Summary of Key Points

WHO Position Paper on BCG Vaccine, February 2018

World Health Organization

Introduction

- This position paper replaces the 2004 WHO position paper on Bacille Calmette-Guérin (BCG) vaccine and the 2007 WHO revised BCG vaccination guidelines for infants at risk for human immunodeficiency virus (HIV) infection.
- It incorporates recent developments in the field of tuberculosis (TB), provides guidance on the immunization of children infected with HIV, re-emphasizes the importance of the BCG birth dose and outlines the urgent need for research in the development of new vaccines
- This position paper also includes recommendations for the prevention of leprosy.

Background

- **Tuberculosis (TB)** is caused by the bacterium Mycobacterium tuberculosis, which spreads via airborne droplets when individuals infected with active TB cough. HIV infection, malnutrition, tobacco use, and diabetes are predisposing factors for TB.

- **Multi-drug resistant TB (MDR-TB)** is caused when bacteria do not respond to the 2 most powerful first line anti-TB drugs.

- Globally, 1.7 billion people are estimated to be infected with *M. tuberculosis* and in 2016, 1.7 million people died from TB, including 400,000 among people infected with HIV. In children, TB most commonly occurs in those aged <5 years.

Background

- **Leprosy** is caused by *Mycobacterium leprae* and mainly affects the skin and peripheral nerves. More than 200,000 cases of Leprosy were reported in 2016, including 12,819 new cases with visible deformities.

- **Buruli ulcer** is caused by *Mycobacterium ulcerans* and In 2016, 1,864 new cases of Buruli ulcer were reported from 11 countries.

Vaccines

- Bacillus Calmette-Guérin (BCG) vaccines continue to be the only vaccines in use for prevention of TB.
  - BCG is a live attenuated bacterial vaccine derived from M. bovis.
  - Several BCG vaccines, based on different strains, are available worldwide.
  - BCG has demonstrated significant effectiveness, however protection has not been consistent across all forms in all age groups
- BCG has also shown effectiveness in preventing leprosy (RR from 20-80%), Buruli ulcer (RR of 50% in Africa region) and other non-tuberculosis mycobacterial (NTM) infections.
- Several new vaccine candidates are in development to protect against TB and Leprosy.

Vaccine Safety

- About 95% of BCG vaccine recipients experience a reaction at the injection site that heals within 2-5 months leaving a superficial scar, this is considered normal.
- Adverse events following (AEFI) are dependent on the strain used, number of viable bacilli in the batch and variation in injection technique.
- Disseminated BCG disease may occur between 1.56 and 4.29 cases per million doses and can have an incidence of up to 1% of infants and HIV-infected children.

Vaccine Effectiveness

- A systematic review of 12 cohort studies found protection against Pulmonary TB (PTB) ranged from 44-99% in 11 studies and no protection in one study.

- Protection varies by age:
  - Neonatal vaccination provided 82% protection against TB (RR 0.18, 95% CI: 0.15–0.21).
  - In school-age TST-negative children BCG was 64% protective against PTB (RR 0.36, 95% CI: 0.30–0.42).

- A systematic review of 5 studies found BCG was effective in preventing leprosy (RR 0.45 CI: 0.34–0.56) however there was considerable heterogeneity (I^2=98%)

WHO Position

- BCG vaccination is recommended in countries or settings with a high incidence of TB and/or high leprosy burden as well as where Buruli ulcer occurs.
- A single dose should be given to all healthy neonates at birth. If the vaccine cannot be administered at birth, it should be given at the earliest opportunity thereafter.
- Countries with low incidence of TB or leprosy may choose to selectively vaccinate high-risk neonates.
- Countries with declining rates of TB are encouraged to evaluate the epidemiology of TB and leprosy and consider a switch to selective risk group vaccination.

WHO Position

- Standard dose of BCG vaccine is an intradermal injection of 0.05 mL of the reconstituted vaccine for infants <1 year, and 0.1 mL for those >1 year.
  - BCG multi-dose vials should be used despite any wastage.
- BCG vaccine can be safely co-administered with other routine childhood vaccines including the hepatitis B birth dose.
- Revaccination is not recommended even if the tuberculin skin testing (TST) reaction or result of an IFN-ɣ release assay (IGRA) is negative.

WHO Position

Special Populations

- BCG is recommended for unvaccinated, TST-negative or IGRA-negative school children for those coming from or moving to high incidence/burden settings, as well as older groups at risk through occupational exposure.
- As a precaution, BCG vaccination is not recommended during pregnancy.
- BCG vaccination is contraindicated for immunocompromised persons and for patients undergoing immunosuppressive treatment.

WHO Position

- Children who are HIV-infected should not receive BCG vaccination.
- HIV-infected individuals, including children, who are receiving anti-retroviral therapy (ART), are clinically well and immunologically stable should be vaccinated.
- Neonates born to women of unknown HIV status should be vaccinated.

WHO Position

- Neonates with unknown HIV status born to HIV-infected women should be vaccinated if they have no clinical evidence suggestive of HIV infection, regardless of whether the mother is receiving ART
- Neonates with HIV infection should delay BCG vaccination until ART has been started and are immunologically stable.
- Neonates born to mothers with pulmonary TB should receive BCG vaccination if they are asymptomatic, have no immunological evidence of TB and are HIV-negative

Future Research Needs

- Further reporting of TB cases is needed to better understand the safety and effectiveness of BCG vaccination at different ages and in different populations, especially of HIV-infected children including those receiving ART.
- Further evidence of programmatic strategies such as timeliness and wastage is needed.
- Development of additional vaccines that provide greater protection for all ages and populations.
  - More effective vaccines against leprosy is needed

For more information on the WHO BCG position paper, please visit the WHO website:

www.who.int/immunization/documents/positionpapers

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