

Tetanus immunisation policy in England and Wales – an overview of the literature

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Summary: Current UK policy on immunisation for tetanus has changed in the light of evidence that five doses of vaccine probably provides sufficient protection as long as high-risk wounds are managed with tetanus immunoglobulin. This paper reviews the evidence base for tetanus immunisation policy in England and Wales: the epidemiology of tetanus, vaccination coverage and response to tetanus toxoid, and population immunity to tetanus. The paper highlights gaps in our current knowledge of tetanus vaccination and policy implementation, and makes recommendations for further investigations.

Key words:
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Introduction

Tetanus is an acute disease acquired through the inoculation of wounds with spores of *Clostridium tetani*. The tetanus bacillus grows anaerobically at the site of an injury, and causes significant mortality and morbidity. Tetanus spores are ubiquitous in the environment and contaminate wounds of all types. The disease is completely preventable through adequate immunisation and wound management.

Prior to 1950 (i.e. from 1938) tetanus toxoid was available mainly to military personnel and there was only patchy cover of the rest of the population; but in 1961 universal active immunisation with tetanus toxoid was introduced in England and Wales. The tetanus immunisation schedule in the United Kingdom (UK) focuses on children, with the primary course of tetanus being given at 2, 3, and 4 months of age. This is followed by a pre-school booster and school-leaving booster (introduced later in the 1960s). Uptake of toxoid up to 5 years of age is monitored using the COVER (Cover of Vaccination Evaluated Rapidly) programme, but little is known about uptake in older age groups. Note that those born before 1961 may be less well or not at all protected because they may not

have had an opportunity to be vaccinated.

The current UK Department of Health's guidelines on immunisation recommend that a full course of tetanus for life-long protection consists of five doses in childhood after which further booster doses are not required, apart from travellers to areas where medical attention may not be accessible should a tetanus-prone injury occur. In the past, where ten years had elapsed since the last dose of tetanus vaccination, policy has been to give a booster after injury, and ten yearly tetanus toxoid boosters have also been recommended. However, policy changed in the light of evidence that five doses of vaccine probably provide sufficient protection as long as high-risk wounds are managed with tetanus immunoglobulin (TIG). (<http://www.dh.gov.uk/assetRoot/04/08/73/89/04087389.pdf>).

Rational immunisation policies require knowledge of tetanus epidemiology, of vaccination coverage, of levels of tetanus immunity in the population, and of levels of immunity after immunisations. This paper reviews the evidence base for tetanus immunisation policy in England and Wales.

Tetanus epidemiology in England and Wales

Between 1984 and 2000, 175 cases of tetanus were reported in England and Wales². Only 20 of these cases were reported in individuals born after childhood immunisation was introduced in 1961. Death was recorded as an outcome in 29% of cases. The number of cases reported annually ranged from 2 to 20 cases with a falling trend during the 17-year period. The majority occurred after a wound sustained at home or in the garden. The average annual incidence was 0.2 per million population; with the highest incidence in the South West of England. Those over the age of 64 accounted for the highest number of tetanus cases. The incidence of disease in this age group was 0.66 per million, over six fold that of the 15 to 44 age group and 3.5 times that of the 45 to 64 year age group. The majority of reported cases had no history of previous tetanus immunisation, and

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unimmunised individuals tended to have more severe forms of the disease. The case fatality rate increased with increasing severity of illness.

An outbreak of tetanus among intravenous drug users (IDUs) occurred in 2003 and continued into 2004 resulting in at least 20 cases, most of whom had serious illness. One person died. Most cases were un-immunised and most had tetanus antibodies below the protective threshold on admission to hospital³. (<http://www.hpa.org.uk/cdr/PDFfiles/2004/cdr0904.pdf>)

The incubation period for tetanus is usually 3–21 days, but it may be as short as 24 hours or extend to several months^{4–5}. For the shorter incubation periods, tetanus toxoid boosters at the time of injury are unlikely to produce an anamnestic response in time to protect the individual and TIG is required to prevent tetanus developing. Worldwide, more than 30% of the cases of tetanus develop in wounds so small that they are not professionally treated⁶. It is therefore imperative that individuals maintain adequate immunity throughout life.

Population immunity to tetanus

In 1937 the protective level of tetanus antitoxin was estimated by bioassay in guinea pigs as 0.01U/ml⁷. This was later confirmed by demonstrating that at such a level a challenge with '2–3 fatal doses' produced no tetanus in human subjects. Enzyme immunoassays are now more widely used to measure tetanus antitoxin levels, and levels of greater than 0.1–0.15 IU/ml have been described as protective, although the cut-off level remains controversial. Tetanus can occur in people who are apparently fully protected, although the disease is usually mild when it occurs in such individuals.

