

Patient Recall of Td Booster History Is Reliable

BY MIRIAM E. TUCKER
Senior Writer

BALTIMORE — In settings with good access to care and high immunization rates, asking patients if they've received a tetanus booster in the last 10 years is a fairly accurate way to determine if they need one, Dr. M. Hassan Murad and his associates said in a poster presentation at a conference on vaccine research sponsored by the National Foundation for Infectious Diseases.

Patients who answer "yes" are probably right and do not need readministration of the vaccine. But those who say either "no" or "I don't know" should receive a tetanus-diphtheria (Td) booster as long as there are no contraindications, said Dr. Murad of the division of preventive medicine at the Mayo Clinic, Rochester, Minn.

Although previous studies have demonstrated poor accuracy of patients' recall of their last Td booster, this has not been evaluated previously in settings where im-

munization rates are high and good documentation is available. In this study, 572 patients of an employee health clinic of a large health care organization were asked whether they had a Td booster in the last 10 years. Of those, 65.6% were able to answer either "yes" or "no."

Comparison of their responses with their charts yielded high sensitivity (92.4%) and low specificity (26.5%). Accuracy of recall did not differ by age or gender, Dr. Murad and his associates reported.

The results from this study patient population are likely generalizable to those of other working-age adults of similar education level. "Since the results rely in significant part on human memory of a rare event—a once-every-10-years shot—they probably reflect useful information. ... The general characteristics of our population are they were mostly working age, education generally high school graduate or greater, and nearly all have good access to routine office care. That is probably similar to many office practices around the country," Dr. Murad said in a follow-up interview.

The advantage to conducting this study at the Mayo Clinic is that the institution keeps exceptionally good electronic immunization records of all employees, he noted. "In addition, we believe that our results are generalizable to the newer form of the vaccine [tetanus-diphtheria-acellular pertussis] since it is given at the same interval and in similar situations."

ProQuad Supply Shortage Could Last Until 2008

A projected shortage of the quadrivalent measles-mumps-rubella-varicella vaccine means that children who require immunization for these diseases will need to get two shots instead of the single combination vaccine until supplies of the latter are replenished, according to the Centers for Disease Control and Prevention.

The quadrivalent vaccine (ProQuad) shortage is expected to begin in July, although actual timing will depend on market demand, and last at least through the end of 2007 (MMWR 2007 May 11;56:453).

Attributing the shortfall to lower-than-expected amounts of varicella zoster virus (VZV) in its recent batch of bulk vaccine, manufacturer Merck & Co. notified the CDC earlier this year of its intent to use its available supply of VZV in the production of its varicella-only vaccine (Varivax) and its zoster vaccine (Zostavax) and to temporarily halt the production of ProQuad.

In anticipation of the shortage, Merck is requesting that physicians begin transitioning from the quadrivalent vaccine to the measles-mumps-rubella vaccine (MMR-II) and the varicella vaccine. The company expects to have adequate supplies of both of the latter vaccines to fully implement the recommended immunization schedules, according to the notice.

"This will allow for continued use of varicella vaccine for all age groups, including the routine two-dose schedule for children aged 12-15 months and 4-6 years, catch-up vaccination with the second dose for children or adolescents who received only 1 dose, and vaccination with two doses for other children, adolescents, and adults without evidence of immunity," the notice said. The company expects to have an adequate supply of zoster vaccine for routine vaccination of adults over age 60.

—Diana Mahoney

03 042470-942500

Typhoid Vi Polysaccharide Vaccine Typhim Vi®

Rx Only

Brief Summary: Please see package insert for full prescribing information.

INDICATIONS AND USAGE

Typhim Vi vaccine is indicated for active immunization against typhoid fever for persons two years of age or older.

Immunization with Typhim Vi vaccine should occur at least two weeks prior to expected exposure to *S typhi*.

Typhim Vi vaccine is not indicated for routine immunization of individuals in the United States (US).¹

Selective immunization against typhoid fever is recommended under the following circumstances: 1) travelers to areas where a recognized risk of exposure to typhoid exists, particularly ones who will have prolonged exposure to potentially contaminated food and water, 2) persons with intimate exposure (ie, continued household contact) to a documented typhoid carrier, and 3) workers in microbiology laboratories who frequently work with *S typhi*.¹

Typhoid vaccination is not required for international travel, but is recommended for travelers to such areas as Africa, Asia, and Central and South America where there is a recognized risk of exposure to *S typhi*. Current CDC advisories should be consulted with regard to specific locales. Vaccination is particularly recommended for travelers who will have prolonged exposure to potentially contaminated food and water. However, even travelers who have been vaccinated should use caution in selecting food and water.²

An optimal reimmunization schedule has not been established. Reimmunization every two years under conditions of repeated or continued exposure to the *S typhi* organism is recommended at this time.

