Tetanus Toxoid Immunization

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Neonatal tetanus was estimated to be responsible for over half a million neonatal deaths globally in early 1980s. Estimates suggest that these deaths have been reduced, but that still some 130 000 babies died around the year 2004 from this very preventable disease. Despite this impressive progress, two global elimination target dates have been missed, most recently in 2005, to a rate of ‘less than 1 case per 1000 livebirths in every district of every country’. Most of the remaining deaths from neonatal tetanus occur in a limited number of large countries with low coverage of facility births and tetanus toxoid immunization, such as India and Nigeria.

Neonatal tetanus is an acute disease presenting initially with loss of ability to suck, followed by generalized rigidity and painful muscle spasms as the disease progresses. The disease is caused by tetanus toxin produced by Clostridium tetani. The commonest port of entry for the tetanus spores is the unhealed umbilical cord. Most (90%) cases of neonatal tetanus develop symptoms during the first 3 days to 14 days of life with the majority presenting at 6 days to 8 days. Mortality tends to be very high: in the absence of medical treatment, case fatality approaches 100%; with hospital care 10% to 60% of NT cases die, depending on the availability of intensive care facilities. Clearly, prevention measures for tetanus are more effective than case management even if full intensive care were available, and certainly much more cost-effective.

Even before tetanus vaccine was available, neonatal tetanus became increasingly rare in most of Europe and North America through hygienic childbirth practices and cord care. The advent of the vaccine resulted in further reduction in high-income countries, and also opened opportunities for progress in low-income settings. The vaccine is an inactivated toxin (toxoid) that was first produced in 1924. It became commercially available in 1938 and was successfully used extensively during the Second World War. In the late 1940s, it was combined with diphtheria and pertussis vaccines to produce the DTP triple vaccine used in many childhood immunization programmes. A trial in Papua New Guinea published in 1961 was the first demonstration that use of two or more doses of tetanus toxoid during pregnancy could prevent neonatal tetanus. In the mid-1970s, tetanus toxoid vaccination of pregnant women was included in the WHO’s Expanded Program on Immunization.

Concentrations of tetanus anti-toxin exceeding 0.1 IU/ml to 0.15 IU/ml, measured by standard (indirect) enzyme linked immunosorbent assay, are considered protective. These are achieved 24 weeks after the second dose of tetanus toxoid in 90% of adults. Although immunity wanes over time, more than three-quarters of women will maintain ‘protective levels’ for 3 years. A third dose given 6 months to 12 months after the first two doses increases both the level of neutralizing IgG antibody and duration of immunity for at least an additional 5 years. Additional doses given at least 1 year apart further prolong duration of protection; after the fifth dose, protective antibody levels last for at least 20 years.

Tetanus antitoxin is actively transported by the placenta from an immunized mother to her fetus, providing passive protection against tetanus during the neonatal period and the following month or two of life. Maternal and neonatal tetanus antibody concentrations at the time of delivery are usually similar. However, placental antibody transfer may be reduced in the presence of maternal malaria and HIV infections.

While tetanus immunization is now a standard practice, the evidence base to support the mortality effect estimate for use in the LiST tool is limited, mainly because the vaccine was accepted for practice before the era of randomized controlled trials. The Cochrane review (‘Vaccines for women to prevent neonatal tetanus’) includes two trials, one from Columbia in 1966 and the second from Bangladesh in 1980.