Need to conserve the use of critically important antimicrobials for managing severe infections in children

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President Elect 2021
Indian Academy of Pediatrics
Back ground

**AMR : the hidden threat lurking behind COVID-19: Need of one health approach**

- Based on current trends, global deaths related to AMR will rise from the current figure of 700,000 to 20 million per year by 2050.

- 70% to 80% of antibiotics manufactured in USA & Europe are used for veterinary practice. In India, exact data not known but on higher side.

- Among 75000 hospitals in India less than 1% is running an effective AMR Program; in USA - 80% hospitals running Antibiotic stewardship program.
One Health & AMR

• Zoonotic diseases represent more than 60% of emerging and re-emerging infectious disease worldwide.

• The destruction of natural environment, globalised trade and travel have created numerous pathways for new pathogens to jump between animals and humans.

• Critical intersection between human health, domestic and wild animal health and the environment requires a new integrated framework — a paradigm called ‘One Health’

• The integral components of AMR Program are infection prevention control, antibiotic stewardship program, rational antibiotic therapy and AMR surveillance
ANTIMICROBIAL RESISTANCE – A BIG PUBLIC HEALTH ISSUE

GLOBAL

A failure to address the problem of antibiotic resistance could result in:

10m deaths by 2050

Costing £66 trillion
Five ways antimicrobial resistance disrupts the Sustainable Development Goals.
Antimicrobial resistance is a complex issue

Human

Environment
- Pharmaceutical
- Farms
- Hospitals
- Household & unused or expired drugs

Animal-food
- Treatment & control
- Disease prevention
- Growth promotion

Major health, food security, environment & economic threat
<table>
<thead>
<tr>
<th>Antimicrobial class</th>
<th>Antimicrobials (examples)*#</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cephalosporins</strong> (third-, fourth- and fifth-generation)</td>
<td>Cefixime, cefodizime, cefoperazone, cefotaxime, cefpodoxime, cefquinome, ceftazidime, ceftriaxone, ceftizoxime, ceftriaxone</td>
</tr>
<tr>
<td>Glycopeptides*</td>
<td>Avoparcin, teicoplanin, vancomycin</td>
</tr>
<tr>
<td><strong>Macrolides and ketolides</strong></td>
<td>Azithromycin, clarithromycin, erythromycin, flurithromycin, roxithromycin, spiramycin, tulathromycin, tylosin, tylvalosin</td>
</tr>
<tr>
<td>Polymyxins</td>
<td>Colistin, polymyxin B</td>
</tr>
<tr>
<td><strong>Quinolones</strong> **</td>
<td>** Ciprofloxacin, danofloxacin, enrofloxacin, flumequine, gatifloxacin, levofloxacin, lomefloxacin, moxifloxacin, nalidixic acid, norfloxacin, ofloxacin, oxolinic acid</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Critically important antimicrobials^</th>
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<tbody>
<tr>
<td><strong>Aminoglycosides</strong></td>
</tr>
<tr>
<td><strong>Ansamycins</strong></td>
</tr>
<tr>
<td><strong>Carbapenems and other penems</strong></td>
</tr>
<tr>
<td><strong>Glycylcyclines</strong></td>
</tr>
<tr>
<td><strong>Lipopeptides</strong></td>
</tr>
<tr>
<td><strong>Monobactams</strong></td>
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<tr>
<td><strong>Oxazolidinones</strong></td>
</tr>
<tr>
<td><strong>Penicillins (antipseudomonal)</strong></td>
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<tr>
<td><strong>Penicillins (aminopenicillins)</strong></td>
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<tr>
<td><strong>Penicillins (aminopenicillins with beta-lactamase inhibitors)</strong></td>
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<tr>
<td><strong>Phosphonic acid derivatives</strong></td>
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<tr>
<td><strong>Drugs used solely to treat tuberculosis/mycobacterial diseases</strong></td>
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</tbody>
</table>
Specific examples wherein critically important antimicrobials are recommended for human health in India


- Ceftriaxone for use in adults but is also in children for septicaemia, neonatal meningitis, severe pneumonia, complicated or severe UTI, antimicrobial coverage for paediatric surgical procedures.


- Ciprofloxacin for treatment of cornea infections, multi-drug resistant bacterial infections, acute inflammatory infective diarrhoeas, serious infected diabetic ulcers, infected burn wounds, severe acute pelvic inflammatory disease, acute prostatitis.

