衞生防護中心
Centre for Health Protection

Scientific Committee on Enteric Infections and Foodborne Diseases

Epidemiology and Prevention of Typhoid Fever in Hong Kong

Purpose

This paper reviews the global and local epidemiology of typhoid fever in order to formulate prevention and control strategy for Hong Kong.

The Pathogen and disease transmission

2. Typhoid fever is a systemic bacterial disease caused by the highly virulent and invasive *Salmonella enterica* serovar Typhi (*S.* Typhi) and affects only human. *S.* Typhi is a motile Gram-negative facultative anaerobic rod-shaped bacterium that is closely related to *Escherichia coli* in the family *Enterobacteriaceae*.[1] Its principal habitat is the intestinal tract of humans. Humans can excrete the bacteria during and after the disease, if they remain carriers. It grows optimally at 35-37°C, with growth greatly reduced below 15°C or above 45°C.[3] The bacterium can remain viable on food surface for a long time (190 days on chocolate biscuits, 230 days on sweets). It can survive in seawater and sewage water for up to 9 days and for weeks, respectively. It is not completely inactivated by freezing and can survive in ice for 90 days. *S.* Typhi can accumulate (but does not multiply) within shellfish and survive for 4 days even if the shellfish is stored at 10-13°C.

3. Typhoid fever is transmitted by ingestion of food or water contaminated by faeces or urine of patients or carriers. Important vehicles include shellfish, raw fruits and vegetables fertilised by human excrement and eaten raw, contaminated milk / milk products, and undiagnosed cases. Flies may also act as mechanical carrier and infect food in which the bacteria multiply to infective dose. An oral dose of at least 10^5 *S.* Typhi cells are needed to cause typhoid in around 50% of human volunteers.[4] It penetrates the intestinal mucosa and multiplies in the mesenteric lymph nodes, from which viable bacteria may enter the bloodstream. The incubation period ranges from 7 to 21 days.

Clinical presentation and outcome

4. Symptoms of typhoid fever include sustained fever, malaise, poor appetite, vomiting, severe headache, relative bradycardia, splenomegaly.[5] In adults, constipation is more common than diarrhoea. Nonproductive cough can occur in the early stage. Rose spots appear on the trunk of 25% of patients, but maybe harder to be seen in patient with darker complexion.

5. The clinical severity varies and can range from a mild illness of low grade fever and gastroenteritis without systemic involvement to those with multiple complications. Complications occur in 10-15% of all cases, and include intestinal haemorrhage or perforation, pneumonia, delirium, psychosis, meningitis, and hepatosplenomegaly.

6. Untreated case fatality rate was as high as 10-20% during the pre-antibiotic era, whereas with antibiotics treatment the case fatality rate is now about 1%.[5] Relapse, generally with milder symptoms, may occur in 15-20% of patients. About 10% of untreated patients are infective within 3 months of disease onset, and 2-5% will become chronic carriers.[5] Reinfections by typhoid fever are rare, as primary infection normally results in lifelong immunity.

Laboratory diagnosis and management

7. Diagnosis of typhoid fever is confirmed by isolation of *S.* Typhi from clinical specimen from normally sterile sites.[6, 7] The bacteria can be isolated from blood in the early stage and from urine and faeces after the first week. While blood culture is most commonly used for diagnosis, bone marrow culture is more sensitive and can be used to detect *S.* Typhi from patients whose blood cultures are negative while receiving antibiotic. The traditional Widal test has moderate sensitivity and specificity only because of cross- reactivities with other salmonellosis, although it can be more useful for diagnosis in young children.

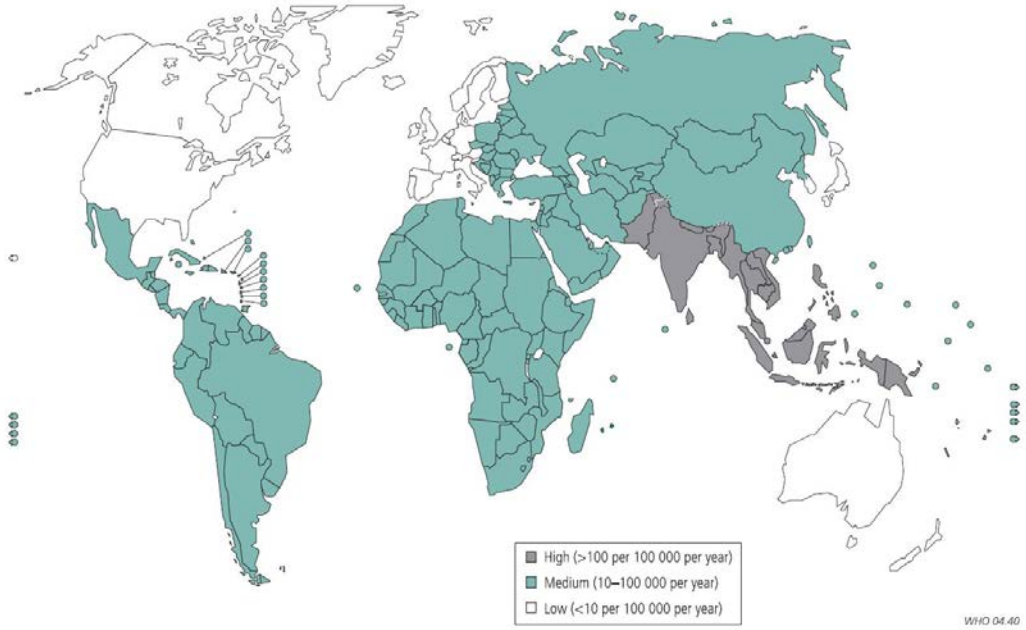
8. Supportive measures are important in the management of typhoid fever. [6, 7] The fluoroquinolones (ofloxacin, ciprofloxacin) are widely regarded as optimal for the treatment of typhoid fever in adults, as they are well tolerated and more rapidly and reliably effective than the former first-line drugs. The emergence of multi-drug resistance strains and resistance to fluoroquinolone is a growing concern and has reduced the choice of antibiotics. Third-generation cephalosporins (e.g. cefotaxime, ceftriaxone) are also commonly used, particularly in cases with isolates resistant to nalidixic acid (a marker of reduced susceptibility to fluoroquinolones). The exact regimen to be used depends on severity of the case. Severe cases usually require a longer time of treatment. Cases with intestinal haemorrhage need intensive care, monitoring, and blood transfusion. Surgical repair should not be delayed for cases with intestinal perforation.

