Typhoid vaccination

The typhoid vaccination inoculates against typhoid fever, which is a systemic infection caused by the Gram-negative bacillus Most salmonella types only cause local infection of the gastrointestinal tract; however, *S. typhi* is an invasive organism which can result in serious systemic infection. It is characterised by sustained fever, headache, nausea, loss of appetite, and 'pea soup' diarrhoea. Neuropsychiatric symptoms are sometimes seen. Intestinal haemorrhage and perforation may be life-threatening, as may organ failure due to sepsis.

Typhoid is spread by the faecal-oral route and is therefore associated with poor sanitation and ineffective personal hygiene. Following typhoid infection, excretion may continue for a prolonged period, allowing the disease to spread easily through communities in areas where conditions are right. Populations are particularly vulnerable in situations of natural disaster, war, population displacement and breakdown of infrastructure.

- Typhoid is a notifiable disease in the UK. Over 300 cases are notified in Britain each year. Most are contracted from people visiting friends and relatives in India, Pakistan and Bangladesh.
- Typhoid is endemic to areas of poor sanitation - eg, Africa, Southeast Asia, South Asia, Central and South America and the Caribbean.
- Avoiding contaminated water can help in preventing infection, but vaccination is recommended.
- Around 10% of people infected can excrete the bacteria for up to three months. Nearly half become long-term carriers [1] .

Available typhoid vaccines [2]

Typhoid vaccination is available on the NHS. There are three typhoid vaccines, of which two are available in the UK: the Vi polysaccharide vaccine which is given by injection, and the live attenuated oral vaccine.

The Vi polysaccharide vaccine - eg, Typherix®, Typhim Vi®

- Composed of purified polysaccharide from *S. typhi* capsule.
- The dose consists of 25 micrograms of antigen in 0.5 ml.
- It is administered subcutaneously or intramuscularly as one dose. Additional doses do not further boost antibody levels.
- A significant rise in antibody titres is detectable seven days after immunisation but maximum antibody response is reached at four weeks.
- Children aged under 2 years respond suboptimally, and the vaccine is no longer licensed for use in children under 2 years. There are few efficacy data for children under 18 months. Nevertheless, Public Health England recommends that children aged 12-24 months be offered the vaccination if travelling to high-risk areas.
- Children under 12 months of age should not usually be given the vaccine. Adults should be advised to observe standards of hygiene if travelling with young children to endemic areas.
- Re-vaccination (single dose) is recommended every three years.
- The cumulative three-year efficacy of this typhoid vaccine has been assessed in field trials and levels of 55% (95% CI 30-71%) in children and 75% (95% CI 49-87%).
- Protective antibody titres fall over time. Re-vaccination is needed if continued protection is required. It returns antibody levels to those reached after the primary immunisation.
- Because of the limited protection offered by the vaccine, scrupulous attention to personal, food and water hygiene must be emphasised to travellers.
- Polysaccharide typhoid vaccine is also available as a combined vaccination with hepatitis A, for adults and for adolescents aged 15 years and over. If boosted within 6-12 months of the first dose, it confers immunity against hepatitis A for ten years, but against typhoid for only three years.

The Ty21a vaccine - eg, Vivotif®

- A live attenuated strain of *S. typhi* and it is an oral typhoid vaccine.
- When administered as three doses on alternating days (0, 2, 4), immunity is achieved seven days after the last dose.
- A repeat, full three-dose course is recommended every year in endemic areas.
- Oral typhoid vaccine is given as enteric-coated capsules and is licensed from 5 years of age.
- The capsule must be swallowed whole, without chewing, with cold or lukewarm water, as soon as possible after placing it in the mouth.
- More immunogenic oral vaccines are being researched currently, as protective efficacy of the vaccine can vary.
- A liquid formulation was shown to have 79% efficacy for up to five years after vaccination in a population of Chilean schoolchildren aged 5-19 years [3] .

Inactivated whole-cell vaccine

- This has been largely superseded in the UK, but is still available in developing countries.
- It is an injectable, killed, whole-cell typhoid vaccine containing heat-inactivated phenol-preserved *S. typhi* organisms.
- A parenteral vaccine of two doses, four weeks apart.
- The three-year efficacy rates are thought to be about 70%.
- A high percentage of recipients have fever and systemic reactions so for this reason this vaccine is no longer used in the UK [4] .

Indications for typhoid vaccination

- Travellers to areas where typhoid is endemic, especially those visiting or staying with local people.
- Travellers to endemic areas, especially where frequent or prolonged exposure to poor sanitation and food hygiene is likely.
- Laboratory personnel whose work may expose them to *S. typhi*.

