### Summary of Key Points

# Tetanus vaccines: WHO position paper – February 2017



### **Background**

- Tetanus is an acute infectious disease caused by toxigenic strains of the bacterium Clostridium tetani (C. tetani).
- The spores of C. tetani are present in the environment irrespective of geographical location; they enter the body through contaminated skin wounds or tissue injuries including puncture wounds.
- The majority of reported tetanus cases are birth-associated, occurring in low income countries among insufficiently vaccinated mothers and their newborn infants, following unhygienic deliveries and abortions and poor postnatal hygiene and cord care practices.
- The disease remains an important public health problem in many parts of the world where immunization programmes are suboptimal, particularly in the least developed districts of low income countries.



### **Disease and Diagnosis**

- Incubation period:
  - In non-neonatal tetanus varies between 3 and 21 days after infection.
  - In neonatal tetanus, symptoms usually present 3 to 14 days, averaging
     7 days, after birth in 90% of cases.
- Characteristic features of the disease are muscular spasms.
- Case-fatality rates vary from 10% to 70% depending on treatment, age and general health of the patient. Among patients in the youngest and oldest age groups without intensive care, case-fatality rates approach 100%.
- The diagnosis of tetanus is primarily based on clinical features and does not depend on laboratory confirmation.



#### **Treatment**

- Management of tetanus cases:
  - Human tetanus immune globulin (TIG).
  - Antibiotics.
  - Benzodiazepines.
  - Supportive care.
- Wound management for prevention of tetanus:
  - Tetanus prophylaxis depends on the nature of the lesion and patient's immunization history. It may include TIG and tetanus toxoid (TT)- containing vaccines (TTCV).
  - All wounds should be cleaned and debrided promptly and appropriately.



#### **Tetanus toxoid vaccines**

- TT vaccine was first produced in 1924 and used extensively for the first time among soldiers during World War II. Since then, immunization programmes using TTCVs have been highly successful in preventing maternal and neonatal tetanus (MNT) as well as injury-associated tetanus.
- TT is available as a single-antigen vaccine and in combination vaccines to protect against other vaccine-preventable diseases including diphtheria, pertussis, poliomyelitis, hepatitis B and illness caused by *Haemophilus influenzae* type b (Hib).



### Immunogenicity, Efficacy and Effectiveness Maternal Immunization

- A non-randomized controlled trial reported vaccine effectiveness during pregnancy to prevent neonatal tetanus:
  - 94% for 3 doses;
  - 65% for 2 doses;
  - No effect for 1 dose.
- Observational studies have confirmed suboptimal seroconversion following a single dose and that protection conferred by tetanus vaccination is incremental.
- A systematic review concluded through a meta-analysis that the vaccine effectiveness of 2 or more properly timed doses of TT given to pregnant women or women of reproductive age (WRA) against neonatal tetanus mortality was 94% (95%, CI: 80–98%).



# Immunogenicity, Efficacy and Effectiveness Infant, children and adolescent immunization

- A 3-dose primary series induces protective immunity in almost 100% of vaccinated infants.
- Although tetanus antibody levels are high after 3 primary TTCV doses in infancy, they decline over time.
- Data from serological studies suggest that a primary series of 3 TTCV doses in infancy plus a booster during the second year of life will provide 3–5 years of protection.
- A further booster dose (e.g. in early childhood) will provide protection into adolescence, and another booster during adolescence will induce immunity that lasts through much of adulthood, thus protecting women through their childbearing years.
- Protective immunity persisting for 20–30 years after a sixth dose of TTCV has been suggested in several studies.



### Vaccine safety

- TT used alone or in various fixed combinations is considered very safe. Mild local reactions such as pain and erythema are common, however, more serious reactions are rare.
- TTCVs are considered safe for pregnant women. There is no evidence of adverse pregnancy outcomes or risk to the fetus from the vaccination during pregnancy with TTCVs.
- TTCVs are considered safe and suitable for use in HIVinfected and immunocompromised persons.



#### **WHO Position**

- All children worldwide should be immunized against tetanus.
- The aims of tetanus vaccination are (1) to achieve global elimination of MNT and (2) to ensure lifelong protection against tetanus.
- Every country should seek to achieve early and timely infant vaccination and maintain high coverage of a complete 3-dose primary series plus 3-dose booster series by the time of adolescence.
- In countries where MNT elimination (MNTE) has not yet been achieved, and in areas where MNT remains a public health concern, special attention is needed to ensure immunization of WRA.



