Models for Stewardship in Hospital Indian setting: Private hospitals

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Indian Pharmaceutical Industry

- 10% increase in global share per year.
- Organized sector -70%.
- OTCs -940 million USD.
- Largest selling drug products are antibiotics.
Health system - India

- Government sector
  - Primary
  - Secondary
  - Tertiary
- Private sector
  - GPs’
  - Private hospitals
- Unregulated
  - OTC
  - Traditional medicine practitioners

National Health Accounts: India, 2004–05

Distribution of Total Health Expenditure in India 2004–05
- External Flow: 2.28%
- Public Expenditure: 19.67%
- Private Expenditure: 78.05%
# International Comparison of Health Expenditure

<table>
<thead>
<tr>
<th>Country</th>
<th>Total Health Exp. as a % of GDP</th>
<th>Government Exp. on Health as % of Total Exp. on Health</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2004</td>
<td>2005</td>
</tr>
<tr>
<td>USA</td>
<td>15.4</td>
<td>15.2</td>
</tr>
<tr>
<td>Germany</td>
<td>10.6</td>
<td>10.7</td>
</tr>
<tr>
<td>France</td>
<td>10.5</td>
<td>11.2</td>
</tr>
<tr>
<td>Canada</td>
<td>9.8</td>
<td>9.7</td>
</tr>
<tr>
<td>UK</td>
<td>8.1</td>
<td>8.2</td>
</tr>
<tr>
<td>Brazil</td>
<td>8.8</td>
<td>7.9</td>
</tr>
<tr>
<td>Mexico</td>
<td>6.5</td>
<td>6.4</td>
</tr>
<tr>
<td>China</td>
<td>4.7</td>
<td>4.7</td>
</tr>
<tr>
<td>Malaysia</td>
<td>3.8</td>
<td>4.2</td>
</tr>
<tr>
<td>Indonesia</td>
<td>2.8</td>
<td>2.1</td>
</tr>
<tr>
<td>Thailand</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>Pakistan</td>
<td>2.2</td>
<td>2.1</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>4.3</td>
<td>4.1</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>3.1</td>
<td>2.8</td>
</tr>
<tr>
<td>Nepal</td>
<td>5.6</td>
<td>5.8</td>
</tr>
<tr>
<td>India</td>
<td>5.0</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Antimicrobial classes or molecules discovered in the last 70 years that suppress multiplication or suppress growth of, or kill bacteria

1. >25, Cephalosporins
2. >15, Penicillins
3. >10, Quinolones
4. Tetracyclines
5. Macrolides
6. Ketolides
7. Aminoglycosides
8. Carbapenems
9. Dihydrofolate reductase inhibitors
10. Streptogramins
11. Nitrofurans
12. Fusidane
13. Phosphonic
14. Glycopeptides
15. Glycylcyclines
16. Oxazolidinones
17. Everninomicins
18. Clindamycin
19. Lincosamides
20. Nitroimidazoles
21. Rifamycins
22. Phenicols
23. Sulphonamides
24. Polymixins B and E
25. Glycolipopeptides
Ministry of Health discussed Chennai declaration in an official meeting Sept 2013

"The Chennai Declaration"
Recommendations of “A roadmap- to tackle the challenge of antimicrobial resistance” - A joint meeting of medical societies of India

Ghafur A, Mathai D1, Muruganathan A2, Jayalal JA3, Kant R4, Chaudhary D5, Prabhash K6, Abraham OC7, Gopalakrishnan R8, Ramasubramanian V9, Shah SN10, Pardeshi R11, Huigol A12, Kapil A13, Gill JPS14, Singh S15, Rissam HS16, Todi S17, Hegde BM18, Parikh P19
Coordinator, Road map meeting and Antibiotic Stewardship Committee Chairperson, Clinical infectious Diseases Society, 1President CIDS, 2President Elect API, 3Indian Medical Association, 4President, Association of Surgeons of India, 5Indian Society of Critical Care Medicine, 6DM Indian Society of Medical and Paediatric Oncology Secretary CIDS, 7Organising Secretary CIDSCON, 8Organising Chairman, CIDSCON, 9Editor, JAMA, 10Federation of Obstetric and Gynaecological Societies of India, 11President, Indian Society of Organ Transplantation, 12Indian Association of Medical Microbiologists, 13Director, School of Public Health and Zoonoses, GADVASU, 14Chairman, Research Committee, NABH, 15Member, Board of Governors, Medical Council of India, 16Panel member of Ministry of Health expert committee STG on Critical Care, 17Former Vice Chancellor, Manipal Academy of Higher Education, 18Convener, Indian Cooperative Oncology Network
National Policy to Control Antibiotic Resistance
2013
Mission
To promote public health by bringing out authoritative and officially accepted standards for quality of drugs including active pharmaceutical ingredients, excipients, dosage forms and medical devices for use by health professionals, patients and consumers.