A recent analysis was carried out on residual sera submitted to the Public Health Laboratory Service Seroepidemiology Unit in 1996. The study found that more than 80% of those aged between 5 and 39 years had protective tetanus antitoxin levels, but at older ages there was a progressive decline in protection, from 70% protected in the 40 to 49 year age group to 53% in those aged 60 and over. There were two increases in tetanus antitoxin level above 0.1IU/ml starting at 4 and 14 years of age, corresponding to booster doses of tetanus toxoid⁸. The protective levels of tetanus antitoxin in cohorts born prior to 1961 are likely to be due to immunisation as part of military service, catch-up campaigns, or opportunistic immunisation including that for travel.

Poor immunity against tetanus appears to be a general problem among older adults in the western world. A population-based serologic survey in the United States showed that the rate of protective tetanus antitoxin levels was lowest amongst the elderly⁹, and estimates from Australian, Austrian, and Swedish studies have shown that only 40% of elderly persons have detectable immunity; also that only 85% of subjects born after the introduction of general childhood vaccinations are protected.^{10,11,12}

Antibody production and duration of immunity following tetanus vaccination

One dose of tetanus toxoid causes only minimal antibody

production. After a second dose about one month later a more pronounced antibody response is seen, but the serum antibody level wanes rapidly. Only after a third injection is immune protection sustained.^{13,14}

There is little published data on long-term immunity following tetanus immunisation. The literature suggests that primary tetanus vaccination (3 doses) will give protection for up to 10 years, and that revaccination will be necessary to maintain immunity.^{15,16,17} A follow-up study of 91 Danes (aged between 25 to 30 years) with documented primary vaccination and no booster showed that 10% who had been vaccinated in the previous 20 years were unprotected, and 28% of those vaccinated greater than 25 years previously were unprotected. There was a sigmoidal decrease in antitoxin levels with increasing intervals since the primary course⁶.

One study showed that the revaccination (booster) response is inversely related to age at revaccination, time from revaccination, and the interval between the primary vaccination and revaccination. The predicted duration of immunity was difficult to confirm clinically, but there was a sigmoidal fall in antibody, similar to that seen after primary vaccination. However, antitoxin levels were consistently higher following a booster than following a primary vaccination course, relative to the interval since the last dose of tetanus vaccine. This corresponded to a longer duration of immunity¹⁸. Studies of the duration of tetanus immunity using statistical modelling have concluded that protection after four or more doses of tetanus toxoid is greater than 12 years with a confidence level of 99.9%¹⁹. A booster given 5 years after the primary course (i.e. similar to the pre-school booster in the UK which is offered from three and a half years of age) will protect children for up to 20 years, but decrease to about 13 years when given to elderly subjects¹⁸.

There are no published studies evaluating long-term immunity to tetanus after a 5-dose schedule of toxoid, and observational studies in the UK are limited to the interval of less than 40 years for which the programme has been in place. The question of whether further boosters are necessary is important. Giving individuals additional doses of tetanus vaccine that are unnecessary wastes patients' time and health service resources and increases the risk of adverse reactions in individuals who have good antibody levels. Adverse reactions in adults are not usually severe but can be unpleasant, including pain, redness and swelling at the injection site and, less frequently, fever.

Tetanus vaccine coverage

Childhood immunisations began in 1961 in this country, and vaccine uptake is routinely monitored in those up to 5 years of age. However, school leaving doses of tetanus vaccine and vaccinations in adulthood are not routinely monitored. Individuals born before 1961 have not had the benefit of a systematic approach to primary vaccination and pre-school and school leaving boosters, and there are few studies reporting coverage in this older cohort.

The majority of cases of tetanus in England and Wales between 1984 and 2000 have occurred in adults over the

age of 65. Most of these cases were completely unvaccinated². The prevalence of non-protective levels of immunity in the older age groups is due both to lack of adequate vaccination and to waning immunity in those vaccinated in the past.

Because a large proportion of cases of tetanus present some time after an injury, or even in the absence of recognised injury, the objective of a tetanus vaccination policy must be to ensure that individuals maintain adequate immunological memory to produce antitoxin antibodies, rather than rely upon tetanus immunoglobulin post exposure prophylaxis. This can be achieved by completing a full schedule of tetanus vaccination. However, a patient's history of complete vaccination may be unreliable and not a good predictor of serological protection, especially in the elderly and those born before routine tetanus vaccination.^{18,20,21} It is essential that tetanus vaccination is systematically documented and available to health care workers in primary and secondary care settings.