Typhim Vi vaccine has efficacy against typhoid fever caused by *S typhi* infection but will not afford protection against species of *Salmonella enterica* serovar *typhi* other than *S typhi* or other bacteria that cause enteric disease.

For recommended primary immunization and reimmunization see **DOSE AND ADMINISTRATION** section.

Typhim Vi vaccine should not be used to treat a patient with typhoid fever or a chronic typhoid carrier.

CONTRAINDICATIONS

TYPHIM VI VACCINE IS CONTRAINDICATED IN PATIENTS WITH A HISTORY OF HYPERSENSITIVITY TO ANY COMPONENT OF THIS VACCINE.

WARNINGS

Allergic reactions have been reported rarely in the post-marketing experience (see **ADVERSE REACTIONS** section).

The safety and immunogenicity of Typhim Vi vaccine in children under two years of age has not been established. As with other polysaccharide vaccines, the antibody response may be inadequate. The decision whether to vaccinate children under 2 years of age depends upon the risk incurred by the child on the basis of the epidemiological context.

Typhim Vi vaccine provides protection against the risk of infection related to *Salmonella typhi*, but gives no protection against *Salmonella paratyphi A* or *B*.

If the vaccine is used in persons deficient in producing antibodies, whether due to genetic defect, immunodeficiency disease, or immunosuppressive therapy, the expected immune response may not be obtained.

As with any intramuscular injection, Typhim Vi vaccine should be given with caution to individuals with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection (see **DRUG INTERACTIONS** section).

As with any vaccine, vaccination with Typhim Vi vaccine may not protect 100% of individuals.

PRECAUTIONS

GENERAL

Care is to be taken by the health-care provider for the safe and effective use of Typhim Vi vaccine.

EPINEPHRINE INJECTION (1:1000) MUST BE IMMEDIATELY AVAILABLE FOLLOWING IMMUNIZATION SHOULD AN ANAPHYLACTIC OR OTHER ALLERGIC REACTIONS OCCUR DUE TO ANY COMPONENT OF THE VACCINE.

Prior to an injection of any vaccine, all known precautions should be taken to prevent adverse reactions. This includes a review of the patient's history with respect to possible hypersensitivity to the vaccine or similar vaccines.

Acute infection or febrile illness may be reason for delaying use of Typhim Vi vaccine except when in the opinion of the physician, withholding the vaccine entails a greater risk.

A separate, sterile syringe and needle or a sterile disposable unit must be used for each patient to prevent the transmission of infectious agents from person to person. Needles should not be recapped and should be properly disposed.

Special care should be taken to ensure that Typhim Vi vaccine is not injected into a blood vessel.

Safety and immunogenicity data from controlled trials are not available for Typhim Vi vaccine following previous immunization with whole-cell typhoid or live, oral typhoid vaccine (See **ADVERSE REACTIONS** section).

DRUG INTERACTIONS

There are no known interactions of Typhim Vi vaccine with drugs or foods.

No studies have been conducted in the US to evaluate interactions or immunological interference between the concurrent use of Typhim Vi vaccine and drugs (including antibiotics and antimetabolites), immune globulins or other vaccines (including common travelers vaccines such as tetanus, poliomyelitis, hepatitis A, yellow fever and meningococcus). (See **ADVERSE REACTIONS** section.)

As with other intramuscular injections, Typhim Vi vaccine should be given with caution to individuals on anticoagulant therapy.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

Typhim Vi vaccine has not been evaluated for its carcinogenic potential, mutagenic potential or impairment of fertility.

PREGNANCY CATEGORY C

Animal reproduction studies have not been conducted with Typhim Vi vaccine. It is not known whether Typhim Vi vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Typhim Vi vaccine should be given to a pregnant woman only if clearly needed.¹

When possible, delaying vaccination until the second or third trimester to minimize the possibility of teratogenicity is a reasonable precaution.³

NURSING MOTHERS

It is not known if Typhim Vi vaccine is excreted in human milk.

