Pretravel Consultation: Rapid Dipstick Test as a Decision Guidance for the Application of Tetanus Booster Vaccinations

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Background. When deciding whether to administer a tetanus vaccination—for international travel or injury—a subject’s vaccination certificate should be investigated. As many people lack valid vaccination cards and are unable to recall their vaccination history, the Tetanos Quick Stick (TQS) test rapidly detects protective tetanus immunoglobulin IgG antibodies in whole blood, serum, or plasma. This immunochromatographic dipstick test yields a positive or negative result.

Methods. Our study evaluates the effectiveness of the TQS test by comparing the binary TQS test results of 100 sera with the tetanus antibody levels as measured by the standardized enzyme-linked immunosorbent assay (ELISA) method. We used the TQS test to determine whether a person needed a tetanus booster vaccination. If the test showed a clearly visible line that was similar to the control line, the result was determined to be positive.

Results. All positive TQS test results had a concentration of IgG antibodies above 0.5 IU/mL as measured by ELISA, indicating that no booster vaccination was required. Similarly, in all cases with an antibody level below 0.1 IU/mL, where a vaccination would have been recommended based on the ELISA test result, the TQS test yielded a negative result. The positive predictive value and the specificity for the dipstick test were therefore 100%.

Conclusions. The TQS test is a reliable, fast, and cost-effective means of identifying subjects with a preexisting level of tetanus IgG antibodies above approximately 0.5 IU/mL. This can help to avoid unnecessary tetanus vaccinations in travel clinics, emergency departments, and practices of family doctors.

Tetanus is a serious disease caused by Clastridium tetani and has a reported fatality rate of up to 50%; the pathogen can be detected all over the world.1–5 Though tetanus infections can be effectively prevented by prophylactic vaccination, worldwide there is an estimated death rate of 309,000 per year due to this disease.6 The number of clinical cases of tetanus is very low in industrialized countries because highly effective childhood immunization programs have been implemented.7 However, in developing countries, tetanus still is a major problem.

Pretravel counseling is a valuable and common opportunity to check the vaccination status of travelers against relevant diseases including tetanus.8 Protection against tetanus is of special interest particularly in travelers performing high-risk activities abroad such as adventure traveling, tramping, backpacking, or living with natives. Many travelers do not have up-to-date vaccination certificates and cannot remember the date of their last tetanus booster. Anamnestic questioning on tetanus vaccination history is extremely ineffective and discordant with actual serum antibody levels.9–11 This makes it difficult to decide whether a tetanus booster should be applied.

If a pretravel consultation is made sufficiently early, the concentration of antibodies against tetanus...
can be determined by enzyme-linked immunosorbent assay (ELISA). According to the World Health Organization (WHO), concentrations of tetanus antibodies of 0.1 IU/mL as measured in the serum by a standardized ELISA method are “usually considered as a safe estimation” for protection.12

However, this method is rather costly and time consuming and therefore not routinely used. If a subject’s immunity against tetanus is in doubt, a booster vaccination is recommended. However, many physicians as well as travelers hesitate to apply an additional booster, particularly when there is anamnestic evidence of a booster within the past 10 years but no vaccination records are available. Moreover, local side effects (and more rarely systemic reactions) after tetanus vaccinations such as pain, swelling, and redness may occur in up to 80% of vaccinees, and these symptoms are aggravated if a tetanus booster is applied too early.13–15

Many physicians would therefore welcome a method for immediate determination of immune status against tetanus to avoid unnecessary boosters. The Tetanos Quick Stick (TQS) test is a dipstick test for the rapid detection of protective tetanus antibodies from whole blood, serum, or plasma. We investigated the effectiveness of the TQS test as an ad hoc decision criterion for whether a person should be vaccinated against tetanus.

Methods

Serum Specimens

We used 100 randomly selected sera from patients, which were sent to our serologic laboratory for a routine analysis of their tetanus antibody status. All patients had records of at least a completed basic immunization series of three vaccinations.

