 -3 million units IV QID until delivery. or Ampicillin 2 gm IV (Loading dose) then 1 gm QID until delivery	Cefazolin 2 gm IV (Loading Dose) and then 1 gm TID Clindamycin 900 mg IV TID or vancomycin IV or teicoplanin for penicillin allergy	Prevalance very low so the prophylaxis may be required only on culture documented report Associated with high risk of pre-term labour,still birth,neonatal sepsis

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OBSTETRICS AND GYNAECOLOGICAL INFECTIONS

Infections	Likely organism	Primary treatment (presumptive antibiotics)	Alternate treatment	Remarks
Chorioamnionitis	Group B streptococcus, Gram negative bacilli, chlamydiae, ureaplasma and anaerobes, usually Polymicrobial		Clindamycin/ vancomycin/ teicoplanin and cefoperazone-sulbactum If patient is not in sepsis then IV Ampicillin	Preterm Birth, 9-11% death rate in preterm infant's unfavourable neurologic outcome, lesser risk to term infants.
Septic abortion	Bacteroides, *Prevotella bivius,* Group B, Group A Streptococcus, Enterobactereaceae, *C. trachomatis, Clostridium perfringens.*	Ampicillin 500 mg QID + Metronidazole 500mg IV TDS if patient has not taken any prior antibiotic (start antibiotic after sending cultures) If patient has been	Ceftriaxone 2g IV OD	

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OBSTETRICS AND GYNAECOLOGICAL INFECTIONS

Infections	Likely organism	Primary treatment (presumptive antibiotics)	Alternate treatment	Remarks
Obstetric Sepsis during pregnancy	Group A beta-haemolytic Streptococcus, *E.coli*, anaerobes.	If patient is in shock and blood culture reports are pending, then start Piperacillin-Tazobactam or Cefoperazone-sulbactam till the sensitivity report is available and modify as per the report. If patient has only fever, with no features of severe sepsis start amoxicillin clavulanate oral 625TDS/IV 1.2 gm TDS Or Ceftriaxone 2gm IV OD+ Metronidazole 500mg IV TDS +/-gentamicin 7mg/kg/day OD if admission needed. MRSA cover may be required if suspected or colonized (Vancomycin/ Teicoplanin)		
Obstetric Sepsis following pregnancy	*S. pyogenes,* *E. coli,* *S. aureus* *S. pneumoniae*, Meticillin-resistant *S. aureus* (MRSA), *C. septicum* & *Morganella morganii.*	Same as above	Sources of sepsis outside Genital tract Mastitis UTI Pneumonia Skin and soft tissue (IV site, surgical site, drain site etc.)	

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OBSTETRICS AND GYNAECOLOGICAL INFECTIONS

VIRAL INFECTIONS (NO ANTIBIOTICS TO BE GIVEN)

Influenza In pregnancy (seasonal And H1N1) The best preventive strategy is administration of single dose of killed vaccine.	Oseltamivir 75 mg Oral BD for 5 days	Nebulization with Zanamvir respules (2) 5 mg each, BD for 5 days	1. Tendency for severe including premature labor &delivery. 2. Treatment should begin within 48 hrs of onset of symptoms. 3. Higher doses commonly used in non pregnant population (150 mg) are not recommended in pregnancy due to safety concerns. 4. Chemoprophylaxis can be used in significant exposures. 5. Live (nasal Vaccine) is contraindicated in pregnancy.	Direct fetal infection rare Preterm delivery and pregnancy loss.
Varicella	>20 wks of gestation, presenting within 24 hours of the onset of the rash, Aciclovir 800mg Oral 5 times a day IV acyclovir recommended for the treatment of severe complications, > 24 hrs from the onset of rash, antivirals are not found to be useful.	VZIG should be offered to susceptible women < 10 days of the exposure. VZIG has no role in treatment once the rash appears. The dose of VZIG is 125 units / 10kg not exceeding 625 units, IM.		Chickenpox during pregnancy does not justify termination without prior prenatal diagnosis as only. A minority of fetuses infected develop fetal varicella syndrome.

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TREATMENT OF MULTI-DRUG RESISTANT BACTERIAL PATHOGENS

1. Methicillin- Resistant S. aureus (MRSA)

a. 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.