### WHO Position Primary vaccination and booster doses in children

- WHO recommends a 3-dose primary series:
  - The first dose of TTCV should be administered as early as 6 weeks of age.
  - Subsequent doses should be given with a minimum interval of 4 weeks between doses.
  - The third dose of the primary series should ideally be completed by 6 months of age.
- In order to provide lifelong protection, WHO recommends 3 TTCV booster doses, ideally, with at least 4 years between booster doses. These should be given at:
  - 12–23 months of age;
  - 4–7 years of age;
  - 9–15 years of age.



# WHO Position Catch-up schedule in adolescents and adults

- Other tetanus prevention efforts are also needed, including education on clean wound care and on the importance of following standard surgical protocols.
- Opportunistic catch-up:
  - Delivery of TTCV with other vaccination campaigns such as HPV vaccination.
  - During routine entry into military services.
  - Along with voluntary medical male circumcision services.



# WHO Position Vaccinating Pregnant Women

- Pregnant women and their newborn infants are protected from birth-associated tetanus if the mother received 6 doses (documented by card, immunization registry and/or history).
   Vaccination history should be verified in pregnant women.
- Following should be applied in countries where MNT remains a public health problem:
  - Pregnant women for whom reliable information on previous tetanus vaccinations is not available should receive at least 2 doses of TTCV, preferably Td, with an interval of at least 4 weeks between doses and the second dose at least 2 weeks before the birth. To ensure protection for a minimum of 5 years, a third dose should be given at least 6 months later. A fourth and fifth dose should be given at intervals of at least 1 year, or in subsequent pregnancies, in order to ensure lifelong protection.
  - Pregnant women who have received only 3 doses of TTCV during childhood without booster doses should receive 2 doses of TTCV at the earliest opportunity during pregnancy with a minimal interval of 4 weeks between doses and the second dose at least 2 weeks before giving birth. To provide lifelong protection, a sixth dose would be needed at least 1 year after the fifth dose.
  - Women who received 4 TTCV doses during childhood or pre-adulthood need only 1 booster dose, which should be given at the first opportunity. To provide lifelong protection, a sixth dose would be needed at least 1 year after the fifth dose.



# WHO Position Vaccinating Pregnant Women

- "High-risk" approach for countries not having achieved MNTE:
  - Targeting of all WRA in high-risk districts.
  - 3 campaign-style vaccination rounds to provide 3 doses of TTCV, irrespective of previous vaccination status (interval of at least 4 weeks between doses 1 and 2, and at least 6 months between doses 2 and 3).
- Ensuring clean delivery and cord care practices are important complementary activities to prevent maternal and neonatal tetanus.



# WHO Position Immunization in the case of injury

- Although adequate vaccination should provide sufficient protection against tetanus, physicians may give a dose of TTCV, preferably Tetanus-diphtheria (Td, low-dose diphtheria toxoid), in addition to other preventive measures if the injury is severe or the patient's previous tetanus immunization history is unreliable.
- The immunization schedule should be completed as soon as possible for those who have not received all required doses.
- In addition, TIG may be needed for prophylaxis in cases of dirty wounds and for incompletely immunized patients.



# WHO Position Choice of combination vaccines

- WHO recommends to shift from the use of single-antigen TT to combinations containing diphtheria toxoid, pediatric diphtheria-tetanus (DT) formulation or Td vaccines.
- WHO continues to support the use of Td for maternal immunization.



# WHO Position Vaccine co-administration

- All vaccines that are age-appropriate and consistent with the child's prior immunization history should be administered simultaneously.
- When 2 or more vaccines are given during the same visit, they may be injected in different limbs. When 3 vaccines are given, 2 can be injected in the same limb and the third should be injected in the other limb.



# WHO Position Health-care workers and Travellers

 Health-care workers and travellers are generally not at special risk of tetanus. They should follow the vaccine recommendations for the general population and ensure they are up to date with their tetanus vaccinations.



# WHO Position Surveillance

- Improved national surveillance and reporting systems, with district-level data analysis, are essential for rational planning of immunization efforts, including high-risk approaches in support of MNTE.
- The need for improved surveillance systems is underscored by the absence of reliable global estimates of non-neonatal tetanus cases and deaths including maternal tetanus.

# For more information on the WHO Tetanus vaccines position paper, please visit the WHO website:

www.who.int/immunization/documents/positionpapers

