
Cholera

State of the art of new vaccines: research and development

[WHO/IVB/06.01](#)

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The Ty21a (typhoid) vaccine is . . . to be swallowed every other day for one week. It can be taken simultaneously with the attenuated CVD103-HgR *V. cholerae* vaccine.

Contraindications

Typhoid vaccines (WHO position paper)

[WER 2000, vol. 75, 32, pp 257-264](#)

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It is not known whether this live attenuated vaccine (Ty21a typhoid vaccine) can cause fetal harm when administered to pregnant women. Ty21a can be administered to HIV-positive, asymptomatic individuals without risk as long as the T-cell count (CD4) is above 200/mm³.

Typhoid vaccines (WHO position paper)

[WER 2000, vol. 75, 32, pp 257-264](#)

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There are no contraindications (to the Vi polysaccharide typhoid vaccine) other than prior severe reaction to vaccine components. Although the vaccine is safe for HIV-infected persons, the induction of protective antibodies is directly correlated to the levels of CD4 positive T-cells.

Typhoid vaccines: WHO position paper

[WER 2008, vol. 83, 6, pp 49-60](#)

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There are no contraindications to the use of this vaccine other than previous severe hypersensitivity reaction to vaccine components. Although the Vi polysaccharide vaccine is safe for HIV-infected individuals, the induction of protective antibodies is directly correlated to the levels of CD4 positive T-cells.

General

Thermostability of vaccines

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The Vi polysaccharide (typhoid) vaccine is highly stable and does not require a cold chain even in tropical conditions. This is a distinct advantage compared with the other two typhoid vaccines in use (attenuated *Salmonella typhi* strains used as live oral vaccines and inactivated whole cell oral vaccines.)

Typhoid vaccines (WHO position paper)

[WER 2000, vol. 75, 32, pp 257-264](#)

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Decisions on whether or not to incorporate typhoid vaccination into large-scale immunization programmes should be based on detailed knowledge of the local epidemiological situation including data on age-specific incidence and possible subpopulations at particular risk, as well as on information concerning the sensitivity to relevant antimicrobial drugs of the prevailing *S. typhi* strains. Ideally, cost-benefit analyses should be part of the planning process.

Typhoid vaccines (WHO position paper)

Immunization of school-age children is recommended in areas where typhoid fever in these age groups is a significant public health problem, and particularly where antibiotic-resistant *S. typhi* strains are prevalent. In those settings immunization against typhoid fever will be required until socioeconomic improvements finally interrupt transmission of *S. typhi*. Where appropriate the use of typhoid vaccines should be harmonized with the administration of tetanus and diphtheria vaccines.

[WER 2000, vol. 75, 32, pp 257-264](#)
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Typhoid vaccines (WHO position paper)

Although both the Ty21a and the Vi polysaccharide (typhoid) vaccines are safe and of acceptable efficacy in individuals above 5 years of age, further controlled studies on the respective value of these vaccines for large-scale vaccination of children below 5 years of age, both in endemic and epidemic settings, are encouraged.

[WER 2000, vol. 75, 32, pp 257-264](#)
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In spite of positive developments in this field, improved vaccines against typhoid fever are needed. Such vaccines should confer high levels of durable protective immunity in all age groups, preferably without the need for booster doses, and be affordable in the populations at greatest need.

Typhoid vaccines (WHO position paper)

Recommended storage temperature (for Vi polysaccharide typhoid vaccine) is between + 2 C and + 8 C.

[WER 2000, vol. 75, 32, pp 257-264](#)
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Typhoid vaccines (WHO position paper)

The Vi polysaccharide vaccine is administered subcutaneously or intramuscularly as 1 dose of 25 mg to individuals aged > 2 years. The vaccine confers protection 7 days after injection.

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Typhoid vaccines (WHO position paper)

To maintain protection, revaccination (with the Vi polysaccharide vaccine) is recommended every 3 years.

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Typhoid vaccines (WHO position paper)

Protection (provided by the Ty21a vaccine) is markedly influenced by the number of doses and their spacing. When the vaccine is given in 3 doses 2 days apart, protective immunity is achieved 7 days after the last dose. In endemic areas a booster dose is recommended every 3 years. Travellers from non-endemic to endemic regions are recommended a booster on a yearly basis. There are currently no field trial data to document the efficacy of this vaccine in children aged < 3 years.

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Typhoid vaccines (WHO position paper)

The (Ty21a typhoid) vaccine is usually administered orally as entericcoated capsules and is registered for use from 6 years of age.

A liquid formulation of the Ty21a (Ty21a typhoid) vaccine can be taken by children as young as 2 years and has proved more immunogenic than the capsular formulation.

