Typhoid vaccine policy and practice: update from the Coalition against Typhoid (CaT)

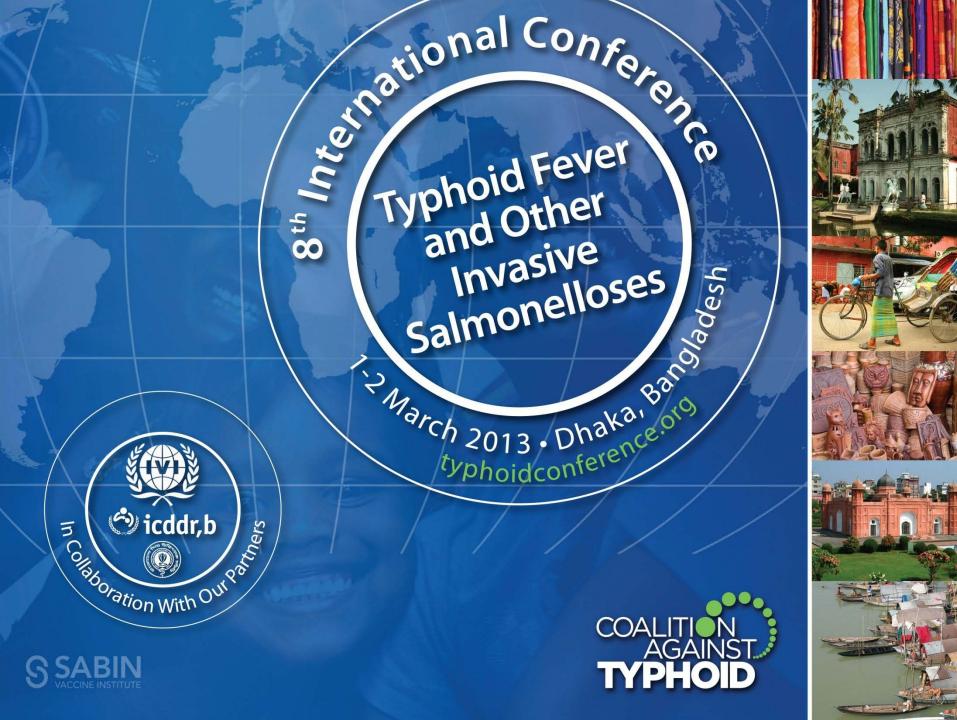
Christopher B. Nelson, PhD MPH
Director, Coalition against Typhoid (CaT) Secretariat

www.COALITONagainstTYPHOID.org // CaT@sabin.org

1 March 2013







Typhoid Fever has impacted populations since antiquity



430–424 BC: plague of Athens killed one third of the population, including their leader Pericles. The balance of power shifted from Athens to Sparta, ending the Golden Age of Pericles and Athenian dominance in the ancient world.

International Journal of Infectious Diseases (2006) 10, 206-14. Image: http://www.pbs.org/empires/thegreeks/keyevents/430_c.html Alexander the Great (356-323 BC) dies from typhoid fever in Babylon.



Oldach DW, Richard RE, Borza EN, Benitez RM. N Engl J Med. 1998 Jun 11;338(24):1764-9. Alexander fighting the Persian king Darius III. From Alexander Mosaic, Pompeii. Naples National Archaeological Museum. Naples, Italy.





Typhoid Fever has impacted populations since antiquity

Zhang Zhong-Jing (150 – 219 A.D.)

- compiled the "Shanghan Zabing Lun", or "Treatise on Febrile and Miscellaneous Diseases"
- addresses typhoid fever

GSABIN

- the work was later divided in two parts:
 - "Shang han lun" or "Treatise on Febrile
 Diseases Caused by Cold" (description of
 epidemic disease causing fever);
 - 2) "Jin kui yao lue" or "Synopsis of prescriptions of the golden chamber" (compendium of clinical experience).
- in the preface the author notes that of the approximately 200 inhabitants in his village, more than two-thirds died within the course of 10 years and 70% of these deaths were due to typhoid.

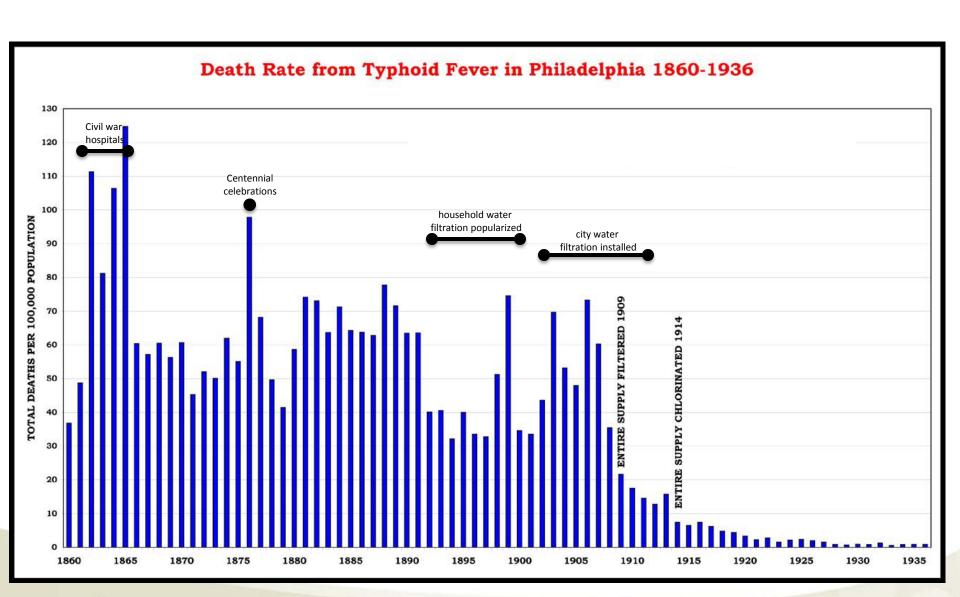


G. Maciocia. ZHANG ZHONG JING.1980. Journal of Chinese Medicine. 4. Spring/summer. http://homepage.mac.com/sweiz/files/article/4-2.pdf

