WEEKLY EPIDEMIOLOGICAL REPORT

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Enteric Fever (Part II)

This is the second in series of two articles on Enteric Fever

Vaccines

Currently, there are 2 vaccines available for the prevention of typhoid fever. The Ty21a vaccine is a live, attenuated, oral vaccine containing the S. Typhi strain Ty21a and the parenteral Vi vaccine is based on the S. Typhi Vi antigen. Ty21a is available as enteric capsules and is licensed for use in children 02 years of age (but licensed in the United States for children aged 06 years of age). The Vi-based vaccine is licensed for children aged 02 years. The effectiveness of parenteral Vi vaccine has recently been confirmed in young children, and the protection of unvaccinated neighbours of Vi vaccinees has been demonstrated. A new conjugate vaccine under development, Vi-rEPA, includes Vi antigen bound to a nontoxic recombinant protein that is antigenically identical to Pseudomonas aeruginosa exotoxin. It has been shown to be safe and immunogenic in Vietnamese children aged 2–5 years, providing protective efficacy of 91.5%, and is undergoing evaluation in younger age groups. In addition, efforts are underway to develop and evaluate improved live attenuated oral vaccines with the goals of maintaining safety while improving efficacy and reducing the number of doses required.

Because S. Paratyphi lack the Vi antigen, Vi -based vaccines are unlikely to provide protection against paratyphoid fever. There is evidence from pooled analyses of randomized controlled field trials done in Chile that Ty21a provides some limited protection against S. Paratyphi B and a descriptive analysis of national enteric fever surveillance data among Israeli travelers suggests that Ty21a may offer protection against S. Paratyphi A. Despite some preliminary efforts, there are currently no licensed vaccines against S. Paratyphi, which is a matter for concern, given the evidence for the emergence of this pathogen.

Despite having been evaluated in populations in middle and low-income countries of endemicity, typhoid fever vaccines have historically been used predominantly among travellers from high-income countries and have been only occasionally used in settings of endemicity However, this situation is changing because of the availability of high-quality burden of disease data from countries of endemicity; the experience of typhoid vaccination programs in Thailand, China, Vietnam and India; and vaccine demonstration projects in 5 Asian countries . Furthermore, a 2008 World Health Organization (WHO) position paper on the use of typhoid vaccines provides a mandate to member states by suggesting that countries should consider the programmatic use of Ty21a and Vi vaccines for controlling endemic disease. The position paper indicates that the use of vaccine should be based on an understanding of the local epidemiology of typhoid fever to target vaccine to groups at high risk of disease, such as pre-school-or school-age children and that vaccine should be implemented in the context of broad disease control efforts. Ultimately, the adoption of typhoid vaccine in settings of endemicity would be greatly aided by the availability of vaccines that are efficacious in infants to facilitate integration with Expanded Programs of Immunization, that can be administered as a single dose and that are produced locally to reduce cost.

Opinion about the use of typhoid vaccines to curtail epidemics has developed over time. Historically, expert groups have recommended to the WHO that epidemic typhoid control focus on the antimicrobial treatment of acute cases and on improvements in water and sanitation. The conser-

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vative approach to the use of vaccine was based on the requirement for multiple doses, the risk for adverse reactions and concern that vaccination campaigns would divert resources from attention to the source, usually sanitation and water problems. The effect of antimicrobial resistance on patient treatment, the availability of safe vaccines with simpler dosing regimens, the logistic challenges of rapidly addressing major water and sanitation infrastructure problems, and the success of mass vaccination programs in countries where typhoid fever is endemic have led to vaccine being more widely considered for epidemic control.

Antimicrobial Resistance and Patient Management

Antimicrobial resistance is a major public health problem in both S. Typhi and S. Paratyphi and timely treatment with appropriate antimicrobial agents is important for reducing the mortality associated with enteric fever.

Multidrug resistance

Resistance to the traditional first-line antimicrobial agents ampicillin, chloramphenicol and trimethoprim-sulfamethoxazole defines multidrug resistance (MDR) in S. enterica. The MDR phenotype has been shown to be widespread among S. Typhi for many years and is present, albeit at lower rates, among S. Paratyphi. Surveillance studies demonstrate considerable geographic variation in the proportion of S. Typhi isolates that are MDR in the same region, with sites in India, Pakistan and Vietnam having higher rates of MDR isolates than sites in China and Indonesia. Furthermore, longitudinal studies at the same site showed marked changes in the proportion of S. Typhi and S. Paratyphi A with MDR over time, including reductions in the proportion of isolates with MDR.