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

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:** is an I.V. 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.

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2. Vancomycin Resistant Enterococcus (VRE)

- The acquisition of resistance to vancomycin by enterococci has seriously affected the treatment and infection control

- 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.
  - Linezolid may be particularly useful in patients who require oral or outpatient therapy (when I.V. is undesirable), or intolerant to glycopeptides, or impaired renal function.
  - Linezolid toxicity when administered for prolonged courses may limit its use in VRE endocarditis.

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2. Vancomycin Resistant Enterococcus (VRE)

- **Ampicillin:** Isolates that remain relatively susceptible to penicillin or ampicillin may be treated with high dose

- **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.

- **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.

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2. Vancomycin Resistant Enterococcus (VRE)

- **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.

- **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.*

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

- ESBLs confer resistance to broad spectrum β- lactam antibiotics
- 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.***

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

- The emergence of ESBL producing enterobacteriaceae is related to indiscriminate use of 3rd generation cephalosporins.

- 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.

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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, but should be on the principle of 'highest safe' rather than 'minimum potentially effective; durations should be as standard for the infection type.***

- **Colistin - Case reports of successful use in a range of infections due to carbapenemase producers.**

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Carbapenem- Resistant Enterobacteriaceae (CRE)

- **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).

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

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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 cephalosporins

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GUIDELINES FOR OPTIMIZING USE OF KEY ANTIMICROBIALS

Guidelines For Optimizing Use Of Key Antimicrobials

Antimicrobial Prescribing: Good Practice

Send for the appropriate investigations in all suspected infections as recommended.

↓

Rapid tests, such as Gram stain, can help determine therapeutic choices when empiric therapy is required

↓

Differentiation between contamination, colonization and infection to prevent overuse of antimicrobials

↓

Prescribing antibiotics just in case an infection is present is rarely justified

↓

In hospitalized patients close observation is usually a better option till the diagnosis is made.

↓

Use the most effective, least toxic and least expensive antibiotic for the precise duration of time

↓

Clinical Diagnosis: The antibiotic treatment chosen must be based on presumptive diagnosis

↓

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Guidelines For Optimizing Use Of Key Antimicrobials

Antimicrobial Prescribing: Good Practice

Empiric Therapy:

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.

The need for antimicrobial therapy should be reviewed on a daily basis

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

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B. Reserve Antimicrobials

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

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

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B. Reserve Antimicrobials…

- **The following criteria has been proposed for initiating Colistin –**
  - Pan-resistant organism as per culture report with evidence of invasive disease – fever/ leucocytosis/elevated procalcitonin (PCT) or culture from a sterile site.
  - Clinical failure of all other classes of antibiotics over 72 hours.

- **The following criteria has been proposed for initiating Rifampicin –**
  - 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**

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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 the guidelines are**

1. ciprofloxacin,
2. ceftazidime,
3. cefotaxime,
4. ceftriaxone,
5. vancomycin (or teicoplanin),
6. imipenem,
7. levofloxacin,
8. meropenem,
9. moxifloxacin,
10. piperacillin-tazobactam,
11. linezolid (oral/IV)
12. voriconazole,
13. caspofungin,
14. valganciclovir,
15. ertapenem and
16. newer preparations of amphotericin.

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PREVENTIVE STRATEGIES FOR HEALTHCARE ASSOCIATED INFECTIONS

Health Care Associated Infections

- Health Care Associated Infections (HCAI) are a worldwide phenomenon.
- HCAI have been defined variously at different times and by different organizations.
- **Current definitions** incorporate infections which were neither incubating nor did they manifest or present, during the period of admission in patients admitted in the hospital but were present on or after the 3rd calendar day of admission, (the day of hospital admission being calendar day 1).

