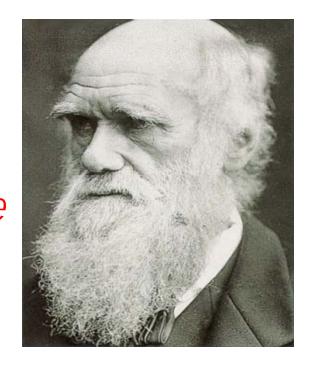
# AMR SURVEILLANCE Framework in human health and possible integration



Dr. Sunil Gupta
Addl Director
National Centre for Disease Control, Delhi
Aug 17

It is not the strongest in the species that survive or the most intelligent..

but the ones most responsive to change



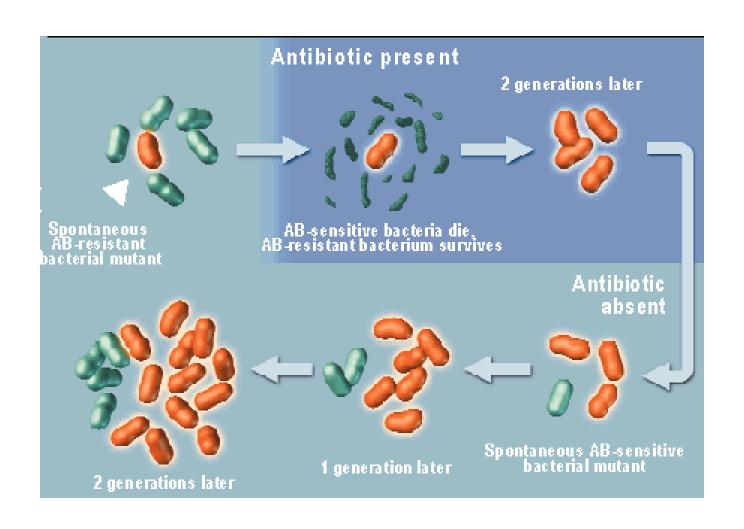
**Charles Darwin** 

"Drug resistance follows the drug like a faithful shadow."

- Paul Erhlich 1854-1915



#### **Antibiotic Selection for Resistant Bacteria**



#### Why Do Microbes Develop Resistance

- Development of Persisters (Metabolically inactive forms), L forms (Mycoplasma), Biofilms
- Continuously Occuring Changes in Genetic Material (Mutation)
- Acquisition of Genetic Material (plasmids) from other Previously Resistant Organisms
- Selection and spread of resistant organisms in the presence of antimicrobials facillitated by
- 1) Irrational use of drugs
- 2) Self medication and
- 3) Misuse of drugs

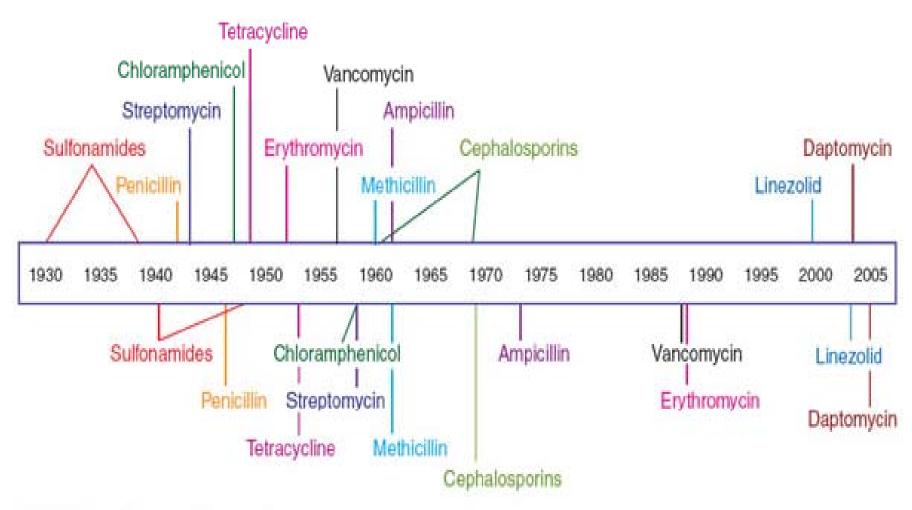
#### Mechanism of Antimicrobial Resistance

- Production of inactivating enzymes
   Chloramphenicol, aminoglycosides, Penicillin etc
- Alteration of drug targets penicillins, methicillins, Oxacillin, Macrolides, quinolones etc
- Altered drug uptake/Increased Efflux eg, Penicillins
  ,Tetracycline
- Altered Metabolic Pathway eg Sulfa Drug Resistance

#### Why AMR surveillance

- AMR Confirmation : Laboratory evidence only
- Feed back to Clinicians/Field epidemiologists
- Feed back to Disease Programme Managers
- Feed back to regulatory authoroties
- Feed Back to Policy makers
- Feed back to researchers

#### Antibiotic deployment



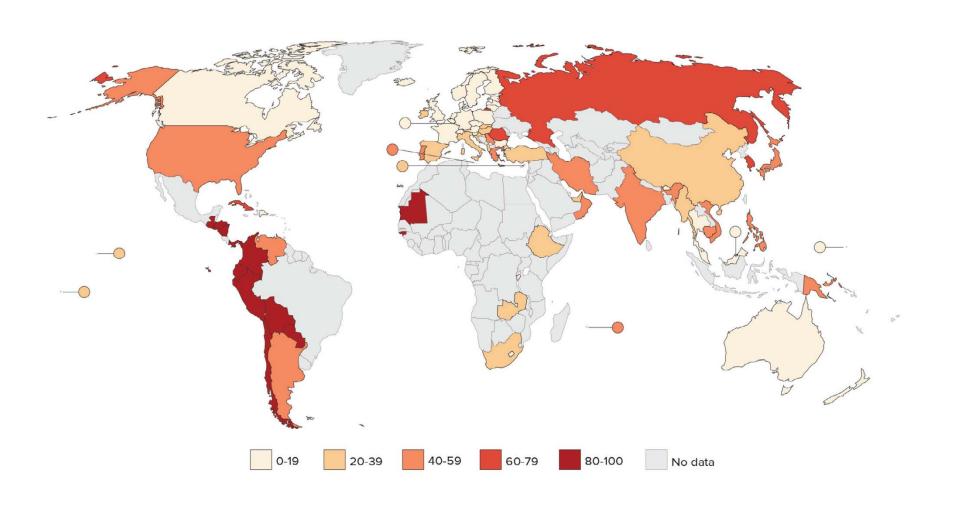
Antibiotic resistance observed

#### **Increasing Prevalence of AMR**

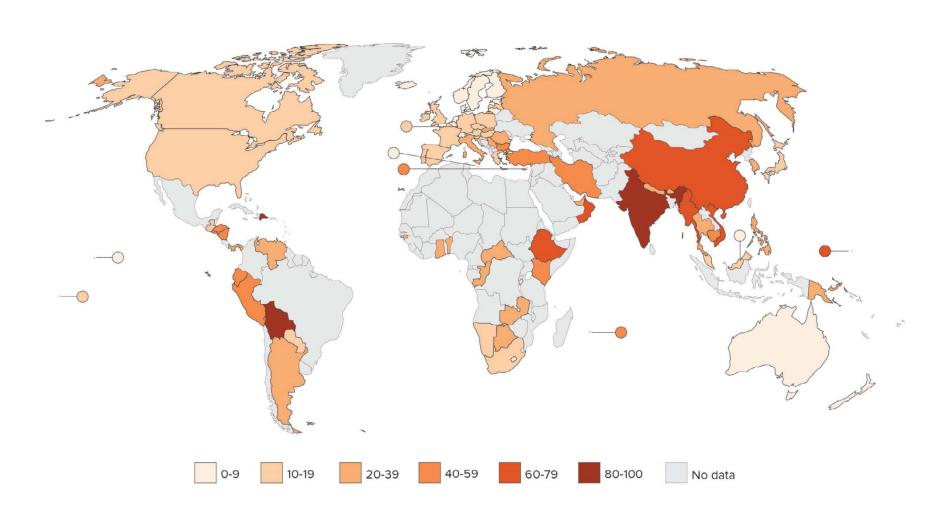
- Community-acquired infections: Multidrug resistant pneumococci, H. influenzae, Salmonella, Shigella, Gononococci, Multidrug-resistant M. tuberculosis, Drug-resistant Malaria, Drug-resistant HIV
- Hospital-acquired infections: Methicillin-resistant staphylococci(MRSA), Vancomycin-resistant enterococci(VRE), ESBL positive and Carbapenem res Gram-negative bacteria, Azole-resistant yeasts

