INTERNATIONAL VACCINE INSTITUTE

The Typhoid Fever Surveillance in Africa Program (TSAP)

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Introduction

Present global disease burden model for typhoid fever (TF)

- Studies conducted in the period of 1990-2011 covered
- Data available from the below sites:

Central America: none
South America: none

North Africa: 2
West Africa: 1
East Africa: 3
Central Africa: none

East Asia: 2
South Asia: 7
Southeast Asia: 4
Central Asia: none

Introduction

Extrapolation of available data to a wider region

Introduction – Kilifi 2009

Meeting on invasive Salmonelloses convened by the IVI in Kilifi, Kenya in January 2009

Question:
Is there typhoid fever in Africa?
If so, how much?

Outcome:
Recommendation that a sentinel network of field sites be created across Africa that follows similar standards and study procedures.

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Conference Summary

Meeting on Establishment of Consortium to Study Invasive Salmonelloses in Sub-Saharan Africa

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Estimates of typhoid fever in Africa have been based exclusively on placebo group incidence rates during vaccine trials in the Arab Republic of Egypt and the Republic of South Africa (1–4); population-based data on infections caused by *Salmonella enterica* serotype Typhi have not been available. In the Gambia, Mabey et al. described a series of 5,466 febrile patients hospitalized during 1979–1984 from whom blood cultures were taken (5). Of the 246 blood cultures from which bacteria were isolated, 45 (18%) were positive for *Salmonella* serotype Typhi and 71 (28%) were positive for non-Typhi serotypes of *S. enterica*. The importance of *S. enterica* non-Typhi serotypes in febrile illness also has been demonstrated in other studies (6–9), including a population-based study (9). In that study, of 1,094 children with bacteremia admitted to the hospital during 1998–2002 in Kilifi, Kenya, 166 (15%) had *S. enterica* non-Typhi serotypes and 1 had *Salmonella* Typhi; *S. enterica* non-Typhi serotypes were the second most frequently isolated bacterial species.

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http://www.cdc.gov/EID/content/15/7/e2.htm

TSAP – Objective, procedures and study sites

Objective:

to generate standardized data on incidence of invasive *Salmonella* bloodstream infections in sub-Saharan Africa

Standardized procedures:

- Protocol

  1) Inclusion criteria
  2) Clinical procedures
  3) Laboratory procedures

- Logistics incl. sample shipment
- Health care utilization survey (HCUS)
- Database/Data management