Vision
To promote the highest standards for drugs for use in humans and animals within practical limits of the technologies available for manufacture and analysis.

Objective in Focus
To revise and publish the National Formulary of India on a regular basis.
Current scenario - 2013

• National Antibiotic Policy on hold. (OCT 3, 2011; Need measures to ensure supply in rural areas

October 2013 AB dispensation  OTC without valid prescription is banned
Government eliminates antibiotics for growth promotion in animals?

A new directive from the DGHS & CDSCO directs the Drug Controller of all states to stop the use of antibiotics as growth promoters in animal industry, in a letter dated 3rd June (102-74/2014-Trade). Interestingly the letter predates the study on antibiotic residues in chicken that created national headlines (see CIDS newsletter, August 2014). The letter specifically directs states to stop the use of antibiotics and hormones as growth promoters, and mandates withdrawal periods (time between last use of antibiotic and use of animal as food) as 7 days for eggs or milk, 28 days for poultry and other meat and “500 degree days” (not sure what that means?) for fish meat.

Great news: first step is to have a rule or law, next step is implementation. This will go a long way in reducing antibiotic abuse, human exposure to antibiotics in food and combating resistance. Hope this is enforced rather than just being on the books!
Chennai Declaration: Five year plan

Chennai Declaration Implementation-Five Year Plan

The “Chennai declaration-five year plan” is designed as a companion document to the original “Chennai declaration”. Details on various components of the five-year plan are already elucidated in the declaration document. The proposal provides a time bound action plan to various recommendations of the declaration. Readers are encouraged to refer to “The Chennai declaration” document for details.

<table>
<thead>
<tr>
<th>STRATEGY</th>
<th>ONE YEAR</th>
<th>TWO YEAR</th>
<th>FIVE YEAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>OVER THE COUNTER SALE OF ANTIBIOTICS (SCHEDULEH1)</td>
<td>24 antibiotics included in the Restricted list (as per the modified H1 list published)</td>
<td>60% of all antibiotics to be included in the restricted list</td>
<td>90% of all to be included antibiotics in the restricted list</td>
</tr>
</tbody>
</table>

Coordinator: DCGI/State Drug Control Authority

Stop prescribing antibiotics for fever, cold, IMA will tell docs

‘Overuse Of Meds A Major Health Risk’

Durgesh Nandan Jha
@timesgroup.com

New Delhi: Faced with the scary prospect of losing lives to simple infections in future, India is waking up to the dangers of reckless antibiotic use. The Indian Medical Association, a pan-India voluntary organization of doctors, will on Sunday launch a nationwide awareness programme on overuse of these life-savers, a practice that has led to emergence of drug-resistant organisms.

IMA will also ask fellow practitioners to avoid unnecessary prescriptions such as recommending antibiotics for patients with fever and cold, which are generally caused by viral infections.

“In the past two decades, almost no new antibiotic has been discovered while bacteria have learnt to overcome existing ones. If we don’t conserve the existing antibiotics, a day will come when simple infections will become life threatening,” warned Dr Narender Saini, IMA secretary general.

Saini said Sunday onwards IMA plans to hold public lectures and ‘training of trainers’ aimed to press for rational use of drugs among the medical fraternity.

The association, he added, has almost 2.5 lakh member doctors registered with its 1,700 branches across the country and all of them will be part of the initiative.

Several studies, including those conducted by WHO in India, have revealed that over-the-counter sale and purchase of antibiotics is rampant in the country.

There is also lack of knowledge about the exact use of each antibiotic among physicians.

“Over-prescription of antibiotics is a reality and we must act to check it. I welcome IMA’s move,” said Dr Anoop Misra, chairman, the Centre of Excellence for Diabetes, Obesity, Metabolic Diseases and Endocrinology (Fortis-C-DOC).

He said government should put in place a mechanism to audit prescription of antibiotics, particularly the second and third generation ones, in all hospitals and nursing homes. “Disease causing microorganisms have evolved at a higher speed than drug development. If we don’t check overuse of existing antibiotics, we will hit a dead-end soon,” said Dr Sumit Ray, vice-chairman, critical care medicine at Sir Ganga Ram Hospital.

Health experts say no new groups of antibiotics have been developed since the 1990s. “Carbapenem is the last group of antibiotics developed worldwide. There have been modifications to the available antibiotics but no new drug has come up. This is despite an increase in drug-resistant microorganisms. The New Delhi superbug or New Delhi Metallo-B-Lactamase 1 (NDM1) is just one example,” said Dr Ray.