9. To prevent secondary cases within hospital, patients should be nursed with Standard Precautions, such as hand washing, gloves for contact with body fluids and contaminated items, eye protection and gown for splashes of body fluids.[7, 8] Contact Precautions, such as single room and gowns / gloves for patient contact, should be considered for diapered / incontinent patients or for controlling institutional outbreaks.

Global disease burden

10. Typhoid fever remains an important cause of enteric disease in Africa, Latin America and particularly in developing areas of Asia (Figure 1). Multi-drug resistant strains of *S.* Typhi are becoming increasingly common worldwide, which makes treatment by antibiotics more difficult and costly.

Figure 1. Global distribution of typhoid fever*.[2]



* From Bulletin of the World Health Organization 2004;82:346-353 (http://www.who.int/bulletin/volumes/82/5/346.pdf), with permission from the World Health Organization.

Nonetheless, the true burden of typhoid fever in developing countries is difficult to estimate. This is due to lack of inexpensive rapid diagnostic tools, infrequency of laboratory testing, poor disease reporting systems and the fact that the clinical presentation of the disease is often confused with those of other common febrile illnesses.

11. WHO estimated in 2004 that the global burden was at 21 million cases and 216,000 to 600,000 deaths per year, with children of school age or younger mostly affected.[2, 9] Asia, with 274 cases per 100,000 persons has the highest incidence of typhoid fever cases worldwide, especially in Southeast Asian countries and on the Indian subcontinent, followed by sub-Saharan Africa and Latin America with 50 cases per 100,000 persons. The estimates of case fatality of the disease range from 1-4%, with ninety percent of deaths occur in Asia.

12. Prospective population-based surveillance studies conducted by the Diseases of the Most Impoverished (DOMI) Program in five Asians sites (North Jakarta, Indonesia; Karachi, Pakistan; Hechi, China; Hue, Vietnam and Kolkata, India) have revealed that pre-school and school-aged children in urban slum areas still suffer high rates of typhoid fever.[10] In three urban slums in Karachi, Kolkata and North Jakarta, incidence of blood-confirmed typhoid fever cases among children 5-15 years of age ranged from 180 cases to 494 cases per 100 000 persons. Assuming that blood cultures are only 50% sensitive for detecting typhoid, the actual incidence rates among 5-15 year olds may double these figures.[11]

13. Multi-drug resistant strains of *S.* Typhi continue to increase and spread in many parts of Asia. MDR typhoid has been associated with more severe illness and higher rates of complications and deaths, especially in children under two years of age.[12] Data from the DOMI studies confirm that multi-drug and nalidixic acid resistance is a serious problem in several sites, where 67% of isolates in Karachi, 22% in Hue and 7% in Kolkata were multi-drug resistant, and high rates of nalidixic acid resistance were found in all three sites.[10] Ciprofloxacin-resistant strains are now reported in India as well.

14. Apart from high incidences reported in endemic areas, several large outbreaks also occurred in developing countries as a result of contamination or breakdown in water supplies and sanitation systems. In the Democratic Republic of Congo, 42 564 cases were reported to WHO over a four-month period in 2004/2005.[13] This outbreak caused 214 deaths (case fatality ratio, 0.5%) and 696 severe cases of peritonitis and intestinal perforations. Another large outbreak occurred in Tajikistan between 1996 and 1998, affecting more than 24,000 people with a case fatality rate of around 1%.[14-16] This was the first reported epidemic of ciprofloxacin-resistant typhoid.

15. Typhoid fever has become rare in industrialised countries with improvements in water and sanitation systems and hygiene education. The sporadic cases of typhoid fever reported in developed countries are mostly imported from endemic areas. For example, the average yearly number of typhoid notifications in the past 5 years is 391 and 207 for USA and UK respectively. However, outbreak can still occur occasionally. In 2010, a multistate outbreak of typhoid fever occurred in the California and Nevada states of USA.[17] A total of 9 persons were affected with 7 of them hospitalised. There was no fatal case. Epidemiological investigation traced the source of infection to frozen fruit pulp used in milkshake or smoothie. The related food products were recalled.