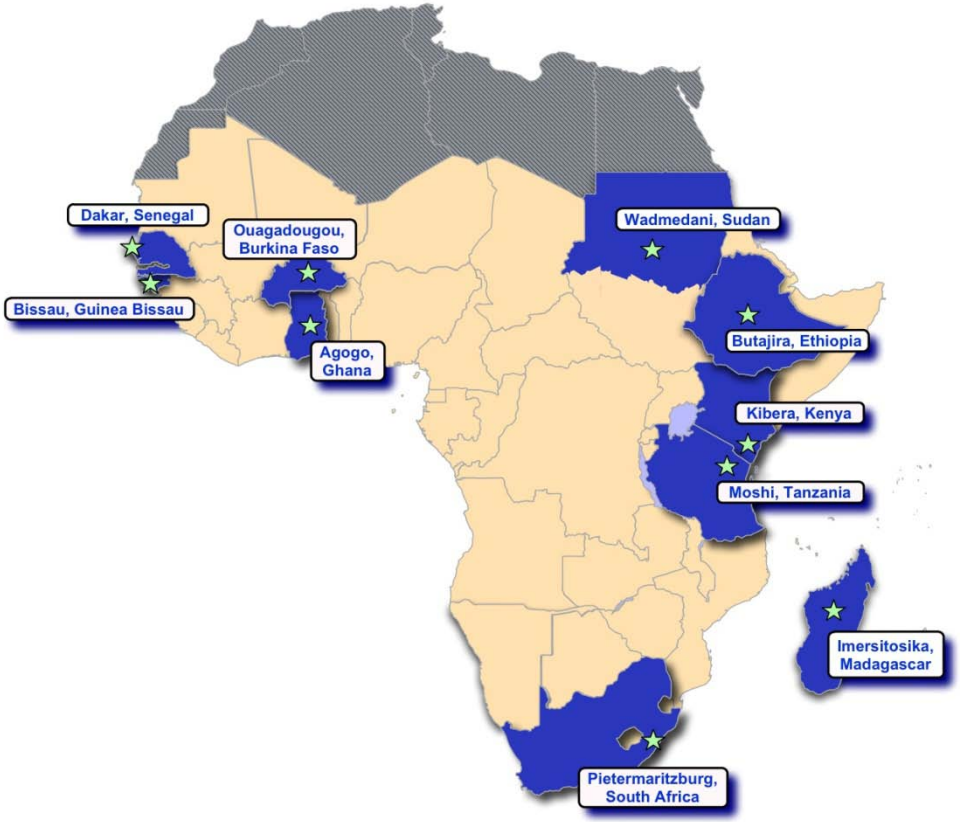

Fig. Location of TSAP study sites

TSAP – Outcomes

Research Topics	Expected outcomes
Incidences for typhoid/paratyphoid fever and NTS infections	Identification of risk groups/target groups for preventive interventions
Antimicrobial susceptibility patterns	Adaption of treatment with adequate antibiotics/Re-evaluation of national guidelines/Awareness raising
Other organisms identified	Information on further causes of febrile diseases (i.e. incidence of viral infections in particular risk groups/per season)
Co-infection with malaria	Occurrence of *P. falciparum* on invasive bacterial infections
Clinical data/risk factor assessment	Determination of risk factors associated with enteric fever
Information on *Salmonella* carrier status	Proportion of *Salmonella* carriers in population

TSAP – Extrapolation model

To develop and validate a disease burden prediction model using standardized data

Improvement of the current disease burden model to

- Predict burden of disease at population level and
- Identify populations at higher risk of *Salmonella* infections, using standardized data incl. risk factors collected at TSAP sites.

Step 1: Decision on input variables that are transferable and available/or easily determinable

Step 2: model to be calibrated against known output variables such as current disease burden estimates and validated in at least three TSAP sites on its ability to predict what it projected.

This model intends to enable the global community to predict the disease burden based on input variables in differing countries or geographical locations and help inform GAVI/country-level decision-making for vaccine introduction.

Active, household-level surveillance

***Active* household-level surveillance of fever cases**

Rationale:

- **Avoid self-treatment of fever with antibiotics** (leading to reduced microorganism detection rates in blood culture diagnostics)
- Capture patients and perform diagnostics early in the course of the disease (when bacteremia is high)
- **Adjust for the differing health systems**/health-seeking behaviors in TSAP countries, which might lead to incomparable incidence calculations

***Active* household-level surveillance** of febrile cases in selected TSAP countries where health-care seeking attendance is hampered due to lack of health-are systems and at sites with considerable antibiotic self-treatment prior to fever diagnostics

Summary

- Standardized surveillance established and running in 10 sites
- Initial data indicate *S.* Typhi and NTS disease burden in study sites
- One year of surveillance data insufficient
- Design/validation of extrapolation model where data feed into

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THANK YOU

Published *S.* Typhi incidence: Asia*

Site	Hechi, China	Kolkata, India	North Jakarta, Indonesia	Karachi, Pakistan	Hue, Viet Nam	Total	*P*-value[a]
Site setting	Urban / rural	Urban slums	Urban slums	Urban slums	Urban	–	–
Total population from the study census [year of census]	112 889 [2001]	56 946 [2003]	160 261 [2002]	101 937 [2001, 2003][b]	281 781 [2002]	713 814	–
Surveillance period	1 Aug 2001 to 31 Jul 2002	1 Nov 2003 to 30 Oct 2004	1 Aug 2002 to 31 Jul 2003	1 Aug 2002 to 31 Jul 2004[c]	1 Jun 2002 to 30 Jun 2003	–	–
Surveillance target population (age in years)	5–60	All ages	All ages	2–15	5–18	–	–
Typhoid Incidence (per 100 000/year)	**15.3**	**214.2**	**81.7**	**451.7**	**21.3**	**107.6**	< 0.0001
By age							
0–1 years	NA	89.2	0.0	NA	NA	21.6	0.0777
2–4 years	NA	340.1	148.7	573.2	NA	364.8	< 0.0001
5–15 years	29.3	493.5	180.3	412.9	24.2	170.8	< 0.0001
≥ 16 years	12.4	119.7	51.2	NA	10.9	46.8	< 0.0001

- **Ochiai *et al*., Bull WHO 2008**