There is no data to warrant the use of this product in nursing mothers for passive antibody transfer to an infant.

PEDIATRIC USE

Safety and effectiveness of Typhim Vi vaccine have been established in children 2 years of age and older.^{4,5} (See **DOSE AND ADMINISTRATION** section.) FOR CHILDREN BELOW THE AGE OF 2 YEARS, SAFETY AND EFFECTIVENESS HAVE NOT BEEN ESTABLISHED.

ADVERSE REACTIONS

Adverse event information is derived from clinical trials and worldwide post-marketing experience.

DATA FROM CLINICAL TRIALS

Safety of Typhim Vi vaccine, the US licensed liquid formulation, has been assessed in clinical trials in more than 4,000 subjects both in countries of high and low endemicity. In addition, the safety of the lyophilized formulation has been assessed in more than 6,000 individuals. The adverse reactions were predominantly minor and transient local reactions. Local reactions such as injection site pain, erythema and induration almost always resolved within 48 hours of vaccination. Elevated oral temperature, above 38°C (100.4°F), was observed in approximately 1% of vaccinees in all studies. No serious or life-threatening systemic events were reported in these clinical trials.^{4,5}

Adverse reactions from two trials evaluating Typhim Vi vaccine lots in the US (18- to 40-year-old adults) are summarized in TABLE 1. No severe or unusual side effects were observed. Most subjects reported pain and/or tenderness (pain upon direct pressure). Local adverse experiences were generally limited to the first 48 hours.^{4,5}

TABLE 1^{4,5} PERCENTAGE OF 18- TO 40-YEAR-OLD US ADULTS PRESENTING WITH LOCAL OR SYSTEMIC REACTIONS WITHIN 48 HOURS AFTER THE FIRST IMMUNIZATION WITH TYPHIM VI VACCINE

REACTIONS	Trial 1 Placebo N=54	Trial 1 Typhim Vi vaccine N=54 (1 Lot)	Trial 2 Typhim Vi vaccine N=98 (2 Lots combined)
Local			
Tenderness	7 (13.0%)	53 (98.0%)	95 (96.9%)
Pain	4 (7.4%)	22 (40.7%)	26 (26.5%)
Induration	0	8 (14.8%)	5 (5.1%)
Erythema	0	2 (3.7%)	5 (5.1%)
Systemic			
Malaise	8 (14.8%)	13 (24.0%)	4 (4.1%)
Headache	7 (13.0%)	11 (20.4%)	16 (16.3%)
Myalgia	0	4 (7.4%)	3 (3.1%)
Nausea	2 (3.7%)	1 (1.9%)	8 (8.2%)
Diarrhea	2 (3.7%)	0	3 (3.1%)
Feverish (subjective)	0	6 (11.1%)	3 (3.1%)
Fever ≥100°F	0	1 (1.9%)	0
Vomiting	0	1 (1.9%)	0

No studies were conducted in US children. Adverse reactions from a trial in Indonesia in children one to twelve years of age are summarized in TABLE 2.^{4,5} No severe or unusual side effects were observed.

TABLE 2^{4,5} PERCENTAGE OF INDONESIAN CHILDREN ONE TO TWELVE YEARS OF AGE PRESENTING WITH LOCAL OR SYSTEMIC REACTIONS WITHIN 48 HOURS AFTER THE FIRST IMMUNIZATION WITH TYPHIM VI VACCINE

REACTIONS	N=175
Local	
Soreness	23 (13.0%)
Pain	25 (14.3%)
Erythema	12 (6.9%)
Induration	5 (2.9%)
Impaired Limb Use	0
Systemic	
Feverishness*	5 (2.9%)
Headache	0
Decreased Activity	3 (1.7%)

* Subjective feeling of fever.

In the US Reimmunization Study, subjects who had received Typhim Vi vaccine 27 or 34 months earlier, and subjects who had never previously received a typhoid vaccination, were randomized to placebo or Typhim Vi vaccine, in a double-blind study. Safety data from the US Reimmunization Study are presented in TABLE 3.^{4,6} In this study 5/30 (17%) primary immunization subjects and 10/45 (22%) reimmunization subjects had a local reaction. No severe or unusual side effects were observed. Most subjects reported pain and/or tenderness (pain upon direct pressure). Local adverse experiences were generally limited to the first 48 hours.^{4,6}

