Summary of the WHO Position Paper on BCG vaccines: WHO position paper – February 2018

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 tuberculosis (TB) field, provides revised guidance on the immunization of children infected with HIV, and re-emphasizes the importance of the birth dose. This position paper also includes recommendations for the prevention of leprosy.

Background

Tuberculosis

The causative agent of TB is the bacterium *Mycobacterium tuberculosis.* In children, TB occurs most commonly in those aged <5 years. While TB typically affects the lungs, it may also affect other sites of the body (extrapulmonary TB). 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.

Leprosy

Leprosy is caused by *Mycobacterium leprae* and mainly affects the skin and peripheral nerves, if it presents with deformities it can result in lifelong disability. Cases tend to occur in clusters and mainly affect adults but can also occur in children. More than 200 000 cases were reported in 2016, including 12 819 new cases with visible deformities.

Buruli ulcer and other non-tuberculous mycobacterial (NTM) infections

Buruli ulcer is caused by *Mycobacterium ulcerans*. In 2016, 1 864 new cases of Buruli ulcer were reported from 11 countries. Other non-tuberculous mycobacterial infections can cause a wide spectrum of diseases and are treated by combinations of antibiotics.

Bacille Calmette-Guérin (BCG) vaccines

BCG is a live attenuated bacterial vaccine derived from *M. bovis*. Several BCG vaccines, based on different strains, are available worldwide. While BCG has demonstrated significant effectiveness, protection has not been consistent against all forms in all age groups. BCG has also shown effectiveness in preventing leprosy (RR from 20-80%) and Buruli ulcer (RR of 50% in Africa region).

WHO Recommendations

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. Additionally, 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.

The standard dose of BCG vaccine is and intradermal injection of 0.05 mL of the reconstituted vaccine for infants <1 year, and 0.1 mL for those >1 year. BCG vaccine can be safely co-administered with other routine childhood vaccines including the hepatitis B birth dose. BCG multi-dose vials should be used despite any wastage. Studies have shown minimal or no evidence of any additional benefit of repeat BCG vaccination against TB or leprosy. Therefore, revaccination is not recommended even if the tuberculin skin testing (TST) reaction or result of an IFN-ɣ release assay (IGRA) is negative.

Vaccination of older age groups, special populations, contraindications and precautions
Older age groups -. BCG vaccination of unvaccinated, TST-negative or IGRA-negative school children is recommended for those coming from or moving to high incidence/burden settings, as well as older groups at risk through occupational exposure.

Pregnant - As a precaution, BCG vaccination is not recommended during pregnancy.

Immunocompromised and HIV-infected person - BCG vaccination is contraindicated for immunocompromised persons and for patients undergoing immunosuppressive treatment. Infants exposed to immunosuppressive treatment in utero or via breastfeeding should not receive BCG.

Children who are HIV-infected should not receive BCG vaccination. However, if HIV-infected individuals, including children, are receiving anti-retroviral therapy (ART), are clinically well and immunologically stable they should be vaccinated with BCG.

Neonates born to women of unknown HIV status should be vaccinated. However, 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. Additionally, neonates with HIV infection should delay BCG vaccination until ART has been started and are immunologically stable.

Neonates born to mothers with pulmonary TB – BCG vaccination is recommended if an infant is asymptomatic, has no immunological evidence of TB, and is HIV-negative.

Further Monitoring and Research Needs

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, reporting of TB cases is encouraged. Additionally, further evidence is needed on programmatic strategies of BCG vaccination, such as timeliness of vaccination and wastage.

There is also a need for development of vaccines that provide greater protection than BCG on all forms of TB for all age groups including persons infected with HIV. The development of more effective vaccines against leprosy is also encouraged.