The medical fraternity in Europe has been observing antibiotic awareness day since year 2008. Public health experts say it is good that India has woken up to the need finally.
Management of Infectious Diseases

Manoj Jain
Dilip Mathai

JAYPEE
Antimicrobial Stewardship (ASP)

• Not only about reducing but improving AB use
• Currently “most pts with infection” receive empiric (broad spectrum) rather than appropriate (focused) therapy; OTC (or phone call treatment, kerb consultation)
• Currently no national AB policy exists (to guide GP’s) who require evidence based guidelines.
• Difference in choice of AB in medical literature across continents/ countries/ medical societies cause confusion.
Present Status:

- **AB Stewardship** - ICMR: Developing AB policy guidelines, monitor AB prescription at community levels (pharmacy, private clinics, GP’s, secondary hospitals) & national drug policy
- **Infection control** – Policy manuals, NABH, HICC, society
DIRTY NATION

68.8 MN tonnes of waste per year - 41 MN missing toilets - 597 MN defecating in the open

HOW MODI CAN DELIVER A CLEAN INDIA
Centre sets March 31 deadline for industries polluting Ganga

New Delhi: All polluting industries along the river Ganga will have to set up sensor-based real-time online effluent monitoring system by March 31 next year. The government on Wednesday said it was serious about the deadline with water resources minister Uma Bharti issuing a veiled threat to industries—mend your ways or face the consequences.

The government also said that its long-term goal was to implement “zero liquid discharge” where all the water used by industries could be recycled and re-used.

Sending a tough message to polluting units, Bharti said that if she had to choose between the Ganga and industry, she would choose the river unless polluting industries adhere to all environment norms and the deadline.

Using the analogy of a delivery procedure where a mother’s life may be at stake, the minister said she would ideally like both the mother (Ganga) and child (industry) to survive. But, if she has to choose between the two, she would choose “Ma” (mother Ganga), she said.

"If the child (industry) would suck mother’s (Ganga) blood, she would prefer the mother to survive", said Bharti. While claiming she was running out of patience, the minister refrained from using harsh words at a time when industries are voluntarily turning up to hold consultations for finding a solution.

Bharti underlined the fact that whatever the government was doing to rejuvenate the Ganga, would serve as a template for all rivers across the country.

Her remarks came after several rounds of consultation with representatives of polluting industries.
Risk factors for MDR and XDR-TB in a Tertiary Referral Hospital in India

- Department of Microbiology, Christian Medical College Vellore, Vellore, Tamil Nadu, India
- Retrospective chart review based on positive cultures isolated in a high volume mycobacteriology laboratory between 2002 and 2007.
- 47 XDR, 30 MDR and 117 susceptible controls were examined.
- Drug resistant cases were less likely to be extrapulmonary, and had received more previous treatment regimens.

CONCLUSIONS:

- There is significant selection bias in the sample available.
- **Selection pressure from previous treatment and an inadequate initial regimen increases risk of drug resistance.**

Local patients and those requiring financial subsidies may be at lower risk of XDR-TB.

Multivariate Analysis: Risk factors for XDR.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio for XDR</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous treatment with a fluoroquinolone and an injectable agent (other than streptomycin)</td>
<td>7.00</td>
<td>1.14–43.03</td>
</tr>
<tr>
<td>Initial treatment regimen did not follow national guidelines</td>
<td>5.68</td>
<td>1.24–25.96</td>
</tr>
</tbody>
</table>

Including smoking, alcohol, HIV, TN state, payment, regimen 1 adequate, extrapulmonary TB, cavitary, number of regimens, previous treatment with fluoroquinolone and injectable.

Only significant associations shown.

Model based on 69 cases with complete data.

MDR/XDR/TDR – TB

- MDR TB - early 1990s,
  - New York City: Homelessness, prison outbreaks and HIV.
  - Successful Case Management Strategy
    - Aggressive identification
    - Treatment - direct observation of patients taking their pills
- XDR TB - 2005 — Resistance to the three 1st line and several 2nd line drugs
  - Kwazulu-Natal: HIV
  - effective treatment with the few drugs that work against XDR-TB
  - ? more patients than available treatment slots
- TDR TB – Resistance to the three 1st line and all Nine 2nd line drugs
  - 2003 - Italy: 2 women with HIV
  - 2009 - Iran: 15 patients
  - 2011 – Mumbai, India - 12 Cases

Tuberculosis Transmission

• Early Detection:
  – Xpert®, Cepheid, 2 hr test for MTB and RIF resistance
  – Bill & Melinda Gates Foundation / PEPFAR/ USAID/ UNITAID supports 40% cost at US$9.98 for 145 developing countries, 08 Aug 2012

• Household Transmission

• Hospital Spread:
  – Nurse at NYC Maternity/ Newborn Nursery ¹

• Occupational Spread:
  – South African Gold Miners exposed to Silica ²

• Feasibility of Respiratory Isolation in Developing Countries

¹ http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5450a2.htm
PVT. Hospitals
THEY AIM FOR ACCREDITATION

• National/International – Hospital, Laboratory
• NABH/NABL/JCI etc
• Sets the bar high, expected of a tertiary care set-up
1. AMSP DOCUMENT

• Every hospital – crisp written document – all aspects of the hospital’s AMSP programme. ie, infectious conditions and prescriptions required for antimicrobials
  Hospital Drug Formulary/Essential Drug list – Essential Antibiotic list

• Clarity is the key – programme to be understood/implemented by all hospital personnel
2. AMSP TEAM

• Large hospitals – separate teams for each of the major clinical departments, to push the programme

• Chaired – respective Heads of Departments (HODs)
3. INFECTIOUS DISEASES (ID) DEPARTMENT

• Recommended for all medical colleges, large tertiary care institutes.