- Amikacin for pyelonephritis, pneumonia and in children for urinary tract infection, septicaemia or pneumonia in infants with severe sepsis.

- Gentamicin for endocarditis, obstetric sepsis during pregnancy, corneal infections, osteomyelitis, septic arthritis and in children for the treatment of neonatal meningitis, septicaemia, pneumonia.

- Ampicillin for infective endocarditis, group B streptococcal disease, septic abortion, peritonitis, vancomycin resistant enterococcus and neonatal meningitis, severe pneumonia, neonatal septicaemia.

- Amoxicillin is advised for the treatment of cellulitis, acute pharyngitis, rhinosinusitis, acute bacterial exacerbation of chronic obstructive pulmonary disease, asymptomatic bacteriuria (an obstetrics and gynaecology infection), obstetric sepsis during pregnancy, acute otitis media, acute rheumatic fever and other acute ear infection.
Indian Priority Pathogens List

Critical priority
*Enterobacteriaceae* (*Klebsiella pneumoniae* and *Escherichia coli*): Carbapenem, tigecycline and colistin-R
Non-fermenting bacteria (*Acinetobacter baumannii* and *Pseudomonas aeruginosa*): Carbapenem and colistin-R

High priority
*Staphylococcus aureus*: methicillin-resistant *S. aureus*, heterogenous vancomycin-intermediate *S. aureus*, daptomycin-NS, linezolid-R
*Enterococcus* species: Vancomycin and linezolid-R, daptomycin-NS
*Salmonella* species (typhoidal and non-typhoidal): Azithromycin, third-generation cephalosporins and carbapenem-NS

Medium priority
*Streptococcus pneumoniae*: Cephalosporin, fluoroquinolones and linezolid-R
*Staphylococcus*, coagulase-negative: Vancomycin and linezolid-R
*Shigella* species: Third-generation cephalosporins and azithromycin-R
*Haemophilus influenzae*: Third-generation cephalosporin and carbapenem-NS
*Neisseria meningitides*: Fluoroquinolones and third-generation cephalosporins-NS

Note: R: resistant; NS: non-susceptible; Mycobacteria, including *Mycobacterium tuberculosis*, were not included in this prioritization exercise as it is a well-established global and national priority for which innovative new treatments are urgently needed and being developed.
# Resistance and susceptibility trends in bacteria against critically important antimicrobials

<table>
<thead>
<tr>
<th>Antibiotic (class)</th>
<th>S. aureus</th>
<th>Enterococcus sp.</th>
<th>E. coli</th>
<th>Klebsiella sp.</th>
<th>Pseudomonas sp.</th>
<th>Acinetobacter sp.</th>
<th>S. aureus</th>
<th>E. faecalis</th>
<th>E. faecium</th>
<th>E. coli</th>
<th>K. pneumoniae</th>
<th>P. aeruginosa</th>
<th>A. baumannii</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotaxime (third-, fourth- and fifth-generation cephalosporins)*</td>
<td>-</td>
<td>-</td>
<td>78.0</td>
<td>79.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>14.5</td>
<td>21.3</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Ceftazidime (third-, fourth- and fifth-generation cephalosporins)*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>53.0</td>
<td>78.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>20.0</td>
<td>25.3</td>
<td>63.1</td>
<td>12.2</td>
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<tr>
<td>Ciprofloxacin (quinolones and fluoroquinolones)*</td>
<td>66.0</td>
<td>77.0</td>
<td>79.0</td>
<td>71.0</td>
<td>54.0</td>
<td>65.0</td>
<td>178</td>
<td>16.4</td>
<td>8.0</td>
<td>20.8</td>
<td>36.0</td>
<td>57.7</td>
<td>-</td>
</tr>
<tr>
<td>Levofloxacin (quinolones and fluoroquinolones)*</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>19.0</td>
<td>35.0</td>
<td>56.5</td>
<td>19.1</td>
</tr>
<tr>
<td>Erythromycin (macrolides and ketolides)*</td>
<td>60.0</td>
<td>80.0</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Gentamicin (aminoglycosides)</td>
<td>23.0</td>
<td>48.0</td>
<td>-</td>
<td>-</td>
<td>49.0</td>
<td>55.0</td>
<td>-</td>
<td>57.5</td>
<td>35.0</td>
<td>-</td>
<td>-</td>
<td>62.2</td>
<td>-</td>
</tr>
<tr>
<td>Amikacin (aminoglycosides)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>47.0</td>
<td>45.0</td>
<td>60.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>79.2</td>
<td>50.1</td>
<td>679</td>
<td>20.4</td>
</tr>
<tr>
<td>Ampicillin (penicillins)</td>
<td>-</td>
<td>61.0</td>
<td>870</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>80.8</td>
<td>18.1</td>
<td>-</td>
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</tr>
</tbody>
</table>
# WHO AWARe classification .. 2017