#### **AMR: Global Scenario**

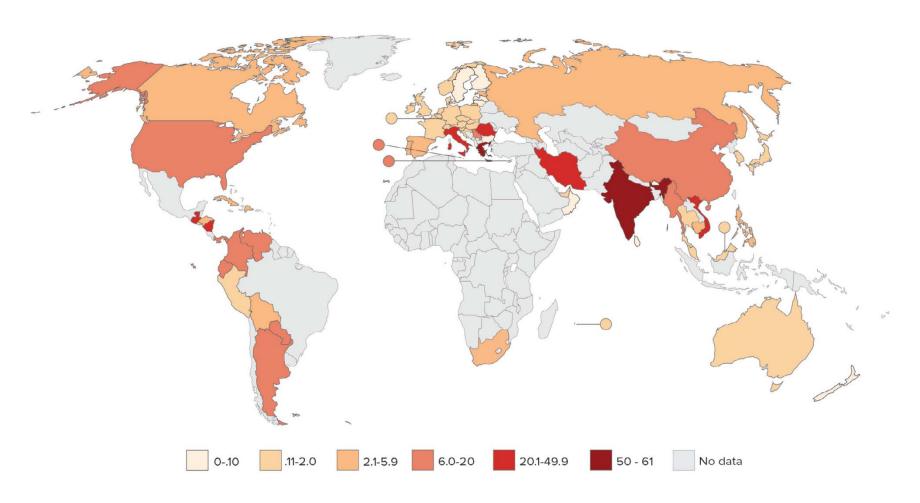
## Percentage of (MRSA), by country (most recent year, 2011–14)



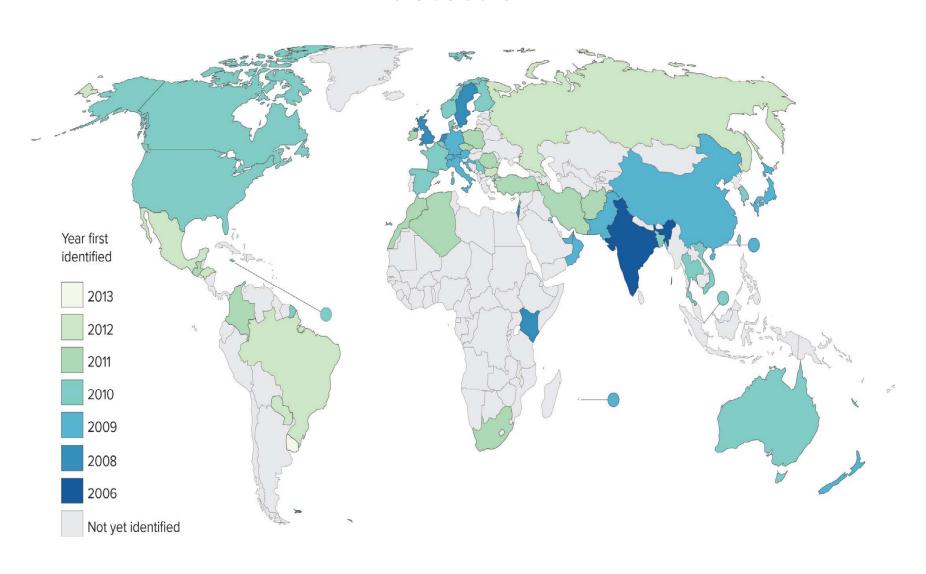
## Percentage of ESBL producing Escherichia coli (2011–2014)



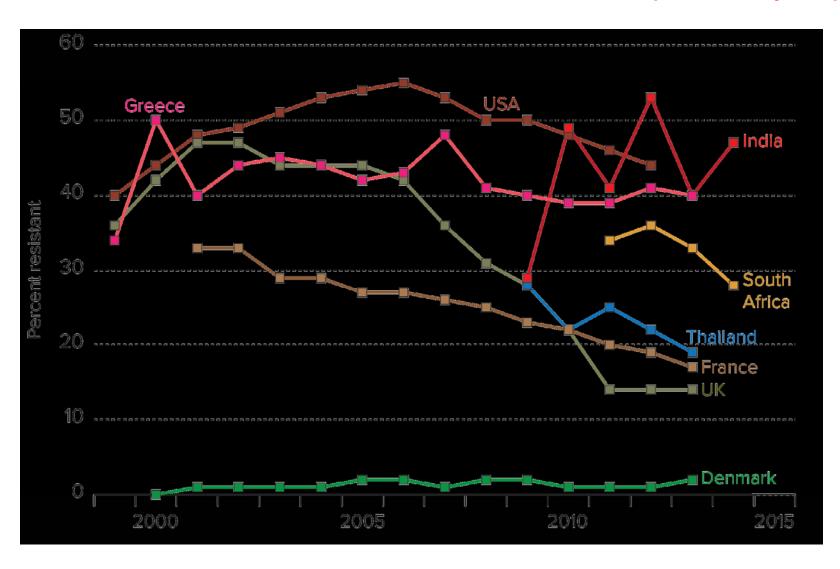
## Percentage of carbapenem-resistant Klebsiella pneumoniae, by country (most recent year, 2011–2014)



### Spread of New Delhi metallo-beta-lactamase-1: first detection



### Percentage of Staphylococcus aureus isolates that are methicillin resistant (MRSA) in selected countries, 1999–2014 (GARP report)



#### **AMR** Surveillance: India

- Data available from some public health programmes eg RNTCP, NVBDCP, NLEP, NACO for specific diseases/pathogens
- GASP for Gonococcus(network of 15 labs)
- Indiaclen: Data generated by (India clinical epidemiology network) through IBIS and CAMR surveillance for Pneumococcus, H.inf
- INSAR (2008-10): Network of 20 labs with WHO support not existent anymore
- However, till couple of years back No national AMR surveillance for other pathogens eg Salmonella, Shigella, Staph, Klebsiella, Acinetobacter etc
- ICMR initiated AMR surveillance with Network of 4 Centres/6 labs
- DGHS/NCDC initiated AMR surveillance with network of 10 labs

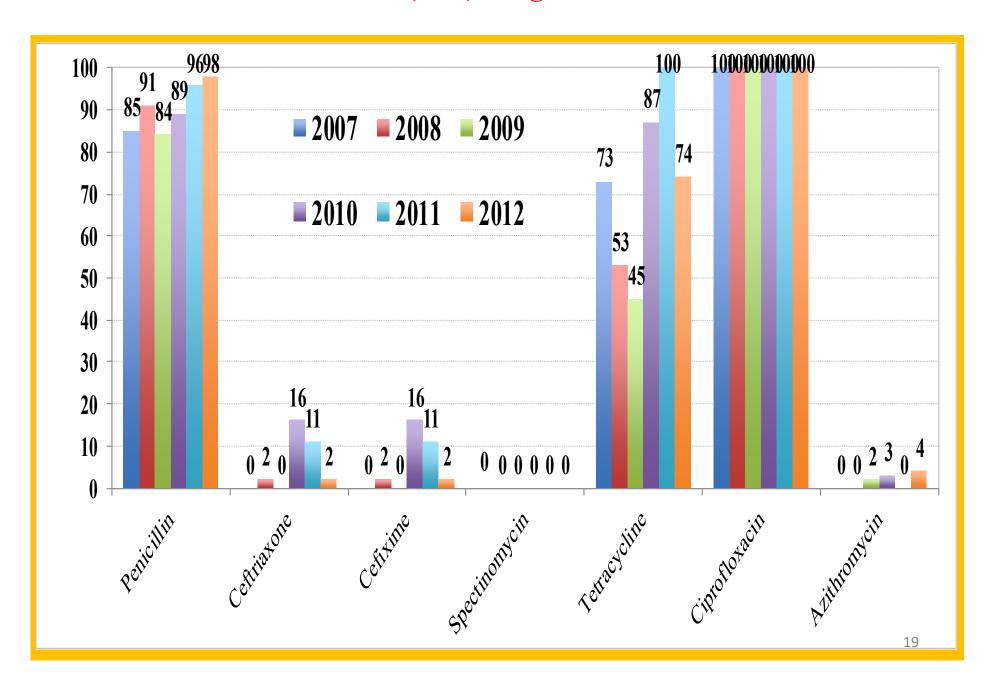
#### AMR SURVEILLANCE: INDIAN ....

- Very few Quality assured labs for antibiotic St testing
- Insufficient data analysis
- Not much Networking of labs
- Precise quantitation and trend analysis very sketchy
- Increasing drug resistance trends in the country based on available data

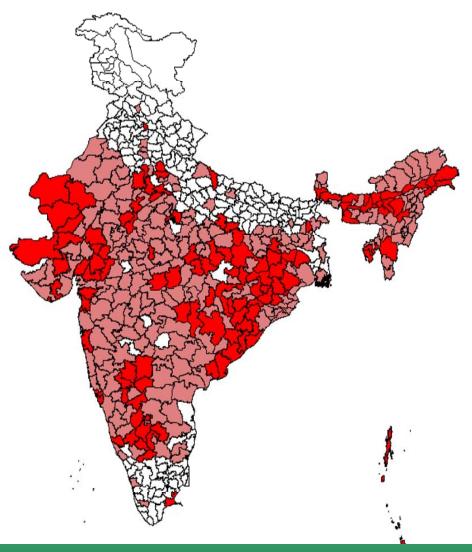
#### **AMR trends: India**

- Enteric Fever: Chloramphenicol, Ampicillin, Co-trimoxazole (10-15 %), Quinolones
   (up to 30%), recently reversal seen to Chloro, Cotrimoxazole and Ampicillin
- Meningococcal Infections: Penicillin (5-10%) Co-trimoxazole, Ciprofloxacin and Tetracycline (50-100%)
- Gonococcal Infections: Penicillin (50-80%), Ciprofloxacin (20-80%), Ceftriaxone (2-10%)
- ESBL: 30-60%, MRSA: 20-30%
- Malaria : Chloroquine(30-40%) and Sulpha-Pyrimethamine(25%) Res in Falciparum
   Malaria
- TB: MDR: 3-5% in new cases, 10-15% In treated cases XDR: 4-7% of MDR Cases, High MDR in Sikkim, Mumbai
- HIV: Primary and secondary low level resistance reported.