THE URBAN PENALTY: TYPHOID FEVER



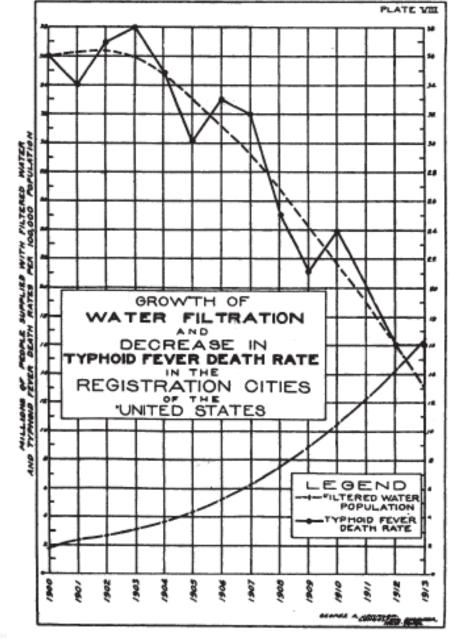








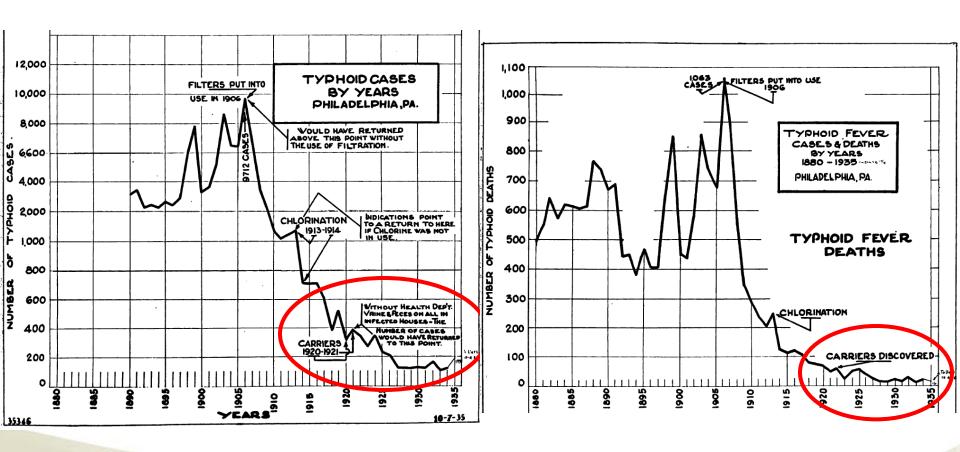
The widespread adoption of improved water (filtration +/- chlorination) by American cities in the early 20th century is followed by dramatic decreases in typhoid mortality







After water filtration +/- chlorination,
Public health measures contributed to the control of typhoid fever:
Pasteurization of milk, epidemiologic investigation of cases and outbreaks with hospitalization of cases, immunization of contacts, and occupational restrictions for carriers (pre-antibiotic era)







nttp://www.historyofvaccines.org/

Typhoid Mary – a chronic carrier



- Mary Mallon worked as a cook for wealthy New York families
- Families for whom Mallon had worked as a cook had fallen ill with typhoid fever.
- Was the first identified healthy carrier of typhoid: she carried the typhoid bacteria and spread them to others, but did not fall ill herself.
- In 1907, detained by the New York City Department of Health for three years
- In 1915, while working under an assumed name, was associated with 25 typhoid cases, one of whom died.
- Detained at North Brother Island and remained there for the next 23 years until her death in 1938.
- At the time of her death in 1938, she was officially and directly linked to 10 outbreaks totaling 51 cases of typhoid fever, and three deaths from the disease.





Erasing the Urban Penalty



During the early 20th century, the provision of clean water (filtration +/-chlorination) to major American cities led to:

- the near-elimination of typhoid fever (>90% reduction)
 - 26% almost immediately
 - Add'l 65% over 5 years
- a 74% decrease in infant mortality
- a 62% decrease in child mortality





POPULATIONS W/O ACCESS TO SAFE WATER AND BASIC SANITATION:

DEVELOPMENT, IMPLEMENTATION AND IMPACT OF THE FIRST TYPHOID VACCINES





S. Typhi is observed and cultured for the first time in the early 1880's

Philadelphia Water Department
Historical Collection CHAPTER XX.

Downloaded from

www.phillyh2o.org/filtration.htm

Typhoid fever—Study of the organism concerned in its production— Its morphological, cultural, and pathogenic properties—Bacillus coli—Bacillus paratyphosus—Its resemblance to Bacillus typhosus.

BACILLUS TYPHOSUS.

THE organism discovered in the tissues of typhoid cadavers microscopically by Eberth (1880–81), and subsequently isolated in pure culture and described by Gaffky (1884), is now generally recognized as the etio-

Fig. 70. Fig. 71.

Bacillus typhosus, from culture twenty-four hours old, on agaragar.

logical factor in the production of typhoid fever. It may be described as follows:

Bacillus typhosus, showing flagella stained by Löffler's method.

It is a bacillus about three times as long as broad, with rounded ends. It may appear at one time as very short ovals, at another time as long threads, and both

426





The Widal agglutination test was described in 1896

first used in municipal hospitals later that year (Johnston 1896) including the New York city Health Department (Guerard 1897)



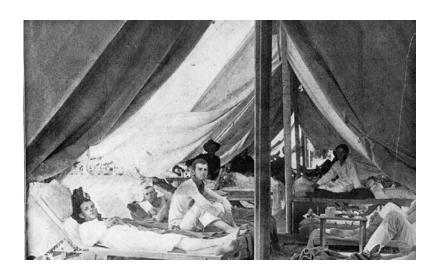
achaise.net/appl/article.ph article=2038

General conclusions.—From an analysis of the results which have so far been obtained in the application of the Widal test, it would seem, in the first place, that the serum reaction is by no means specific, in the strict acceptation of the term. In the second place, it is evident that this test has certain limitations in its practical utility, and that unless properly applied with a due appreciation of these limitations, it is liable to lead to false conclusions. The chief

When the subject of the serum diagnosis of typhoid fever was first brought before the public, it was hoped that at last the long-sought infallible diagnostic test for typhoid fever had been discovered, which was at once rapid, simple and suitable for clinical use at the bedside. With the non-fulfillment of these hopes, some physicians have come to look upon Widal's test as practically useless for diagnostic purposes. But,

AR Guerard. JAMA. 29. 1897.

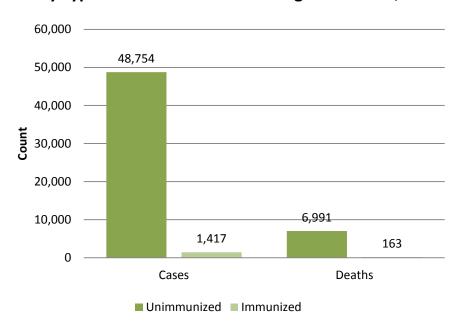
Hx of Typhoid Vaccines: UK



1897 English bacteriologist Almroth Wright introduces a killed (heat-inactivated, phenol-preserved, whole-cell) typhoid vaccine in Britain.

1898-9 Trials in the Indian army produced excellent results and typhoid vaccination was adopted for the use of British troops serving in the Second Boer War (1899).

Early Typhoid Vaccine Use in the Anglo-Boer War, 1899



Cantlie N. History of the Army Medical Department, Vol. II. Edinburgh and London: Churchill Livingstone, 1974:230, 373.

