Your travel medicine provider has given you the oral typhoid fever vaccine, Vivotif®. Unlike other vaccines that are given as a shot, this vaccine is contained in four capsules and is taken orally.

This easy-to-understand guide provides answers to Frequently Asked Questions. Please read this handout carefully. As with any drug, it is important that you follow the instructions carefully.

Do I have to take all 4 doses?
Yes. You must take all 4 capsules to get the full long term effect of the vaccine.

Just as important, you need to skip a day between capsules. Remember to take a capsule EVERY OTHER DAY.

The last dose must be taken at least 1 week before you enter a high-risk area.
How does the oral typhoid fever vaccine work?
This oral vaccine is contained in a special type of capsule. This capsule is designed to dissolve only when it reaches the small intestine. Once there, the vaccine is absorbed into the body to begin providing protection.

Can I drink alcohol?
After taking a capsule, wait at least TWO hours before taking a drink of an alcoholic beverage. The alcohol can cause the capsule to dissolve before reaching the small intestines. Also, alcohol itself can destroy the vaccine.

Does each dose have to be taken at the same time of day?
Taking the vaccine at approximately the same time will make it easier for you to remember. Many patients find it easiest to take the capsule as soon as they wake up in the morning.

Is there an easy way to help remind me of when to take each dose?
A sticker is available to help you remember when to take each of the 4 capsules. Write the day you are supposed to take each of them in the space provided and put it somewhere you will see it each day. Your travel medicine provider may also have other helpful materials for you.

Precautions
Do not take the oral vaccine if you:
• Are taking antibiotics
• Have had any bad reactions to this oral typhoid vaccine or enteric coated capsules in the past
• Have a fever
• Have continued vomiting
• Have diarrhea or a stomach illness.

Be sure to tell your travel medicine provider if you are pregnant, nursing or immunodeficient.

You should still avoid potentially contaminated food or water, as not all people will be fully protected against typhoid fever.

If you have any additional questions, please discuss them with your travel medicine provider.

Do I have to take the capsule with water?
Yes. It is best to swallow each capsule with a full glass of cool or room temperature WATER. Don't open or chew the capsule — remember that the vaccine capsule needs to reach the small intestine before it dissolves.

Can I take each capsule with food?
No. The oral vaccine must be taken on an empty stomach. That means you should take the capsule either 1 hour before eating a meal or 2 hours after eating a meal.

Why is it important to take on an empty stomach?
If there is any food in the stomach, the capsule will remain in the stomach for a much longer time where the stomach acids can dissolve the capsule. Once the capsule is destroyed, the vaccine will also be destroyed before it can be absorbed into the intestine. One hour after taking the capsule, you can eat some food.

Side Effects
In clinical trials, the most frequently reported side effects were abdominal pain, nausea, headache, fever, diarrhea, vomiting and skin rash. Although infrequent and mild, nausea was the most mentioned side effect. You should report any serious side effect to your doctor or directly to the Vaccine Adverse Event Reporting System (1-800-822-7967).

Can a child take the vaccine?
Yes, children 6 years and older can take the oral typhoid vaccine.
lipopolysaccharide (1). The protective immune response is dependent upon the bacteria possessing a complete barrier, colonize the intestinal tract, penetrate the lumen and enter the lymphatic system. These non-symptomatic carriers are the natural reservoir for S. typhi. 2–4% of acute typhoid cases result in the development of a chronic carrier state (8). In 340 cases acquired in the United States between 1977 and 1979, 23% of the cases were associated with typhoid carriers, 24% were due to food outbreaks, 23% were associated with the ingestion of contaminated food or water, 6% due to household contact with an infected person and 4% following exposure to S. typhi in a laboratory setting (6).

The majority of typhoid cases respond favorably to antibiotic therapy. However, the emergence of multi-drug resistant strains has greatly complicated therapy and cases of typhoid fever that are treated with ineffective drugs can be fatal (7). Approximately 2–4% of acute typhoid cases result in the development of a chronic carrier state (8). These non-symptomatic carriers are the natural reservoir for S. typhi and can serve to maintain the disease in its endemic state or to directly infect individuals (3).