#### **AMR(%R)**: N.gonorrhoeae



#### **Chloroquine Resistance in Pf in India**



Districts with CQ treatment failure ≥10% (red) in any trial between 1978 and 2007 and Pf endemic areas (pink)

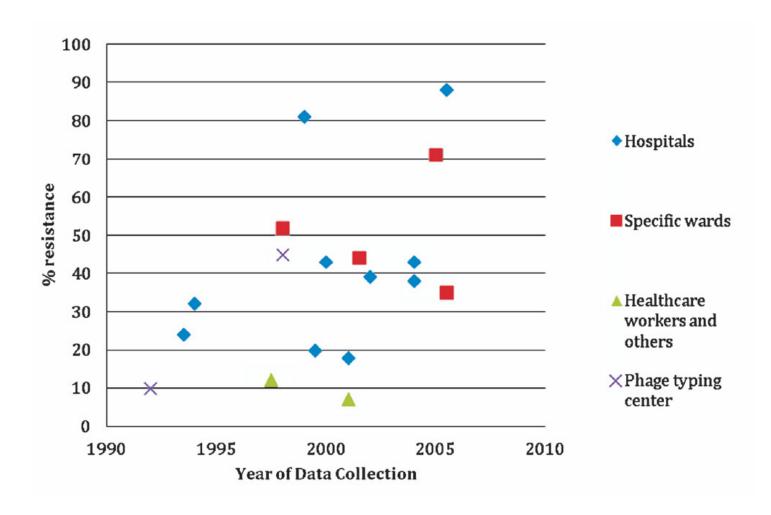
#### **AMR: MENINGOCOCCUS**

- No Res In India reported till 2005
- Following 2005 outbreak in Delhi increasing resistance (50-100%) seen towards Co-trimoxazole, Ciprofloxacin, Vancomycin and Tetracycline
- Other flouroquinolones (Ofloxacin, Levofloxacin, Gatifloxacin) (40-80%) also observed
- Increasing Res to Penicillin (0 -10%)
- No res to Ampicilln ,Rifampicin, Macrolides,
- Increased MIC to Chloro, Cephalosporins except 3<sup>rd</sup> Generation
- Similar trends seen in Meghalaya (2008) and Tripura (2009) outbreaks

#### **AMR: Strept. Pneumoniae**

- T/t failure in Pneumococcal meningitis/Pneumonias increasingly reported since mid 90,s
- Increasing penicillin resistance PRSP(penicillin resistant Str.pneumoniae)(10-30%)
- Chloro (10-15%), Tetracycline (20-40%), Cotrimoxazole (50-65%),
   Oxacillin (10-15%)
- Increasing low level Resistance also seen towards macrolides (0-4%), flouroquinolones (0-2%), Cephalosporins (1-2%)
- However, so far No Res to 3<sup>rd</sup> Generation Cephalosporins

## MRSA resistance rates from various Indian studies vary but appear to increase over time



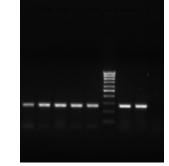
#### **Carbapenem Resistance**

- Since 2005, more and more resistance to various carbapenems being reported in various Gram Negative pathogens eg Klebsiella, Acinetobacter, Pseudomonas from different parts of the country
- Reports of occurrence of NDM-1 strains from India (Reported in lancet Infectious disease August 2010) raised a lot of hue and cry specially on the issue of naming these strains as NDM-1( New Delhi Metallo b lactamse-1) and linking the origin of these strains from India, though these have been reported in many other countries also.

Prevalence of ESBL, Carbapenem resistance in E.coli in

#### **Environment & Community**

**NCDC Study (2011-2014)** 



- **1. Community: 763 E.Coli isolates** obtained from stool samples (Healthy children ).
- ESBL production: 13 % 15 %, Carbapenem Res: 6-10% NDM-1 production: 3.2% 4.5%
- 2. Sewage: Seven collection sites selected in Delhi for study from October2011 to Dec 2014, total of 976 E. coli isolates obtained from sewage samples

**ESBL**: 20-60%, **Carbepenem** Res: 12-20%, **NDM-1**: 5-7.2 %

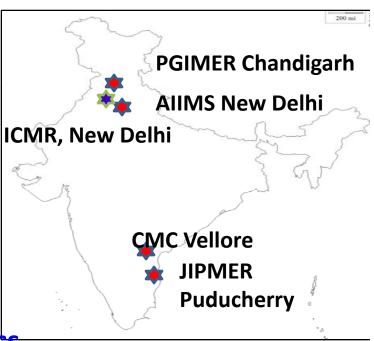




#### AMR Surveillance ICMR

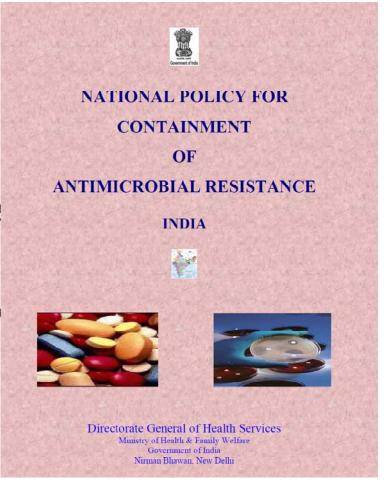
- Nodal centres are focal points for six pathogenic groups:
  - Enterobacteriaceae / sepsis (PGIMER)
  - Gram negative non-fermenters (CMC)
  - Enteric fever organisms (AIIMS)
  - Diarrhoeagenic organisms (CMC)
  - MRSA, Enterococcus (JIPMER)
  - Fungal pathogens (PGIMER)
  - Data management unit in Bioinformatics
     Center, ICMR Hqs
- 15 Regional Centres (RC) proposed

**Nodal Centres** 



#### The National Policy for Containment of Antimicrobial Resistance

- A National task force was set in 2010 under t chairpersonship of the DGHS review AMR situation in t country and formulate a strate for containment.
- The National Policy for AN containment were formulated
   2011 with following objectives.



## JAIPUR DECLARATION ON AMR BY HEALTH MINISTERS OF THE SOUTH-EAST ASIA REGION

**Sept 2011** 

Strong commitment to tackle AMR in the Region

#### National Programme on Containment of Antimicrobial Resistance

- As per National Policy, National Programme on AMR was developed and approved for implementation during 12<sup>th</sup> Five Year Plan.
- ➤ National Centre for Disease Control, Delhi identified as the nodal institution for this activity

#### Specific areas covered under National antibiotic policy

- I. Review the current situation regarding manufacture, use & misuse of antibiotics in the country.
- II. Design for creation of a National Surveillance System for Antibiotic Resistance.
- III. Initiate studies documenting prescriptions patterns & establish a Monitoring System for the same.
- IV. Enforce and enhance regulatory provisions for use of antibiotics in human, veterinary and industrial use.
- V. Recommend specific intervention measures such as rationale use of antibiotics & antibiotic policies in hospitals which can be implemented as early as possible.
- VI. Diagnostic Methods pertaining to antimicrobial Resistance Monitoring

## Activities Envisaged Under AMR containment

- National advocacy meetings with State Health Ministers, Health Secretaries, Technical Officers, Hospital Authorities etc.
- ➤ Establishment of Quality Assured AST Lab Network for AMR surveillance.
- Surveillance of antibiotic usage & operational research.
- Strengthening of diagnostic tools to prevent misuse of antimicrobials.

## Activities Envisaged Under AMR containment..2

- Co-ordination with DCGI/FSSAI for regulatory issues.
- Monitoring implementation of Hospital Infection Control and rational drug use policies in public and private sectors.
- Technical manpower training and development.
- IEC /BCC about rational use of antibiotics.
- ➤ Interface with Animal Husbandry/Agriculture etc. to rationalize use of antibiotics.

#### **Action taken:**



Promote rationale use of antibiotics.(National treatment guidelines developed)

AMR surveillance established

Schedule H1 enacted to regulate sale of antibiotics (March 2014)

 Hospital Infection control: To strengthen hospital infection control guidelines and practices (Draft guidelines developed)

#### Regulatory mechanism is being strengthened by adding Schedule H1 for use of antibiotics as well as starting Pharmaco-vigilance activity under DCGI.