NB: whole-cell inactivated vaccine, one dose regimen, soldiers.





Hx of Typhoid Vaccines: USA

Typhoid vaccination for US soldiers during WWI. *Image from the History of Medicine (NLM)*. The History of Vaccines. http://www.historyofvaccines.org/

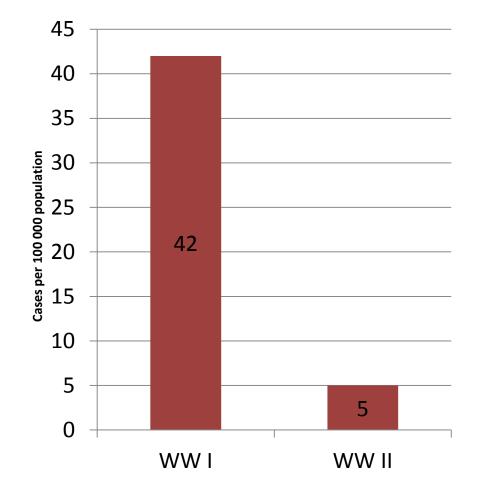


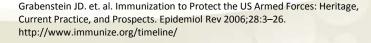
Typhoid vaccination in the US armed forces

- 1909 starts in US Army
- 1911 required for entire US Army and Navy

The impact of typhoid vaccination in the US armed forces

- World War I, 1917–1918
 - 2 000 typhoid cases, 227 deaths (11.4% CFR)
 - 42 typhoid cases per 100 000 soldiers
- World War II, 1941–1945
 - 5 typhoid cases per 100 000 soldiers









Hx of Typhoid Vaccines: USA



Doctor administering a typhoid vaccination at a school in San Augustine County, Texas. Photograph by John Vachon, April 1943.

Typhoid vaccination in the general population

- 1914 Typhoid vaccine first licensed for the U.S. general population
- July 16, 1952 Heat-phenol inactivated typhoid vaccine by Wyeth licensed in US.
- Dec 15, 1989 A live, oral typhoid vaccine (Ty21a, Vivotif Berna by Swiss Serum Institute) licensed in US.
- Nov 28, 1994 Typhoid Vi polysaccharide inactivated injectable polysaccharide vaccine (Typhim Vi by Aventis Pasteur) licensed in US.

http://www.immunize.org/timeline/ Grabenstein JD. et. al. Immunization to Protect the US Armed Forces: Heritage, Current Practice, and Prospects. Epidemiol Rev 2006;28:3–26.





THE URBAN PENALTY: TYPHOID FEVER

A CONTINUING PROBLEM
IN LOWER AND LOWER MIDDLE INCOME COUNTRIES





Populations at Risk for Typhoid Fever

Typhoid fever is prevalent in populations with

- inadequate access to safe water
- inadequate access to basic sanitation

Levine MM. Vaccines. Typhoid fever vaccines. In: Plotkin SA, Mortimer EA, Orenstein W, editors. Vaccines 5th Edition. Philadelphia: WB Saunders Company; 2008.

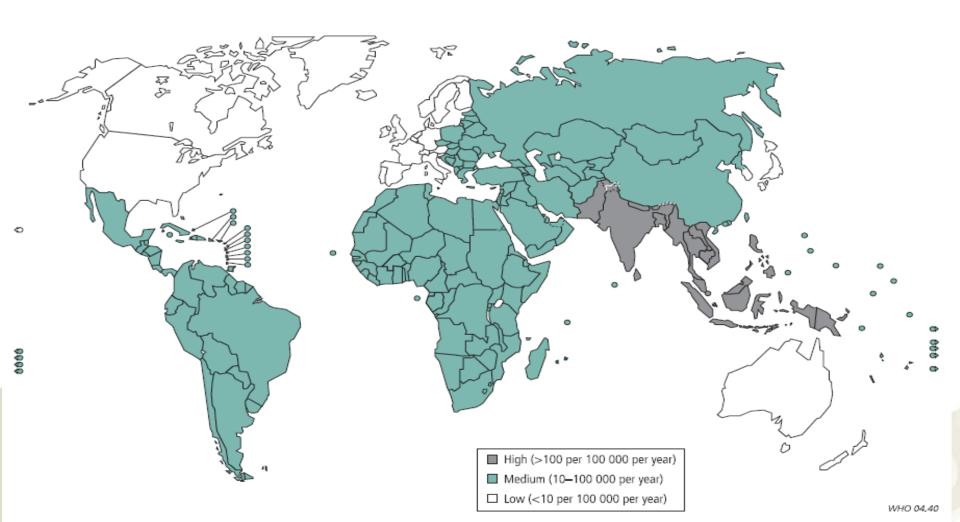




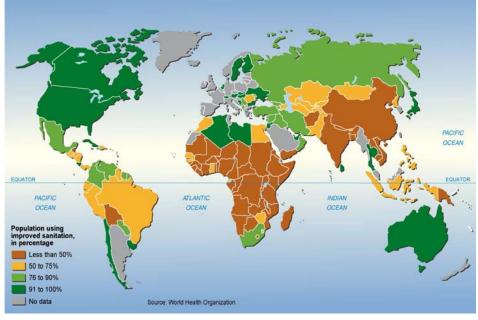
Estimated Global Burden of Typhoid Fever

- WHO estimates 21 million cases and 216,000 600,000 deaths are caused by S. Typhi, every year.
 - Ivanoff et al. (1994) 17 million cases and 600,000 deaths
 - Crump et al. (2004) 21.6 million cases and 216,000 deaths

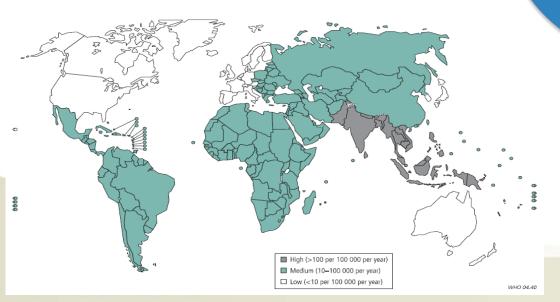
Geographical distribution of typhoid fever



