Typhoid Fever: *Salmonella enterica* Serovar Typhi.

- Endemic in Indian Subcontinent
- Diagnosis: Often jeopardized.
- Treatment: Become a challenge due to drug resistance.
- Prevention: Should be planned properly.
  - Sanitation
  - Vaccine
Laboratory Diagnosis of Typhoid fever

- Blood culture
  - Gold standard
  - Limitations: only 50-60% of the cases are positive in the first week of disease.
- Serological: Widal test.
- Stool and/or Urine culture
  - Both of them are rarely positive and stool culture needs special procedure.
Serological tests

- Widal → widely used test in the endemic region. 
  Cut off point →
  - Varies from place to place and time
  - Significance for diagnosis and prognosis

- Bangladesh Perspective →
  - TO ≥1:160 and/or TH ≥1:320
    - Clinical correlations →
      - Non-specific reactions, previous clinical/subclinical infections.
      - Common questions ………

BLOOD CULTURE AND RECENT ADVANCES.

♣ Conventional
  • Time consuming
♣ Advance technologies: FAN, Vitek, Bactech etc.
  • Expensive and Needs Automation.
♣ Lysis-direct plating/centrifugation method.
Schematic diagram of LDP/LC method.

- The device is made indigenously.
- Method is simple.
- Can be adapted in any lab with minimum facilities.
Growth of S. typhi after 18 hours of incubations.
Blood culture during antibiotic therapy?

- Introduction of any Newer method that usually accompanied with loud fanfares and intensive promotions.
- What is the reality?
  - Sensitivity of the organisms
  - Culturable and non-culturable form of bacteria.
  - Pharmacokinetics of antibiotic(s)

Growth from a partially treated case.

Saha et al. 1992 Trans. Royal Society Tropical Medicine and Hygiene.
Turnaround time for Culture Positive Cases (N=391).

- TAT – Key to create impact on treatment.
- TAT\(^{90} \) was 30 h
- TAT\(^{100} \) was \( \leq 67 \) h
- Antibiogram of randomly selected strains were tested by conventional NCCLS method.
  - The result was identical (±1mm).

**Impact of Report on Therapy.**

<table>
<thead>
<tr>
<th>Empirical Therapy Started</th>
<th>Change Needed from 1st line</th>
<th>Change Needed from 2nd line</th>
<th>Appropriate Therapy</th>
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<tbody>
<tr>
<td>81% (87/108)</td>
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<tr>
<td>54% (47/87) with 1st line of antibiotic</td>
<td>46% (40/87) with 2nd line of antibiotic</td>
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Overall impact is only on 27% \([29(21+8)/108]\) of cases. Cost effectiveness was never a consideration.
Treatment of typhoid fever

1st line of Antibiotic
- Amoxycillin
- Chloramphenicol
- Cotrimoxazole

Recent Problem
- Slow epidemic of multi-drug resistant *S. Typhi* in the subcontinent

Panic among the public health people

Confusion between clinicians and microbiologists

2nd line of antibiotic
- Ceftriaxone - Expensive
- Ciprofloxacin – Widely Used

Saha et al. 1995 J Antimicrobiol Chemotherapy.
Impact of using 2nd line of drugs - Resistance of community vs hospital strains, 1994-1997

- Remarkable difference between hospital and community isolates.
- Ideal practice in Bangladesh and ....
- Hospital Vs community

Saha et al. J Antimicrobial Chemotherapy 1997
Nalidixic Acid Resistance in S. typhi

- Progressive increase in relative resistance to Ciprofloxacin
  - Delay in clinical response
  - Higher dose
  - Treatment failure
  - Recurrence
Trend of drug resistance in last one decade
Prevention

• Improvement of sanitary system and assurance of safe water supply.

• Immunization – designed for school age children
  – Common belief – either not prevalent or benign in early age

• Vaccine type
  – Parenteral
    • LPS – age group dependent
  – Oral
    • Attenuated
Magnitude of S. typhi bacteremia: change in concept of virulence

- Magnitude of Bacteremia is directly proportional to age.
- Disagree with the common belief about
  - Virulence
  - Vaccination.

Saha et al, Pediatric Infectious Disease Journal, 2000
Age group distribution of Typhoid cases 1998-2004: Implication in vaccination policy (N=2074)

New recommendation for vaccination:

- Existing vaccine may not be effective in 98% of cases with conjugate vaccine needed for this group.
- Effective conjugate vaccine required.
- 98% coverage desired.

Saha et al. Pediatric Infectious Diseases Journal, 2000; and unpublished
Conclusions

• Prevalence – Most common cause of febrile illness in the community and hospital
• Treatment – Third generation cephalosporin
• Prevention – Vaccination, Sanitation, Education (?)
  – Vaccination policy – conjugated vaccine at the age of 9 months to 1 year
Thank You All