#### **Treatment Guidelines: The Highlights**

#### Therapy of Common Infections: Syndrome vise

- Gastro-intestinal system
- Central Nervous System
- Cardio-vascular system
- Skin and Soft tissue
- Respiratory tract
- Genitourinary tract
- Pediatric and Neonatal infections
- Obstetrics & Gynecological infections
- Ophthalmic Infections
- Infections of Ear, Nose & Throat

#### **AMR Surveillance(NCDC Network)**

- A total of 30 labs in state medical colleges will be strengthened in a phased manner to carry out surveillance.
- Ten labs selected in the first phase(2015) in different geographical regions, five more being added in 2017
- Pathogens identified
- Panel of antibiotics finalised
- AST (disc Diffusion) methodology finalised based on CLSI guidelines
- Data analysis tools identified





## **AMR Network labs**

- The ten laboratories in the network are as below:
- a) Dr Ram Manohar Lohia Hospital, Delhi
- b) Smt Sucheta Kriplani Hospital, Delhi
- c) Vardhman mahavir Medical college and S.J Hospital, Delhi
- d) GVS Medical College, Kanpur(UP)
- e) SMS medical College, Jaipur(Rajasthan)
- f) B.J Medical College, Ahmedabad(Gujarat)
- g) B.J Medical college, Pune (Maharashtra)
- h) Govt Medical college, Chandigarh
- i) Mysore Medical college, Mysuru (Karnataka)
- j) JIPMER, Puducherry(T.N)
- Five more laboratories would be added in the network this year 1.(I.G.M.C. Shimla) 2. GMC, Assam, 3. NEEIGRHIM, Shillong, 4. MGM college, Indore (M.P) 5. Osmania Medical college, Hyderabad(Telangana)

#### Pathogen selection for AMR surveillance

- To begin with the following bacteria included for the AMR surveillance:(Initially four pathogens out of WHO priority list)
- Klebsiella pneumoniae
- Escherichia coli
- Staphylococcus aureus
- Enterococcus sp
- Typhoidal Salmonella, Pseudomonas aeruginosa and Acinetobacter added 2016/17
- Isolates both from community acquired infections and hospital acquired infections included.

## **Support to Network Labs**

- Manpower: Funds for recruiting Lab technician and data entry operator
- Reagents: Quality antibiotics procured centrally and supplied funds given for purchase of other minor reagents
- Equipments: Funds for purchase as well as Repair/maintenance
- Training: On Data analysis and quality control
- Guidelines: Made available current CLSI Guidelines, SOP,s developed

# AMR SURVIELLANCE METHODOLOGY

# Samples/Isolates to be tested

- CLINICAL -
- OPD
- IPD
- ICU
- (COMMUNITY)
- ENVIRONMENTAL

## Format for Reporting under AMR Surveillance

S. No	Isolat ID	Age	Sex	IPD/ICU/ Community	n Deptt	Provision al Diagnosi s	D.O.Admis sion	Date of sample collection	Clinical Sample	Pathogen Isolated	AST pattern/Zone diameter

# **Antibiotic Panel**

Staphylococcus aureus				
Penicillin	10 units			
Cefoxitin	30μg			
Erythromycin	15 μg			
Clindamycin	2 μg			
Co-trimoxazole	25 μg			
Gentamicin	10 μg			
Ciprofloxacin	5 μg			
Vancomycin	Vanco Screen/MIC			
Teicoplanin	MIC			
Doxycycline	30 μg			
Linezolid	30 μg			
Chloramphenicol	30 μg			
Norfloxacin (urine)	10 μg			
Nitrofurantoin (urine)	300 μg			

E. coli and Klebsiella pneumoniae				
Ampicillin	10 μg			
Amoxicillin-clavulanic acid	20/10 μg			
Cefoxitin	30 μg			
Cefotaxime	30 μg			
Cefotaxime- clavulanic acid	30/10 μg			
Ceftazidime	30 μg			
Ceftazidime - clavulanic acid	30/10 μg			
Co-trimoxazole	25 μg			
Gentamicin	10 μg			
Amikacin	30 μg			
Ciprofloxacin	5 μg			
Piperacillin-tazobactam	100/10 μg			
Imepenem	10 μg			
Meropenem	10 μg			
Colistin	MIC			
Nitrofurantoin (Only urine)	300 μg			

Enterococcus sp.		
Ampicillin	10 μg	
Penicillin	10 units	
Amoxicillin-clavulanic acid	<b>20/10</b> μg	
Gentamicin (high level)	120 μg	
Erythromycin	15 μg	
Vancomycin	30 μg	
Teicoplanin	30 μg	
Chloramphenicol	30 μg	
Ciprofloxacin	5 μg	
Linezolid	30 μg	
Tetracycline	30 μg	
Norfloxacin (urine)	10 μg	
Nitrofurantoin (urine)	300 μg	

Salmonella (Typhoidal)				
Ampicillin	10 μg			
Cefixime	30 μg			
Ceftriaxone	30 μg			
Nalidixic acid	30 μg			
Ciprofloxacin	5 μg			
Chloramphenicol	30 μg			
Tetracycline	30 μg			
Trimethopirim-sulphamethoxazole	25 μg			
Azithromycin	15 μg			
Imipenem	10 ug			

Pseudomonas aeruginosa				
Ceftazidime	30 μg			
Levofloxacin	5 μg			
Tobramycin	10 μg			
Amikacin	30 μg			
Netilmicin	30 μg			
Gentamicin	10 μg			
Colistin	MIC			
Ciprofloxacin	5 μg			
Cefepime	30 μg			
Piperacillin-tazobactam	100/10 μg			
Imipenem	10 μg			
Meropenem	10 μg			
Aztreonam	30 μg			

Acinetobacter baumannii				
Ceftazidime	30 μg			
Levofloxacin	5 μg			
Amikacin	30 μg			
Netilmicin	30 μg			
Colistin	MIC			
Cefepime	30 μg			
Piperacillin-tazobactam	100/10 μg			
Imipenem	10 μg			
Meropenem	10 μg			
Cefoperazone-sulbactam	75/30 μg			
Tetracycline	30 μg			

# **Quality Assurance**

IQC : Being Practiced by network Labs

EQA: 1% isolates sent to NCDC for reconfirmation
 90-95 % concordance in results

Independent EQA: Being explored with IAMM,WHO

 Some of the network labs already participating in EQA run by IAMM and some are NABL accredited

# DATA ANALYSIS /TRANSMISSION & FREQUENCY

WHO Net/Excel

Quarterly/Six monthly Through E mail

# AMR Resistance Trend from Network Labs (2015-16)

LHMC, DELHI (LHMC)

RMLH, DELHI (RML)

SJH, DELHI (SJH)

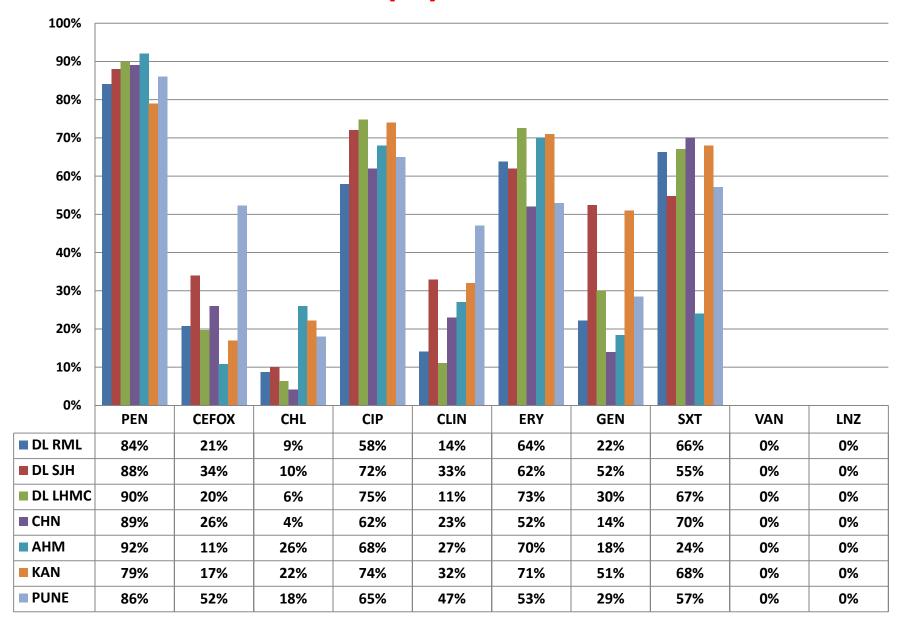
GMCH, CHANDIGARH(CHN)

BJ MC, AHMEDABAD (AHM)

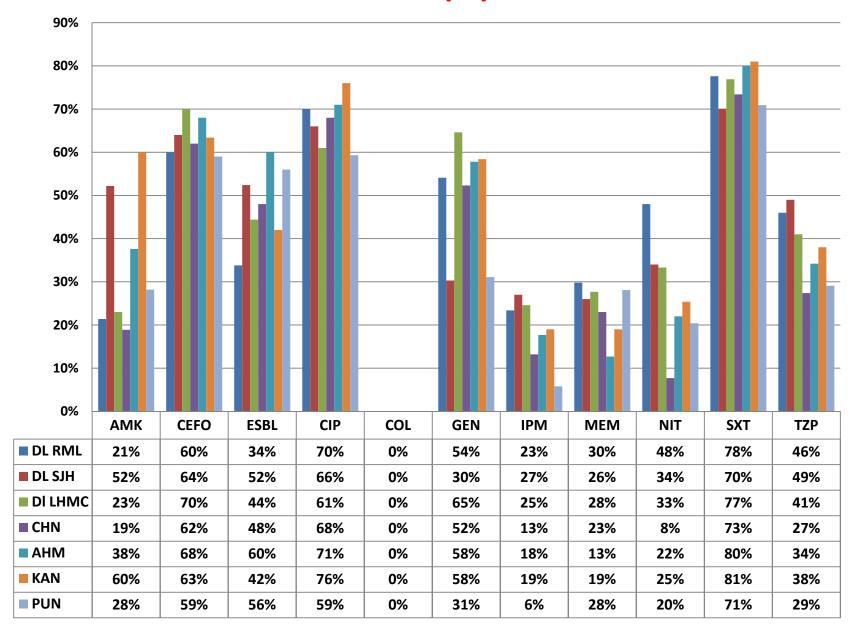
BJMC, PUNE (PUN)