Local epidemiology

16. In the 1950's, around 1000 cases of typhoid fever were reported annually, but the number has dropped substantially over the years. The number of cases from 2000 to November of 2010 was shown in Figure 2. There was a general downward trend except for a spike in 2009, largely due to an increased number of imported cases from endemic places. The average yearly number of cases for 2000 to 2009 was 59.6, equivalent to an average incidence rate of 0.88 case per 100 000 population per year, which is considered to be low by WHO's classification.[2] Hong Kong therefore is not considered as a typhoid fever endemic area. More cases (54%) were notified between May and September (Figure 3).

17. For cases notified from 2000 to November of 2010, the male-to-female ratio was 0.6:1, and the median age was 25 years. The age group distribution is shown in Figure 4, which shows that the age group 20-29 years was the most affected, and accounted for one third of the cases. Ninety-six percent of the cases were hospitalised, and the median length of stay was 10 days. There was one fatal case in 2000 affecting a 79-year-old woman. She developed sepsis and succumbed after being admitted for 3 days.

Figure 2. Number of cases of typhoid fever notified to Department of Health, 2000 to November 2010.

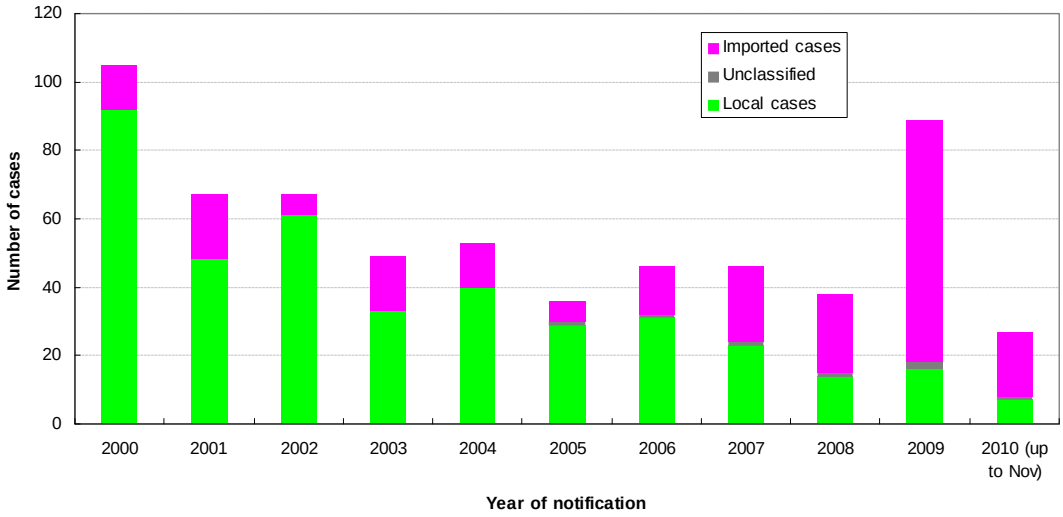


Figure 3. Monthly number of cases of typhoid fever notified to Department of Health, 2000 to 2009.