• Rest – ID physicians

• Fellowship programmes in ID – CMC Vellore, Apollo Hospitals Chennai, PD Hinduja Hospital Mumbai
4. CLINICAL PHARMACISTS

• Clinical Pharmacologist/M Pharm recommended

• For better Antimicrobial agent selection, combinations, dosages, drug interactions and improving overall therapeutics in hospitals
# Antimicrobial Susceptibility Profile of Blood Stream Infection Jan-June 2011

## AST profile of BSI Organisms – Susceptible percentage

<table>
<thead>
<tr>
<th>Drug</th>
<th>Escherichia coli (n=356)</th>
<th>Klebsiella spp. (n=104)</th>
<th>Enterobacter spp (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESBL</td>
<td>24</td>
<td>25</td>
<td>44</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>40</td>
<td>34</td>
<td>56</td>
</tr>
<tr>
<td>Amikacin</td>
<td>88</td>
<td>51</td>
<td>83</td>
</tr>
<tr>
<td>Netilmicin</td>
<td>84</td>
<td>47</td>
<td>73</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>15</td>
<td>27</td>
<td>61</td>
</tr>
<tr>
<td>Pipericillin / Tazobactam</td>
<td>40</td>
<td>30</td>
<td>66</td>
</tr>
<tr>
<td>Cefoperazone / Sulbactam</td>
<td>77</td>
<td>52</td>
<td>83</td>
</tr>
<tr>
<td>Timentin</td>
<td>21</td>
<td>24</td>
<td>51</td>
</tr>
<tr>
<td>Imipenem</td>
<td>95</td>
<td>60</td>
<td>86</td>
</tr>
<tr>
<td>Meropenem</td>
<td>95</td>
<td>59</td>
<td>90</td>
</tr>
<tr>
<td>Tige cycline</td>
<td>99</td>
<td>70</td>
<td>85</td>
</tr>
<tr>
<td>Colistin</td>
<td>100</td>
<td>94</td>
<td>80</td>
</tr>
</tbody>
</table>
Prepared by:
Drs. O. C. Abraham, V. Balaji, Joy Sarojini, Hema Paul and Ms. Catherine Truman

Issued by:
HICC

Approved by:
Dr. Lionel Ganapraj Medical Superintendent

MANUAL: Antibiotic Guidelines - Adults

HOSPITAL INFECTION CONTROL COMMITTEE

ANTIBIOTIC GUIDELINES - ADULTS

REVISION HISTORY

<table>
<thead>
<tr>
<th>Version No.</th>
<th>Revision</th>
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<tr>
<td>1</td>
<td>Jan 2006</td>
</tr>
<tr>
<td>2</td>
<td>Jan 2009</td>
</tr>
<tr>
<td>3</td>
<td>Jan 2011</td>
</tr>
<tr>
<td>4</td>
<td>Aug 2011</td>
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Antimicrobial Protocols
Guidelines for Empirical Antimicrobial Therapy
Questions

- **Ques 2:** Who provides the audit and feedback and to whom?

- **Question 3:** How many hours /week should a physician devote to a bed /bed/day
Initial Choice of Antimicrobial Therapy for Common Infections

• Empiric antibiotic treatment should be limited to conditions where early initiation of antibiotics has been shown to be beneficial. Some examples are:
  – Severe sepsis (sepsis-induced tissue hypoperfusion or organ dysfunction) and septic shock
  – Acute bacterial meningitis
  – Community acquired pneumonia
  – Ventilator associated pneumonia
  – Necrotizing fasciitis.
• Always obtain cultures (two sets of blood cultures and other appropriate samples as clinically indicated – e.g. normally sterile body fluids, deep pus etc.) before starting empiric antibiotic treatment.
• Avoid sending cultures from superficial wounds, decubitus ulcers and chronic draining sinuses. Swab cultures are either inadequate or provide misleading information regarding diagnosis.
• De-escalate the antibiotic regimen (to the narrowest spectrum, least toxic and least expensive antibiotic) once culture and susceptibility reports are available, and the patient has responded to the initial empiric broad-spectrum antibiotics.
• These recommendations are based on CMC Hospital, Vellore antibiograms.
Acute Bacterial Meningitis

| 1. Acute bacterial meningitis (community acquired) | *Strep. pneumoniae*  
*N. meningitides* | CP 20 L units i.v. Q2H  
- Penicillin-resistant pneumococci (MIC $\geq 0.12$ μg/m):  
  Ceftriaxone 2 g i.v. Q12H +  
  Vancomycin 1 g i.v. Q12H | Duration:  
10 - 14 days  
Steroids:  
Indication:  
- Cloudy CSF  
- Bacteria in CSF on Gram's staining, or  
- CSF WBC count $>1000$/ml  
Dose: Dexamethasone 10mg i.v. Q6H x 4 days; first dose 15 min before first dose of antibiotic. |
### VIII. GU Infections