GVSM, KANPUR (KAN)

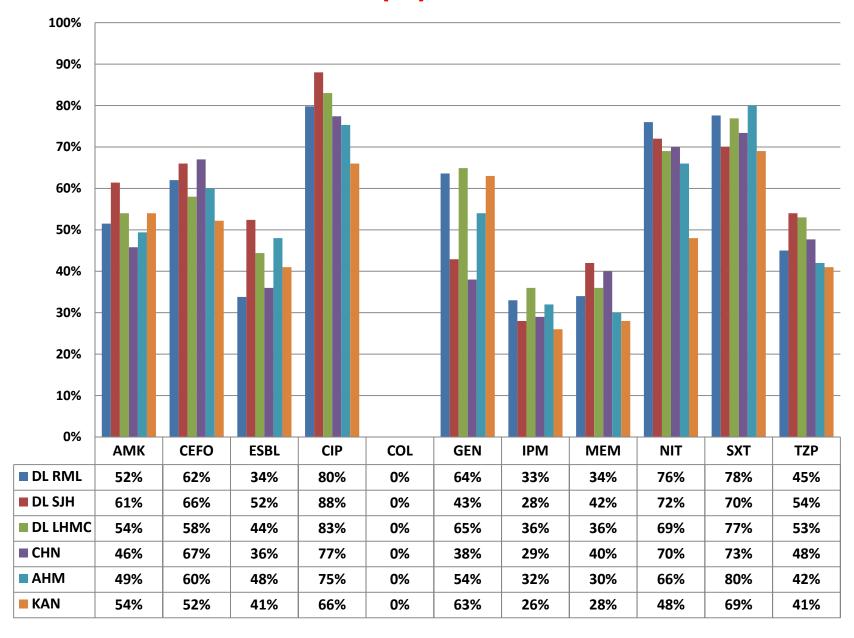
## **RESISTANCE (%) STAPH. AUREUS**



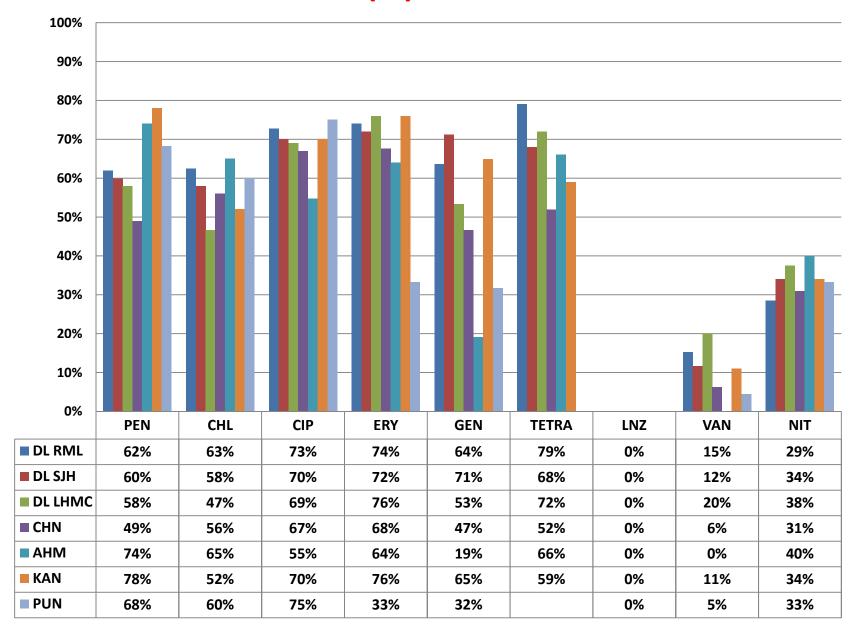
### **RESISTANCE (%) E.COLI**



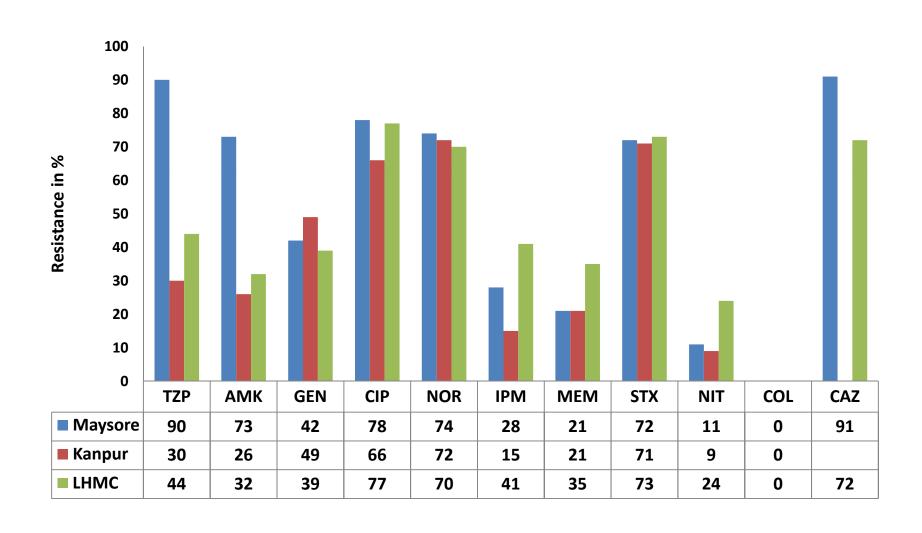
### **RESISTANCE (%) KLEBSIELLA.SP**



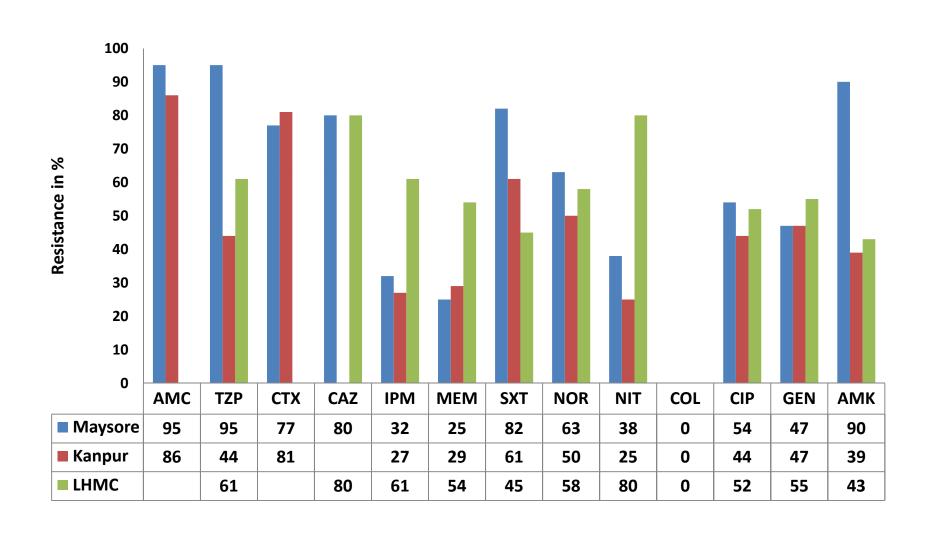
### **RESISTANCE (%) ENTEROCOCCUS**



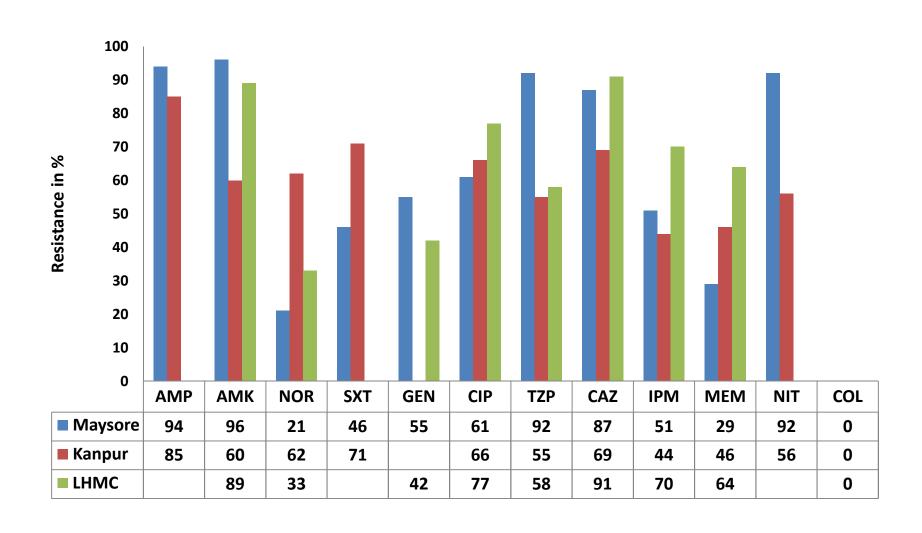
## E. Coli (% Res) – 2016-17



## Klebsiella(%Res): 2016-17



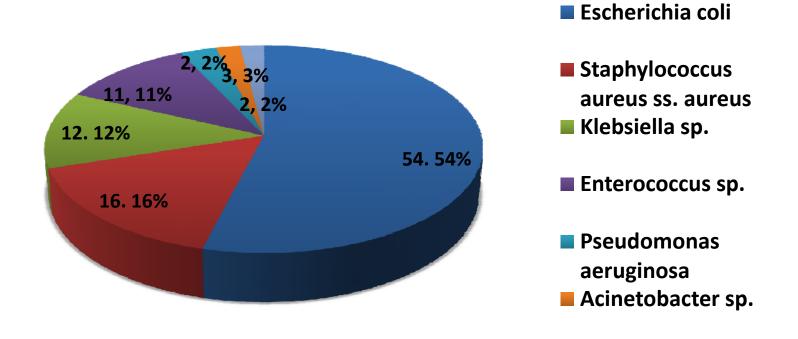