[WER 2000, vol. 75, 32, pp 257-264](#)
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Typhoid vaccines (WHO position paper)

Ty21a (Ty21a typhoid) is remarkably well tolerated. The vaccine may be given simultaneously with other vaccines, including live vaccines against polio, cholera and yellow fever, or the measles, mumps and rubella (MMR) combination. Proguanil or antibiotics should be avoided during the 3 days before and after vaccination.

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Typhoid vaccines (WHO position paper)

The old, heat inactivated whole-cell (typhoid) vaccine may not always be manufactured according to international standards, whereas both the parenteral Vi-based polysaccharide vaccine and the live attenuated oral Ty21a vaccine are of assured quality and safety. The respective duration of protection is not fully established for any of these vaccines. Because of its considerable reactogenicity, the inactivated whole-cell vaccine should now be replaced by the less reactogenic and equally efficacious modern vaccines. However, for mainly economic reasons the old vaccine is still used in some parts of the world.

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Typhoid vaccines (WHO position paper)

Primary immunization with this (old inactivated whole-cell) parenteral (typhoid) vaccine consists of 2 doses given 4 weeks apart; a single booster dose is recommended every 3 years.

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Typhoid vaccines (WHO position paper)

Neither the Vi-based polysaccharide (typhoid) vaccine nor the Ty21a (typhoid) vaccine is licensed for children aged < 2 years, and with their current formulations they are not considered candidates for inclusion into large-scale vaccination programmes in this age group.

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Typhoid vaccines (WHO position paper)

For the occasional small-scale vaccination in countries of low typhoid endemicity and for individual protection of short-term visitors to highly-endemic areas, either of the 2 modern (typhoid) vaccines is recommended. It should be noted, however, that the vaccines do not provide complete protection and should not replace hygiene precautions.

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There are no contraindications (to the Vi polysaccharide typhoid vaccine) other than prior severe reaction to vaccine components. Although the vaccine is safe for HIV-infected persons, the induction of protective antibodies is directly correlated to the levels of CD4 positive T-cells.

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(W)hile waiting for improved vaccines against typhoid fever, further assessment of the protective efficacy of the currently-licensed vaccines in the youngest age groups seems warranted.

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State of the art of new vaccines: research and development

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State of the art of new vaccines: research and development

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Typhoid vaccines: WHO position paper

[WER 2008, vol. 83, 6, pp 49-60](#)
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In view of the continued high burden of typhoid fever and increasing antibiotic resistance, and given the safety, efficacy, feasibility and affordability of 2 licensed vaccines (Vi and Ty21a), countries should consider the programmatic use of typhoid vaccines for controlling endemic disease. In most countries, the control of the disease will require vaccination only of high-risk groups and populations. Given the epidemic potential of typhoid fever, and observations on the effectiveness of vaccination in interrupting outbreaks, typhoid fever vaccination is recommended also for outbreak control.

Typhoid vaccines: WHO position paper

[WER 2008, vol. 83, 6, pp 49-60](#)
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Decisions on whether or not to initiate programmatic use of typhoid vaccines should be based on knowledge of the local epidemiological situation. Important information includes data on subpopulations at particular risk and age-specific incidence rates, as well as on the sensitivity of the prevailing *S. Typhi* strains to relevant antimicrobial drugs. Ideally, cost-effectiveness analyses should be part of the planning process.

Typhoid vaccines: WHO position paper

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Immunization of school-age and/or preschool-age children is recommended in areas where typhoid fever in these age groups is shown to be a significant public health problem, particularly where antibiotic-resistant *S. Typhi* is prevalent. The selection of delivery strategy (school or community-based vaccination) depends on factors such as the age-specific incidence of disease, subgroups at particular risk and school enrolment rates, and should be decided by the concerned countries.

Typhoid vaccines: WHO position paper

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Typhoid fever vaccination may be offered to travellers to destinations where the risk of typhoid fever is high, especially to those staying in endemic areas for >1 month and/or in locations where antibiotic resistant strains of *S. Typhi* are prevalent.

Typhoid vaccines: WHO position paper

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All typhoid fever vaccination programmes should be implemented in the context of other efforts to control the disease, including health education, water quality and sanitation improvements, and training of health professionals in diagnosis and treatment.

Typhoid vaccines: WHO position paper

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The Vi polysaccharide vaccine: The vaccine is licensed for individuals aged >2 years.

Only 1 dose is required, and the vaccine confers protection 7 days after injection. To maintain protection, revaccination is recommended every 3 years. The Vi polysaccharide vaccine can be co-administered with other vaccines relevant for international travellers such as yellow fever and hepatitis A and with vaccines of the routine childhood immunization programmes.

