Tetanus – A Tale of 50 Years

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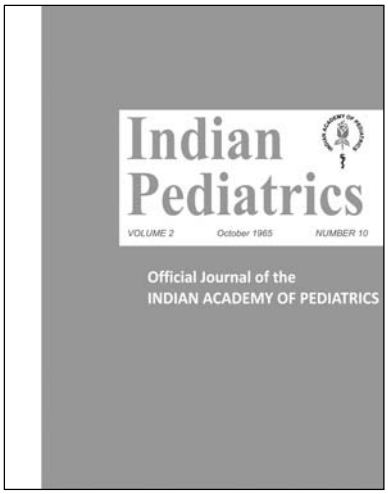
October 1965 issue of *Indian Pediatrics* comprised of 41 pages, including five original research papers. Amongst these, we decided to review the article on "Tetanus in infancy and childhood" [1], considering that patients with tetanus still continue to be admitted at Indian hospitals despite free availability of a highly efficacious and safe vaccine. We also present the current status of tetanus epidemiology and the changes in its management since publication of the reviewed research paper 50 years ago.



THE PAST

The study by Saxena, *et al*. [1], published in October 1965 issue of Indian Pediatrics, is a retrospective review of records of admitted cases at PBM group of hospitals at Bikaner from January 1945 to June 1965. The authors have presented a profile of 175 tetanus cases in infancy and childhood (age 1 mo to 12 y, excluding neonatal tetanus), and assessed factors associated with mortality. The cases were classified into five grades depending upon presence of five severity criteria that included: (*i*) presence of lockjaw, (*ii*) presence of spasms, (*iii*) incubation period of ≤ 7 days, (*iv*) time interval between the appearance of first symptom and spasm of < 48 hours, and (*v*) axillary temperature of >99 ^{o}F within 24 hours of admission. The cases were categorized into grades I to V depending upon number of criteria present. Tetanus constituted 0.5% of the pediatric admissions in the reported period. A mortality rate of 32.2% was observed. Majority (44.4%) of cases belonged to clinical grade IV while the highest mortality (62.5%) was observed in grade V. There were two peaks observed – at ages 4 and 10 years – corresponding to periods of increased susceptibility to infection and trauma. In more than one-third of cases, the probable source of infection was unknown, while trauma and ear infection were responsible for 34.8% and 23.6% cases, respectively. The mortality rate was highest (66.6%) in cases where the focus of injury/ infection was the face, neck and scalp, and lowest in the group with otorrhea (26.3%). The average incubation period – recorded in 78 cases where the information was available – was 13.4 days with maximum deaths observed in cases with incubation period < 7 days. Besides short incubation period, onset of spasms within 24 hours of illness, severe spasms and temperature >99 ^{o}F within 24 hours of admission were the factors associated with grave prognosis. Most (96.8%) deaths occurred within first week of admission. No significant difference in mortality was recorded with different dosage schedules of anti-tetanus serum (ATS) while the use of penicillin was associated with improved outcome.

Historical background and past knowledge: After Hippocrates' primeval description of tetanus in medical literature, no significant advancement in understanding occurred till the early 19th century [2]. The causative agent of tetanus was identified by Rossenbach [3] but isolation of *Clostridium tetani* is credited to Kitasato in 1889 [4]. This gram-positive, spore-forming, motile, anaerobic bacillus constitutes the normal intestinal flora of animals. As the spores are ubiquitous and persist for long time in the soil, these can easily contaminate wounds. Thus, any non- or partially-vaccinated individual is vulnerable to develop tetanus. In 1897, Edmond Nocard established the role of tetanus anti-toxin in inducing passive immunity in humans. Nearly three decades later, tetanus toxoid – developed by Descombey in 1924 – was widely used during World War II. The use of tetanus toxoid as a combined vaccine in the form of DPT (Diphtheria, Pertussis and Tetanus) was licensed in 1949. In the pre-vaccination era, the true burden of tetanus was largely unknown as most neonatal births and deaths occured at home without an account of the either event.

THE PRESENT

Although DPT was introduced in 1950s, it became part of Expanded Program of Immunization (EPI) only in 1974. In the meanwhile, tetanus remained widely prevalent. In

1980's, a significant proportion of global under-five mortality was attributed to tetanus (more than 1 million deaths every year), two-third of this being contributed by neonatal tetanus [5]. With effective implementation of the immunization program, the incidence of tetanus in the developed countries declined sharply during the last three decades, though it remained endemic in developing countries, particularly in Asia and Africa. The incidence in these nations is inversely related to the tetanus toxoid coverage of the population, and has direct relationship with poor hygiene, child-care practices, and wound management. By the end of 20th century, though there was a substantial decline in number of tetanus cases in India with improved vaccination coverage [6], it still constituted a significant burden on the health infrastructure, especially as the case fatality rate continued to be high [7].

During 2000-2013, the global mortality rates for tetanus declined by more than 30% with an impressive annual rate reduction of 8.9% for neonatal tetanus [8]. India has also witnessed reduced death rates from post-neonatal tetanus within last 5 years due to improvement in management strategies, especially supportive care provided to these patients [9]. In May 2015, India achieved the landmark of elimination of neonatal and maternal tetanus [10], certification of which requires incidence of less than 1 case per 1000 live births in all districts of the country for two consecutive years. This has been possible due to the sustained and diligent efforts in improving the vaccination coverage in pregnancy, rate of institutional deliveries, and promoting clean delivery and cord-care practices.

The risk factors associated with poor outcome in tetanus have largely remained unchanged in last 50 years [7,9]. There exists an inverse relationship between severity of disease and short incubation period and the interval between onset of first symptom and development of spasms. The autonomic dysfunction that usually appears in the second week of illness, and other complications like aspiration pneumonia and sepsis encountered frequently in individuals with prolonged hospital stay or in those who are mechanically ventilated, also contribute to mortality.

The use of ATS to neutralize the unfixed toxin has been phased out and replaced by Tetanus Immunoglobulin (TIG). The current recommendation is to use TIG early in course of illness as a single injection (500-2000 U) intramuscularly. Its use via intrathecal route has not been shown to provide any additional benefit [11]. The earlier recommendation to use penicillin has been criticized as it may inhibit the release of GABA, similar to the action of tetanospasmin [12]. Currently, metronidazole has become the drug of choice, to be given intravenously (30 mg/kg/day) every 6 hours for 10-14 days. Benzodiazepines (diazepam and lorazepam) in view of the potent anticonvulsant, sedative and hypnotic properties, continue as the preferred drugs for treatment of the spasms in tetanus since last half a decade [13], while use of barbiturates, phenothiazines, and meprobamate is no longer recommended in view of their serious side effects. Magnesium sulphate has emerged as an adjunctive drug in recent past with an additional benefit of controlling the autonomic symptoms [14]. Its use has been shown to reduce the dose requirement of benzodiazepines and neuromuscular blocking drugs, as well as the need of mechanical ventilation. Use of neuromuscular blocking agents is recommended in experienced hands after securing the airway in an intensive care set up if the above drugs fail to control spasms.

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