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pathogen(s)</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute uncomplicated cystitis in women – dysuria and frequency in healthy, adult, non-pregnant women with normal urinary tract</td>
<td><em>E. coli</em></td>
<td>Nitrofurantoin 100 mg p.o. BID x 5 - 7 days</td>
<td></td>
</tr>
<tr>
<td>Pyelonephritis – uncomplicated (no underlying GU disease)</td>
<td><em>E. coli</em></td>
<td>Non-severe illness: • Amikacin 15 mg/kg i.v. Q24H • Severeill (MODS, septic shock): • Ertapenem 1 g i.v. Q24H</td>
<td>Non-severe illness: • Piperacillin-Tazobactam 4.5g i.v. Q6-8H; Duration: Mild to moderate cases – 7 days; Severe cases – 14 days; hospitalize patient.</td>
</tr>
<tr>
<td>Complicated UTI (underlying GU disease)</td>
<td><em>E. coli</em>, <em>Proteus</em>, <em>Pseudomonas aeruginosa</em>, <em>Acinetobacter spp.</em></td>
<td>Carbapenems (Imipenem / Meropenem); de-escalate as per AST reports</td>
<td>Duration: 10 - 14 days</td>
</tr>
<tr>
<td>Foley catheter associated UTI</td>
<td>Gram-negative bacilli</td>
<td>• As per AST reports • Treat only when patient has systemic symptoms (fever, SIRS)</td>
<td>Urine sample for culture obtained through a new catheter (after removing the indwelling catheter). When this is not possible, obtain sample through catheter port, (and not the drainage bag).</td>
</tr>
</tbody>
</table>
COMMUNITY ACQUIRED PNEUMONIA (CAP) MANAGEMENT PROTOCOL

1. Suspect if patient (not been hospitalized in the previous two weeks; not immuno-compromised) has any combination of the following:
   a. Symptoms: fever, cough (with or without expectoration), pleuritic chest pain, dyspnea
   b. Signs: Temp >38 °C, tachypnea, tachycardia, impaired percussion notes, bronchial breath sounds, crackles, altered VF/VR.
2. Check oxygen saturation (SpO₂) by pulse oximetry; start oxygen if SpO₂ <90%.
3. Confirm with chest x-ray (to be done as soon as possible).
4. Severity assessment based on CURB-65 score:
   a. 6 point score (range 0 - 5)
   b. Gives one point each for:
      i. Confusion (abbreviated mental test score ≤ 8 or new disorientation in person, place, or time)
      ii. Urea >42 mg/dL
      iii. Respiratory rate ≥ 30/min
      iv. Low blood pressure (SBP < 90 mm Hg or DBP ≤ 60 mm Hg)
      v. Age ≥ 65 years
   c. Interpretation
      i. CURB-65 score 0 or 1: low risk of death
      ii. CURB-65 score 2: moderate risk of death
      iii. CURB-65 score ≥3: high risk of death
5. Lab tests
   a. CBC
   b. Urea, creatinine
   c. ABG (only if CURB 65 score ≥2)
   d. Blood culture x 2 (only if CURB 65 score ≥2)
   e. Spurum Gram stain & culture (optional)
      i. Only if CURB 65 score ≥2 & patient can expectorate
      ii. Specimen (expectorated sputum) should be transported promptly to the lab
Question 4

• A great deal of coordination between AMSP Team and HIC/ Hospital Epidemiologist
6. Setting of care
   a. CURB-65 score 0 or 1: out-patient
   b. CURB-65 score 2: in-patient (ward)
   c. CURB-65 score ≥3: in-patient (M-ICU)

7. Antibiotic management:
   *All patients should receive the first dose of antibiotics as soon as the diagnosis of CAP is confirmed*
   a. CURB-65 score 0 or 1
      i. **Preferred:** Amoxicillin 500 mg p.o. Q8H x 5 - 7 days
      ii. **Alternatives:**
         1. Levofloxacin 750 mg p.o. OD x 5 - 7 days
         2. Azithromycin 500 mg p.o. OD x 3 days
         3. Doxycycline 100 mg p.o. BID x 7 days

   b. CURB-65 score ≥2
      i. **Preferred:** Crystalline penicillin 20 L units i.v. Q4H x 7 days

   c. CURB-65 score ≥3
      i. **Preferred:** Piperacillin-Tazobactam 4.5 G i.v. Q6-8H + Azithromycin 500 mg i.v. OD x 7 – 10 days
      ii. **Alternatives:**
         1. Crystalline penicillin 20 L units i.v. Q4H + Azithromycin 500 mg i.v. OD x 7 – 10 days
         2. Ertapenem 1 G i.v. OD + Azithromycin 500 mg i.v. OD x 7 – 10 days

