Typhoid

Typhoid fever is a systemic infection caused by *Salmonella* Typhi, usually through ingestion of contaminated food or water. The acute illness is characterized by prolonged fever, headache, nausea, loss of appetite, and constipation or sometimes diarrhoea. Symptoms are often non-specific and clinically non-distinguishable from other febrile illnesses. However, clinical severity varies and severe cases may lead to serious complications or even death. It occurs predominantly in association with poor sanitation and lack of clean drinking water. According to the most recent estimates, between 11 and 21 million cases and 128 000 to 161 000 typhoid-related deaths occur annually worldwide. A similar but often less severe disease, paratyphoid fever, is caused by *Salmonella Paratyphi* A and B (or uncommonly Paratyphi C).

Three typhoid vaccines are currently recommended by WHO for control of endemic and epidemic typhoid fever:

- an injectable typhoid conjugate vaccine (TCV), consisting of Vi polysaccharide antigen linked to tetanus toxoid protein licensed for children from 6 months of age and adults up to 45 years of age;
- an injectable unconjugated polysaccharide vaccine based on the purified Vi antigen (known as Vi-PS vaccine) for persons aged two years and above; and
- an oral live attenuated Ty21a vaccine in capsule formulation for those over six years of age.

Among the available typhoid vaccines, TCV is preferred at all ages for routine programmatic use in view of its improved immunological properties, suitability for use in younger children and expected longer duration of protection. WHO further recommends that 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.

Gavi, the Vaccine Alliance announced in November 2017 funding support to eligible countries for programmatic use of TCV starting from 2019. There is currently one WHO prequalified TCV product available on the global market. Reviews of the available safety data for TCV by the Global Advisory Committee on Vaccine Safety (GACVS) concluded that the safety profile of the vaccine is reassuring, there are no signals of serious adverse events to date, and no theoretical safety concerns for TCV use.

Interim analysis of the ongoing Typhoid Vaccine Acceleration Consortium trial in Nepal, using the WHO-prequalified TCV, showed a protective efficacy of 1 dose of TCV as 81.6% (95% CI 58.8-91.8) against blood-culture confirmed typhoid fever after 1 year of follow up. This randomized control trial of 20,000 children (approx. 10,000 each in the TCV arm and the control MenA vaccine arm) provides the first efficacy results for a licensed TCV in an endemic population. Furthermore, seroconversion – at least 4-fold increase in Vi IgG level 28 days after vaccination - was reported in 99% of the TCV recipients versus 2% of the control group (in an immunogenicity subgroup of 1343 children). Safety data reported from this trial support the earlier GACVS conclusions and provide further reassuring evidence for TCV use in typhoid endemic settings.