Estimated Global Burden of Typhoid Fever



Geographical distribution of typhoid fever



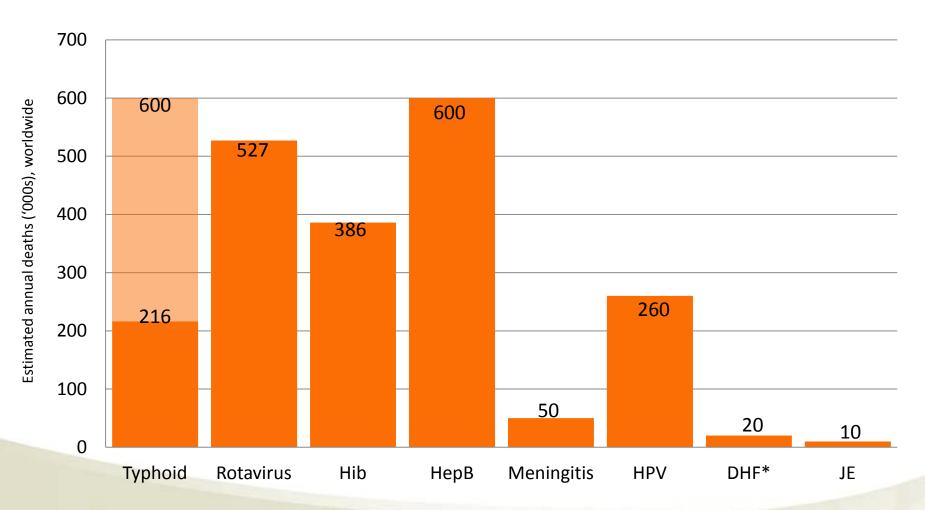
Available burden estimates are limited by:
- Confounding
with other febrile illness dx,
e.g. malaria, dengue
-Poor diagnostics
- lack of
systematic surveillance

Typhoid is a global problem



Typhoid Fever Mortality

is Similar to Other Vaccine Preventable (VP) Diseases

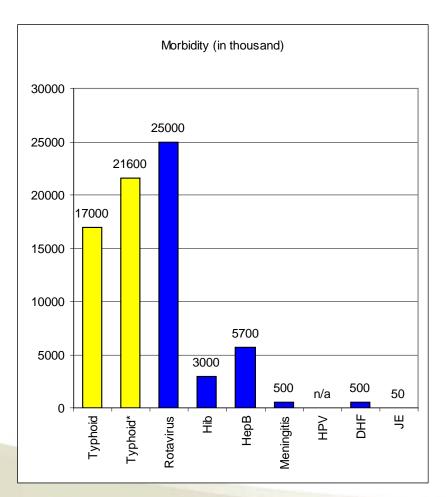


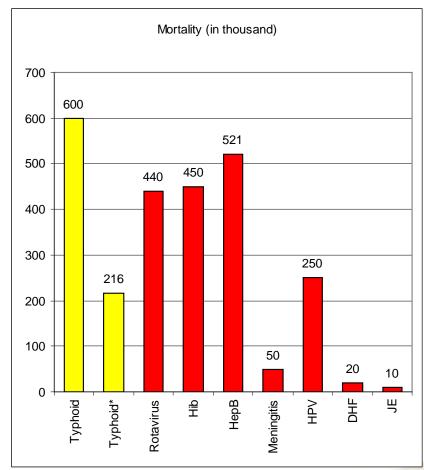




Typhoid Fever Morbidity and Mortality

in Relation to Other VP Diseases









POLICY & PRACTICE: SOUTH AND SOUTHEAST ASIA





WHO recommends typhoid vaccines

2008. 83, 49-60



Organisation mondiale de la Santé

Weekly epidemiological record Relevé épidémiologique hebdomadaire

Vaccins antityphoïdiques:

note d'information de l'OMS

Conformément à son mandat, qui est de

fournir des conseils aux Etats Membres sur

les questions relatives aux politiques de santé,

l'OMS publie une série de notes d'information

régulièrement actualisées sur les vaccins et les

associations vaccinales contre les maladies

qui ont un impact sur la santé publique au

niveau international. Ces notes d'information,

qui portent essentiellement sur l'utilisation

des vaccins dans le cadre de programmes de

vaccination à grande échelle, résument les

considérations générales essentielles sur les maladies et vaccins respectifs et présentent

en conclusion la position actuelle de l'OMS

concernant leur utilisation dans le cadre

mondial. Ces notes ont été soumises à un certain nombre de spécialistes, à l'OMS et à

l'extérieur et, depuis avril 2006, sont examinées

et approuvées par le Groupe stratégique consultatif d'experts de la vaccination de

l'OMS. Elles sont principalement destinées aux

responsables nationaux de la santé publique

et aux administrateurs des programmes de

vaccination. Mais ces notes peuvent également

présenter un intérêt pour les organismes

internationaux de financement, les fabricants

de vaccins, la communauté médicale, les médias scientifiques et le grand public.

La présente note d'information sur la fièvre

typhoïde actualise et remplace la note

correspondante publiée précédemment dans

le Relevé épidémiologique hebdomadaire.

Cette mise à jour des recommandations a été

approuvée par le Groupe stratégique consultatif

8 FEBRUARY 2008, 83rd YEAR / 8 FÉVRIER 2008, 83° ANNÉE

No. 6. 2008. 83, 49-60 http://www.who.let/wor

WHO Position Paper (2008)

(http://www.who.int/wer/2008/wer8306.pdf) Countries should consider the programmatic use of typhoid vaccines for:

- controlling endemic disease (targeting high risk groups / high burden populations)
- outbreak control

An update of the original WHO position paper issued in 2000

(http://www.who.int/docstore/wer/pdf/2000/wer7532.pdf)

Contents

- 49 Typhold vaccines: WHO position paper
- (ii) WHO web sites on infectious

- 49 Vaccins antitypholidiques: note d'Information de l'OMS
- 60 Sites Internet de l'OMS

DE LA SANTÉ

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55N 0049-8114

Typhoid vaccines: WHO position paper

In accordance with its mandate to provide guidance to Member States on health policy matters, WHO issues a series of regularly updated position papers on vaccines and vaccine combinations against diseases that have an international public health impact. These papers, which are concerned primarily with the use of vaccines in large-scale immunization programmes, summarize essential background information on the respective diseases and vaccines, and conclude with the current WHO position concerning their use in the global context. The papers have been reviewed by a number of experts within and outside WHO and, since April 2006, they have been reviewed and endorsed by WHO's Strategic Advisory Group of Experts (SAGE) on immunization. The position papers are designed for use mainly by national public health officials and immunization programme managers. However, they may also be of interest to international funding agencies, the vaccine manufacturing industry, the medical community, scientific media and the

The current position paper on typhoid fever updates and replaces the corresponding paper previously published in the Weekly Epidemiological Record.1 These updated recommendations were endorsed by SAGE in November 2007,2

Summary and conclusions

Typhoid fever is a serious systemic infection caused by the enteric pathogen Salmonella

d'experts en novembre 2007.3 Résumé et conclusions

La fièvre typhoïde est une affection généralisée grave causée par une entérobactérie pathogène,









¹ See No. 22, 2000, pp. 253-264.

² See No. 1, 2008, pp. 1-15.