<table>
<thead>
<tr>
<th>A</th>
<th>Amikacin, amoxicillin, chloramphenicol, Amoxicillin – clavulanic acid, Ampicillin, Cefazolin, Cephalexin, cloxacillin, Procaine benzyl penicillin, clindamycin, doxycycline, gentamicin, metronidazole, nitrofurantoin, sulphadoxine-trimethoprim</th>
</tr>
</thead>
<tbody>
<tr>
<td>WA</td>
<td>Quinolones, 3rd generation cephalosporins with or without beta lactamase inhibitors, macrolides, glycopeptides, antipseudomonal, penicillins + beta lactamase inhibitors, carbapenems, penems</td>
</tr>
<tr>
<td>RE</td>
<td>Aztreomycin, Fosfomycin (IV), 4th generation cephalosporins, LINEZOLID, 5th generation cephalosporins, tigecycline, polymixin, daptomycin</td>
</tr>
</tbody>
</table>
Use of the WHO Access, Watch, and Reserve classification to define patterns of hospital antibiotic use (AWaRe): an analysis of paediatric survey data from 56 countries

Yingfen Hsia, Brian R Lee, Ann Versporten, Yonghong Yang, Julia Bielicki, Charlotte Jackson, Jason Newland, Herman Goossens, Nicola Magrini,
AWaRe Use In Neonates
% of ESBL producers

% of ESBL producers (India)

Acinetobacter spp 65
E. coli 61
Klebsiella spp 62
Pseud. aeruginosa 65
Carbapenem resistance

**Carbapenem resistance (India)**
- *Acinetobacter* spp: 70
- *E. coli*: 12
- *Klebsiella* spp: 51
- *Pseud. aeruginosa*: 42

**Graph:**
- **Blue line:** *Acinetobacter* spp
- **Red line:** *E. coli*

**Graph X-axis:**
- Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Oct, Nov, Dec
Gram positives

Resistance (India)

MRSA 47
VRE 12
What is Antimicrobial Stewardship?

- The commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

- **RIGHT ANTIBIOTIC, AT RIGHT TIME, AT RIGHT DOSE, FOR RIGHT DURATION FOR RIGHT PATIENT.**

- Objectives:
  - Maximum antimicrobial benefit
  - Avoid harm from adverse reactions and drug allergies
  - Improve patient outcomes
  - Decrease antimicrobial resistance
  - Decrease healthcare costs

5 D’s of Antimicrobial Stewardship

- Diagnosis
- Drug
- Dose and Duration
- Discontinuation of Therapy
- De-escalation of Therapy
• Low hanging fruit model for Antibiotic stewardship

a. Antibiotic prescription for inpatients have to be put under a bracket.

b. If WHO RESERVE antibiotics are prescribed, need for the same has to be documented in the case sheet.

c. If de-escalation is not practiced based on susceptibility report, the reason for the same has to be documented in the case sheet.

d. Double anaerobic coverage is redundant. If double anaerobic coverage is given, reason for the same has to be documented in the case sheet.
e. If antibiotics are continued for more than 7 days, reason for the same has to be documented in the case sheet.

f. If surgical prophylaxis is continued for more than 24 hours reason for the same has to be documented in the case sheet.

g. If more than two antibiotics are prescribed, reason for the same has to be documented in the case sheet.
Antibiotic resistance is a slow-motion pandemic – whose speed will increase because of COVID-19. A concentrated global effort is now needed to ensure it is addressed with the same urgency that’s likely to bring us a COVID-19 vaccine in the months ahead...

“ALONE WE CAN DO SO LITTLE; TOGETHER WE CAN DO SO MUCH.”
- Helen Keller
THANK YOU