

### **Typhoid Vaccine**

*Dr. T. Jacob John, Professor and Head, Department of Microbiology and Virology, Christian Medical College Hospital, Vellore, Tamil Nadu 632 004 answers important questions in relation to Typhoid Vaccine. Professor Jacob John, a leading international Vaccinologist, is an Adviser on Immunization to the World Health Organization and other International Agencies. He is the current Chairman of the IAP Committee on Immunization.*

***Q.1.** Following an episode of enteric fever, should typhoid vaccine be administered? If yes, after what period and in how many doses?*

**A.1.** Relapses and recurrences of typhoid fever although rare, illustrate that the immunity due to the disease is not completely protective. An episode of enteric fever usually means that the child lives in an environment in which further exposure to infection is likely. It is, therefore, rational to reinforce immunity by vaccine, even after typhoid fever. However, in real life a second episode of typhoid fever is so rare that postillness immunization has not become a routine practice.

There is no clear recommendation about when to vaccinate.. It is reasonable

to wait at least 4 weeks after complete recovery before vaccinating the child. If a decision is made to vaccinate, on theoretical grounds a single dose of whole cell killed vaccine or of Vi vaccine should suffice to boost or reinforce immunity. Whether the oral vaccine would induce additional protection in a gut recently recovered from *S. typhi* infection is not known. One could also argue that the disease itself may be taken as an immunizing experience and offer the vaccine 3 years later. This is what most of us practice.

***Q.2.** Should unimmunized close contacts of typhoid fever (for example, siblings and children) be vaccinated? If yes, with what vaccine type and schedule?*

**A.2.** The fact that it is unusual to see typhoid fever in more than one child (or person) in a family at a point in time indicates that household contact is not a common mode of transmission. However, the potential for a similar exposure to infection as the index case exists for siblings or parents. Further, there is also the potential for transmission within family. For these reasons, it is reasonable to vaccinate household contacts. At least we may use this as an opportunity to vaccinate and reduce the risk of disease in future.

The timing of vaccination of contacts may either be immediately after making the diagnosis in a child, or after the full recovery of the index child, aiming to avoid the period of possible incubation of infection in them. If given immediately after diagnosis, either oral vaccine or the single-dose Vi vaccine is preferred

in order to achieve rapid immunization. The whole cell killed vaccine, on the other hand, requires 2 doses for primary immunization, hence immunity is delayed. If given after the recovery of the child, any of the 3 vaccines may be chosen since there is no undue hurry to achieve protection. More important than immunization is to give health education for reducing any risk of feco-oral transmission of *S. typhi* within the family setting.

**Q.3.** *After typhoid vaccination, what is the interpretation of Widal test in a febrile child?*

**A.3.** The Widal test measures antibody to O and H antigens; neither Vi vaccine nor oral vaccine induce these antibodies. Therefore, these two vaccines do not interfere with the interpretation of the results of Widal test.

The whole cell killed vaccine induces high levels of H antibody which may persist for a few years, and moderate levels of O antibody which usually persist for a few months only. Caution is therefore, needed in interpreting Widal results in a child vaccinated with this vaccine. Six months or more after vaccination, in a febrile child, elevated H antibodies with low level of O antibodies is a pattern to be interpreted as due to the vaccine. If the vaccine contained killed *S. paratyphi* A also (TA vaccine), then the simultaneous presence of high levels of *S. typhi* H and *S. Paratyphi* H antibodies will give away the clue of previous immunization. If on the other hand, O antibody level is 160 or greater, then it is more likely to be indicative of typhoid fever.

**Q.4.** *What are the optimal storage*

*conditions for various forms of typhoid vaccines?*

**A.4.** All three typhoid fever vaccines should be transported and stored under refrigeration (2°C - 8°C), but not frozen, in order to maintain potency without any loss. However, the live oral vaccine is more susceptible to higher temperatures than the other two. Short periods of exposure of TA or Vi vaccines upto 37°C do not affect their immunogenicity seriously. The oral vaccine should reach 37°C only inside the intestines where it will undergo 4-5 generations of multiplication. If exposed to 37°C during transport or storage, its potency, namely viability of the live organisms, will be seriously affected. Such vaccine should not be used. In our country, where we have no easy measure of the protective efficacy of the vaccine, oral vaccine should be used only if these precautions can be followed scrupulously.

**Q.5.** *Is the uptake of the vaccine adequate in severely malnourished subjects? Can the vaccine be safely given in severely malnourished children?*

**A.5.** Malnutrition affects cell mediated immune responses more adversely than antibody production. Moreover, responses to several vaccines have been shown to be reasonably good in children with malnutrition. Therefore, at least on theoretical grounds, either of the injectable vaccines should induce protective immunity in such children. Since oral vaccine was successfully used in large field trials in developing countries, one may assume that it might offer some protection even in malnourished children. However, a better common-sense approach would be to immunize

after nutritional rehabilitation which should be easily possible within about 4 weeks.

**Q.6.** *Can typhoid vaccine(s) be safely administered during pregnancy?*

**A.6.** Although no specific effect of typhoid fever vaccines on pregnancy or its outcome has been shown, most physicians are reluctant to give a live vaccine during pregnancy. Where the risk of typhoid fever is high and if immunization is considered essential, the parenteral vaccines may be preferred to oral vaccine. If oral vaccine was given without realizing that the subject was pregnant, there is no cause for undue anxiety either.

**Q.7.** *Can typhoid vaccine be given to HIV infected children?*

**A.7.** On theoretical grounds the non replicating vaccines (TA and Vi) may be given to HIV infected children without any fear of adverse effects. There are no data about live oral vaccine's safety in HIV infected children. Since the organisms are inherently incapable of survival without nutritional supplementation, there should be no risk of invasion even in immunodeficient children.

**Q.8.** *Are 4 doses of oral typhoid vaccine superior to the usually recommended 3 doses?*

**A.8.** The oral vaccine consists of 1000 to 5000 million viable Ty 21a organisms per dose. Currently 3 doses are recommended on alternate days. In one field study in Child 2, 3 and 4 doses were compared and 4 doses induced significantly greater protective efficacy than 2 or 3 doses. The dose is fixed at 3 for pragmatic and cost considerations.

**Q.9.** *What is the rationale of combining Typhoid Vi antigen and tetanus conjugate vaccine? Are there any field trials available or being conducted?*

**A.9.** The Vi antigen is polysaccharide in nature. Polysaccharide antigens stimulate B cells directly and T helper cells do not get stimulated. In other words Vi is a T cell-independent antigen. T-independent antigens induce only IgM class antibody since IgM to IgG class switch requires regulation by T helper cells. Moreover, infants and children upto 18-24 months do not respond at all or respond very poorly to such antigens. T-independent antigens do not induce the production of memory T cells or memory B cells. All these disadvantages can be overcome by conjugating polysaccharide antigens to protein moieties, when the complex becomes T-dependent. Currently there are field studies being conducted in South America using protein-conjugated Vi vaccine.

**Q.10.** *Recently in India, there are fears that a proportion of enteric fever may be caused by Vi-negative Salmonella. Is this true? If yes, what is the likely effect on the protective efficacy of various typhoid vaccines?*

**A.10.** There have been no scientific reports that have shown Vi negative *S.typhi* causing typhoid fever. In our own investigations we have found that 98% of fresh *S. typhi* isolates were Vi positive, but 2% to be apparently Vi-negative. However, the patients had developed Vi antibody, thereby indicating that the infecting organisms were Vi positive. We concluded that the current method of testing for Vi by agglutination is not completely reliable.