Typhoid fever

Typhoid or Enteric Fever is a serious systemic infection caused by an enteric pathogen Salmonella Typhi that, in the pre-antibiotic era, had a case fatality of 10% to 20%. Salmonella Paratyphi A and B also cause illness (paratyphoid fever) clinically indistinguishable from typhoid fever. However, where typhoid is endemic, approximately 90% of the clinical cases are due to Salmonella typhi, and the rest, Salmonella paratyphi. Enteric fever is endemic in populated areas with poor access to clean water and where sanitation and hygiene practices are less than ideal. Although it is an endemic disease, S. Typhi has epidemic potential.

World Health Organization estimates the annual global incidence of typhoid fever at 21 million cases, of whom 1-4% end fatally. Regions of south-central Asia and south-east Asia are considered high incidence for typhoid with rates of >100/100,000 cases/year; the rest of Asia, Africa, Latin America and the Caribbean, and Oceania except for Australia and New Zealand experience medium incidence with rates of 10-100/100,000 cases/year while countries of Europe, North America and the rest of the developed world have low incidence with typhoid fever rates of <10/100,000 cases/year.

The incidence rate of typhoid fever in Sri Lanka is 11.48 per 100,000 populations in 2009. But this distribution is uneven throughout the country. The highest incidence rate 390.56/ 100,000 population has been reported from Vavuniya District, then from Mannar District (140.76/100,000). The medium level incidence reported from Jaffna (98.27/100,000), Nuwara Eliya (27.21/100,000) and Puttlam Districts (10.32/100,000).

A study of typhoid in five Asian countries show that 57% of blood culture confirmed typhoid occurred in children aged 5-15 years and the annual incidence (per 100,000 per year) among this age group varied from 24.2 to 29.3 in sites in VietNam and China to 180.3 in sites in Indonesia, and to 412.9 to 493.5 in sites in Pakistan and India.

Even though, the Epidemiological information is limited for Sri Lanka, the age distribution of Typhoid fever can be described based on the routine surveillance date. In 2008, 58.66% reported cases of Typhoid fever were within the 1-14 year age group.

More importantly, typhoid vaccination should not be seen in isolation, but as a component of an integrated approach to typhoid control that includes efforts to improve access to clean water, better sanitation and hygiene and education on hand washing, in addition to prompt diagnosis and appropriate treatment of cases identified. Vaccination for Typhoid can be provided with other public health services such as: Immunization programmes, School Medical Inspection and Maternal and Childcare Services.

General Approach to Typhoid Immunization

Even within typhoid endemic districts, typhoid epidemiology can vary significantly from location to location. Therefore, typhoid vaccination is recommended as a risk-based strategy and targeted only for high-risk groups and population. According to the incidence rate of Typhoid fever Vavuniya, Mannar, Jaffna, Nuwara Eliya and Puttlam are considered as high risk Districts. Several MOH areas of other districts such as Soranathota, Ambalangoda, Haldumulla, Bibile and Municipal area Matale were also reported high incidence in the surveillance data of 2008. Although Batticaloa, and Trincomalee districs are not in the category of high incidence, they are potential for out breaks due to re-settlement, high mobilization of people and lack of facilities.

Typhoid vaccines

There are two internationally licensed vaccines against typhoid. A Vi capsular polysaccharide vaccine which contains extracted cell surface Vi polysaccharide of Salmonella enterica serovar Typhi, S typhi Ty2 strain in a

sterile solution. It is an injectable vaccine, recommended for intramuscular use. It is produced by several internationally recognized vaccine manufacturers and easily available globally.

The other vaccine is the Ty21a live attenuated, formulated as a capsule for oral administration. Protection from Ty21a vaccine is based on different surface antigens, including O- and H-antigens; it lacks Vi-antigen and protection is therefore independent of Vi-expression by the bacteria. In the past a liquid formulation of the same was also available, but not available now. The capsule is recommended for children aged ≥ 5 years of age, but the liquid formulation can be administered even to younger children (aged ≥ 2 years).

Vi polysaccharid vaccine

The Vi polysaccharide is a T-cell independent antigen and, therefore, is poorly immunogenic in children aged <2 years. Further, unlike a conjugate vaccine a polysaccharide vaccine does not confer long-term immune memory and, thus, the protection conferred is of limited duration. Although there is not much experience with ViPS typhoid vaccine per se, there is some experience from the use of 23-valent pneumococcal polysaccharide vaccine with regards to the safety and efficacy of administering repeated doses of polysaccharide vaccine.

There is evidence that those who were revaccinated were more likely than those who were receiving the vaccine for the first time to experience local adverse reactions, although mild and rapidly self-limiting ones. Adverse events considerations would be even more important in populations with high rates of HIV infection or other immunocompromised individuals.

Immunogenicity and efficacy of typhoid vaccines

The single dose ViPS injectable vaccine provides about 70% protection against blood-culture confirmed typhoid fever. More recently a cluster randomised effectiveness trial of Vi Typhoid vaccine in India showed a 80% protection in children who were vaccinated between ages 2 and 5 years. More importantly even among the unvaccinated the protection was 44%, thus demonstrating significant herd effect with the use of ViPS vaccine. In clinical studies, seroconversion was observed in >95% of recipients when measured at two weeks after administration.