Virent strains of S. typhi upon ingestion are able to pass through the stomach acid barrier, colonize the intestinal tract, penetrate the lumen and enter the lymphatic system and blood stream, thereby causing disease. One possible mechanism by which disease may be prevented is by evoking a local immune response in the intestinal tract. Such local immunity may be induced by oral ingestion of a live attenuated strain of S. typhi Ty21a. Results from clinical studies indicate that adults and children greater than 6 years of age may be protected against typhoid fever following the oral ingestion of 4 doses of Vivotif® (Typhoid Vaccine Live Oral Ty21a). The efficacy of the S. typhi Ty21a strain has been evaluated in a series of randomized, double-blind, controlled field trials. Suspected typhoid cases, detected by passive surveillance, were confirmed bacteriologically either by blood or bone marrow culture. The first trial was performed in Alexandria, Egypt with a study population of 32,388 children aged 6 to 7 years. Three doses of vaccine, in the form of a freshly reconstituted suspension administered after ingestion of 1 g of bicarbonate, were given on alternate days. Immunization resulted in a 95% decrease (95% confidence interval (CI) = 77%–99%) in the incidence of typhoid fever over a 3-year period of surveillance (9). A series of field trials were subsequently performed in Santiago, Chile to evaluate efficacy when the vaccine was administered in the form of a single dose (10). The initial trial involved 82,543 school-aged children, and compared 1 or 2 doses of vaccine given one week apart. After 24 months of surveillance vaccine efficacy was 29% (95% CI = 4%–47%) for the single dose schedule and 59% (95% CI = 41%–71%) for the 2-dose schedule (10). A further field trial was performed in Santiago, Chile involving 109,594 school-aged children (13). Three doses of enteric-coated capsules were administered either on alternate days (long immunization schedule) or 21 days apart (long immunization schedule). Following 36 months of surveillance vaccine attributable risk of typhoid fever in the short immunization schedule group and a 49% reduction (95% CI = 24%–66%) in the long immunization schedule group. After 48 months of surveillance the short immunization schedule resulted in a 69% (95% CI = 55%–80%) decrease in typhoid incidence of level of 0.15 increase in optical density units over baseline determined in an enzyme linked immunosorbent assay (ELISA) was compared in an open study between adults living in an endemic area (Chile) and non-endemic areas (United States and Switzerland) after the ingestion of 5 doses of Ty21a over a 3-year period of surveillance (11). After 30 months of surveillance vaccine efficacy for all age groups was 42% (95% CI = 23%–57%).

Vaccine organisms can be shed transiently in the stool of vaccine recipients (16). However, secondary transmission of vaccine organisms has not been documented. Ty21a has not been isolated from blood cultures following immunization. At present, the precise mechanism(s) by which Vivotif® confers protection against typhoid fever is unknown. However, it is known that immunization of adult subjects can elicit a humoral anti-S. typhi LPS antibody response. Taking advantage of this fact, the seroconversion rate (defined as ≥ 0.15 increase in optical density units over baseline determined in an ELISA) was compared in an open study between adults living in an endemic area (Chile) and non-endemic areas (United States and Switzerland) after the ingestion of 5 doses of Ty21a over a 3-year period of surveillance (11). After 30 months of surveillance vaccine efficacy for all age groups was 42% (95% CI = 23%–57%).

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Vivotif®
Typhoid Vaccine Live Oral Ty21a

Information for Patients

It is essential that all 4 doses of vaccine be taken at the prescribed alternate-day interval to obtain a maximal protective immune response. Vaccine potency is dependent upon storage under refrigeration (between 2 °C and 8 °C [35.6 °F–46.4 °F]). The vaccine should be stored under refrigeration at all times. It is essential to replace unused vaccine in the refrigerator between doses. The vaccine capsule should be swallowed approximately 1 hour before a meal with a cold or luke-warm (temperature not to exceed body temperature, e.g., 37 °C [98.6 °F]) drink. Care should be taken not to chew the vaccine capsule. The vaccine capsule should be swallowed as soon after placing in the mouth as possible.