WHO Regions and Countries: SEAR

WHO South East Asia (SEA)
Regional Office
Immunization
Technical Advisory Group (ITAG)

July 2008:

Recognizing that typhoid fever may be a significant cause of morbidity and mortality in the region, the ITAG encourages countries to identify their disease burden and at-risk populations in order to consider vaccines introduction as part of a comprehensive disease control package.

WHO South East Asia (SEA) Region Countries

May 2009:

Countries in WHO's SEA region prioritize typhoid vaccines for 'immediate' introduction

WHO SEARO. Report of the South-East Asia Regional Vaccine Prioritization Workshop.

Bangkok, Thailand, 11-13 May 2009. SEA-Immun.- 56. Available at:

http://www.who.int/immunization/sage/Report SEARO Vaccine Prioritization wshop.pdf (Accessed 23 June, 2011)







WHO Regions and Countries: SEAR

WHO SEAR Immunization Technical Advisory Group (ITAG)

March 2011:

The ITAG recommends establishing sub-groups to review and make recommendations on specific issues such as health resource management and vaccine introduction (rubella, hepatitis B and typhoid) with each subgroup consisting of an ITAG member as a focal point, WHO staff as secretariat and invited experts from relevant areas.

- WHO-SEARO-ITAG chair: Professor Lalitha Mendis
- WHO-SEARO-ITAG Typhoid, Paratyphoid and Cholera working group chair: Dr Jacob John
- WHO-SEARO-ITAG Members:
 Professor Lalitha Mendis, Dr. Jacob John,
 Dr. Supamit Chunsuttiwat, Dr. Nyoman
 Kandun, Dr. A. M. Zakir Hussain, Dr. Lalit
 Kant., Dr. M. H. Maskey, Dr. N. K. Arora, Dr.
 Triono Soendoro, Dr. Khin Pyone Kyi, Dr.
 Brent Burkholder





Pediatric Associations recommend typhoid vaccines



the Indian Academy of
Pediatrics Committee on
Immunization (IAPCOI)
recommends the use of
ViPS typhoid vaccines in
children 2-15y



the Indonesian Pediatric Society recommends the use of typhoid vaccines

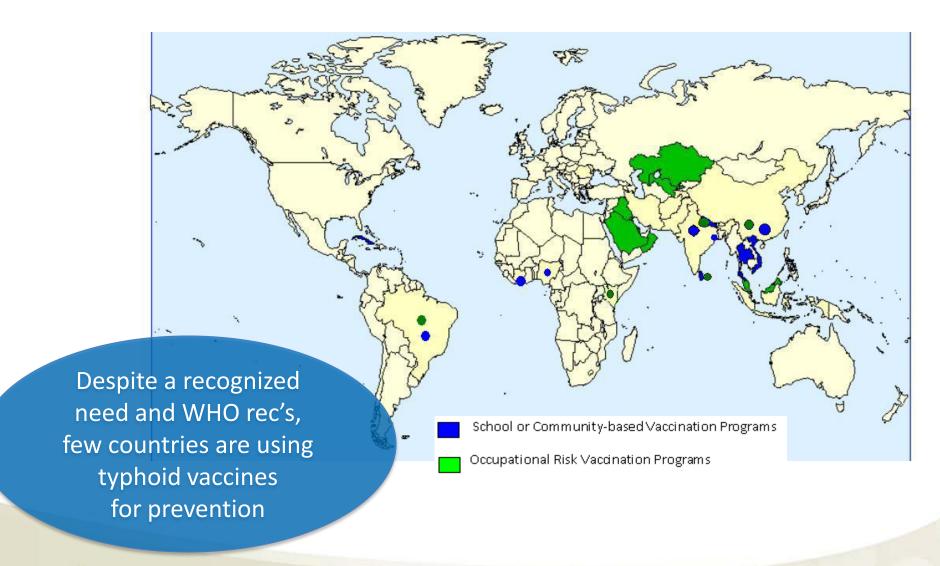
Indian Academy of Pediatrics Committee on Immunization. IAPCOI 2011 Recommendations on use of individual vaccines. Typhoid Vaccines: Recommendations for use. Available at:

for use. Available at: http://www.iapcoi.com/hp/pdf/11-TYPHOID%20VACCINES.pdf (Accessed May, 2012)





Summary of typhoid vaccination programs: 1980-present







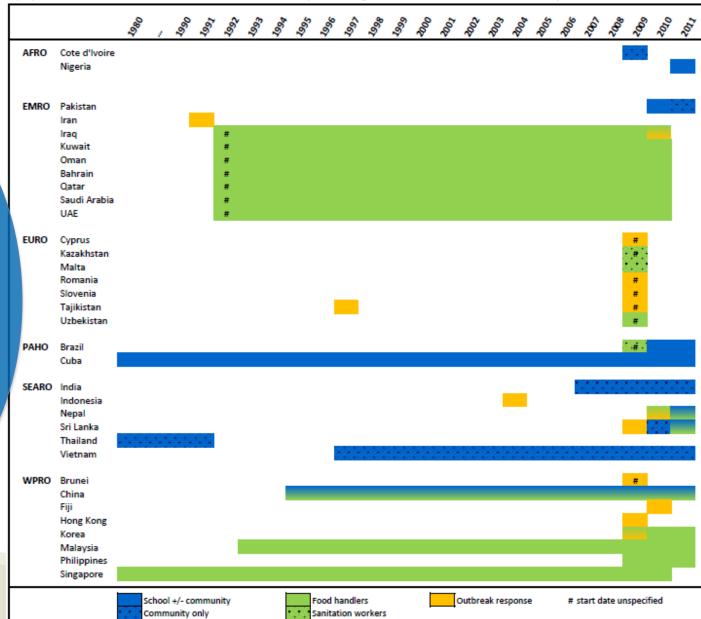
Summary of typhoid vaccination programs: 1980-present

Existing typhoid vaccination programs

Food handlersGen'l Population

and

in place many yearsstarted recently







WHAT HAS BEEN THE IMPACT?





Programmatic Effectiveness of existing Typhoid Vaccine

Old generation killed whole cell vaccine

- School-based vaccination program in Thailand
 - More than 5 million children vaccinated (1977-84)
 - Sharp decline in typhoid fever incidence (note: no formal assessment)

Live attenuated Ty21a vaccine

- School-based vaccination in Santiago, Chile
 - Half a million school aged children through large school-based, randomized, controlled vaccine trials
 - Conferred protection and decline in typhoid cases noted

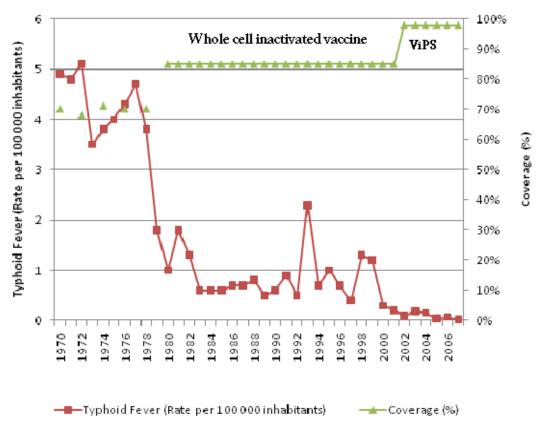




Cuba Vaccine Impact

Vaccination Coverage and Rate of Typhoid Fever in Cuba, 1970 - 2007

(in 2002, Cuba switched from whole-cell inactivated vaccine to Vi PS, one dose regimen, 10-16y school children.)