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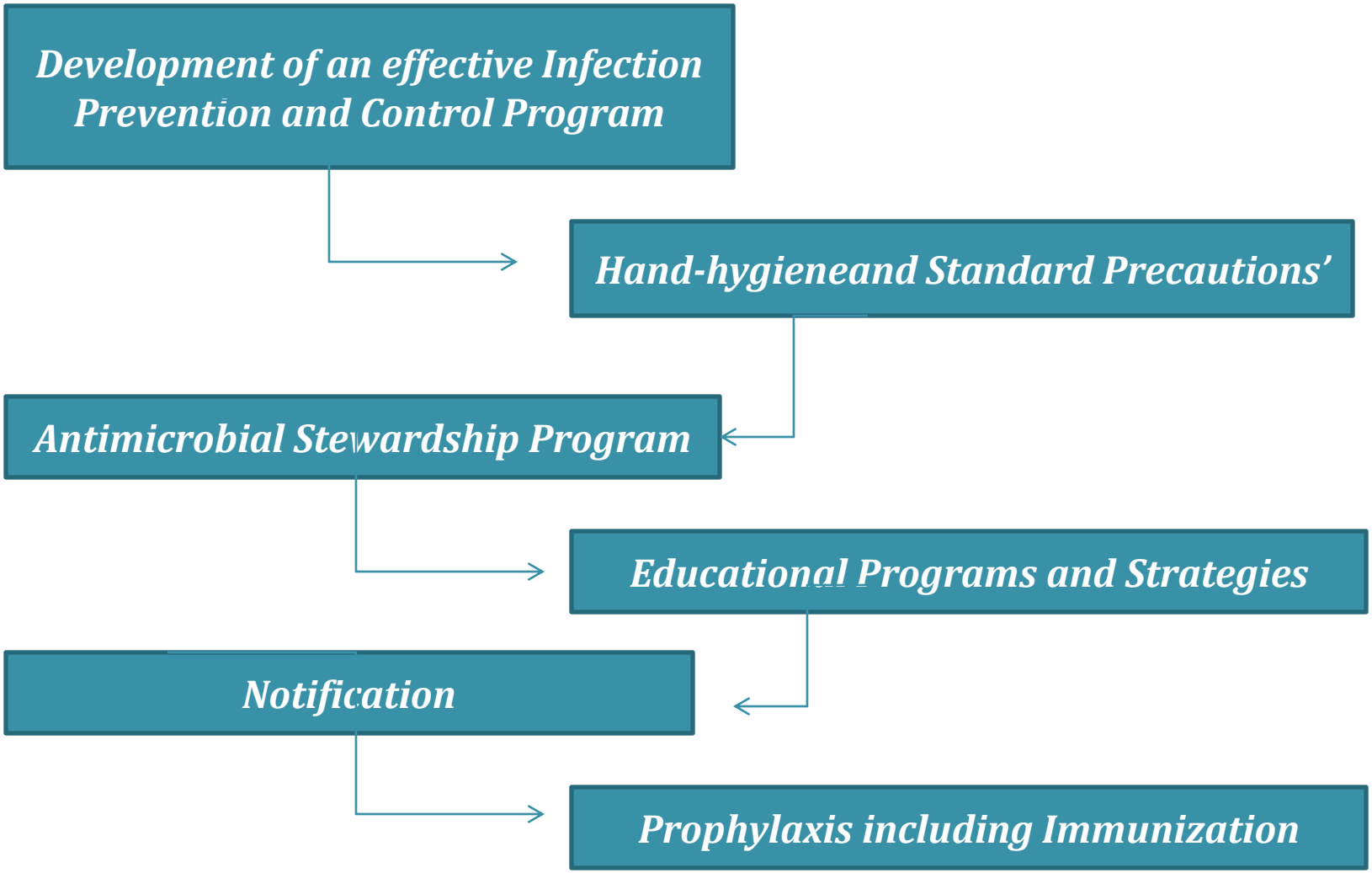
Reducing the risk of Health care associated infections



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MONITORING ANTIMICROBIAL USE