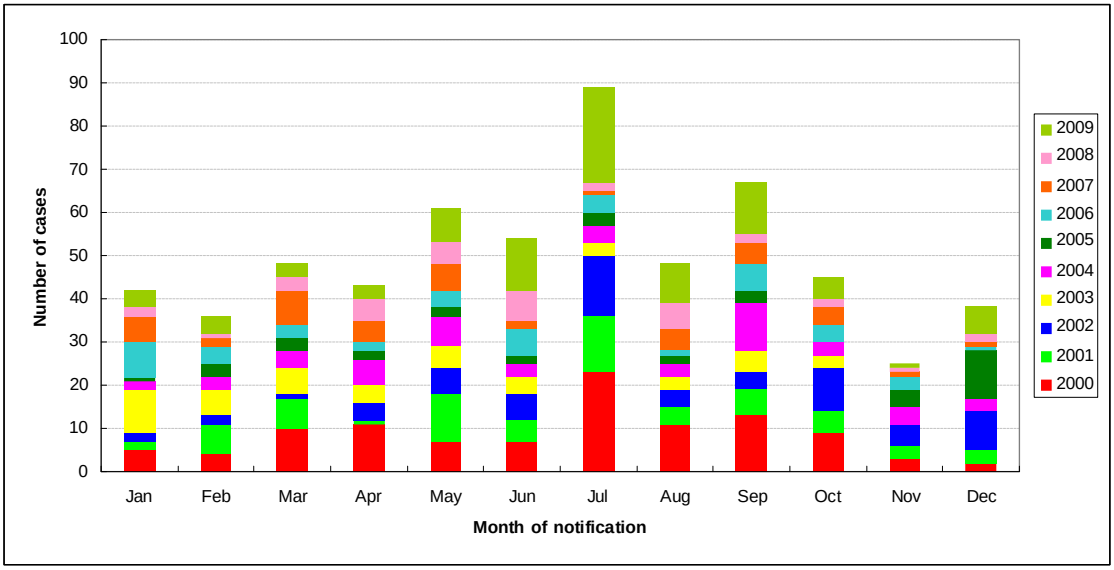
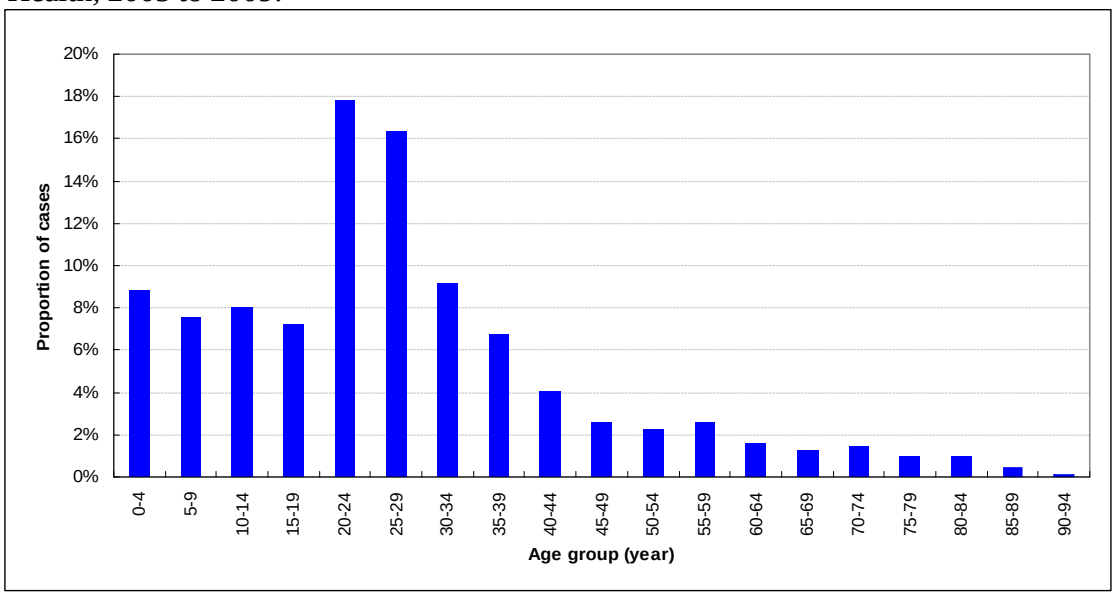


Figure 4. Distribution by age group for typhoid fever cases notified to Department of Health, 2005 to 2009.



18. A significant proportion of the typhoid fever cases reported from 2000 to November 2010 were classified as imported (36%) after epidemiological investigation. Further analysis on the place of origin for the imported cases reported since 2005 is shown in Figure 5. The proportion of imported cases has been increasing from 17% in 2005 to 80% in 2009. Overall, the most notable places of origin among imported cases were Indonesia and India, with an overall percentage of 61% and 18% respectively.

19. In 2009, an upsurge of cases imported from Indonesia was noted, accounting for 82% of the 71 imported cases. Of the 58 imported cases from Indonesia, 57 of them were Indonesian domestic helper. Epidemiological investigation was carried out for each reported case and neither secondary transmission in Hong Kong nor a common source in Indonesia was identified. A similar increase of imported case from Indonesia was also observed in Taiwan during the summer of 2009.[18] The CHP issued a press release in July 2009 urging travellers to Indonesia to observe good personal hygiene to prevent typhoid fever. The health authority of Indonesia was also informed. The proportion of imported cases from Indonesia gradually decreased in the end of 2009 and in 2010 (up to November), with the proportion of imported cases from Indonesia (6 cases) only accounted for 22%.

Figure 5. Place of origin of typhoid fever cases from 2005 to November 2010

	2005	2006	2007	2008	2009	2010 (up to Nov)
Hong Kong	29	31	23	14	16	7
Unknown	1	1	1	1	2	2
Sri Lanka	0	0	0	0	0	1
Myanmar	0	1	0	0	0	0
Korea, Republic of	0	0	0	1	0	0
Cambodia	0	0	1	0	0	0
Mainland China	1	0	1	0	0	0
Bangladesh	0	0	1	0	1	1
Nepal	1	1	2	0	0	1
Philippines	0	1	2	3	1	1
Pakistan	1	0	0	1	6	2
India	2	3	5	6	5	6
Indonesia	1	8	10	12	58	6

20. In November 2005 to January 2006, a cluster of 14 locally acquired typhoid fever cases was identified and all of them reported patronizing food premises in Yuen Long within one month of disease onset. Positive *S.* Typhi isolates were available from 13 of the cases and they were confirmed to be of the same genetic pattern by pulse field gel electrophoresis (PFGE). Nevertheless, there was no common source of food shared by all patients and none of the cases worked as a food handler. The exact nature of the vehicle remains elusive despite detailed epidemiological and environmental investigations.