Fluoroquinolone resistance

The widespread distribution and high prevalence of MDR among Salmonella species has led to fluoroquinolones assuming a primary role in the therapy for invasive salmonellosis. Some investigators have noted increases in the prevalence of S. Typhi and S. Paratyphi strains susceptible to traditional first-line antimicrobials coinciding with a switch to fluoroquinolones for the management of enteric fever. However, the widespread use of fluoroquinolones has also been associated with decreased susceptibility and increases documented resistance to this class of drugs. A single chromosomal mutation in the quinolone resistance determining region of the gyrA gene may be sufficient to result in decreased ciprofloxacin susceptibility. Nalidixic acid resistance in the presence of ciprofloxacin susceptibility had been thought to be a reliable indicator of decreased ciprofloxacin susceptibility; however, this is now known not to be the case and many have suggested that decreased ciprofloxacin susceptibility is most reliably determined by measurement of the ciprofloxacin minimum inhibitory concentration. Patients with enteric fever due to isolates with decreased ciprofloxacin susceptibility are more likely to have prolonged fever clearance times and higher rates of treatment failure. In addition to decreased ciprofloxacin susceptibility, ciprofloxacin resistance has been reported among both S. Typhi and S. Paratyphi A.

Future concerns in antimicrobial resistance

As fluoro-quinolone use continues to expand and as decreased ciprofloxacin susceptibility and fluoroquinolone resistance drives the use of third-generation cephalosporins and other agents for the management of enteric fever, new patterns of antimicrobial resistance can be anticipated. Patterns of antimicrobial resistance seen in non-Typhi Salmonella species and Enterobactericeae may emerge in S. Typhi and S. Paratyphi. Although quinolone resistance among Enterobactericeae usually arises as the result of mutations in the quinolone resistance determining region of gyrA, plasmid-mediated resistance is increasingly recognized. Plasmid-mediated quinolone resistance is associated with qnr genes that encode a protein that protects DNA gyrase from ciprofloxacin and by aac(6′)-Ib-cr, an aminoglycoside-modifying enzyme with activity against ciprofloxacin. Plasmids bearing qnr or aac(6′)-Ib-cr may also contain an extended-spectrum cephalosporin resistance gene, which would pose a threat to the success of 2 major antimicrobial classes for the management of invasive salmonellosis. Indeed, an S. Typhi isolate producing an SHV-12 extended-spectrum β-lactamase and extended-spectrum β-lactamase-producing S. Paratyphi A have recently been reported. Of further concern, rare non-Typhi Salmonella isolates have been described that contain the carbapenemase blaIMP-4 and qnrB4 conferring both meropenem resistance and decreased ciprofloxacin susceptibility.

Antimicrobial management of enteric fever

Optimal antimicrobial treatment of patients with enteric fever depends on an understanding of local patterns of antimicrobial resistance and is enhanced by the results of antimicrobial susceptibility testing of the Salmonella isolated from the individual patient. Ciprofloxacin continues to be widely used, but clinicians need to be aware that patients infected with Salmonella with decreased ciprofloxacin susceptibility may not respond adequately. In this circumstance, third-generation cephalosporins, such as ceftriaxone, may be used. However, the cost and route of administration make ceftriaxone less suitable for patient treatment in some low and middle-income countries and the oral third-generation cephalosporin cefixime appears to be inferior to other oral agents both in terms of fever clearance time and treatment failure. In these circumstances, recent clinical trials suggest that azithromycin treatment (500 mg once daily for 7 days for adults or 20 mg/kg/day up to a maximum of 1000 mg/day for 7 days for children) is useful for the management of uncomplicated typhoid fever. Because of its pharmacokinetic profile, gatifloxacin has potential as a new agent for treating patients infected with isolates with decreased ciprofloxacin susceptibility but carries risk for dysglycemia, which may limit its widespread use.