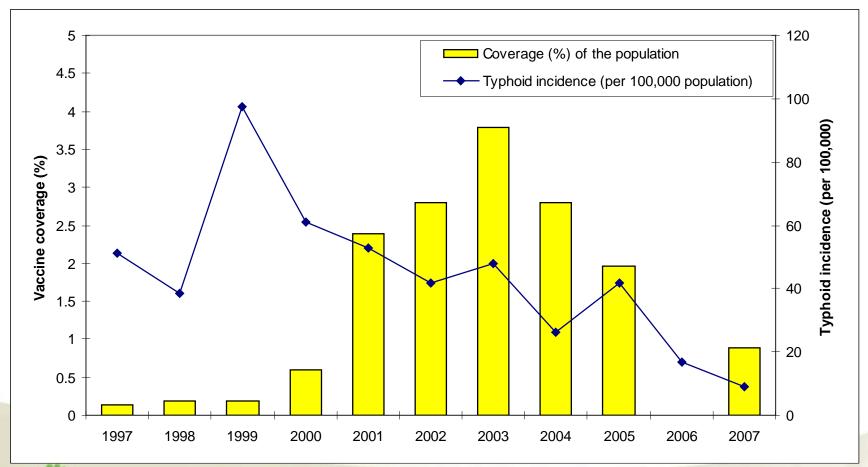




Galindo MA. Programa Nacional de Inmunización, Cuba. PowerPoint presentation at FINSA, November 2006, Havana. Available at: http://mediccreview.medicc.org/articles/mr_56.pdf. (Accessed 17 August, 2011).

Vaccine Coverage and Typhoid Incidence in Northwestern Region of Vietnam



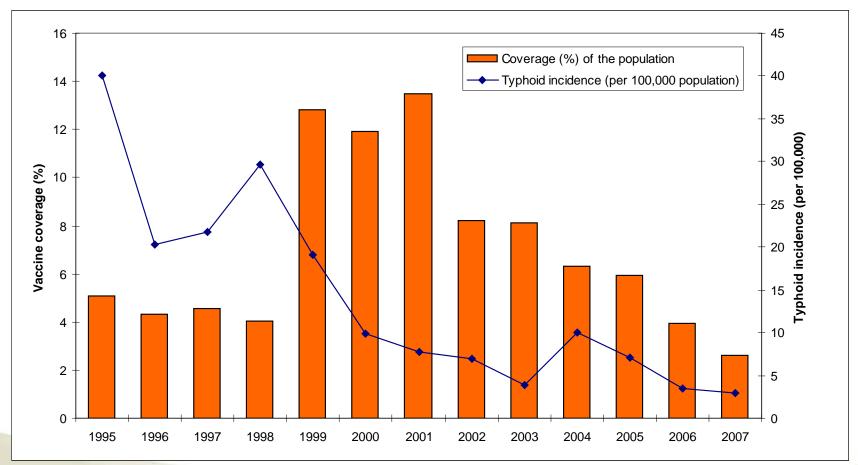






Vaccine Coverage and Typhoid Incidence Guilin, Guangxi Province, China









POLICY & PRACTICE: SOUTH AND SOUTHEAST ASIA

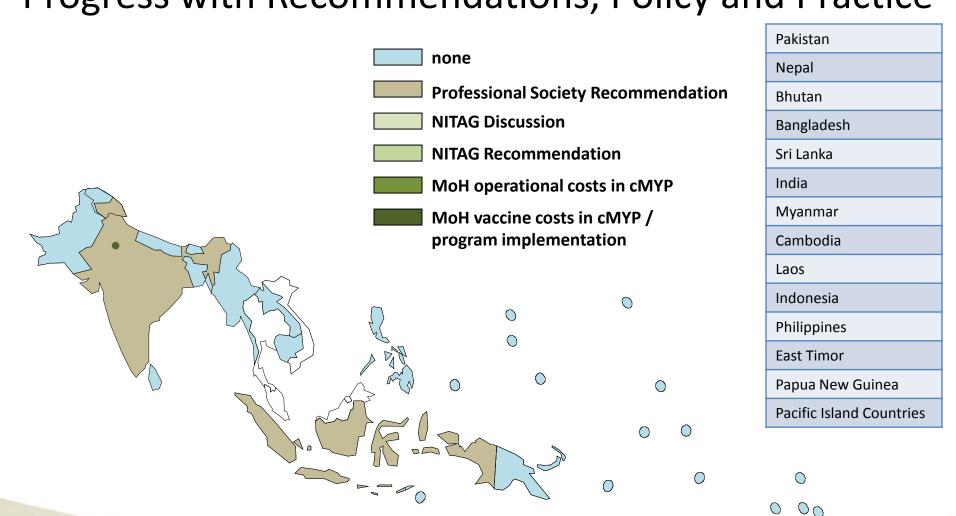




High Typhoid Burden Countries, without existing typhoid immunization programs

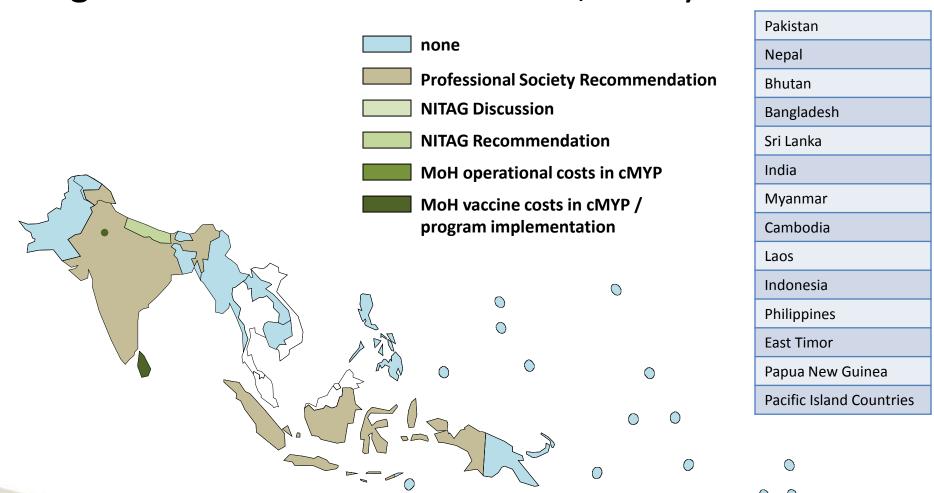


2009 - High Priority Countries: Progress with Recommendations, Policy and Practice