21. Apart from the above community-wide outbreak, sporadic clusters of typhoid fever cases did occur. On the average (2000 to 2009), there was around 1 cluster per year and most of them were of domestic nature with a median size of 2 affected persons. There was no institutional outbreak of typhoid fever reported so far in Hong Kong.

22. Multidrug-resistant (MDR) typhoid fever, that is, resistant to all 3 of the first-line antibiotics (chloramphenicol, ampicillin, and trimethoprim - sulphamethoxazole) is associated with more severe illness and higher rates of complications and death, and is also associated with a high rate of becoming asymptomatic carriers after treatment.[19] The pattern of antibiotics resistance of *S.* Typhi isolated in Hong Kong from 2005 to November 2010 is shown in Table 1. As shown, the overall percentage of resistant isolates for the first-line antibiotics was below 8%. However, percentage resistant to nalidixic acid

(often associated with poorer response to fluoroquinolone) was 23.1%. From 2005 to November 2010, there were 1, 3, and 1 MDR isolates from 2006, 2009, and 2010 respectively. The MDR isolate from 2006 was also resistant to nalidixic acid.

Table 1. Number of antibiotic resistant and sensitive *S.* Typhi isolates from 2005 to November 2010

Antibiotics	**Resistant**	**Sensitive**	**% resistant**
Amoxycillin	0	13	0.0%
Ampicillin	17	220	7.2%
Cefotaxime	0	58	0.0%
Ceftriaxone	1	163	0.6%
Chloramphenicol	7	132	5.0%
Ciprofloxacin	2	141	1.4%
Levofloxacin	0	32	0.0%
Nalidixic Acid	12	40	23.1%
Ofloxacin	0	6	0.0%
Septrin / Cotrimoxazole / TMP-SMX	13	171	7.1%
Tetracycline	3	70	4.1%

Prevention and control for typhoid fever in Hong Kong

Statutory notification and case investigation

23. In Hong Kong, typhoid fever had been notifiable together with paratyphoid fever as enteric fever since 1946, and then as typhoid fever alone since 1957. All registered medical practitioners are required to report suspected or confirmed cases to the CHP for investigation and public health control measures. Cases are defined as persons with compatible clinical features and laboratory confirmation. Asymptomatic carriages are not recorded as cases. They would, however, be investigated and followed up. During investigation, clinical, laboratory, and treatment information is obtained from clinician. History of exposure to food, travel and other risk factors is elicited to identify the possible source and mode of transmission. Food collaterals, travel collaterals and household contacts are traced and put under medical surveillance. When food items or food handlers from food premises are involved, the Food and Environmental Hygiene Department (FEHD) will be informed so that control measures can be implemented. PFGE is also used to assist in outbreak detection and trace the source of the outbreak.

24. According to the Public Health and Municipal Services Ordinance, CAP. 132 sub. leg. X Section 24 Restriction on employment of persons likely to spread diseases, a Health Officer may notify a person in writing and thereafter such person shall cease to work or take part in any food business, if the Health Officer is satisfied that the person is suffering from any communicable disease, or is likely to communicate to any other person any

communicable disease. As such, if the case is a food handler, the patient would be referred to FEHD for suspension from employment in food handling work until clearance of pathogen. Close contacts are advised not to participate in food handling work until bacteriological result is available. If stool culture is positive, the contact would also be referred to FEHD for suspension from employment in food handling work.

25. Since infected patients may shed the bacteria for a variable period, post-treatment stool specimens are collected for monitoring of bacterial clearance. If any of the stool cultures is positive, stool specimens would be collected at intervals until bacterial shedding is no longer observed. If patients excrete the bacteria persistently, they will be referred to specialist for treatment and investigation. Chronic carriers who excrete *S.* Typhi for one year or more will be monitored and followed up with annual stool culture for life.

Pre-employment screening for food handler

26. The World Health Organization published a report on health surveillance and management procedures for food handling personnel, indicating that pre-employment or routine medical and laboratory examinations of food handling personnel are of no value in the prevention of foodborne diseases.[20] The report recommended those governments, industries and institutions that rely on medical examination of food handling personnel for the prevention of foodborne disease should discontinue the practice. On the other hand, known carriers of *S.* Typhi (or Paratyphi) should be prevented from handling unwrapped foods to be consumed raw or without further cooking.[20] In addition, WHO also stressed that importance of providing education and training in good hygienic practices to all food handling personnel.

27. In United States, United Kingdom, Singapore, and Taiwan, there is no legal requirement on pre-employment laboratory screening for *S.* Typhi with food handlers.[21-24] Food handlers are required to have the skills and knowledge in food safety and food hygiene by attending training course or through on-the-job training.

28. Similar to other areas, no pre-employment and routine medical examination for *S.* Typhi for food handlers is required by the laws in Hong Kong. Nonetheless, the Food Business Regulation under Public Health and Municipal Services Ordinance (Cap 132X) requires food handlers to observe personal cleanliness and restricts sick food handlers from handling open food. For instance, person who is suffering from a discharging wound or sore on any exposed part of the body, or from a discharge of the ear or from attacks of diarrhoea or vomiting or from a sore throat is restricted from taking any part in the handling of open food.

