Use of Typhoid fever vaccine

The burden of typhoid infections remains high in many parts of the world and the emergence and spread of antimicrobial resistant strains of S. Typhi is increasing. In February 2018, WHO recommended use of available conjugate (TCV) vaccine for prevention and control, and to prevent emergence of drug resistant strains of the disease, especially in high burden countries.

Editorial note

Typhoid fever is an acute generalized infection, caused by a highly virulent and invasive enteric bacterium—Salmonella Typhi (S. Typhi). Typhoid fever is an important public health problem in many low and middle income countries. Global estimates of typhoid fever burden shows more than 20 million cases and 0.15 million deaths annually. The majority of cases occur in South/South-East Asia, and sub-Saharan Africa.

Increasing prevalence of typhoid fever in high burden countries is mainly sustained by inadequate safe water and poor sanitation infrastructure. Further, uncontrolled urbanization in poor urban slums, and extremes of weather such as frequent flooding due to climate change have only served to exacerbate the problems of poor water and sanitation in these high typhoid burden countries.

Emergence of typhoid resistance to antibiotics commonly used in treatment of the disease is increasing in high burden countries. This poses significant threat to prevention and control of the disease. It also underscores the urgent need for strengthening alternative prevention and control measures including environmental interventions such as improvement of water and sanitation infrastructure, and vaccination interventions.

Regarding use of typhoid vaccine for prevention and control, three types of typhoid vaccines have been licensed (see table). Among these, typhoid conjugate vaccines (TCV) is preferred for all age groups in view of its improved immunological properties, suitability for use in younger children and longer duration of protection.

Characteristics of Typhoid fever vaccines

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Typhoid conjugate vaccine (Typbar-TCV®)</th>
<th>Unconjugated Vi polysaccharide vaccine</th>
<th>Live attenuated Ty21a vaccine</th>
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</thead>
<tbody>
<tr>
<td><strong>Composition</strong></td>
<td>25 µg of purified Vi capsular polysaccharide conjugated to TT</td>
<td>25 µg of purified Vi capsular polysaccharide</td>
<td>2 to 6 × 10⁹ CFU of Ty21a (attenuated Ty2 strain of S. Typhi)</td>
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<tr>
<td><strong>Route and dose</strong></td>
<td>IM, 1 dose</td>
<td>IM/SC, 1 dose</td>
<td>Oral, 3 (4 in USA and Canada) doses every second (alternate) day</td>
</tr>
<tr>
<td><strong>Presentation</strong></td>
<td>Liquid</td>
<td>Liquid</td>
<td>Enteric-coated capsules</td>
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<tr>
<td><strong>Recommended target age for vaccination</strong></td>
<td>Adults and children ≥6 months to ≤45 years of age</td>
<td>Adults and children ≥2 years of age</td>
<td>Adults and children older than 6 years</td>
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</table>

Typhoid fever vaccines: few facts

**Vaccine safety:** No safety signals were identified for Typbar-TCV based on the evaluation of immunogenicity and safety during the trials.

**Special populations:** Pregnant and lactating women – There are no data on safety and immunogenicity of any of the 3 types of typhoid vaccines in pregnant and lactating women. Immunocompromised and HIV-infected persons – There are currently no data on TCV use in this population.

**Co-administration:** Currently available data for these vaccines shows that, they can be co-administered with other routine and need based vaccines; as MMR, yellow fever, polio, cholera and with routine childhood vaccines.

**Cost-effectiveness:** Available modelling data indicate that routine vaccinaton of infants with TCV plus catch-up vaccination of older cohorts provides additional benefits towards routine vaccinaton of infants with TCV and provision of additional protective benefit of reducing extensive use of antibiotics and slowing down of emergence and spread of antibiotic resistant strains.

Reactive use of typhoid vaccine in response to confirmed outbreaks of typhoid fever can be critical in containing upsurge of cases. Furthermore, by reducing the number of susceptible individuals and occurrence of new cases of the disease, the use of the vaccine has the added benefit of reducing extensive use of antibiotics and slowing down of emergence and spread of antibiotic resistant strains.

However, data on the use of typhoid vaccine for outbreak control are very limited. Priority should be given to generating data that will further support typhoid vaccination policy and immunization programmes. This include safety and immunogenicity in special populations such as malnourished children, immuno-compromised persons, and pregnant women (see above); duration of protection after a single dose of TCV and the potential need for revaccination.

Despite its value, use of typhoid vaccine should be part of a comprehensive typhoid prevention and control strategy that should also include behavioral interventions, improvement of water safety, and better sanitation infrastructure.

Update on outbreaks in the Eastern Mediterranean Region

**MERS in Saudi Arabia:** cholera in Somalia; cholera in Yemen; Polio in Pakistan.

Current public health events of international concern [cumulative N* of cases (deaths), CFR %]

- **Avian influenza:** 2006-2017
  - Egypt (A/H5N1) [359 (122), 34%]
  - Egypt (A/H9N2) [4 (0)]

- **Ebola virus disease (EVD):** 2018
  - Democratic Republic of Congo (DRC) [52 (22), 42.3%]

- **Lassa fever:** 2018
  - Nigeria [446 (117), 26.2%]
  - Liberia [84 (22), 26.1%]

- **Cholera:** 2017-2018
  - Somalia [3 547(23), 0.6%]
  - Yemen [1 098 737 (2 288), 0.2%]
  - Tanzania [1 856 (36), 1.9%]

- **Diphtheria:** 2018
  - Yemen [1 778 (93), 5.2%]
  - Bangladesh [6 887 (42), 0.6%]

- **MERS:** 2012-2018
  - Saudi Arabia [1 833 (715), 39.0%]

- **Yellow Fever:** 2017-2018
  - Brazil [1 266 (415), 32.7%]