Enteric Fever Outbreaks in Africa: Same old Foe but Emerging New Challenges in Management

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Lecture outline

• Epidemiology of typhoid in Africa
• New clonal expansions and Antimicrobial Resistance
• Current issues on diagnosis
• Prospects for vaccine use in disease prevention strategies
Introduction

• Few population-based data on incidence and mortality due to salmonellosis in Africa (SETA initiative)

• Most data from hospital-based studies of community-acquired bloodstream infection
  – Non-Typhi *Salmonella* predominate in west, central, east, and southern Africa
  – More cases of S. Typhi now reported from informal settlements in sub-Saharan Africa
  – Differences in regional prevalence and epidemiology is poorly understood
A long way to go on matters overcrowding and sanitation

Mukuru kwa Njenga and Mukuru Reuben are among the many villages in the larger slum

### Catchment population for Mukuru

<table>
<thead>
<tr>
<th>Description</th>
<th>Population</th>
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<tbody>
<tr>
<td>Total catchment population</td>
<td>150,000</td>
</tr>
<tr>
<td>Children under 1yr(12months)</td>
<td>22,000</td>
</tr>
<tr>
<td>Children under 5 yrs (60months)</td>
<td>30,000</td>
</tr>
<tr>
<td>Children under 15 yrs</td>
<td>37,000</td>
</tr>
<tr>
<td>Adults (24-59yrs)</td>
<td>50,000</td>
</tr>
<tr>
<td>Elderly (over 60yrs)</td>
<td>11,000</td>
</tr>
</tbody>
</table>
Endemic and Hyperendemic typhoid regions
Global Collection and analysis of S. Typhi

~ 1,800 isolates
63 countries
6 continents

In sub-Saharan Africa, where does Typhoid Fever cluster?

Non-H58 S. Typhi

H58 S. Typhi
West Africa:

Molecular Surveillance Identifies Multiple Transmissions of Typhoid in West Africa.

South Africa:

Typhoid Fever in South Africa in an Endemic HIV Setting.

Carriage prevalence of Salmonella enterica serotype Typhi in gallbladders of adult autopsy cases from Mozambique.

A Qualitative Study Investigating Experiences, Perceptions, and Healthcare System Performance in Relation to the Surveillance of Typhoid Fever in Madagascar.

Rapid emergence of multidrug resistant, H58-lineage Salmonella Typhi in Blantyre, Malawi.

Central Africa:

Salmonella Typhi in the Democratic Republic of the Congo: fluoroquinolone decreased susceptibility on the rise.
East Africa:

Typhoid in Kenya is associated with a dominant multidrug-resistant Salmonella enterica serovar Typhi haplotype that is also widespread in Southeast Asia.

Diagnosis of imported Ugandan typhoid fever based on local outbreak information: A case report.

A large and persistent outbreak of Typhoid fever caused by consuming contaminated water and street-vended beverages: Kampala, Uganda, January - June 2015.

A large outbreak of typhoid fever associated with a high rate of intestinal perforation in Kasese District, Uganda, 2008-2009.

Massive lineage replacements and cryptic outbreaks of Salmonella Typhi in eastern and southern Africa.

Diagnosis and Treatment of Typhoid Fever and Associated Prevailing Drug Resistance in Northern Ethiopia.

Transcontinental MDR spread:
A Multicountry Molecular Analysis of Salmonella enterica Serovar Typhi With Reduced Susceptibility to Ciprofloxacin in Sub-Saharan Africa.

In all endemic settings MDR is a major challenge in Africa
Global dissemination of S. Typhi H58

Kenya as an early hub of S. Typhi H58 from SE Asia
What are the major challenges in tackling Typhoid in SSA?
Challenges in Diagnosis

• Clinical Diagnosis

• High index of suspicion
• Knowledge of the local epidemiology
• Clinical presentation is usually non specific
Laboratory tests: from when are they useful?

- Blood culture or BM culture: Week 1
- Serological Methods: Week 2 (Widal Test most common)
- Stool Ag Test: Week 2
- Urine culture: Week 4
- PCR: Week 1
- WGS and metabolomics technology can be adopted for bedside Dx

# Diagnostic accuracy of the TUBEX-TF and OnSite Typhoid IgG/IgM Combo tests with culture as the gold standard (Zimbabwe outbreak of 2014)

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUBEX-TF (n = 131)</td>
<td>100</td>
<td>94.12</td>
<td>63.16</td>
<td>100</td>
</tr>
<tr>
<td>OnSite Typhoid IgG/IgM Combo (n = 136)</td>
<td>100</td>
<td>94.34</td>
<td>63.16</td>
<td>100</td>
</tr>
</tbody>
</table>

Only point-of-care rapid tests available, but LOW to MODERATE sensitivity and specificity

*Talupiwa et al., BMC Res Notes. 2015 Feb 24;8:5*
• Challenges in treatment options and vaccine use in Africa
Issues of antibiotic Rx in face of MDR S. Typhi

• For MDR infections fluoroquinolones widely used for treatment.
• For fully susceptible S. Typhi (ciprofloxacin MIC< 0.06 μg/mL) Rx very effective
• Later generation fluoroquinolone, gatifloxacin, clinically more effective against MDR infections
• Azithromycin MIC ≤ 16 μg/mL
• Ceftriaxone and cefotaxime, reliable reserve drugs particularly for hospital admitted cases
Vaccines

• WHO recommends targeted vaccination of high risk populations as a short- to medium-term measure.

• Locally, only private clinics stock Vi conjugate vaccine for travel vaccination and for workers in hospitality industry

• Prices still too high for widespread public health use

• Governments in Africa have not prioritized use of vaccine even in endemic settings
Conclusion 1

• With increasing informal settlements with little or no infrastructure, we will continue to experience outbreaks, we have to prepare!

• Accurate diagnosis a major challenge in our settings – we need to adopt simple affordable rapid kits that can be deployed under field conditions.

• Burden of disease data and economic implications important to document as these mobilize action!
Conclusion 2

- Resistance to commonly available antibiotics and high cost of effective alternatives should persuade policy makers to consider low cost vaccine, with options for technology transfer and bulk purchase.

- Improving hygiene, clean water supply and reduced overcrowding long term goals.
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