Public health education

29. As typhoid fever is transmitted by ingestion of food or water contaminated, it is important to emphasise good personal and environmental hygiene and safe food-handling practices. The public should always wash their hands with soap and water after using the bathroom, changing diapers and before preparing food and eating. They should be advised to cook food adequately before consumption. Travellers to countries endemic for typhoid fever should receive vaccination at least 3 to 4 weeks before departure and observe strict personal, food and water hygiene, including the avoidance of drinking water and/or ice of unknown purity and the eating of uncooked shellfish, uncooked fruits and vegetables that are not self-peeled or prepared. Further information on the preventive measures for typhoid fever is available on CHP's website.

30. Food handlers should be adequately trained to reduce the risks of foodborne infection from under-cooked seafood and meat. The Centre for Food Safety of Hong Kong generally recommends to cook food thoroughly and use a food thermometer to check that the core temperature reaches 75°C or above for at least 30 seconds. Hot and cold food should be kept at >60°C or =<4°C respectively.

31. Besides Chinese and English, CHP also provides health education materials on personal and environmental hygiene in languages such as Hindi, Indonesian, Nepali, Tagalog (for Filipinos), and Thai.

Typhoid fever vaccines

Heat-phenol-inactivated whole-cell vaccine

32. There are 3 commercially available typhoid fever vaccines.[4, 9, 25-27] The first is an old heat-phenol-inactivated whole-cell vaccine administered subcutaneously.[9] The reported protective efficacy rates reach 51-67% in controlled studies, but it has a relatively high reactogenicity. It has been shown to associate with fever and systemic reactions in 9-34% of vaccinees, and with short school or work absenteeism in 2-17% of cases. No fatality or chronic disabling condition attributable to this vaccine has been reported, but there were sporadic reports of severe reactions such as hypotension, chest pain, and shock.[28] It is still used in some developing countries. The Center for Disease Control and Prevention of the USA (CDC) strongly discourages the use of this vaccine and its used has been discontinued in USA. WHO also recommends that this vaccine should be replaced by the two newer vaccines described below. In USA, there was another form of acetone-inactivated parenteral vaccine, but it was only available to US Armed Forces.

Vi polysaccharide vaccine

33. There are now 2 newer vaccines (Table 2), the parenteral Vi polysaccharide vaccine and the live oral Ty21a vaccine.[9] Both are with proven safety, efficacy, and programmatic impact. The Vi polysaccharide vaccine was developed by the US National Institutes of Health and was first licensed in USA in 1994. It comprises of purified Vi capsular polysaccharide from the Ty2 *S.* Typhi strain. It can be administered subcutaneously or intramuscularly and elicits a T-cell independent IgG response that cannot be boosted by additional doses. This vaccine does not have patent protection and its technology is readily transferrable to other vaccine producers. It is registered in Hong Kong as Typhim Vi from Sanofi-Aventis Hong Kong Limited, and as Typherix from GlaxoSmithKline Limited.

34. The WHO recommended schedule of the Vi vaccine is shown in Table 2. It can be co-administered with other vaccines for international travellers, e.g. yellow fever and viral hepatitis A, or with vaccines used in childhood immunization programmes.

35. The field effectiveness of the Vi vaccine has been demonstrated in several cases.[14, 29, 30] For example, in an outbreak scenario in the typhoid fever endemic Xing-An County of Guangxi Province of Mainland China, it was estimated that receipt of Vi vaccine was associated with 73% protection among the 1260 students immunized before the outbreak. For the 411 students immunised after the onset of the outbreak, immunisation was associated with 71% lower rate of typhoid fever. This supports the use of Vi vaccine as a public health tool to control typhoid fever in endemic area and during outbreak.

Live oral Ty21a vaccine

36. The live oral Ty21a vaccine (Table 2) was first licensed in Europe in 1983 and in the USA in 1989. This is an attenuated Ty2 strain with the Vi gene chemically mutated. The vaccine comes in two formulations, as an enteric coated capsule, which is used for travellers to endemic areas, and as a liquid suspension, which is often used in public health programmes for young children in developing countries. However, the liquid form of the vaccine is no longer manufactured. The capsule form is available and registered in Hong Kong as Vivotif from Amedis Company Limited.

37. The schedule of the Ty21a vaccine is shown in Table 2. Irrespective of the formulations given, this vaccine requires multiple doses taken every other day, and this maybe one of the reason why it is used primarily for travellers and not for controlling endemic cases in developing countries. The exact recommendation for number of doses and revaccination varies among different countries. It can be administered at the same time with other vaccines, including live vaccines against polio, cholera, and yellow fever,

or the measles, mumps and rubella combination. Ty21a vaccine has also been shown to protect partially against *S.* Paratyphi B, but generally this is not an accepted way to vaccinate against paratyphoid fever.

Considerations when administrating typhoid vaccines

38. All of the above vaccines have an efficacy of 51-78% only, and may not prevent typhoid fever against a large infecting dose.[31] Medical practitioners administrating typhoid vaccine should remind vaccinees not to have a false sense of security. Persons at risk should also be reminded to observe good personal hygiene, such as adhering to safe food-handling practices. Also, both the Vi polysaccharide vaccine and the live oral Ty21a vaccine are not licensed for children aged <2 years since their efficacy in this age group has not been demonstrated.

