

## Typhoid Vaccine(s) – To Give or Not to Give

The two articles on typhoid vaccination(1,2) published in the February 2009 issue of *Indian Pediatrics* raise some pertinent questions.

The author of the first article(1) does not consider the burden of typhoid in India high enough to merit this being included in the national immunization program or, for that matter, even important for individual immunization. On the other hand, the very study that has been quoted(3) not only makes out that India is a country with a high incidence of typhoid disease but also makes a case for conjugate vaccine to enable this to be given to children below 5 years.

The author has based his assessment of disease burden entirely on culture positive cases. However, majority of cases in India are diagnosed and treated without opting for blood culture and sensitivity report which is not routinely available at all places. There are many reports emanating from different parts that incidence of typhoid is even going up even in children around two years of age(4,5). The author also challenges the Cochrane review in this regard, which is considered to be a robust evidence pertaining to any clinical entity, interventions and therapy. They are not based on “assumption by extrapolation”. The conclusion reached by the author that typhoid is not a major public health problem in India, therefore, needs clarification. It may not have high mortality burden but definitely has high morbidity. Further, the author states that the two dose typhoid vaccine was abandoned from the national immunization schedule because of “lack of robust evidence”. However, the reasons for withdrawing this vaccine were the “reports of severe drug reaction including the reports of septic shock like picture and sudden deaths following these vaccines”(6).

In response to the second article(2), we have several queries. Which evidence on vaccines should

be considered as acceptable and which one as non acceptable? What are the minimum standards laid down for accepting studies on vaccines as authentic in terms of the place of study, the authors, the number of cases undertaken in the study, the number and type of publications, the manufacturers etc? What is the status of data from our own country? Do we have ICMR data or any other data which we would be willing to accept? On this count of lack of indigenous data, even licensure of many new vaccines such as Rotavirus, JE SA-14-14-2 etc can also be challenged.

What is the procedure of licensing a vaccine for use in our country? Does not the national licensing/regulatory authority satisfy itself on all accounts before granting permission for its use? What is the liability/accountability of the regulatory authority if vaccines supposedly not meeting the standards are licensed? What is the liability of medical practitioners in case they decide to give or not to give the vaccine on the basis of conflicting opinions? What is the liability of academic forums from where these vaccines are launched to give them a degree of credibility?

The IAP needs to address these questions and lay down guidelines in respect to all vaccines as a matter of ethical importance.

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## Typhoid Fever and Vaccination in India: Clarifications

There is no fixed cut-off figure of disease burden that dictates a national vaccination policy for an infectious disease. This decision has to be based on calculations taking into account burden of disease (number, complications, morbidity/mortality), epidemiology with respect to host and organism, transmission pattern, efficacy and effectiveness of the intervention (vaccine), safety profile, absolute cost of vaccine and vaccination program, cost-effectiveness, expected short and long term outcome, and the likely impact of the absence of a policy on the same. Although the investigators of the paper(1) claimed that the burden of typhoid is large enough to warrant vaccination in India, their data do not support this assertion.

The importance of a specific definition of typhoid (based on blood culture) is that (i) this is what has been used to calculate disease burden in various studies; (ii) calculation of vaccine efficacy from various trials is based on this definition; (iii) the ratio of blood-culture negative to blood-culture positive ‘typhoid cases’ is not known; and (iv) if a more sensitive but less specific definition/test of typhoid is used, many non-typhoid cases would be included(2) in whom the vaccine(s) would be expected to be efficacious, but will not be. Thereby overall effectiveness would decrease, and not increase.

Neither the detection of culture proven typhoid cases nor the ‘large’ number of suspected typhoid cases in young children can be taken as evidence that “*the incidence is going up even in children around two years of age.*”

Cochrane reviews are meant to aid decision-making processes, and not dictate the decision to be taken. However, it should be noted that the review on typhoid vaccines(3) did not identify trials comparing different typhoid vaccines against each other; in fact most trials compared one of the typhoid vaccines with a placebo/control vaccine. Therefore interpreting this information to suggest that a particular typhoid vaccine is superior, indeed amounts to assumption by extrapolation.

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## Licensing of New Vaccines

Several issues raised by the authors are beyond the scope of discussion as my original article did not cover those topics. Following are some of my thoughts relevant to remarks by Drs Kalra and Vashishtha.

To me the first and foremost important authority is the local regulatory authority in any country as far as a ‘stamp’ of authenticity is concerned. However other bodies like ICMR/IAP etc recommending use of any vaccine will make it more acceptable for the