Typhoid vaccine schedule

- A single dose of inactivated typhoid vaccine should be given two weeks before travel, to allow protection to develop fully.
- It can be administered with other inactive vaccines - eg, tetanus, poliomyelitis, hepatitis A, meningococcal meningitis, rabies, Japanese B encephalitis and tick-borne encephalitis. It may also be administered at the same time as live vaccines.
- Injectable typhoid vaccines given simultaneously should be given at different sites, at least 2.5 cm apart, and preferably in different limbs.
- They should be given with separate syringes at separate sites.
- The date, title and batch number should be recorded in the recipient's notes. If more than one vaccine is given, the sites of each should also be recorded.
- Booster vaccines are required after three years. The combined vaccine requires booster hepatitis A after 6-12 months, but can be given up to 36 months later.
- Typhoid vaccine is not 100% effective. This is particularly so if exposed to large doses of *S. typhi*. Attention should be paid to personal, food and water hygiene at all times.

Interactions

The oral vaccine Vivotif® is inactivated when antibacterials and some antimalarials are taken at the same time.

- Antibacterials should not be taken for the three-day period before and the three-day period following oral vaccination.
- Mefloquine: the oral vaccination should ideally be completed at least three days before the first dose of mefloquine. If this is not possible, mefloquine should be avoided for at least twelve hours before or after oral typhoid.
- Other antimalarials: oral typhoid vaccination Vivotif® should be completed at least three days before the first dose of the antimalarial.

- Atovaquone with proguanil may be given concomitantly with oral typhoid vaccine Vivotif®.

Contra-indications to typhoid vaccine

- HIV-positive individuals should not receive the oral typhoid vaccine Vivotif®.
- The effectiveness of Typhim Vi® may be reduced by immunosuppressive treatment or immunodeficiency. In such cases it is recommended to postpone typhoid vaccination until the end of the disease or treatment.
- Nevertheless, vaccination (with Typhim Vi®) of subjects with chronic immunodeficiency such as HIV infection is recommended even if the antibody response might be limited.
- Oral typhoid vaccination Vivotif® is contra-indicated in acute gastrointestinal illness.
- Anaphylaxis:
    - The typhoid vaccine should not be given to those who have had a confirmed anaphylactic reaction within 72 hours of a previous dose of the same vaccine [5] .
    - This also applies if there has been confirmed reaction to a constituent of the vaccine; both combined and single typhoid vaccines contain traces of neomycin.
- Other severe adverse reactions. This means an extensive area of redness and swelling affecting a large area of the arm or leg, accompanied by a fever of 39.5°C or higher, within 48 hours of the injection.
- Accidental intradermal injection can cause a severe local reaction.

The following **DO NOT** contra-indicate typhoid vaccination:

- A personal or family history of asthma, allergy, hay fever or eczema.
- Febrile convulsions - advice regarding post-immunisation pyrexia should be given before immunisation.

- Prematurity.
- Stable neurological conditions - eg, cerebral palsy, Down's syndrome or epilepsy.
- Contact with infectious disease.
- Treatment with antibiotics or local corticosteroids.
- A child being breastfed.
- Being underweight.
- Taking replacement corticosteroids.

Special circumstances

- Acute illness - postpone immunisation until recovered[5] . Minor infections, without fever or systemic upset, are not reasons to postpone.
- Pregnancy - the oral vaccine should be avoided, but termination of pregnancy following inadvertent use is not recommended. There is no evidence of risk from the injectable (inactivated) vaccine.
- Immunosuppression - oral typhoid vaccination should be postponed until at least three months after stopping high-dose systemic corticosteroids, six months after stopping other immunosuppressant drugs or generalised radiotherapy, and twelve months following bone marrow transplantation.
- Evolving neurological problems (eg, poorly controlled epilepsy or neurological problems with no known cause) - immunisation should be avoided until the condition is stable.

General advice

- Patients visiting friends and relatives in India, Pakistan and Bangladesh are least likely to attend General Practice for vaccination before travel. They may benefit from targeted opportunistic health promotion strategies informing them of vaccination and hygiene practices while abroad[6] .
- Reassure patients that the overall risk of contracting infectious diseases from abroad is very low if sensible precautions are taken.

- Risk of infection varies according to region visited, length of stay and time of year of travel, and age and general health of the traveller. Some people may be more susceptible to infection.
- Remind travellers that typhoid immunisation confers only partial protection. At the same time remind them that the most common infectious diseases cannot be prevented by vaccination - eg, traveller's diarrhoea, malaria and sexually transmitted infections. Other sensible precautions are also necessary.

Dr Mary Lowth is an author or the original author of this leaflet.

Further reading

- Travel Health Pro; National Travel Health Network and Centre (NaTHNaC)
- Neupane DP, Dulal HP, Song J; Enteric Fever Diagnosis: Current Challenges and Future Directions. Pathogens. 2021 Apr 1;10(4). pii: pathogens10040410. doi: 10.3390/pathogens10040410.

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