## Acinetobacter (%Res): 2016-17



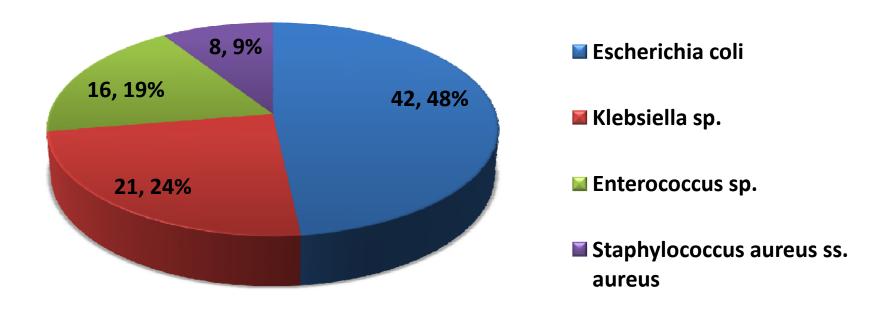
**Antimicrobial Resistance: 2015** 

SJ Hospital/VMMC, DELHI Blood Urinary isolates

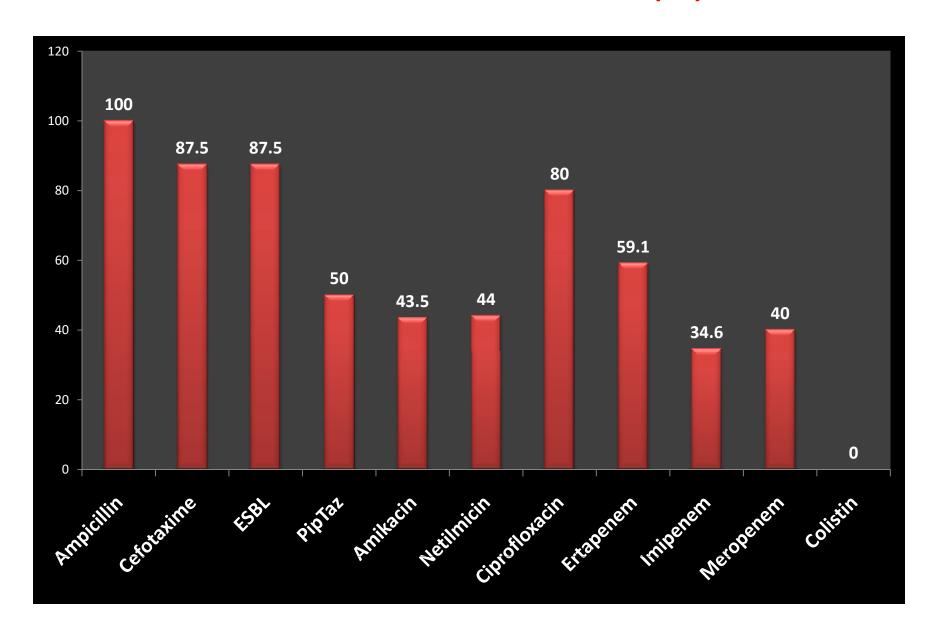
#### **Urinary Isolates Outpatients (84)**



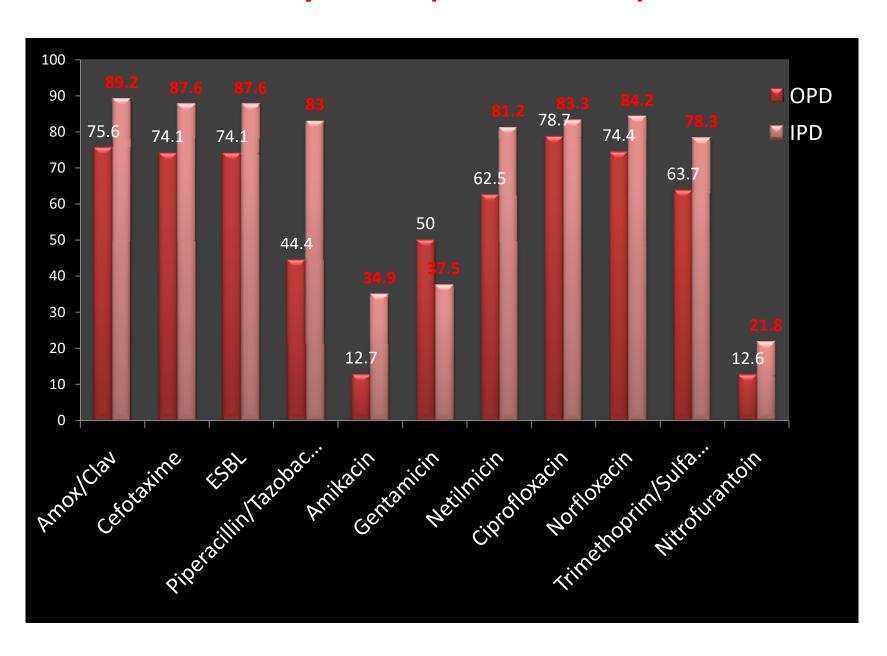
## **Urinary isolates: IPD**



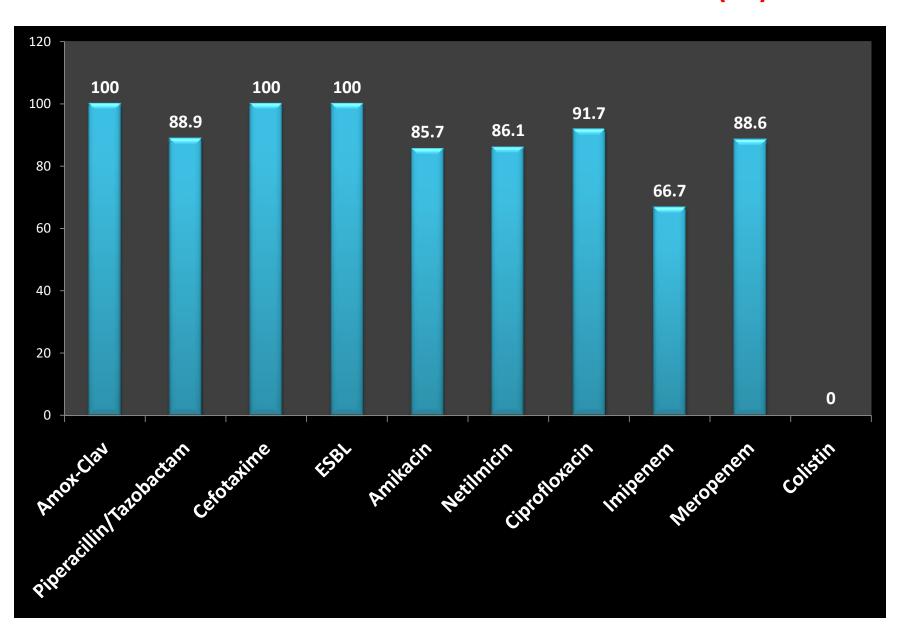
#### % Resistance in E. coli Blood isolates (36)



