piecemeal and not complete. The safety and immunogenicity data are not available for the subjects receiving unconjugated Vi vaccine (control) arm for comparison with those receiving Pedatyph^{R} vaccine. Again, one is misled to believe that Pedatyph^{R} vaccine is same as the Vi-rEPA vaccine by repeated highlighting the work done by Szu, *et al.*(2) and Kossaczka, *et al.*(3) (which is for Vi-rEPA vaccine), stating field efficacy data of Vi-rEPA vaccine (which is different from Pedatyph^{R} and then linking it to Pedatyph^{R} which in fact is totally different vaccine then the Vi-rEPA.

To conclude, it will be more reassuring to have direct clinical efficacy data with Pedatyph^{R} which will make us more confident to use the vaccine in our day to day practice.

Nitin K Shah,
Consultant Pediatrician,
PD Hinduja National Hospital & Research Centre, Mumbai, India.
drnitinshah@hotmail.com.

REFERENCES

1. Engels EA, Matthew EF, Joseph L, Michael LB. Typhoid fever vaccines: a meta-analysis of studies on efficacy and toxicity. British J Med 1998; 316: 110-116.
2. Szu SC, Stone AL, Robbins JD, Schneerson R, Robbins JB. Vi capsular polysaccharide-protein conjugates for prevention of typhoid fever: preparation, characterization, and immunogenicity in laboratory animals. J Exp Med 1987; 166: 1510-1524.
3. Kossaczka Z, Lin FY, Ho VA, Thuy NT, Bay PV, Thanh TC, *et al*. Safety and immunogenicity of Vi conjugate vaccines for typhoid fever in adults, teenagers, and 2- to 4-year-old children in Vietnam. Infect Immun 1999; 67: 5806-5810.
4. Lin FY, Vo AH, Kheim HB, Trach DD, Bay PV, Thanh TC, *et al*. The efficacy of a *salmonella typhi* Vi conjugate vaccine in two-to-five-year-old children. N Engl J Med 2001; 344: 1263-1269.
5. Richard LG, Margaret KM. Polysaccharide conjugate typhoid vaccine. N Eng J Med 2001; 344: 1322-1323.

Conjugate Typhoid Vaccine(s) in the Indian Context

The recent conference presentations and advertisements for 'indigenous' conjugate typhoid vaccine prompt the following considerations.

IS TYPHOID A SIGNIFICANT PUBLIC HEALTH PROBLEM IN INDIA TO MERIT VACCINATION?

(*a*) It is usually taken for granted that typhoid is a major public health problem in developing countries. However, careful analysis of data from current(1) and previous studies(2) shows that the absolute incidence of blood-culture proven typhoid episodes is only about 0.2% per year and, it contributes to a very small proportion of the total febrile episodes across all age groups (***Table* I**). This is a very important observation because vaccination can/will protect only against typhoid episodes and not febrile episodes believed to be typhoid and/or loosely labelled 'enteric fever' and treated as typhoid.

(*b*) Increasing antibiotic resistance(3) is often cited to emphasize the public health significance of typhoid. However, the latest multi-centric international study reported resistance in India to

TABLE I SIGNIFICANCE OF TYPHOID IN INDIA

Age-group	Febrile episodes/ 100,000/y	Typhoid episodes/ 100,000/y	Contribution of typhoid episodes among total febrile episodes
< 2 years	13920	89.2	0.64%
2-4 years	12040	340.1	2.82%
5-15 years	9490	493.5	5.2%
> 16 years	6620	119.7	11.7%
Overall	7690	214.2	2.79%

Data from the latest multicentric study (*1*)

be less than 10% to chloramphenicol, ampicillin, trimethoprim - sulphamethoxazole, combination of all three, and ciprofloxacin; and about 2% to ceftriaxone, but almost 60% to nalidixic acid(1). For unexplained reasons, bacterial resistance in India was much lower than other developing countries in the region; if true, this further reduces the public health significance of typhoid.

(*c*) The National immunization schedule included two doses of typhoid vaccine at school entry over two decades back; however this was not based on robust evidence and was abandoned. Changes in living conditions, hygiene practices, sanitation etc since then must also be factored-in if/when typhoid vaccination is considered in the present day.

DOES CONJUGATE TYPHOID VACCINE MERIT CONSIDERATION IN INDIA?

(*a*) The main advantage of vaccine(s) with polysaccharide antigen(s) conjugated to proteins is the stimulation of T-cell dependent immune responses. The implication of this is that infants with relatively less mature immune systems would respond, which does not happen with polysaccharide alone. This would be a major benefit only if the disease (here typhoid) is a significant problem among young infants. This is often implied in literature by calculating the absolute number or relative proportion of typhoid cases among infants(1,2). However, it is more important to assess the importance of typhoid (and hence prevention) as an issue of public health significance rather than only as a clinical problem. ***Table* 1** constructed from latest data(1) shows that typhoid is responsible not only for a very small proportion of febrile episodes in infants, but the proportion is less than in older children. Therefore, based on current information the conjugate vaccine has limited role in the Indian context, although this is the exact opposite of what is suggested(1). It should be noted that this conclusion need not be similar for other developing countries(4).