TABLE 3^{4,6} US REIMMUNIZATION STUDY, SUBJECTS PRESENTING WITH LOCAL AND SYSTEMIC REACTIONS WITHIN 48 HOURS AFTER IMMUNIZATION WITH TYPHIM VI VACCINE

REACTIONS	PLACEBO (N=32)	FIRST IMMUNIZATION (N=30)	REIMMUNIZATION (N=45*)
Local			
Tenderness	2 (6%)	28 (93%)	44 (98%)
Pain	1 (3%)	13 (43%)	25 (56%)
Induration	0	5 (17%)	8 (18%)
Erythema	0	1 (3%)	5 (11%)
Systemic			
Malaise	1 (3%)	11 (37%)	11 (24%)
Headache	5 (16%)	8 (27%)	5 (11%)
Myalgia	0	2 (7%)	1 (2%)
Nausea	0	1 (3%)	1 (2%)
Diarrhea	0	0	1 (2%)
Feverish (subjective)	0	3 (10%)	2 (4%)
Fever ≥100°F	1 (3%)	0	1 (2%)
Vomiting	0	0	0

* At 27 or 34 months following a previous dose given in different studies.

DATA FROM WORLDWIDE POST-MARKETING EXPERIENCE

The following adverse events have been reported during post-approval use of Typhim Vi vaccine. These events have been very rarely reported; however, because they were reported voluntarily from a population of uncertain size, it is not always possible to reliably calculate their frequencies or to establish a causal relationship to Typhim Vi vaccine exposure.

- Gastrointestinal disorders
Nausea, vomiting, diarrhea
- General disorders and administration site condition
Local Reactions: injection site pain, injection site inflammation, injection site induration, injection site erythema, and lymphadenopathy.
Fever, asthenia, malaise, flu-like episode, abdominal pain.
- Immune system disorders
Allergic-type reactions such as pruritus, rash, urticaria, difficulty breathing, hypotension.
Serum sickness.
- Musculoskeletal and connective tissue disorders
Myalgia, arthralgia, cervical pain.
- Nervous system disorders
Headache, loss of consciousness, tremor.

Additional Adverse Events:

Post-marketing reports of glomerulonephritis, neutropenia, bilateral retinitis, and polyarthritis have been reported in patients who had also received other vaccines; however a causal relationship has not been established.

DOSE AND ADMINISTRATION

Before administration, parenteral drug products should be checked visually for any deviation from normal appearance including container integrity. The syringe or vial and its packaging should also be inspected prior to use for evidence of leakage, premature activation of the plunger, or a faulty tip seal. If evidence of such defects are observed, the syringe should not be used.

For intramuscular use only. DO NOT inject intravenously.

Typhim Vi vaccine is indicated for persons two years of age and older.

The immunizing dose for adults and children is a single injection of 0.5 mL. The dose for adults is given intramuscularly in the deltoid, and the dose for children is given IM either in the deltoid or the vastus lateralis. The vaccine should not be injected into the gluteal area or areas where there may be a nerve trunk.

A reimmunization dose is 0.5 mL. Reimmunization consisting of a single dose for US travelers every two years under conditions of repeated or continued exposure to the *S typhi* organism is recommended at this time.¹

The syringe is intended for single use only, must not be reused, and must be disposed of properly and promptly following its use.

The skin at the site of injection first should be cleansed and disinfected. Tear off upper seal of vial cap. Cleanse top of rubber stopper of the vial with a suitable antiseptic and wipe away all excess antiseptic before withdrawing vaccine.

STORAGE

Store between 2°–8°C (35°–46°F). DO NOT FREEZE.

REFERENCES

1. Recommendations of the Immunization Practices Advisory Committee (ACIP). Typhoid Immunization. MMWR 43: No. RR-14, 1994
2. CDC. Health Information for International Travel 1992. U.S. Department of Health and Human Services, Public Health Service
3. ACIP: Update on Adult Immunization. MMWR 40: No. RR-12, 1991
4. Unpublished data available from Sanofi Pasteur, Inc., compiled 1991
5. Unpublished data available from Sanofi Pasteur, Inc.
6. Keitel WA, et al. Clinical and serological responses following primary and booster immunization with *Salmonella typhi*/Vi capsular polysaccharide vaccines. Vaccine 12: 195-199, 1994

sanofi pasteur

Product Information as of
December 2005

Manufactured by:
Sanofi Pasteur SA
Lyon France
US Govt License #1724
MKT12690

Distributed by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA
1-800-VACCINE (1-800-822-2463)