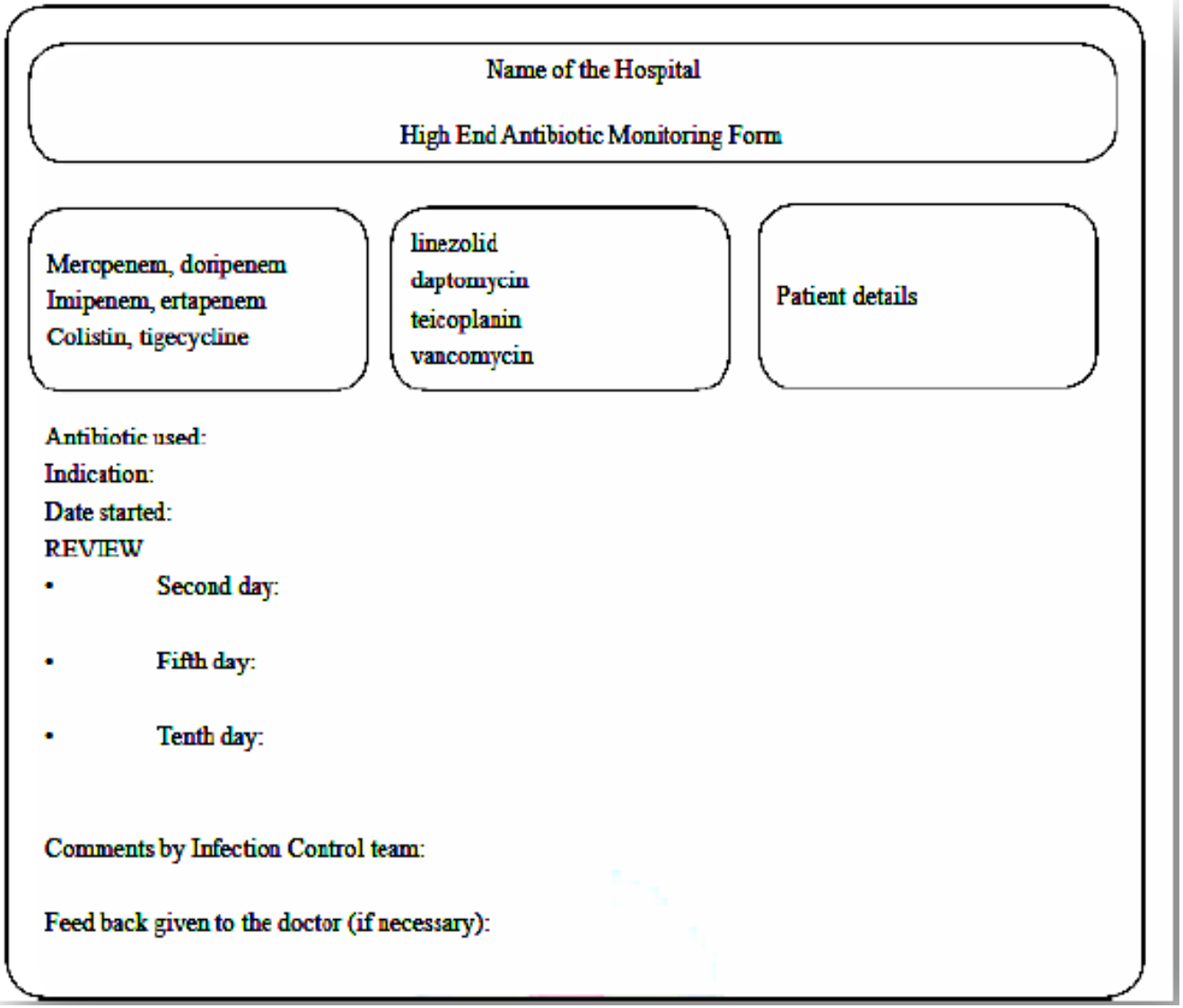
Antibiotic Surveillance: Need of the hour

Antibiotic Surveillance: Need of the hour

- Ministry of health has launched 'National programme for AMR Containment'.
  - **Key activity** - AMR surveillance with a network of ten laboratories across the country

- Imperative to have standardized national treatment guidelines:
  - To contain the further development of antimicrobial resistance with no new drug on the horizon and
  - Reduce the existing levels of reported resistance in the country,

High-end Antibiotic Monitoring Sheet



Name of the Hospital

High End Antibiotic Monitoring Form

Meropenem, doripenem
Imipenem, ertapenem
Colistin, tigecycline

linezolid
daptomycin
teicoplanin
vancomycin

Patient details

Antibiotic used:
Indication:
Date started:
REVIEW

- Second day:
- Fifth day:
- Tenth day:

Comments by Infection Control team:

Feed back given to the doctor (if necessary):

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Surgical Prophylaxis Monitoring Sheet

Name of the Hospital

Surgical antibiotic prophylaxis monitoring sheet

Patient Details	Date of Admission: Name of Surgeon:

Date of Surgery:

Type of surgery:

Date of Discharge:

Prophylactic antibiotic used:

Dose:

Duration:

Reason if antibiotic given for more than the recommended duration:

Signature of the Doctor

Comments by Infection control Team

Feed back given to the doctor (if necessary)

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SUMMARY

CO-AMOXICLAV

Condition	Likely Causative Organisms	Empiric (presumptive) antibiotics
Obstetric Sepsis during pregnancy	Group A beta-haemolytic Streptococcus, E.coli, anaerobes.	If patient has only fever, with no features of severe sepsis start amoxicillin clavulanate oral 625TDS/IV 1.2 gm TDS
Mastitis without abscess	S. aureus	Amoxycillin clavulunate
Diverticulitis Mild-OPD treatment	Gram-Negative Bacteria Anaerobes	Amoxycillin-Clavulanate 625mg TDS for 7 days
Liver Abscess	Polymicrobial	Amoxycillin-clavulanate/ 3rd generation cephalosporin + Metronidazole 500mg I.V.TID / 800mg oral TID for 2 weeks
Cellulitis	Streptococcus pyogenes(common), S.aureus	Amoxicillin-Clavulanate 1.2gm IV TDS/625 mg oral TDS
Furunculosis	S.aureus	Amoxicillin-Clavulanate 1.2gm IV/Oral 625 TDS
Ludwig's angina Vincent's angina	Polymicrobial (Cover oral anaerobes)	Amoxicillin-Clavulanate 1.2gm IV

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Condition	Likely Causative Organisms	Empiric (presumptive) antibiotics
Acute otitis media	S. pneumoniae H. influenzae Morexella catarrahalis	Amoxicillin+clavulanate 90/6.4mg /kg/day bid
Acute bacterial rhinosinusitis	Viral, S. pneumoniae, H.influenzae, M. catarrhalis	Amoxicillin-clavulanate 1gm oral BD for 7 days
Acute bacterial exacerbation of COPD	S. pneumoniae H. influenzae M. catarrhalis	Amoxicillin-clavulanate 1gm oral BD for 7 days
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 1.2 g IV TDS **Severe cases** Amoxycillin-clavulanate 1.2 g IV TDS
Obstetric Sepsis during pregnancy	Group A beta-haemolytic Streptococcus, E.coli, anaerobes.	If patient has only fever, with no features of severe sepsis start amoxicillin clavulanate oral 625TDS/IV 1.2 gm TDS
Mastitis without abscess	S. aureus	Amoxycillin clavulunate

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Summary

- The convergence of factors such as poor public health infrastructure, rising incomes, a high burden of disease, and cheap, unregulated sales of antibiotics has created ideal conditions for a rapid rise in resistant infections in India.

- Over-the-counter, nonprescription sales contribute to growing resistance

- Improving regulation of drug production and sales, better managing physician compensation, and encouraging behavior change among doctors and patients are of immediate priority

Summary

- It is emphasized that antimicrobials should be prescribed only when they are necessary in treatment following a clear diagnosis.
- Not all patients need antibiotics; non–drug treatment may be suitable and this has been emphasized in these guidelines.
- In all cases, the benefit of administering the medicine should be considered in relation to the risk involved.
- This is particularly important during pregnancy where the risk to both mother and foetus must be considered

MICRO LABS LIMITED

Avoid Self Handling

biotics

MYTHS AND FACTS ON ANTIBIOTICS Series

MISSION - AAA

Avoid Antibiotic Abuse


thank you
danke
謝謝
ngiyabonga
شكراً جزيلاً
teşekkür ederim
спасибо
Баярлалаа
dank je
gracias
tapadh leat
bedankt
dziękuję
hvala
mochchakkeram
go raibh maith agat
obrigado
sukriya
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