Vaccines under development

39. Newer vaccines are under development, but will not be available within the next few years.[25] They aim to confer higher levels and more durable protective immunity in all age groups, including those age <2 years, preferably without the need for booster doses. A prototype Vi conjugate vaccine, using a recombinant exotoxin A of *Pseudomonas aeruginosa* (Vi-rEPA) as a carrier protein to increase the immunogenicity, has shown to confer 89% efficacy over 46 months of follow-up.[32] However, this conjugate vaccine is likely to require a regimen of at least 2 doses. There are at least 3 oral live attenuated being developed, and all of them aim at conferring protection by a single dose.[4, 25] No efficacy data is available yet.

Table 2. Comparison of the parenteral Vi polysaccharide vaccine and the live oral Ty21a vaccine

	Vi polysaccharide vaccine	Ty21a*
Licensed age group	Aged ≥ 2 years	Aged ≥ 5 years
Schedule	Only 1 dose is required, and immunity is achieved after 7 days.	Three doses[#], every other day Immunity is achieved 7 days after the third dose.
Revaccination	Every 3 years	For people in endemic area, 1 booster dose 3-7 years after primary immunization. The need for subsequent dose requires further investigation. For travellers from non-endemic to endemic area, 1 booster dose is recommended after 1-7 years of primary immunization.
Contraindication	History of severe local or systemic reactions to any components of the vaccine Not for patient having fever	Not for patient who is immunocompromised Not for patient having gastrointestinal illness Anti-malarial and anti-bacterial drug may harm live bacterial vaccine Not known if it may cause foetal harm when given to pregnant women

Efficacy	64-72%, last 3 years	53-78%, last 3-7 years The duration of protection following Ty21a immunisation is not well defined and may vary with vaccine dose and possibly with subsequent exposures to *S.* Typhi (natural booster). Seven years after the final dose the protective efficacy is 67% in residents of endemic areas but may be less for travellers.[33]
Adverse reaction	Minimal (local side-effects)	Remarkably well tolerated
Storage	Recommended at 2-8OC, 6 months at 37OC, 2 years at 22OC	Recommended at 2-8OC, 14 days at 25OC

* A liquid formulation of Ty21a for 2 2 years was once available but the production was discontinued.[33]
# In North America, the vaccine is given in four doses. [33]

Usage of the typhoid vaccines in other areas

Vaccine use in endemic areas

40. WHO published a WHO position paper in 2008 that replaced the one published in 2000 and outlined several recommendations.[9, 25, 26, 33, 34] It recommends that for endemic countries, they should consider the programmatic use of typhoid vaccines for controlling endemic disease. Immunisation of school-age and/or preschool-age children is recommended in areas where typhoid fever in these age groups is a significant public health problem. However, the decision should be based on detailed local epidemiology situation. One of the essential information includes data on antibiotics resistance pattern of *S.* Typhi. Cost-effectiveness should also be a factor during consideration.

Vaccine use in non-endemic areas

41. The policy and recommendation on the usage of typhoid vaccines in selected non-endemic countries are summarized in Table 3. There are similarities and differences among different countries, and some of these can be justified by their respective local situation.

42. The use of typhoid vaccines for travellers to endemic area is recommended by all health authorities. It was estimated that the attack rate for UK travellers to endemic area like the Indian subcontinent is 17.3 cases per 100 000 visits, as compared to 0.05 case per 100 000 visits to countries in the rest of the world.[35, 36] Some health authorities also emphasise the concept of the VFR (Visiting Friends and Relatives) traveller group, as these peoples are more likely to be at risk due to heightened exposure to contaminated water and food.

43. Many health authorities of the developed countries, such as that of UK, USA, and Canada do not recommend the use of typhoid vaccine during an outbreak in non-endemic areas. It was also advised that it is of limited value to immunise nursing contacts that have been or may be exposed to active cases.

44. For outbreak in an institutional setting, there is no evidence to support the use of typhoid vaccine as an outbreak control measure. HPA states that typhoid vaccine would not be used during an outbreak and that the vaccine is not recommended for persons in close contact with typhoid cases or carriers. The maintenance of a high standard of environmental sanitation, active finding of cases and carriers, and isolation of infected residents maybe more effective in breaking the chain of transmission.

45. WHO recommends the use of typhoid vaccine for high-risk groups and populations, but it does not specify what kind of person is at risk. Most health authorities do recommend those who work with *S.* Typhi in laboratory to get vaccinated.[37] The USA, Canada, and Taiwan recommend the use of typhoid vaccine for household contacts of known carriers.

Recommendations

46. After reviewing the global and local epidemiology, and the published guidelines and recommendation from other health authorities and WHO, the following recommendations are made.

47. Travellers who visit endemic areas of typhoid fever, particularly those visiting their friends and relatives, or performing volunteer services, are advised to receive typhoid vaccines and the dosage required depends on the type of vaccine. They are advised to seek medical practitioners for advice on vaccination and other travel health measures required at least 4 weeks before departure. The public can also refer to Travel Health Service's website (www.travelhealth.gov.hk) and Travel Health Centres of the Department of Health for further health advice.