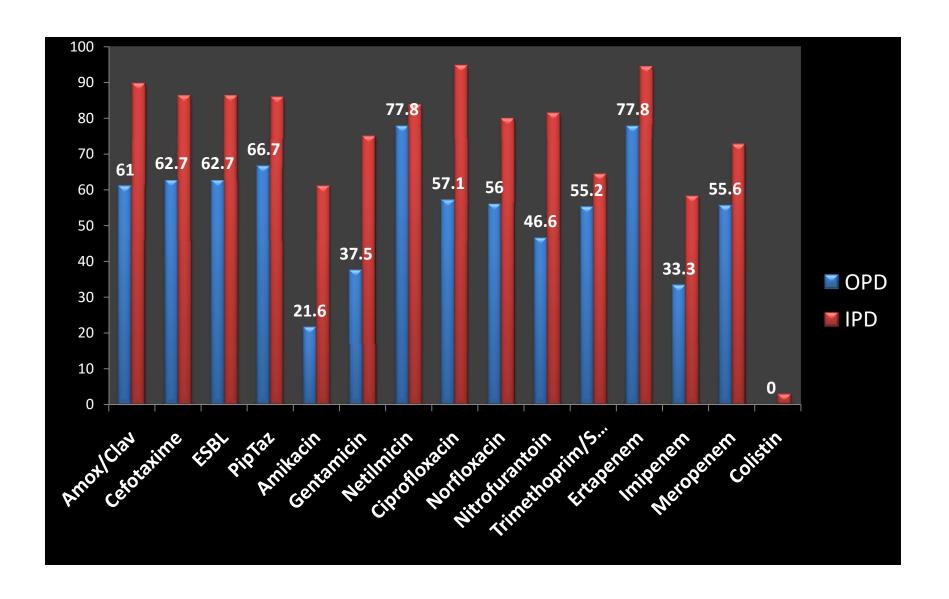
#### % Res Urinary E. coli (OPD and IPD)



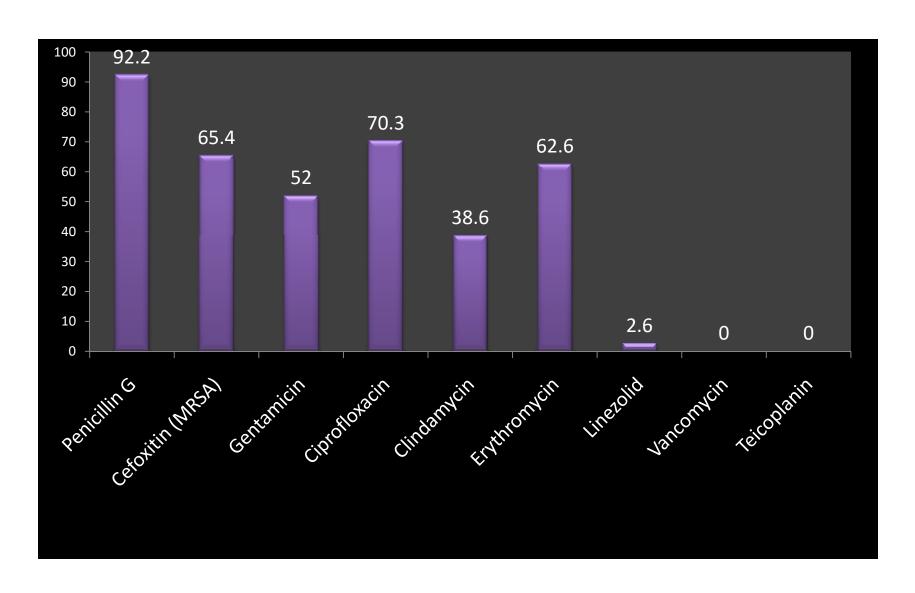
#### % Resistance in Klebsiella Blood isolates (36)



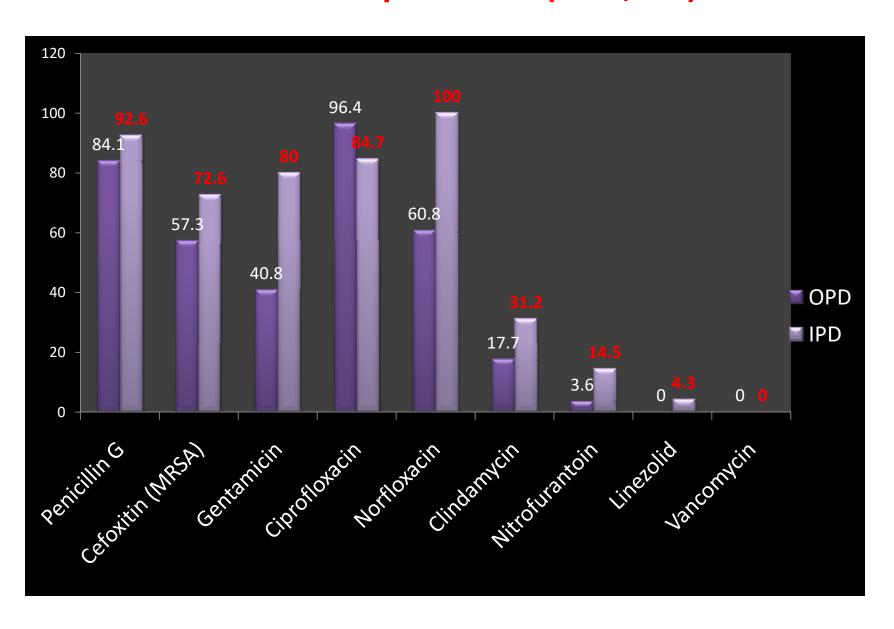
#### % Res Urinary Klebsiella (OPD,IPD)



## % Res S. aureus: Blood (133)

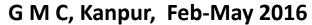


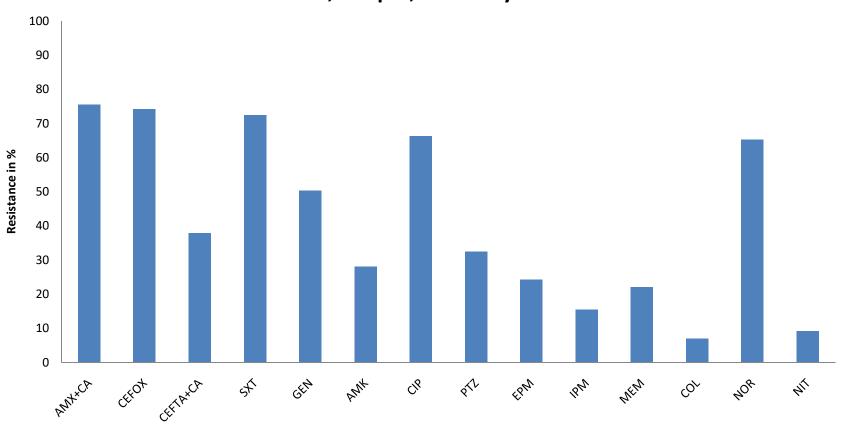
#### % Res Urine: Staph aureus (OPD,IPD)