   * Change to an oral regimen as soon as clinical improvement occurs and the temperature has been normal for 24 h, and there is no contraindication to the oral route.
   * Modify antibiotic regimen based on results of culture & susceptibility reports.
Community Acquired Pneumonia- Treatment
CMC Hospital Protocol

• Ambulatory : Amoxycillin ± macrolide (if atypical organism suspected)
• Hospitalised : Crystalline penicillin 10 lakh units I.V q4h 7-10 days
• Hospitalised with (COPD, CCF, DM) : Cefotaxime 1gm IV q8h 10-14 days
• Hospitalised in ICU : Cefotaxime 1gm IV q8h or Levofloxacin 500 mg p.o / IV + Erythromycin 1 gm p.o q6h or Azithromycin 0.5 gm IV od / od X 10-14 days
Initial antibiotic choice in 100 patients diagnosed to have CAP in CMC

1. Monotherapy

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th>No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{st} generation cephalosporins</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>2\textsuperscript{nd} generation cephalosporins</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>3\textsuperscript{rd} generation cephalosporins</td>
<td>17 (17%)</td>
</tr>
<tr>
<td>4\textsuperscript{th} generation cephalosporins</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Penicillins</td>
<td>34 (34%)</td>
</tr>
<tr>
<td>Quinolones</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Macrolides</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Glycopeptides</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Other : Augmentin</td>
<td>6 (6%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>45 (43.26%)</strong></td>
</tr>
</tbody>
</table>
### Initial antibiotic choice in 100 patients diagnosed to have CAP in CMC

#### 2. Combination therapy

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th>No. of patients (%)</th>
<th>Antibiotic class</th>
<th>No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st CPS + MC</td>
<td>0 (0%)</td>
<td>PCN + FQ</td>
<td>2 (1.92%)</td>
</tr>
<tr>
<td>1st CPS + FQ</td>
<td>0 (0%)</td>
<td>PCN + AG</td>
<td>3 (2.88%)</td>
</tr>
<tr>
<td>1st CPS + AG</td>
<td>0 (0%)</td>
<td>Other : 3rd CPS + AG + MC</td>
<td>3 (2.88%)</td>
</tr>
<tr>
<td>2nd CPS + MC</td>
<td>0 (0%)</td>
<td>Other : 3rd CPS + CBP</td>
<td>1 (0.96%)</td>
</tr>
<tr>
<td>2nd CPS + FQ</td>
<td>0 (0%)</td>
<td>Other : 3rd CPS + PCN + FQ</td>
<td>1 (0.96%)</td>
</tr>
<tr>
<td>2nd CPS + AG</td>
<td>0 (0%)</td>
<td>Other : 3rd CPS + PCN + MC</td>
<td>2 (1.92%)</td>
</tr>
<tr>
<td>3rd CPS + MC</td>
<td>7 (8.65%)</td>
<td>Other : 3rd CPS + PCN + AG</td>
<td>3 (2.88%)</td>
</tr>
<tr>
<td>3rd CPS + FQ</td>
<td>1 (1.92%)</td>
<td>Other : PCN + ATT</td>
<td>2 (1.92%)</td>
</tr>
<tr>
<td>3rd CPS + PCN</td>
<td>11 (10.57%)</td>
<td>Other : FQ + ATT</td>
<td>1 (0.96%)</td>
</tr>
<tr>
<td>4th CPS + MC</td>
<td>0 (0%)</td>
<td>Other : 3rd CPS + PCN + AG + MC</td>
<td>2 (1.92%)</td>
</tr>
<tr>
<td>4th CPS + FQ</td>
<td>0 (0%)</td>
<td>Other : 3rd CPS + PCN + MC + CBP</td>
<td>1 (0.96%)</td>
</tr>
<tr>
<td>4th CPS + AG</td>
<td>0 (0%)</td>
<td>Other :</td>
<td></td>
</tr>
<tr>
<td>PCN + MC</td>
<td>5 (5.76%)</td>
<td>TOTAL</td>
<td>(59 (56.73 %))</td>
</tr>
</tbody>
</table>
Computer based Surveillance

- Can facilitate good ASP
- Tracking of AMR
- Patients' specific culture and susceptibility data.
- Molecular epidemiology investigations of outbreaks (A-III)
- Unintended consequences of antimicrobial uses evaluations by outcomes (A-III)
5. HOSPITAL EPIDEMIOLOGIST

• For better planning /research of Health Care Associated Infections (HCAI)
• Critical member of the Hospital Infection Control (HIC) team – early identification/control of an epidemic
6. HIC TEAM