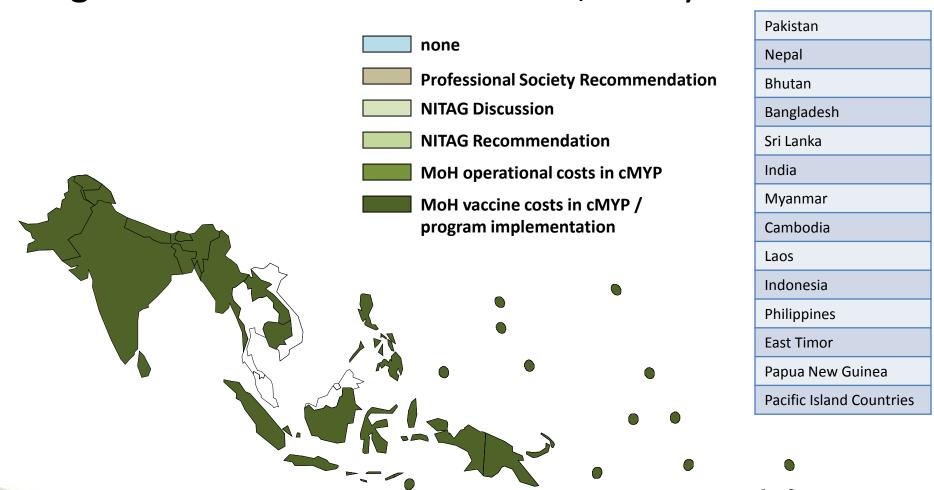


2012 - High Priority Countries:

Progress with Recommendations, Policy and Practice



Goal - High Priority Countries: Progress with Recommendations, Policy and Practice



TYPHOID VACCINES: CURRENT AND FUTURE





Current Typhoid Vaccine Characteristics

| | Ty21a vaccine | Vi polysaccharide vaccine | Vi conjugate vaccine (future) |
|--------------------------------------|----------------------------|---------------------------|-------------------------------|
| Туре | Live attenuated | Subunit | Subunit |
| Route of administration | Oral | IM/SC | IM/SC |
| Doses / regimen | 4 (USA) | 1 | 1-3 |
| Revaccination | 5-7 years | 3 years | never – 4y |
| Efficacy | 35-67% | 55-72% | 90+% |
| Duration of efficacy | 62% at 7 years | 55% at 3 years | 90+% at 4y -life |
| Herd protection | Yes | Yes | Likely |
| Cross-protection against paratyphoid | Yes | No | No |
| Age | ≥ 5 years (ex-USA; USA) | ≥ 2 years (WHO; USA) | ≥ 6 weeks / 9 months (TBD) |





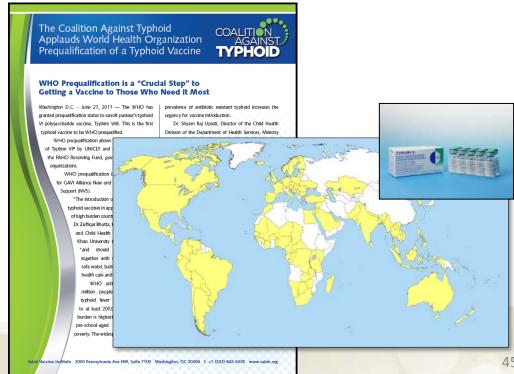
Current Typhoid Vaccines WHO Pre-Qualification Status

Applied for WHO PQ

Crucell-Vivotif (Ty21a)

WHO Pre-Qualified

 Sanofi Pasteur–Typhim Vi (June 2011)







Future Typhoid Vaccines Vi Conjugate (ViCV) and Live Attenuated Vaccines

| ViCV | | Live Attenuated | |
|-----------|--|-----------------|--|
| Vi-rEPA | NIH (USA) Lanzhou Institute (China) | M01ZH09 | Prokarium (July 2012) |
| Vi-CRM197 | NVGH (Italy) ? | Ту800 | Avant Immuno- therapeutics |
| Vi-TT | Bharat Biotech (India) | CVD909 | Center for Vaccine Development , UMD & NIAID |
| Vi-DT * | IVI/Shantha Biotechnics (India) | | |
| Vi-DT * | IVI/SK Chemicals (S Korea) | | |
| Vi-DT * | IVI/Biofarma (Indonesia) | | |
| Vi-DT | DAVAC (Vietnam) | | |
| Vi-DT | Finlay Institute (Cuba) | | |





Development of WHO ECBS Guidelines for Prequalification of Typhoid Vi Conjugate Vaccines

- 5-7 September 2012
 - KFDA/WHO Joint Meeting of Working Group on Quality, Safety and Efficacy of Typhoid Vi Capsular Polysaccharide Conjugate Vaccine, Jeju, Republic of Korea
- 1-31 March 2013
 - first public consultation of the draft document through WHO website
- 29-30 April 2013
 - Follow-up meeting of Working Group on Quality, Safety and Efficacy of Typhoid Vi Capsular Polysaccharide Conjugate Vaccine, Geneva, WHO
- 28 June 2013
 - Submission of final draft for ECBS review
- August September 2013
 - Second public consultation of the draft document through WHO website publication
- 21-25 October 2013
 - ECBS meeting and discussion, Geneva



Review and Discussion of Typhoid Models

- Disease Burden
- Transmission models
 - Interventions effectiveness
 - Cost-effectiveness





GAVI Supports Typhoid Vi Conjugate Vaccines

- In 2008, the GAVI Board approved
 the Vaccine Investment Strategy GAVI's strategic approach
 - 4 vaccines: Human Papillomavirus (cervical cancer), Japanese Encephalitis, Rubella, and
 Typhoid conjugate
 - Reflects a type and degree of commitment to countries, suppliers, and Alliance partners.
 (2010)
- In 2010 and 2011, the GAVI Programme and Policy Committee (PPC) recommended and the GAVI Alliance Board re stated their commitment to typhoid conjugate vaccines
 - Board-recommended Vaccine Investment Strategy (VIS) vaccines: Human Papillomavirus (cervical cancer), Japanese Encephalitis, Rubella, and Typhoid conjugate





THE COALITION AGAINST TYPHOID (CaT)