Tetanus policy — recommendations based on available evidence

It is clear that there are two main groups to be considered when making tetanus immunisation policy in the UK.

Firstly, the cohort of people born before 1961. There is no data on coverage amongst this group in the UK, but the evidence of effectiveness of vaccination together with the epidemiology of tetanus suggests that many did not receive a primary series of tetanus toxoid. Apart from the recent outbreak in IDUs, most cases of tetanus are in inadequately immunised older age groups.

Policy should recommend full protection of these individuals against tetanus, ideally by ensuring that anyone who is found to be unimmunised or partially immunised receives a full primary course of vaccinations or boosters as required. The most cost-effective way to do this is through the good practice of assessing vaccination status of everyone in contact with health services and vaccinating opportunistically. Influenza vaccination is indicated routinely for people in the age groups which are most likely to have missed out on tetanus immunisation and this provides an annual opportunity to check each patient's immunisation status, hence reducing opportunity costs.

The need for a centralised approach to implementation of policy is demonstrated by the failure of a policy for 10-yearly boosters in the United States where only 27% to 36% of individuals over the age of 65 reported receiving a tetanus vaccination in the last 10 years²². This policy has also been a failure in Canada due to the lack of a systematic programme for delivering vaccination to adults²³.

Secondly, for the cohort of people born after the implementation of systematic childhood immunisations, the evidence shows that tetanus antitoxin levels wane with increasing intervals since the primary course. However, modelling suggests that a booster given five years after the primary course will protect children for a further 20 years. Extrapolating this further, a fifth dose given at age 15 will confer immunity until the age of 35, or older. This

estimated minimum duration of protection is consistent with what we observe, in that there is no evidence of significant waning immunity. Cases are not seen routinely in the UK in individuals in the fourth decade of life and older who completed the full recommended series of vaccinations in the 1960s. Protection may last even longer, but this will need assessing through continued surveillance.

There are no clinical trials to determine the decrease in antitoxin levels specifically after a fifth vaccination. However, given that the length of immunity depends upon post-vaccination response, and the fact that vaccination response depends upon the interval since the last vaccination, pre-vaccination immune levels and age, it could be argued that the minimum length of protection would be 20 years. Boosters could be offered every 20 years, thereby reducing the cost of vaccinations and the rate of adverse events compared with 10-yearly boosters. Severe adverse reactions to primary immunisation with tetanus toxoid are rare. Following booster doses, local reactions are common. Oedema and erythema occur in 25 to 30% of recipients of boosters, rates increasing with increasing number of doses²⁴. Severe local reactions occur rarely (less than 2%) and are thought to be associated with high levels of circulating antitoxin resulting from over-immunisation.

The change in UK policy to recommend a schedule of 5 doses of tetanus toxoid immunisation without further boosters is a reflection of the concern about such adverse reactions. This will probably ensure that continuous protective levels are achieved. In New Zealand, however, the pragmatic approach is to offer booster doses at ages 45 and 65, following 6 previous doses by the age of 11. In Australia, a single booster is offered at age 50 following 6 doses by the age of 19, and this has been supported as a second option in the United States. Cost-effectiveness analyses have shown that the optimal policy should focus on improving rates of complete primary immunisation in adults and children, and on reducing the number of booster doses^{25,26,27}.

The main effort should continue to be towards completion of 5 doses of tetanus vaccination. Continued surveillance is vital to ensure that the current UK programme is effective at providing life-long protection.

Recommendations for further investigations

It is evident from the review of the literature that there are gaps in our knowledge of tetanus vaccination per se, and of policy implementation. We therefore recommend several areas for further investigation.

1. A thorough knowledge of tetanus vaccination coverage is essential in the planning of future programmes, so further study of tetanus vaccination coverage in adults should be undertaken to estimate the number of people who require further booster doses, and to inform how best to implement the current policy. Coverage of the school-leaving booster should be incorporated into the COVER programme.
2. Further work should be undertaken to ascertain the extent of booster response in different age groups,

and how the response may be affected by the time since the last vaccination. This will define optimal timing of further booster doses of tetanus toxoid.

3. Policymaking requires evaluation of the impact of current vaccination programmes, and making appropriate changes in response to the evaluation. An audit of current practice for tetanus vaccination in A&E and General Practice should be conducted to determine how closely current policy is being followed before conclusions about the effectiveness of the current policy are made.

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