Typhoid vaccines: WHO position paper

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There are no contraindications to the use of this vaccine other than previous severe hypersensitivity reaction to vaccine components. Although the Vi polysaccharide vaccine is safe for HIV-infected individuals, the induction of protective antibodies is directly correlated to the levels of CD4 positive T-cells.

Typhoid vaccines: WHO position paper

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The Ty21a vaccine:

The capsules are licensed for use in individuals aged >5 years; the liquid vaccine can be administered from the age of 2 years. Both versions of the vaccine are administered every other day; a 3-dose or, in Canada and USA, a 4-dose regimen is recommended for the capsules, whereas the liquid form requires 3 doses. The Ty21a vaccine may be given simultaneously with other vaccines, including live vaccines against polio, cholera, and yellow fever, or the measles, mumps and rubella (MMR) combination.

HIV/AIDS and immunosuppression

Typhoid vaccines (WHO position paper)

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It is not known whether this live attenuated vaccine (Ty21a typhoid vaccine) can cause fetal harm when administered to pregnant women. Ty21a can be administered to HIV-positive, asymptomatic individuals without risk as long as the T-cell count (CD4) is above 200/mm³.

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New Vaccines

Typhoid vaccines (WHO position paper)

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The old, heat inactivated whole-cell (typhoid) vaccine may not always be manufactured according to international standards, whereas both the parenteral Vi-based polysaccharide vaccine and the live attenuated oral Ty21a vaccine are of assured quality and safety. The respective duration of protection is not fully established for any of these vaccines. Because of its considerable reactogenicity, the inactivated whole-cell vaccine should now be replaced by the less reactogenic and equally efficacious modern vaccines. However, for mainly economic reasons the old vaccine is still used in some parts of the world.

Typhoid vaccines (WHO position paper)

[WER 2000, vol. 75, 32, pp 257-264](#)
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Neither the Vi-based polysaccharide (typhoid) vaccine nor the Ty21a (typhoid) vaccine is licensed for children aged < 2 years, and with their current formulations they are not considered candidates for inclusion into large-scale vaccination programmes in this age group.

Policy

Thermostability of vaccines

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The Vi polysaccharide (typhoid) vaccine is highly stable and does not require a cold chain even in tropical conditions. This is a distinct advantage compared with the other two typhoid vaccines in use (attenuated Salmonella typhi strains used as live oral vaccines and inactivated whole cell oral vaccines.)

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In spite of positive developments in this field, improved vaccines against typhoid fever are needed. Such vaccines should confer high levels of durable protective immunity in all age groups, preferably without the need for booster doses, and be affordable in the populations at greatest need.

Typhoid vaccines (WHO position paper)

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(W)hile waiting for improved vaccines against typhoid fever, further assessment of the protective efficacy of the currently-licensed vaccines in the youngest age groups seems warranted.

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State of the art of new vaccines: research and development

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Pregnant Women

Typhoid vaccines (WHO position paper)

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Research

Typhoid vaccines (WHO position paper)

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Schedule

Typhoid vaccines (WHO position paper)

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Travellers

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Typhoid fever vaccination may be offered to travellers to destinations where the risk of typhoid fever is high, especially to those staying in endemic areas for >1 month and/or in locations where antibiotic resistant strains of *S. Typhi* are prevalent.

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Vaccine Administration

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Typhoid vaccines: WHO position paper

All typhoid fever vaccination programmes should be implemented in the context of other efforts to control the disease, including health education, water quality and sanitation improvements, and training of health professionals in diagnosis and treatment.

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Typhoid vaccines: WHO position paper

The Ty21a vaccine:
The capsules are licensed for use in individuals aged >5 years; the liquid vaccine can be administered from the age of 2 years. Both versions of the vaccine are administered every other day; a 3-dose or, in Canada and USA, a 4-dose regimen is recommended for the capsules, whereas the liquid form requires 3 doses. The Ty21a vaccine may be given simultaneously with other vaccines, including live vaccines against polio, cholera, and yellow fever, or the measles, mumps and rubella (MMR) combination.

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Vaccine Handling

Thermostability of vaccines

The Vi polysaccharide (typhoid) vaccine is highly stable and does not require a cold chain even in tropical conditions. This is a distinct advantage compared with the other two typhoid vaccines in use (attenuated *Salmonella typhi* strains used as live oral vaccines and inactivated whole cell oral vaccines.)

[WHO/GPV/98.07](#)
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Typhoid vaccines (WHO position paper)

Recommended storage temperature (for Vi polysaccharide typhoid vaccine) is between + 2 C and + 8 C.

[WER 2000, vol. 75, 32, pp 257-264](#)
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Typhoid vaccines (WHO position paper)

(Ty21a typhoid vaccine) requires storage between + 2 C and + 8 C.

[WER 2000, vol. 75, 32, pp 257-264](#)
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