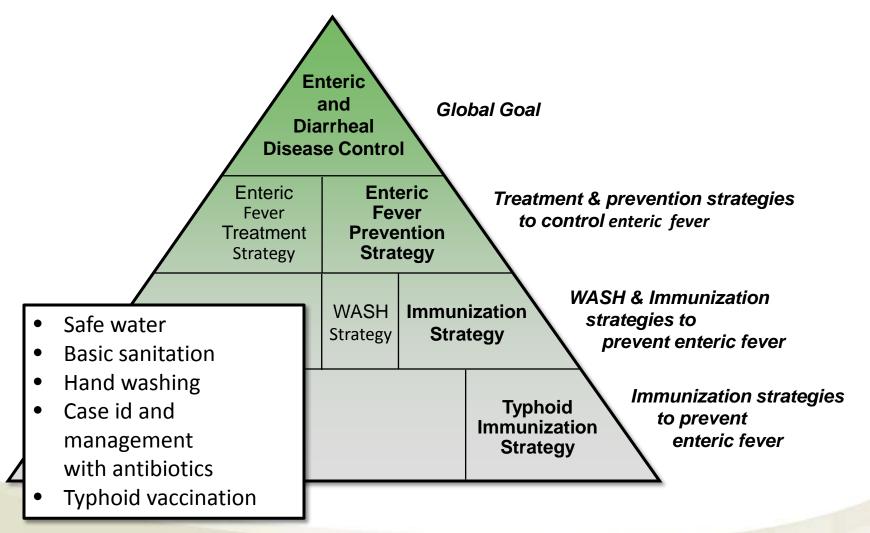






CaT's aim is to expedite and sustain rational, evidence-based decisions regarding the use of typhoid vaccines.

Our aim is defined within the context of Enteric and Diarrheal Disease Control and specifically Enteric Fever Control







CaT's success is based on the collective action of its membership. It is not a highly funded organization in the style of previous new vaccine initiatives.



15th International Congress on Infectious Diseases

BANGKOK, THAILAND • JUNE 13-16, 2012



Organized by the International Society for Infectious Diseases



In collaboration with the Infectious Disease Association of Thailand

Second Announcement



ASTMH 61st Annual Meeting (2012)

November 11-15, 2012
Atlanta, Georgia USA
http://www.astmh.org/Home.htm

CaT symposium

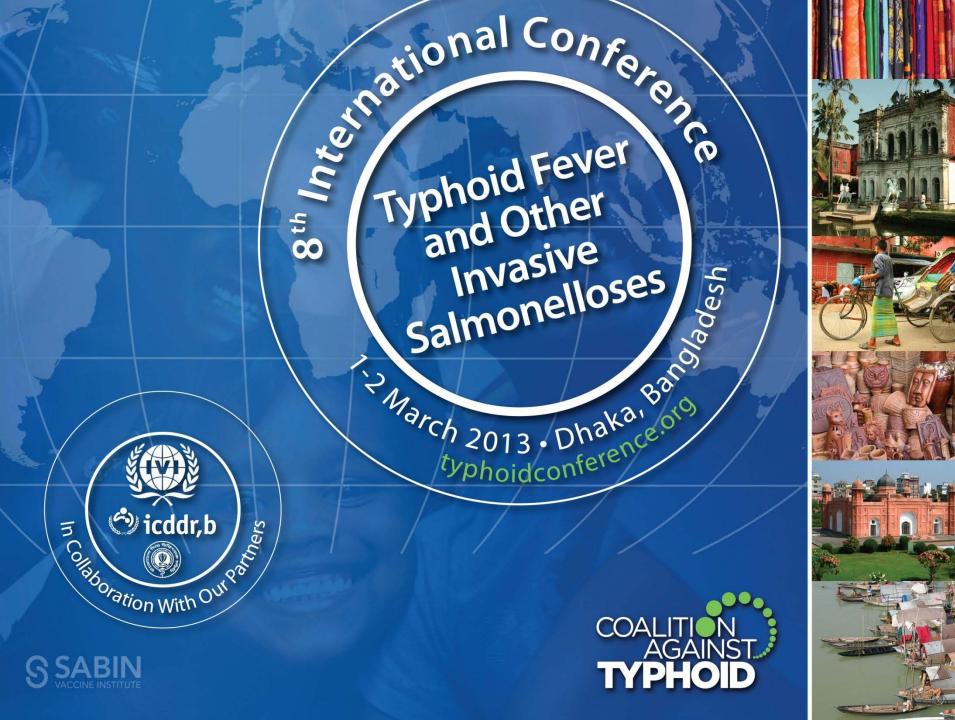
Organizer: Chris Nelson, Coalition against Typhoid (CaT)/Sabin Vaccine Institute, Washington DC USA Co-chair: Zulfi Bhutta, Founding Chair, Women and Child Health Division, the Aga Khan University, Karachi, Pakistan

Advances in typhoid fever epidemiology and control

- Non-malaria febrile illness, J Crump
- Enteric fevers: diseases in need of better diagnostics, G
 Vernet
- Progress with typhoid conjugate vaccines, S Szu
- Typhoid fever transmission models, I Longini







VACCINES FOR ENTERIC DISEASES

6-8 November 2013, The Royal Orchid Sheraton Hotel & Towers, Bangkok, Thailand

ASTMH 62nd Annual Meeting

November 13-17, 2013 Marriott Wardman Park Hotel Washington, DC USA

http://www.astmh.org/Home.htm



The American Society of Tropical Medicine and Hygiene Advancing global health since 1903



8TH WORLD CONGRESS
OF THE WORLD SOCIETY FOR
PEDIATRIC INFECTIOUS DISEASES (WSPID)

CAPE TOWN, SOUTH AFRICA, NOVEMBER 19-22, 2013





















vww.COALITONagainstTYPHOID.org

ÄGAINST TYPHOID

SSABIN



THE BURDEN

SOLUTIONS

ACTIVITIES GET INVOLVED RESOURCES ABOUT CaT



TYPHOID NEWS

AUGUST 05, 2011 Typhoid Epidemic Sweeps Philippines: Regional health officials declare typhoid incidence up 40%...

SEPTEMBER 25, 2011 Focus on Typhoid at ICID: The 15th International Congress on Infectious Diseases will feature...

OCTOBER 13, 2011 Indian Academy on Pediatrics Recommends Typhoid Vaccine Use: In a reversal of an earlier recommendation, the IAP COI recently...

CaT NEWS & EVENTS

Hyper-endemic Typhoid in Africa Takes Spotlight in Cannes

Important new evidence revealing hyper-endemic typhoid in Africa will be presented by global health experts and scientists...



VIEW ALL

RESOURCES

Community Acquired Bacteremia in Young Children from Central Nigeria A Pilot Study

A team led by researchers from Michigan State University found similar typhoid infection rates...





COALITION AGAINST TYPHOID

Q SEARCH

THE BURDEN

SOLUTIONS

ACTIVITIES GET INVOLVED RESOURCES ABOUT CAT



TYPHOID NEWS

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