(*b*) The other purported advantage of typhoid conjugate vaccine is the belief that it confers superior protection as compared to the currently available vaccines. A recent Cochrane review(5) reported protective efficacy of 48% (95% CI=34-58%) at 2.5-3.0 years with three doses Ty21a vaccine; 55% (95% CI=30-70%) at 3.0 years with one dose Vi-polysaccharide vaccine and 87% (95% CI=56-96%) at 2.3 years with two doses Vi-rEPA (conjugate) vaccine, giving the impression that the conjugate vaccine is superior. However it is inappropriate to draw conclusions by comparing data between studies; the superiority of conjugate vaccine (if any) needs to be established through a randomized controlled comparative trial, rather than assumption by extrapolation.

CURRENT STATUS OF CONJUGATE TYPHOID VACCINE

(*a*) A Vi-rEPA conjugate vaccine prepared in USA was reported to have excellent protective efficacy in clinical trials conducted in Vietnam nearly a decade back(6). However, this vaccine also underwent clinical trials in China simultaneously; inexplicably the data is not available in the public domain. It is also surprising that no subsequent clinical trials have been reported with the vaccine.

(*b*) An Indian manufacturer has reportedly developed and tested a Vi-TT conjugate vaccine, but the trial design, outcome-measures, reporting format and conclusions are of questionable validity and more data is required to draw a definite conclusion.

WHAT CAN WE CONCLUDE?

Need for a vaccine is determined by clearly understanding disease burden (not synonymous with number/frequency), epidemiological factors and public health significance. Data on effectiveness (does the vaccine protect?), efficacy (does the vaccine generate immune responses?) and safety, should guide decisions once the need is justified. Using/recommending/promoting vaccine(s) merely because they are available in the market(7) relegates science to the background. In the context of typhoid conjugate vaccines, the need, effectiveness and efficacy have not been clearly established; hence it cannot be recommended at present.

Joseph L Mathew,
Advanced Pediatrics Centre,
PGIMER, Chandigarh 160012, India.
Email: jlmathew@rediffmail.com

REFERENCES

1. Ochiai RL, Acosta CJ, Danovaro-Holliday MC, Baiqing D, Bhattacharya SK, Agtini MD, *et al.* A study of typhoid fever in five Asian countries: disease burden and implications for controls. Bull WHO 2008; 86: 260-268.
2. Sinha A, Sazawal S, Kumar R, Sood S, Reddaiah VP, Singh B, *et al.* Typhoid fever in children aged less than 5 years. Lancet 1999; 354: 734-737.
3. Kumar S, Rizvi M, Berry N. Rising prevalence of enteric fever due to multidrug-resistant Salmonella: an epidemiological study. J Med Microbiol 2008; 57: 1247-1250.
4. Saha SK, Baqui AH, Hanif M, Darmstadt GL, Ruhulamin M, Nagatake T, *et al.* Typhoid fever in Bangladesh: implications for vaccination policy. Pediatr Infect Dis J 2001; 20: 521-524.
5. Fraser A, Goldberg E, Acosta CJ, Paul M, Leibovici L. Vaccines for preventing typhoid fever. Cochrane Database Syst Rev 2007, Issue 3.
6. Szu SC, Stone AL, Robbins JD, Schneerson R, Robbins JB. Vi capsular polysaccharide-protein conjugates for prevention of typhoid fever: preparation, characterization, and immunogenicity in laboratory animals. J Exp Med 1987; 166: 1510-1524.
7. Indian Academy of Pediatrics Committee on Immunization (IAPCOI). Consensus recommendations on immunization, 2008. Indian Pediatr 2008; 45: 635-648.

Setting the Scene to Blame the GOI for Failure of Polio Eradication

The recommendation of the 2nd National Consultative Meeting of the IAP on Polio Eradication (PE) has been published in the Journal(1). It seems appropriate at this time to look at what was accomplished by the 1st consultation(2). Last time, the committee suggested that India stockpile vaccine 'now' (as if the imported live-vaccine has an indefinite shelf-life) so that the country is 'no longer dependent on the WHO' if there is a resurgence of the disease. There was no protest in the journal about the illogical recommendation. It was simply ignored by the membership and the Government of India (GOI).

This year the committee says the GOI must take urgent measures to attain 90% coverage with UIP vaccines by the end of 2008, 'if the goal of polio eradication is to be achieved'. At present the committee says 38% children are fully immunized)(3). Does anyone imagine 90% immunization is possible by the year-end? Are we to infer that polio eradication is not possible just as 90% coverage under routine immunization (RI) by 2008 is not achievable?

PE was started with the goal to eradicate the virus by 2000 so that 'children need not be immunized perpetually(4)' It is now accepted that even if PE is successful (defined as absence of circulation of wild polio virus for 3 years) polio immunization will still be needed perpetually. The reason is that we now know that local strains of poliovirus can resurface decades after PE(5). International organizations spearheading the campaign for PE had seriously miscalculated and they will be keen to defect the blame (on to the GOI or any one else) for its failure. It is unfortunate that the IAP should participate in this game plan to lay blame on the GOI.

Siddharth and Jacob Puliyel,
Department of Pediatrics,
St Stephens Hospital,
Tis Hazari,
Delhi 110 054,
India.
E-mail: puliyel@gmail.com