• Implement the tenets of the AMSP programme – executive arm of the programme
• Concise document – objectives of the HIC team, recommended guidelines
• Regular weekly/emergency review meetings - chaired by the Medical Superintendent (MS)
• Regular/emergency investigative activity - various hospital departments
7. HIC GUIDELINES – COMPLIANCE AUDIT

• Are the guidelines being adopted?
• Outcome – ?Improved HIC practices
  ? Changes to the HIC policy
8. HCAI LIST

• Must have - every hospital’s AMSP
• Training of healthcare personnel – early identification/ management of these infections
• Periodic revisions to this list
9. OUTBREAK GUIDELINES

• Guidelines - Concise, Clear
• Identifying the Cause – Route of transmission
• Controlling the outbreak – Blocking the route
• Awareness – hospital’s IT department
10. IT DEPARTMENT

• Strong IT team – efficient planning/management of the HIS with HIC/AMS Team.
• Regular updates with current information - made available to all personnel, keep them in the loop about developments
11. HIC IN HIS

- Hospital Information Systems (HIS) – easy access to guidelines
  - reports
  - minutes of meetings
  - online prescriptions, autoreview of antimicrobial agents selected
    (as developed by clinical pharmacists)
  - bulletins etc
- HIS training – all hospital personnel
12. ANTIMICROBIAL RESISTANCE DATA ANALYSIS

• Frequency – performed monthly, communicated half-yearly & annually
• Data analysed as per –
  CAI(?catheter), HCAI, ICU (and sub-units)
  Site of infection (or subsite) Ex: Urinary tract
  Specific pathogen (not groups like Gram +ve, Gram –ve)
  Sentinel drug / bug
13. AMA Agents – Usage data

- As per the recommended Anti-Microbial Agents (AMA) - Essential drug list
- New adverse effects identified – added to formulary if statistically significant
- Notice to department/individual – Non-compliance (esp. if repeated multiple times)
14. AMSP STRATEGIES

• Customized - Local requirements
  Antimicrobial Resistance Data
  (hospital/community)
  Cost/Efficacy (drug formulary)
15. AMA PRESCRIPTION GUIDELINES

• Department –wise for various conditions
• Involved the HOD and respective department members
• Regular review/update – most current developments
16. AMA PRESCRIPTION AUDIT/FEEDBACK

- Separate audit teams – each major clinical department
- Chaired by the HOD
- Should target –
  AMA compliance – as per specific conditions
  Adverse drug effects identified
  Suggested improvements
  Recognition – significant achievements by a dept.
17. AMSP IMPLEMENTATION OUTCOMES

• Pre/Post implementation data – collected, compared
• Efficacy of AMSP activities – corrections if any
• Report – made available to all hospital personnel
18. PRESCRIPTION AUTONOMY

• Surveys at regular intervals – oppositions to the AMSP by clinicians
• Address issues effectively
Supplemental AB Stewardship Strategy

• Education is considered to be an essential element of any program designed to influence prescribing behavior and can provide a foundation of knowledge that will enhance and increase the acceptance of AB Stewardship (A-III). However, education alone, without incorporation of active interventions, is only marginally effective in changing antimicrobial prescribing practices and has not demonstrated a sustained impact (B-II).
Public health in a crisis

India's public health sector is in urgent need of policies and regulatory frameworks to save it from maladies such as commercialisation, pharma-regulator nexus, unethical practices and urban bias.
Communicable diseases on the rise

- Kerala - best health indicators in India
- Confronted by the threat of increasing communicable diseases.
- Ten types of communicable diseases, including three variants of hepatitis, have been reported in Ernakulam district till September in addition to cases of fever and acute diarrhoea. A total of 1.10 lakh fever cases and 14,478 cases of acute diarrhoea have been reported in the district so far this year.

KOCHI, September 15, 2011

http://www.thehindu.com/todays-paper/tp-national/tp-kerala/article2454955.ece
Protocol for the management of adult patients with acute undifferentiated fever.

Fever

- **Sepsis?**
  - Yes: Follow Sepsis protocol
  - No: Localizing signs?

- **Localizing signs?**
  - Yes: Treat appropriately
  - No: Day of fever?

- **Day of fever?**
  - Day 1 or 2: Defer investigations & antimicrobials
  - Day 3 or 4: Total blood count, Differential count, Malaria parasite quantitative buffy coat, urinalysis
  - Day 5 or greater: As per day 3 or 4, plus blood culture

- Antimicrobials based on investigations and clinical judgement
Indian Society of Critical Care Medicine (ISCCM) recommendations

• Most common causes are:
  – dengue hemorrhagic fever,
  – rickettsial infections/scrub typhus
  – malaria (usually *falciparum*), typhoid, and
  – leptospira bacterial sepsis and
  – common viral infections like influenza.

• The committee recommends a ‘syndromic approach’ to diagnosis and treatment of critical tropical infections
Indian Society of Critical Care Medicine (ISCCM) recommendations

• It has identified five major clinical syndromes:
  – undifferentiated fever
  – fever with rash / thrombocytopenia
  – fever with acute respiratory distress syndrome (ARDS)
  – fever with encephalopathy and
  – fever with multi organ dysfunction syndrome

• Evidence based algorithms are presented to guide critical care specialists to choose reliable rapid diagnostic modalities and early empiric therapy based on clinical syndromes.