Not all recipients of Vivotif® (Typhoid Vaccine Live Oral Ty21a) will be fully protected against typhoid fever. Travelers should take all necessary precautions to avoid contact or ingestion of potentially contaminated food or water. Several anti-malaria drugs, such as mefloquine, chloroquine and proguanil (not approved for use in US) possess antibacterial activity which may interfere with the immunogenicity of Vivotif®. Clinical results (see Warnings – Drug-Interactions) indicate that mefloquine and chloroquine can be administered together with Vivotif®. Proguanil should be administered only if 10 days or more have elapsed since the final dose of Vivotif® was ingested. A serious adverse reaction occurred in the administration of the vaccine should be reported to your health care provider. You may also report an adverse reaction directly to the Vaccine Adverse Event Reporting System (1-800-822-7967) (20). Your health care provider should inform you of the benefits and risks of the vaccine, the importance of taking all 4 capsules in the correct schedule, and the importance of proper storage temperature of the capsules.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals with Vivotif® have not been performed to evaluate carcinogenic potential, mutagenic potential or impairment of fertility.

Pregnancy Category C

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

Nursing Mothers There is no data to warrant the use of this product in nursing mothers. It is not known if Vivotif® is excreted in human milk.

Pediatric Use The safety and efficacy of Vivotif® has not been established in children under 6 years of age. This product is not indicated for use in children under 6 years of age.

Adverse Reactions

More than 1.4 million doses of Ty21a have been administered in controlled clinical trials and more than 150 million doses of Vivotif® (Typhoid Vaccine Live Oral Ty21a) have been marketed world-wide. Active surveillance for adverse reactions of enteric-coated capsules was performed in a pilot study (21) and in a subgroup of a large field trial (14) involving a total of 483 individuals receiving three vaccine doses. The overall symptom rates from both studies when vaccinated with capsules were combined and shown to be: abdominal pain (6.4%), nausea (5.8%), headache (4.8%), fever (3.3%), diarrhea (2.9%), vomitting (1.5%) and skin rash (1.0%). Only the incidence of nausea shown to be: abdominal pain (6.4%), nausea (5.8%), headache (4.8%), fever (3.3%), vomiting (1.5%) and skin rash (1.0%). One isolated, non-fatal anaphylactic shock considered to be an allergic reaction to the vaccine was reported.

Doseage and Administration

One capsule is to be swallowed approximately 1 hour before a meal with a cold or luke-warm (temperature not to exceed body temperature, e.g., 37 °C [98.6 °F]) drink on alternate days, e.g., days 1, 3, 5 and 7. Immunization (ingestion of all 4 doses of Vivotif® (Typhoid Vaccine Live Oral Ty21a) should be completed at least 1 week prior to potential exposure to S. typhi.

The blister containing the vaccine capsules should be inspected to ensure that the foil seal and capsules are intact. The vaccine capsule should not be chewed and should be swallowed as soon after placing in the mouth as possible. A complete immunization schedule is the ingestion of 4 vaccine capsules as described above.

Re-immunization

The optimum booster schedule for Vivotif® has not been determined. Efficacy has been shown to persist for at least 5 years. Further, there is no experience with Vivotif® as a booster in persons previously immunized with parenteral typhoid vaccine. It is recommended that a re-immunization dose consisting of four vaccine capsules taken on alternate days be given every 5 years under conditions of repeated or continued exposure to typhoid fever (7).

How Supplied

A single foil blister contains 4 doses of vaccine in a single package.

Storage

Vivotif® (Typhoid Vaccine Live Oral Ty21a) is not stable when exposed to ambient temperatures. Vivotif® should therefore be shipped and stored between 2 °C and 8 °C (35.6 °F–46.4 °F). Each package of vaccine shows an expiration date. This expiration date is valid only if the product has been maintained at 2 °C–8 °C (35.6 °F–46.4 °F).

Manufactured by
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References

15. Data on File, Swiss Serum and Vaccine Institute Berne, Switzerland.

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