practitioners. There is a mention of demerits of the conjugate Vi vaccine marketed in India in the IAP Immunization Guidebook 2008(1).

Typically any new vaccine (or for that matter any new drug) has to undergo phase 1 (early safety and dosing study), phase 2 (safety, dosing and immunogenicity study) and phase 3 (field efficacy and further safety study) trials before being licensed(2). In case one brand of the concerned vaccine with satisfactory efficacy data is already licensed, and serological correlates of protection for the vaccine are clearly known, a new brand need not do efficacy trials and can be licensed provided it shows non-inferiority (not more than 10% lower than for the lower CI) in comparative immunogenicity trials. Such non-inferiority results will assume and extrapolate similar efficacy for the new brand as compared to the existing vaccine (what is called bridging studies)(3). The new brand has to show non-inferiority over the existing brand in seroconversion (not more than 10% lower for the lower confidence interval compared to the existing brand) and GMCs (not less than 0.5 times as compared to the existing brand).

However if the serological correlates of protection are not known for a vaccine, one has no choice but to conduct field efficacy trials to prove non-inferiority compared with the existing licensed vaccine, example of such vaccines being pertussis vaccines for which huge and expensive field efficacy trials were conducted by most manufacturers(4); and typhoid vaccines. Serological correlates of protection are not known for the existing unconjugated Vi vaccine, oral Ty21a vaccine or the old whole cell killed typhoid vaccines. This is the reason why for each of these vaccines field efficacy trials have been conducted and reported(5). This is the reason why other Indian manufacturers are busy conducting field efficacy trails with their own candidate conjugate Vi vaccine(2).

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

REFERENCES

1. Singhal T, Amdekar Y, Agarwal R. IAP Guidebook on Immunization: IAP Committee on Immunization 2007-2008. New Delhi: Jaypee; 2009; p. 57.
2. Clemens J. Translational research to generate evidence for rational and efficient introduction of new vaccines in developing countries: The experience of the International Vaccine Institute. Ann Nestle 2008; 66: 81-91.
3. Jódar L, Butler J, Carlone G, Dagan R, Goldblatt D, Käyhty H, *et al*. Serological criteria for evaluation and licensure of new pneumococcal conjugate vaccine formulations for use in infants. Vaccine 2003; 21: 3265-3272.
4. Cherry JD. Comparative efficacy of acellular pertussis vaccines: an analysis of recent trials. Pediatr Infect Dis J 1997;16: S90-96.
5. 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.

Alleviation of Pain Associated with Immunization Injections

I often come across prescriptions recommending hot fomentation for relief of post vaccination pain and tenderness over the injection site. Many pediatricians prescribe ice packs/cold compress; others prescribe Thrombophob ointment application, besides paracetamol. What is the stand of IAP on this vital issue?

Shyam S Sidana
Consultant Pediatrcian,
Pedicare, Ratu Road,
Ranchi 834 001, India.
rch_sssidana@rediffmail.com.

Reply

Comfort measures, such as distraction (e.g., playing music or pretending to blow away the pain),

ingestion of sweet liquids, use of pacifier, breast feeding, cooling of the injection site, and topical or oral analgesia, can help infants or children cope with the discomfort associated with vaccination. Pretreatment (30-60 minutes before injection) application of 5% topical lidocaine-prilocaine emulsion can decrease the pain of vaccination by causing superficial anesthesia. Topical lidocaine-prilocaine emulsion should not be used for infants who are receiving treatment with methemoglobin-inducing agents. Use of a topical refrigerant (vapocoolant) spray immediately before vaccination can reduce the short-term pain associated with injections and can be as effective as lidocaine-prilocaine cream. Administration of multiple injections simultaneously rather than sequentially also helps in reduction of pain. Use of the correct size needle and the correct site also reduces procedural pain and so does the application of pressure at the site of injection. Withdrawing the plunger after insertion to check for blood in the syringe prolongs the process of injection and is no longer recommended.

One study indicates that acetaminophen or ibuprofen used immediately and for 24 hours following DTwP vaccination reduces fever, discomfort and pain following vaccination in young infants. There is no evidence to suggest that using these agents prophylactically following DTwP in older children, or DTaP or other vaccines at any age is of any help in reducing post vaccination pain.

Tanu Singhal
Convener, IAP Committee on Immunization,
Tanu.Singhal@relianceada.com

REFRENCES

1. Schechter NL, Zempsky WT, Cohen LL, McGrath PJ, McMurtry CM, Bright NS. Pain reduction during pediatric immunizations: evidence-based review and recommendations. Pediatrics 2007; 119: e1184-1198.
2. Kroger AT, Atkinson WL, Marcuse EK, Pickering LK; Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2006; 55(RR-15): 1-48.
3. Manley J, Taddio A. Acetaminophen and ibuprofen for prevention of adverse reactions associated with childhood immunization. Ann Pharmacother 2007; 41: 1227-1232.

Vi Conjugate Typhoid Vaccine

The introduction of the conjugated typhoid vaccine in India (Peda Typh^{TM}), and for the first time in the world, has come as one of the vaccines on the wish list of pediatricians living in the South of Globe. This novel vaccine has been found to be safe and effective in inducing very high levels of immune response (>90%) in infants, young children and adults. Since this vaccine induces 'T' cell dependent response, it would get boosted by field exposure and is expected to confer long lasting immunity. This new vaccine can be used to vaccinate and protect patients after clinical recovery and thus prevent disease carriers and relapses. We wish to offer our views on the previous correspondence on this issue(1,2).

Serologic correlates of typhoid immunity induced by Vi antigen was first reported by Felix and Pitt in 1935(3). Over the years the protective immunity conferred by Vi antigen has been well established and adopted by the WHO(4). The commonly known antigens of *S. typhi* viz 'O' & 'H' antigens induce serological response which are not protective in nature.

The valuable suggestion for bridging studies can only be taken up when an equivalent vaccine becomes available(1). Clinical trials are suggested involving more volunteers of all age groups over longer periods to establish that results of Peda Typh^{TM} vaccine shall be similar to the Vi-rEPA vaccine in the Vietnam trials. Bio-Med (P) Ltd shall support any such initiative to bring more scientific information. Already more than 30000 doses of Peda Typh^{TM} have been used over past 6-7 months all over India in all age groups. If doctors cooperate by providing serum samples for analysis, huge database can be created.