Shelf Life

The expiry date of the vaccine is indicated on the label and packing.

Prioritized groups for vaccination in Sri Lanka

High risk districts and MOH areas (Annexure 1) were identified according to the incidence rate and other factors associated with the spread of Enteric Fever (Typhoid and Paratyphoid) in Sri Lanka. After scrutinizing of local and international reports, the Epidemiology Unit suggests to administer the vaccine only for high risk groups in the high risk areas shown in the annexure 1.

High risk categories

- Food handlers: People involved in food processing, cooking at the hotels, common community kitchens in pilgrimage and IDP camp settings.
- People who do not use or do not have proper toilet facilities
- Close contacts of typhoid patients (eg. family members)
- Children getting frequent episodes of diarrhoea (eg. more than 4 attacks in preceding six month)
- Communities do not access to safe water
- Health care workers associate with typhoid patients

Formulation, Dosage and Administration

The ViPS is an injectable vaccine (liquid) that is available as single dose pre-filled syringe, 5 and 20-dose vials. Vaccines [Single dose, 5 doses, 20 doses] are presented as a clear, colourless, liquid form and need to be shaken before use. Vaccines should be inspected for any foreign particulate matter and/or variation of physical aspect pror to administration. In the event of either being observed, discard the vaccine. ViPS is to be administered intramuscularly, 0.5 ml preferably using an auto-disable syringe. The injection is given in the deltoid region of the arm.

Interchangeability

The ViPS and the Ty21 vaccines work through different mechanisms. The ViPS does not stimulate any immune memory whereas the oral Ty21a does. There is no harm in completing a Ty21a series with ViPS. Possibility of co-administration is tested with inactivated hepatitis A vaccine [Havix 1440 Adult] and administration to different sites is identified to develop adequate immunogenicity. Simultaneous administration of other vaccines has not specifically been tested and does not anticipate any adverse outcome.

Typhoid vaccine should not be mixed with other vaccines in the same syringe under any circumstances.

Storage temperature and shelf life

The vaccine is recommended to be stored at $+2^0$C to $+8^0$C, and freezing should be avoided.

Contraindications

There are no specific contraindications to the use of this vaccine other than established previous hypersensitivity reaction to vaccine components. HIV positivity is not a contraindication for the ViPS, but induction of protective antibodies is directly correlated to the levels of CD4 positive T-cells. Precaution should be taken for the patient having bleeding disorders and Thrombocytopenia to prevent the bleeding at the injection site. Vaccination should be postponed for patients having acute febrile illness.

Use in pregnancy and Lactation

Adequate human data on use during pregnancy or lactation and adequate animal reproduction studies are not available

Adverse events following immunization (AEFI)

Adverse reactions were predominately minor and transient local reactions, such as injection site pain, erythema and induration; these local reactions almost always resolved within 48 hours of vaccination. Further, the ViPS can be coadministered with other routine childhood vaccines. Anaphylaxis, allergic reactions including anaphylactoid reactions and urticaria have been reported very rarely.

Revaccination

Three years after the first vaccination.

Documentation

1. Prepare a *Typhoid Vaccination Card* as the format given in figure i, complete and hand over for each vaccine recipient.

2. A *Typhoid Vaccination Register* should be prepared as the format given in figure ii, and completed at the vaccination centre.

3. A *Monthly Consolidated Report of Typhoid Vaccination* should be prepared as the format given in figure iii by the Regional Epidemiologist. This consolidated report is completed with the information of the Typhoid vaccines registers of all vaccination centres in the district. A copy of the Monthly Consolidated Report of Typhoid Vaccine should be sent to the Epidemiology Unit before the end of the following month.

Figure i. Typhoid Vaccination Card

Typhoid Vaccination Card	
Name of recipient	
Date of Birth	Male/Female
Address of recipient	
Date of Vaccination	
MOH Area	
Vaccinator's Name	Vaccinator's Designation
Notes (if any)	

Figure ii. Typhoid* Vaccination *Register

Serial No	Name	Age	Sex	Category of recipient *	Date of immunization	Batch No	AEFI reported

Category of recipient*

Children 2-15 years
Food handlers
Healthcare workers
Others

Figure iii. Monthly Consolidated Report of Typhoid Vaccination

Name of District		**Month**
Number of doses received in 2010		
Number of doses used in this month		
Doses remaining at hand		
Number of vaccination according to recipient	Children 2-15 years	
	Food handlers	
	Healthcare workers	
	Others	
Number of AEFI reported		

Name of Regional Epidemiologist: …….
Signature: ……
Date: ……

Annexure 1

Distribution of Typhoid vaccine

Divisions
COLOMBO
COLOMBO MUNCIPALITY
KALUTARA
KANDY
MATALE
NUWARA ELIYA
JAFFNA
MANNAR
VAVUNIYA
MULLATIVU
BATTICALOA
TRINCOMALEE
KURUNEGALA
PUTTALAM
ANURADHAPURA
POLONNARUWA
BADULLA
MONARAGALA
RATHNAPURA
KEGALLE