Source-
Global Trends in Typhoid and Paratyphoid Fever- available from

http://cid.oxfordjournals.org/content/50/2/241.full

Compiled by Dr. Madhava Gunasekera of the Epidemioogy Unit

Table 4: Selected notifiable diseases reported by Medical Officers of Health 19th – 25th October (43rd Week)

RDHS	Dengue Fever		Dysentery		Encephalit		E Fever		F Poisoning		Leptospirosi		T Fever		V Hepatitis		H Rabies		Chicken-		Meningitis		Leishmani-		WRCD %	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	T*	C**
Colombo	164	8152	2	178	0	17	0	132	3	56	3	185	0	7	4	75	0	1	7	381	1	59	0	0	**77**	**23**
Gampaha	49	3080	4	180	2	20	2	48	5	36	14	361	1	19	3	170	0	0	5	154	1	84	0	5	**73**	**27**
Kalutara	22	1530	2	160	0	20	2	76	2	25	2	355	0	6	0	24	0	0	10	242	2	67	0	0	**69**	**31**
Kandy	17	1545	5	143	0	11	0	25	0	10	1	69	2	96	6	111	0	0	4	125	1	15	0	4	**96**	**4**
Matale	3	412	3	88	0	4	0	24	0	8	1	59	0	4	0	47	0	0	1	44	0	34	0	11	**85**	**15**
NuwaraEliya	4	222	3	145	0	2	0	14	0	217	1	28	1	59	0	22	0	0	5	112	0	12	0	0	**69**	**31**
Galle	6	758	7	110	0	19	0	6	0	89	1	195	2	55	0	14	0	2	3	289	0	45	1	1	**74**	**26**
Hambantota	7	293	2	55	0	3	0	15	1	33	1	161	0	63	0	86	0	0	0	95	1	48	1	290	**67**	**33**
Matara	5	417	2	76	0	13	0	28	1	28	3	139	1	81	1	139	0	2	5	243	4	75	2	86	**100**	**0**
Jaffna	19	627	17	364	0	10	3	306	3	99	1	9	3	335	0	17	0	1	0	137	0	55	0	0	**100**	**0**
Kilinochchi	0	59	1	38	0	0	1	15	0	5	0	9	0	16	0	0	0	2	0	2	0	7	0	11	**50**	**50**
Mannar	2	67	0	72	0	3	2	64	0	36	0	14	0	19	0	2	0	0	0	11	0	5	0	4	**60**	**40**
Vavuniya	1	67	0	55	0	13	0	12	0	20	0	50	0	3	0	3	0	2	0	22	0	34	0	10	**25**	**75**
Mullaitivu	0	113	1	20	0	2	1	10	0	43	0	38	0	7	0	1	0	2	0	8	0	6	0	15	**80**	**20**
Batticaloa	1	511	7	288	0	5	0	10	0	73	0	33	0	2	0	14	0	3	2	44	0	8	0	0	**86**	**14**
Ampara	2	177	9	167	0	1	0	5	1	12	2	36	0	1	0	9	0	0	4	86	0	18	0	3	**86**	**14**
Trincomalee	3	186	1	61	0	3	0	6	0	3	0	59	0	15	0	3	0	1	1	39	0	4	0	28	**58**	**42**
Kurunegala	21	2548	8	170	4	40	0	38	0	26	8	294	3	44	3	55	0	1	3	329	0	96	1	51	**85**	**15**
Puttalam	6	812	0	74	0	7	0	16	0	36	0	42	1	13	0	7	0	1	0	78	1	33	0	9	**62**	**38**
Anuradhapur	8	474	0	100	0	16	0	3	1	62	3	306	0	23	0	25	0	2	1	160	1	93	10	383	**63**	**37**
Polonnaruwa	12	410	3	77	0	2	0	14	0	64	1	161	0	3	0	29	0	2	2	123	1	18	1	151	**86**	**14**
Badulla	7	459	9	189	0	5	0	18	0	11	2	56	0	81	1	45	0	0	1	119	1	66	0	7	**76**	**24**
Monaragala	5	234	4	113	0	4	0	23	0	26	0	196	1	58	3	163	0	1	2	50	0	24	0	10	**73**	**27**
Ratnapura	19	1598	2	346	0	83	1	39	0	17	9	334	1	66	21	466	0	1	10	168	0	76	0	13	**89**	**11**
Kegalle	34	1026	3	123	0	16	0	28	0	11	17	224	1	72	5	213	0	0	2	299	3	103	0	2	**91**	**9**
Kalmune	1	493	1	141	0	2	0	3	1	118	1	10	0	2	0	5	0	0	2	83	0	9	0	1	**62**	**38**
SRI LANKA	**418**	**26270**	**96**	**3533**	**06**	**321**	**12**	**978**	**18**	**1164**	**71**	**3423**	**17**	**1150**	**47**	**1745**	**0**	**24**	**68**	**344**	**17**	**1094**	**16**	**1095**	**78**	**22**

Source: Weekly Returns of Communicable Diseases (WRCD).

