Where are we with diagnosing typhoid fever?

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Searching for the elusive typhoid diagnostic

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Abstract
Typhoid (enteric) fever is still a common disease in many developing countries but current diagnostic tests are inadequate. Studies on pathogenesis and genomics have provided new insight into the organisms that cause enteric fever. Better understanding of the microorganisms explains, in part, why our current typhoid methodologies are limited in their diagnostic information and why developing new strategies may be a considerable challenge. Here we discuss the current position of typhoid diagnostics, highlight the need for technological improvements and suggest potential ways of advancing this area.

Probably needs an update
Medical advances

• We live in a period of amazing medical technology
• New generation vaccine technology
• Gene therapy
• Microbiome therapy
• Cancer diagnosis and treatment
• Hepatitis C cure
• HIV cure
• Reprogramming of T cells

• What about typhoid?
Things didn’t really work out as we hoped
Non specific febrile diseases
Typhoid isn’t so easy
What do we need?

- A POC test that can identify Typhi/Paratyphi/NTS
- A POC test that can identify viral/bacterial/parasitic infections
- A POC test that can identify MDR/XDR organisms
- A test than can help us measure disease burden and incidence
- A test that can identify and estimate carriage
- A test that can identify environmental circulation
- It is unlikely that one can do all
Reproducible diagnostic metabolites in plasma from typhoid fever patients in Asia and Africa

Elin Näesström1, Christopher M Parry2,3, Ngà Tran Vu Thinh4,5, Rapeephan R Mauds6, Hanna K de Jong7,8, Masako Fukushima9, Olena Rzhepishevska1, Florian Marks1, Ursula Panzner1, Justin Im9, Hyojin Joon9, Seeun Park6, Zabeen Chaudhury9, Aniruddha Ghose10, Rasheda Samad10, Tan Trinh Van4, Anders Johansson11, Arjen M Dondorp4, Guy E Thwaites4,12, Abul Fazl13, Henrik Anttila14, Stephen Baker6,14,16

Interferon-driven alterations of the host's amino acid metabolism in the pathogenesis of typhoid fever

Christoph J. Blohmke1, Thomas C. Darton1, Claire Jones1, Nicolas M. Suarez2, Claire S. Waddington1, Brian Angus3, Liqing Zhou1, Jennifer Hill4, Simon Clare5, Leanne Kane, Subhankar Mukhopadhyay6, Fernanda Schreiber7, Maria A. Duque-Correa8, James C. Wright9, Theodorus I. Roumeliotis10, Lu Yu11, Jyeot S. Choudhury12, Assuncion Mejias13, Ocavio Ramilo14, Milena Shanyinde15, Marcelo B. Stein16, Robert A. Kingeley17, Stephen Lockhart18, Myron M. Levine19, David J. Lynn20, Gordon Dougan21, and Andrew J. Pollard22

Development of a Simple, Peripheral-Blood-Based Lateral-Flow Dipstick Assay for Accurate Detection of Patients with Enteric Fever

Iqbal Hassan Khan2, M. Abu Sayeed2, Nisheen Sultan2, Kameel Islam2, Jakia Anis2, M. Omar Faruk3, Unuma Khan2, Farhana Kanan4, Edward T. Ryan4,5,6, Fradaq Qadri6

An evaluation of purified Salmonella Typhi protein antigens for the serological diagnosis of acute typhoid fever

Journal of Infection (2017) 75, 104–114
“Infection” defined as increase in CdtB in paired samples (3 months apart)

Incidence/Burden

**HlyE** | **Vi** | **Flagellin** | **YncE**
---|---|---|---
No IgG increase | Infected (?) | No IgG increase | Infected (?) | No IgG increase | Infected (?) | No IgG increase | Infected (?)
The environment

Evaluating PCR-Based Detection of *Salmonella* Typhi and Paratyphi A in the Environment as an Enteric Fever Surveillance Tool


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Carriage
Outlook?

• We have made substantial inroads into assessing various aspects of typhoid detection
• We are in a good position to take some of these methods forwards into the typhoid elimination era
• We have the tools and new ones are coming

• However
  • We still lack important data
  • We lack standardized approaches
  • We lack a consensus of what is needed
  • We need to focus our efforts on the best approach

• A POC test for typhoid?
What next?

• We need to capitalize on existing momentum
• Fill some important knowledge gaps
• Use the roll out of TCV as a mechanism to develop appropriate tests
  • Disease burden
  • Impact of vaccine
  • Replacement of Paratyphi A

• Non specific febrile disease/vaccines/AMR
Many thanks

- To the various contributors in the room
- Look forward to seeing more advances in the coming days