Rank order of 1480 blood stream recovered from 7894 blood specimens (5145 patients) seen in CMCH between 1st Jan - 30th June 2005.

<table>
<thead>
<tr>
<th>Rank order</th>
<th>Organisms</th>
<th>Total number of organisms (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Coag neg staph</td>
<td>380 (26)</td>
</tr>
<tr>
<td>2</td>
<td>Ecoli</td>
<td>138 (9)</td>
</tr>
<tr>
<td>3</td>
<td>S. typhi + S.paratyphi</td>
<td>45 (3)</td>
</tr>
<tr>
<td>4</td>
<td>Klebsiella spp.</td>
<td>40 (3)</td>
</tr>
<tr>
<td>5</td>
<td>Enterococcus</td>
<td>39 (3)</td>
</tr>
<tr>
<td>6</td>
<td>Ps. aeruginosa</td>
<td>32 (2)</td>
</tr>
<tr>
<td>7</td>
<td>S. aureus</td>
<td>30 (2)</td>
</tr>
<tr>
<td>8</td>
<td>Alpha streptococcus spp.</td>
<td>23 (2)</td>
</tr>
<tr>
<td>9</td>
<td>Pneumococcus spp.</td>
<td>18 (1)</td>
</tr>
<tr>
<td>10</td>
<td>Enterobacter spp.</td>
<td>13 (1)</td>
</tr>
<tr>
<td>11</td>
<td>Misc.</td>
<td>695 (47)</td>
</tr>
</tbody>
</table>
Typhoid Fever

<table>
<thead>
<tr>
<th>6. Typhoid fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. <em>S. enterica</em> ser. Typhi (<em>S. typhi</em>)</td>
</tr>
<tr>
<td>2. <em>S. enterica</em> ser. Paratyphi A (<em>S. paratyphi A</em>)</td>
</tr>
</tbody>
</table>

| 1. | Ciprofloxacin 750 mg BID p.o. x 14 days (if Nalidixic acid susceptible or cipro MIC <0.125 μg/m/ml) |
| 2. | Azithromycin 1 g p.o. x 7 days (if MDR & NARST or cipro MIC ≥0.125 μg/m/ml) |

- Nalidixic acid resistant *S. typhi* (NARST) and/or cipro MIC ≥0.125 μg/m/ml is associated with failure of ciprofloxacin & ofloxacin treatment
- Empiric choice should be based on local antibiotic susceptibility patterns
- 3rd generation cephalosporins have higher rates of clinical failure when compared to fluoroquinolones (FQ); hence they should only be used in pregnant women with typhoid and failure of FQ treatment
Analysis of First 721 patients

Number of patient Enrolled in this study 1282 / 1432 (90%)
Number of CRF 944/ 1282 (74%)
Bacteria positive 32 / 429 (7.4%)

Duration of fever (Mean value) 6.48
Minimum Duration 1 day

Number of patient Given Antibiotics 644/721 (89%)
1st generation cephalosporin 1/644 (0.15%)
2nd generation cephalosporin 3/644 (0.46%)
3rd generation cephalosporin 508/644 (79%)
Carbapenem 3/644 (0.46%)
Penicillin 48 (7.4%)
Aminoglycoside 55 (8.54%)
Quinolone 17 (2.64%)
Marcrolide 11 (1.7%)
Doxy 273 (42.3%)

Number of patients took Combinational Antibiotics are 198
Diagnostics I: To improve AB use

1. **Clinical need** is to develop rapid tests.
   a. This would help in *easing doctors anxiety* that the action of not starting an antibiotic may result in poor outcome
   b. May not change management but their use of antibiotic
   c. Determining whether they need urgent care or hospitalization especially elderly – who lack specific clinical symptoms
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   c. Determining whether they need urgent care or hospitalization especially elderly – who lack specific clinical symptoms
Measuring Outcomes

• It's important to measure outcomes
  – % Reduction in ESBL prevalence.
  – % Decrease in PAN resistance PA/AB
  – % Increase amongst *Pseudomonas*.
  – % Reduction in MRSA / VRE

• Share with clinicians with a constant feedback mechanism.
Summary: AMSP in Private Hospitals

Implementation:

- Improve dissemination of information
  a. Educational workshops on antimicrobial stewardship
  b. Provide feedback of
    i. AMR surveillance (prevalence rates, sentinel drug-bug combination)
    ii. AB prescription at community level for common community acquired infections such as fever, skin & soft tissue, diarrhea, UTI and RTI
    iii. AB utilization at hospital level indexed against resistance rates
- Pharmacovigilance Committee institutional & national programs
- Indian medical societies are encouraged to develop their policy statement for national consensus