ELISA Method

We first determined the antibody concentrations of the selected sera using enzyme immunoassay (VaccZyme Anti-Tetanus Toxoid IgG, Enzyme Immunoassay Kit; MK010; The Binding Site, Birmingham, UK) according to the manufacturer’s instructions. The detection limit was 0.0093 IU/mL. The ELISA method is considered as the gold standard for the measurement of the level of tetanus antibodies. We compared these ELISA results to the results produced by a TQS test.

TQS Test

The TQS is an immunochromatographic dipstick test that detects tetanus antibodies. As in many other similar dipstick systems, the sample and a diluent have to be applied to a carrier medium. Ten minutes later, the result can be read. The test window has two fields: the “C” field, where a pink control line has to appear to assure that the dipstick works and the test has been conducted correctly. According to the manufacturer’s specifications in the “T” field, a “clearly distinguishable pink colored line” appears if protective tetanus immunoglobulin G antibodies are present in the given sample (minimal concentration for the whole blood: ≥0.2 IU/mL and for the serum: ≥0.1 IU/mL).

The TQS test was performed with serum according to the manufacturer’s instructions, which has been extensively described previously by Colombet and colleagues.9 In short, the sera were kept at room temperature, and immediately after applying 20 μL of serum on the well of each device with Labsystem micropipettes, three drops of the diluents were added. After incubating the assay for 10 minutes, the results were read.

The TQS tests were conducted and assessed by two blinded operators who had previously been trained in evaluation of dipstick tests. The tests with a clearly visible pink line in the “T” window were considered as positive. The tests showing only a faint line in the “T” window were read as negative results.

Results

In total, 103 TQS tests were performed on 100 sera. The mean age of persons whose sera had been tested was 40.3 years (SD 19.7; minimum: 4.5 y; maximum: 81.0 y). Ten sera were from children aged 10 years and younger and 18 sera were obtained from persons aged 60 years and older. Agreement of the two blinded operators’ readings was present in all cases. Three tests did not show clear pink lines in the “C” window and were repeated. These three sera did not show a control line in the repeated test, either, and had almost no detectable antibody concentration according to ELISA. Thus, 97 test results remained for analysis.

The geometric mean of the antibody concentration (according to the ELISA test) of all tested sera was 0.32 IU/mL [95% confidence interval (CI): 0.22–0.47 IU/mL; minimum: below detection limit of ELISA test; maximum: 13.00 IU/mL]. Comparison of the sera with and without a recommendation for a tetanus booster vaccination (based on results of a TQS test) and ELISA value in IU/mL is shown in Figure 1.
Tetanus Dipstick Test

**Negative TQS Test Results**
Fifty-four TQS tests showed negative test results according to the readers’ opinions. In the ELISA tests, these 54 sera showed a geometric mean antibody level of 0.11 IU/mL (95% CI: 0.07–0.18 IU/mL), and the range was below detection limit and up to 1.42 IU/mL.

**Positive TQS Test Results**
In 43 cases, a clearly visible pink line was present in the “T” window, indicating a positive test result. The antibody concentrations as measured by ELISA of these 43 sera were between 0.51 and 13 IU/mL, with a geometric mean of 1.48 IU/mL (95% CI: 1.18–1.85 IU/mL). None of the TQS test results was false positive, implying a positive predictive value of 100%.

**Sensitivity and Specificity of the TQS Test**
According to our results, the cutoff of the TQS test for a result considered as “positive” corresponded to an antibody concentration of at least 0.51 IU/mL (as determined by ELISA). The sensitivity for the TQS test was 55% when assuming 0.10 IU/mL according to ELISA as the minimum protective antibody concentration. Specificity for the TQS test was 100%. The relation between the antibody concentrations according to ELISA and the outcome of the TQS tests is given in Table 1.

**Discussion**
Many travelers will experience small injuries or wounds during their trip abroad. Therefore, it is of special interest for them to know if their tetanus immunity will be definitely sufficient to protect them even without an ad hoc booster during their trip. This issue gets even more important, as about one quarter of all travelers are not completely immunized against tetanus and 20% of travelers seek medical advice only 2 weeks prior to their trip. TQS, an immunochromatographic bedside dipstick test, is designed to evaluate the immune status against tetanus in serum, plasma, or whole blood. This dipstick test can indicate within 10 minutes whether a booster vaccination should be applied.