48. Pre-employment screening of *S.* Typhi carriage for food handling personnel is not recommended. CHP will continue to refer infected food handler to FEHD for suspension from employment in food handling work.

49. Based on published literatures and policies of overseas health authorities, there is no conclusive evidence to support the use of typhoid vaccine in institutional outbreak in Hong Kong.

50. Public health education on personal, food, and environmental hygiene is of paramount importance, and should be targeted to food handlers and travellers to endemic regions as appropriate. Educational materials should be translated to languages used by the intended target populations. Medical practitioners should remind the recipients of typhoid vaccine not to have a false sense of security.

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Table 3. Recommended usage of typhoid vaccines

Health authority	National vaccination programme	School-age and/or preschool-age children	Travellers to endemic area	Outbreak control	Other high-risk groups and populations
WHO[9]	Yes for endemic country. Cost-effectiveness analyses should be part of the planning process.	Yes, if for these age groups typhoid fever is shown to be a significant public health problem, particularly where antibiotic-resistant *S.* Typhi is prevalent. The choice of school or community-based vaccination would depend on factors such as age-specific incidence, subgroups at risk, and school enrolment rates.	Yes, particularly for those staying in the endemic area for >1 month and/or in locations where antibiotic resistant strains of *S.* Typhi is prevalent.	Yes, for endemic area	Yes
CDC of USA[5, 37-39]	Not part of the routine immunisation programme	Not part of the routine immunisation programme	Yes, particularly if exposure to unsafe food and water is likely, or if there is close contact in rural areas with indigenous populations.	No evidence has indicated that typhoid vaccine is useful in controlling common-source outbreaks.	Yes for those subjected to unusual occupational exposure (e.g. clinical microbiological technicians) and household members of known carriers. Note: However vaccination of sewage sanitation workers is not warranted.
Public Health Agency of Canada[40]	Not part of the routine immunisation programme	Not part of the routine immunisation programme	Recommended for persons travelling to small cities, villages or rural areas of endemic area for >4 weeks, particularly for those living with or visiting families. Not recommended for business travel or short-term (< 4 weeks) holidays in resort hotels in such countries. Also recommended for travellers with reduced or absent gastric acid secretion.	Not for controlling common-source outbreaks, but maybe considered in a control program to limit a typhoid fever epidemic (e.g. in closed communities, refugee settings)	Recommended for people with ongoing household or intimate exposure to an *S.* Typhi carrier, and laboratory workers who frequently handle cultures of *S.* Typhi. Not routinely recommended for workers in sewage plants, or people attending rural summer or work camps or for people in non-endemic areas experiencing natural disasters such as floods
Health Protection Agency / Department of Health of United Kingdom[36, 41, 42]	Not part of the routine immunisation programme	Not part of the routine immunisation programme	Yes, particularly if sanitation and food hygiene are likely to be poor	Not recommended for use during an outbreak Since 2008, HPA no longer recommended vaccination for persons in close contact with typhoid cases or carriers.	Yes for laboratory personnel who may handle *Salmonella* Typhi in the course of their work.

Health authority	National vaccination programme	School-age and/or preschool-age children	Travellers to endemic area	Outbreak control	Other high-risk groups and populations
Department of Health and Ageing, Australia[43]	Not part of the routine immunisation programme	Not part of the routine immunisation programme	Recommended for travellers (include military) > 2 years of age travelling to endemic regions, which include the Indian subcontinent, most southeast Asian countries, many south Pacific nations and Papua New Guinea. Strongly recommended for individuals travelling to endemic regions to visit friends and relatives	Not indicated	Laboratory personnel routinely working with S. Typhi should also be considered for vaccination
Taiwan CDC[44]	Not part of the routine immunisation programme	Not part of the routine immunisation programme	Yes Note: Typhoid vaccine is only recently available in Taiwan.	Not indicated	Recommended for persons with intimate contact with active cases or carriers
China CDC / MoH[45, 46]	Not part of the routine immunisation programme, but typhoid vaccine is administered by some local governments[47, 48]	Not part of the routine immunisation programme, but school-based immunisation programme exists in some regions[47, 48]	Yes, and highly recommended for travellers to countries with MDR strains of S. Typhi	Immunization of high risk groups in outbreak site and in neighbouring area	In 2008, China MoH published a special guideline " 災區預防接種指南"on vaccination after disaster. Vi vaccine will be administered in earthquake affected area if typhoid cases occurred within three years of the earthquake, or after the earthquake. Targeted high risk groups include: sewage sanitation workers, food handlers, victims living in temporary settlement where sanitation and food / water hygiene is poor, and relief workers. If scattered cases of typhoid fever happen throughout the affected area, typhoid vaccine maybe given to all persons aged >5 years. Also, if an cluster of typhoid fever with more than two cases occurs within 14 days in the same temporary settlement site, vaccine will be given to all residents and relief workers aged >5 years in that site.
Our current practice (Travel Health Service / SEB outbreak investigation)[49]	Not part of the routine immunisation programme	Not part of the routine immunisation programme	Yes	No	Recommended for those subjected to unusual exposure to typhoid from occupation, and those living in areas of high endemicity.

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