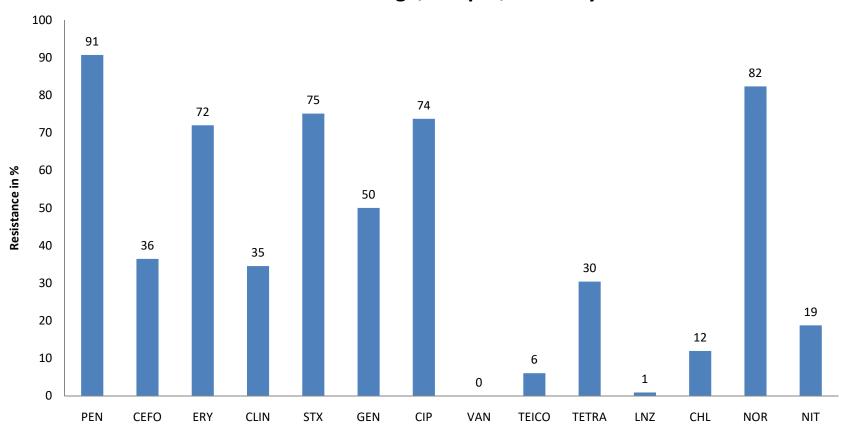
GMC Kanpur: 2016

## **E.Coli Resistance (%)**

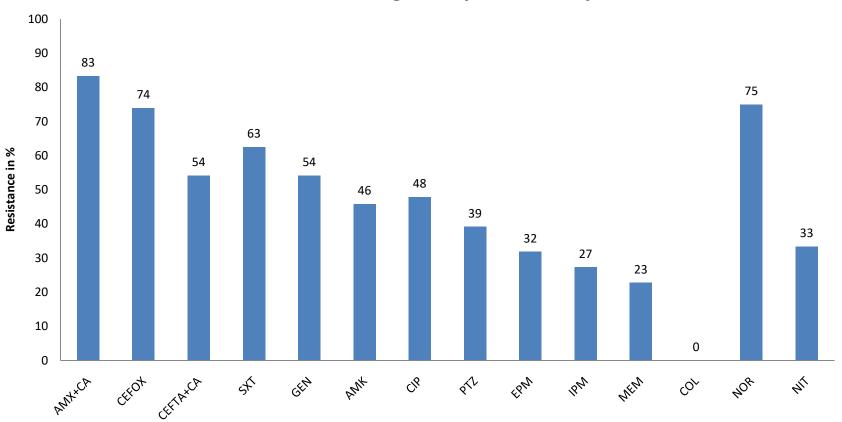




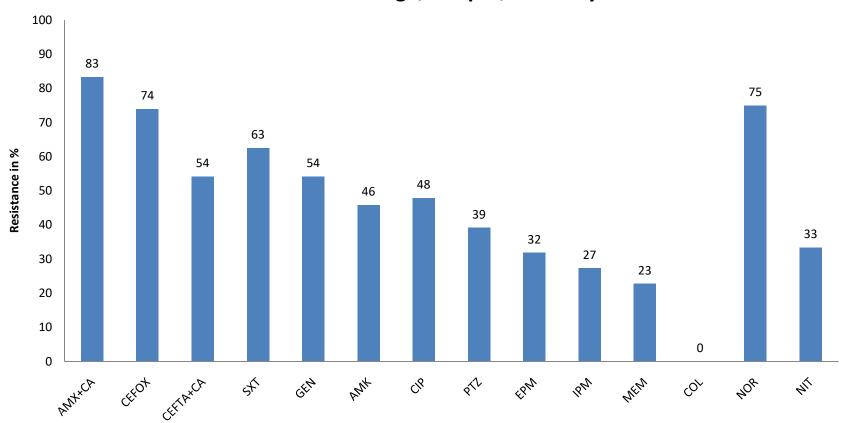
## **S.Aureus Resistance (%)**



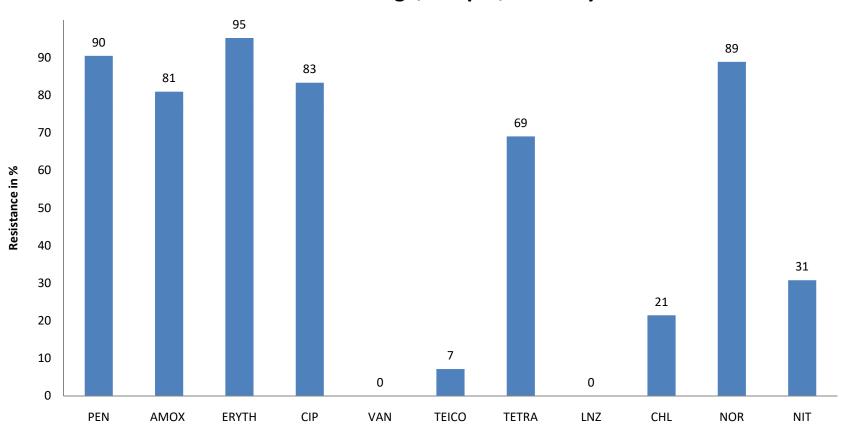
# **Klebsiella Resistance (%)**



## Klebsiella Resistance (%) in IPD



# **Enterococcus Resistance (%)**



## **Proposed New labs NCDC Network**

1. I.G. Medical College, Shimla (H.P)

2. NEEIGRHIM, Shillong (Meghalaya)

3. Gauhati Medical College, Guwahati, Assam

4. M.G Medical College, Indore, MP

5. Osmania Medical college Hyderabad, Telangana

## **Country wide AMR surveillance**

 DGHS written to heads of 200 Medical colleges to provide data on AMR June 2017

H.P(5), Orissa(4), Punjab (3), Rajasthan(6), Kerala(8)

Karnataka (30) Gujarat (16) Bihar(10) Chattisgarh(8)
 U.P (10), Meghalaya (1) Manipur(1) and others

 Encouraging response from some (8 labs) specially from state of kerala

# **Enrollment in GLASS: Requirements**

- Notified National Reference Centre
- Notification of at least One national reference laboratory in the country who should be having state of the art facilities for AST
- There are eight target pathogens for AMR surveillance including E.coli, Klebsiella, Gonococcus, Staph aureus, Pseudomonas, Acinetobacter
- Beginning can be made even with one pathogen
- AMR data from the four target anatomical sites eg Blood, Urine, Stool and Uretheral/Cervical area

# **GLASS Enrollment: India July 2017**



20. A VENUE APPA - CH-1211 GENEVA 27 - SWITZERLAND - TEL CENTRAL +41 22 791 2111 - FAX CENTRAL +41 22 791 3111 - WWW WIND BY

Tel. direct: Fax direct: E-mail : +41 22 791 2320 +41 22 791 2372

In reply please refer to:

Your reference:

Dr Sunil Gupta
Additional Director & Head (Microbiology)
Division of Microbiology
National Center for Disease Control
Ministry of Health and Family Welfare
New Delhi
India

Dear Dr Gupta,

Welcome to the Global Antimicrobial Resistance Surveillance System (GLASS)!

We are pleased to confirm that as of 21<sup>st</sup> of July 2017 the Republic of India is fully enrolled into GLASS. Participation in GLASS is a lifelong journey and we look forward to working together on implementation of the Global Action Plan on AMR through the development of the new global AMR surveillance system.

We will contact shortly the nominated GLASS national focal points with more detailed information on the next steps and credentials to access the GLASS IT platform. Please do not hesitate to contact us for any additional information you may require.

Yours sincerely,

12-12

Dr Carmem L. Pessoa-Silva
a.i. Coordinator
AMR Surveillance Team
AMR Secretariat
Office of the Director General

# Challenges

Data mainly from Tertiary care centres

Quality assurance

Procurement of Quality antibiotic discs

Manpower issues

Data analysis

# National Action plan: AMR surveillance

### **Dev of National Action Plan(NAP)**

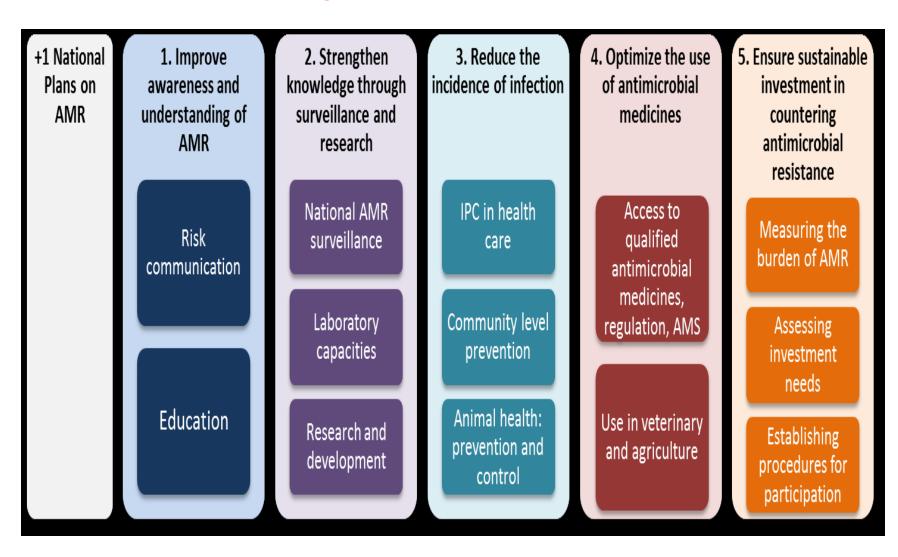
Inter-Ministerial Consultations on Containment of Antimicrobial Resistance

 Three committees constituted to oversee various activities including development and Implementation of national action Plan

- 1. Core Working Group (CWG)
- 2. Technical advisory group (TAG)
- 3. Inter-sectoral coordination committee

- National Action plan drafted endorsed by different stakeholder ministries in interministerial meeting chaired by Hon,ble HFM dated 19<sup>th</sup> April 2017
- Operational plan being developed for implementation
- Shri C.K. Mishra ,Secy(H&FW) written to concerned ministries
   July 2017 inviting inputs

# Strategic objectives WHO global action plan for AMR



# **Strategic priority 2**

# Strengthen knowledge and evidence through surveillance

## **Strengthen AMR Surveillance**

Objective – Strengthen laboratory capacity for AMR surveillance in human, animal/food and environment

#### **Activities:**

- Strengthen laboratories (including private sector) for antimicrobial susceptibility testing (AST) in medical labs (NCDC, ICMR, WHO) S-M
- Strengthen laboratories for antimicrobial susceptibility testing (AST) in Animals, Food, (DAHDF, ICAR, FSSAI FAO,OIE) S-M
- Strengthen laboratories (including private sector) for antimicrobial resistance and antimicrobial residues in the environment (MoEFCC, CPCB, SPCB, ICAR, CSE) S-M
- Develop National Network of Labs for AMR surveillance
  - Short term (S): 15-20
  - Medium term (M): 20-50
  - Long term (L): >50

# Strengthen AMR surveillance....

- Designate national reference laboratories (2-3 pathogen based labs) for AMR surveillance as a pre-requisite for enrolment in GLASS S (NCDC, DADF, ICMR, WHO, FAO)
- Monitor/evaluate performance of microbiology laboratories in humans, animals/food and environment by joint monitoring mission M-L (NCDC, ICMR, ICAR, MOEFCC, WHO, FAO)
- Organize joint training workshops for AST and data harmonization in humans, animals, food and environment S-M

(NCDC, ICMR, WHO) (DAHDF, ICAR, FSSAI, FAO, OIE) (MoEFCC, )

# Way Forward

Strengthen Quality Assurance in network labs

Strengthen Data collection, Reporting, Analysis

Expand Range of Pathogens for surveillance

Expand the AMR Network to District level

 Synergize all AMR surveillance at one platform to be submitted to GLASS

# **Areas/Modalities of Integration**

- Identification of Priority Pathogens for surveillance
- Common Antibiotic Panels for susceptibility testing of Pathogens
- Common Data Collection/Reporting formats
- Common data Entry/Analysis tools
- Sharing of analysed data
- Common Independent External Quality Assurance Systems (EQAS)