The goal of this study was to evaluate the effectiveness of the TQS test. The test’s specificity and positive predictive value were 100%. The cutoff of the test for positive results was approximately 0.5 IU/mL, which is considered to be far above the protective threshold of 0.1 IU/mL. Thus, if the TQS test result obtained from a patient’s serum is positive by showing a clearly visible pink line, it can be assumed that a sufficient antibody concentration is present in serum against tetanus infection for a period of at least 5 years.

Well-known problems of multiple tetanus vaccinations are hyperergic adverse events such as local Arthus-type reactions, which are associated with high antibody levels against tetanus. This is mainly observed in patients who repeatedly received booster doses within short periods of time. To avoid hyperimmunization, the TQS test can be used to identify subjects with high antibody concentrations against tetanus for which a booster is unnecessary.

In our study, all subjects with antibody concentrations of more than 0.5 IU/mL were clearly positive in the TQS test. Not a single subject with an antibody concentration of less than 0.1 IU/mL in the ELISA showed a positive test result in the TQS test. According to the WHO criteria, an antibody concentration of 0.1 IU/mL is considered to be definitely protective. We therefore conclude that...
the TQS test meets the necessary criteria to obtain a clear and concise decision whether a booster vaccination is necessary or not. The low sensitivity of the TQS test has the advantage of an ample safety window. Sensitivity of the TQS test has been reported to be even lower for using whole blood; therefore, the results should be even more conservative and safe in this case.

Subjects that tested “negative” in the TQS test may have low serum antibody concentrations. Some subjects may still have an estimated duration of protection of up to or even more than 5 years, but there were also subjects who had antibody concentrations well below 0.1 IU/mL. Therefore, an additional tetanus booster vaccination seems to be adequate in subjects that tested negative to provide sufficient protection even for a longer period of time, eg, for a longer trip in a country with inadequate medical supplies. In these subjects, an additional booster is not expected to result in strong local side effects due to very high tetanus antibody levels.

The TQS test could also be an option for persons who generally prefer the testing of antibody levels instead of regular booster vaccinations. It should also be taken into account that variables such as age, gender, and body mass index could have a negative influence on immunity. 10,21

Our investigation confirms the results presented in other studies. 9,11 Colombet and colleagues found high sensitivity and specificity evaluating the TQS test results from serum and whole blood. However, the percentage of subjects with tetanus antibody levels below 0.1 IU/mL was smaller than in our investigation. Thus, our data reveal a more conclusive database for people at risk of infection. 9 Stubbe and colleagues 11 performed the test on whole blood and described several “equivocal” TQS test results. Because this dipstick test is qualitative and should only offer a distinct positive or negative result, in our study, only tests that showed an undisputable, clearly visible, and pink line in the “T” window were read as positive results, which was highly effective in our analysis leading to a specificity of 100%. In our investigation, there were three TQS tests that did not show a clearly visible pink line in the “C” window, which might be regarded as inconclusive. As the number of such cases seems to be small, this will not reduce the value of the test in a significant manner: subjects with inconclusive results had a low antibody concentration as determined by ELISA; therefore, the recommendation of a tetanus booster dose in such cases may be given.

Besides travelers and surgical patients, persons at special risk of acquiring a tetanus infection are immigrants, where immunity rates are very low, 11 parenteral drug users, and elderly. 1,2,21 In these groups, the TQS test can be a useful and cheap tool as a decision support for booster vaccination against tetanus.

**Conclusion**

We found that the TQS test is a highly suitable tool to determine the tetanus protection status in unselected persons where a fast decision is needed. High specificity makes the test system a safe and reliable tool to identify subjects who are still protected and do not require a tetanus booster vaccination. The TQS test can therefore help to avoid unnecessary tetanus booster doses in travel clinics, emergency departments, and practices of family doctors.

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**Declaration of Interests**

The authors state that they have no conflicts of interest.

**References**