***T=**Timeliness refers to returns received on or before 25th October , 2013 Total number of reporting units 339. Number of reporting units data provided for the current week:262 C** Completeness

A = Cases reported during the current week. **B** = Cumulative cases for the year.**H Rabies***= Human Rabies, **E Fever***=Enteric Fever, **F Poison*** =Food Poisoning, **T Fever***=Typhus Fever, **V Hepatitis***=Viral Hepatitis

Table 1: Vaccine-Preventable Diseases & AFP 19th October – 25th October 2013 (43rd Week)

Disease	No. of Cases by Province									Number of cases during current week in 2013	Number of cases during same week in 2012	Total number of cases to date in 2013	Total number of cases to date in 2012	Difference between the number of cases to date in 2013 & 2012
	W	C	S	N	E	NW	NC	U	Sab					
AFP*	01	01	00	00	00	00	00	01	01	04	02	81	67	+ 20.9 %
Diphtheria	00	00	00	00	00	00	00	00	00	-	-	-	-	-
Mumps	05	07	04	00	07	01	01	01	03	29	27	1316	3941	- 66.6 %
Measles	32	02	10	00	00	01	09	03	39	98	04	3352	57	+ 5780.7 %
Rubella	00	00	00	00	00	01	00	00	00	00	-	26	-	-
CRS**	00	00	00	00	00	00	00	00	00	00	-	06	-	-
Tetanus	00	00	00	00	00	00	00	00	00	00	00	20	11	+ 81.8 %
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	00	-	00	-	-
Japanese Encephalitis	00	00	00	00	00	00	00	00	00	00	-	68	-	-
Whooping Cough	00	01	00	00	00	00	00	00	00	01	00	73	89	- 18.0 %
Tuberculosis	133	27	35	12	24	00	39	12	01	283	249	6900	7399	- 6.7 %

Key to Table 1 & 2

Provinces: **W**: Western, **C**: Central, **S**: Southern, **N**: North, **E**: East, **NC**: North Central, **NW**: North Western, **U**: Uva, **Sab**: Sabaragamuwa.

RDHS Divisions: **CB**: Colombo, **GM**: Gampaha, **KL**: Kalutara, **KD**: Kandy, **ML**: Matale, **NE**: Nuwara Eliya, **GL**: Galle, **HB**: Hambantota, **MT**: Matara, **JF**: Jaffna, **KN**: Killinochchi, **MN**: Mannar, **VA**: Vavuniya, **MU**: Mullaitivu, **BT**: Batticaloa, **AM**: Ampara, **TR**: Trincomalee, **KM**: Kalmunai, **KR**: Kurunegala, **PU**: Puttalam, **AP**: Anuradhapura, **PO**: Polonnaruwa, **BD**: Badulla, **MO**: Moneragala, **RP**: Ratnapura, **KG**: Kegalle.

Data Sources:

Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Neonatal Tetanus, Whooping Cough, Chickenpox, Meningitis, Mumps., Rubella, CRS,

Special Surveillance: AFP* (Acute Flaccid Paralysis), Japanese Encephalitis

CRS =**Congenital Rubella Syndrome

AFP and all clinically confirmed Vaccine Preventable Diseases except Tuberculosis and Mumps should be investigated by the MOH

Dengue Prevention and Control Health Messages

Thoroughly clean the water collecting tanks bird baths, vases and other utensils once a week to prevent dengue mosquito breeding.

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Comments and contributions for publication in the WER Sri Lanka are welcome. However, the editor reserves the right to accept or reject items for publication. All correspondence should be mailed to The Editor, WER Sri Lanka, Epidemiological Unit, P.O. Box 1567, Colombo or sent by E-mail to **chepid@sltnet.lk. Prior approval should be obtained from the Epidemiology Unit before publishing data in this publication**

ON STATE SERVICE

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