PAPERS AND ORIGINALS

Prevention of Tetanus in the Wounded

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British Medical Journal, 1975, 3, 453-455

Summary

Recommendations for the prevention of tetanus in the wounded have been revised to incorporate the use of human tetanus immunoglobulin, which is now available in the United Kingdom. Surgical toilet is of prime importance for all wounds, and is usually sufficient for tetanus prophylaxis in patients with wounds that are less than six hours old, clean, non-penetrating, and with negligible tissue damage. Human tetanus immunoglobulin should be given to patients with more serious wounds who have had toxoid injections over 10 years earlier, had an incomplete course, or do not know their immunity status. The importance of active immunization is emphasized. The recommendations should be regarded as guidelines as the circumstances in individual cases will differ.

Introduction

In 1966 we published recommendations for the prevention of tetanus in the wounded,¹ which took into account the fundamental importance of active immunization and the need, in non-immune wounded patients, to limit the use of equine antitoxin and to place greater reliance on the use of antimicrobials to supplement careful surgical toilet. The use of human tetanus immunoglobulin was also recommended, as preferable to either equine antitoxin or antimicrobials, but in 1966 the material was scarce.

In 1974 human tetanus immunoglobulin became generally

available in the United Kingdom²; consequently, equine, bovine, and other animal antitoxins may now be regarded as obsolete for tetanus prevention in this country and antimicrobials may no longer be considered to have a primary role. Since 1966 it has become generally recognized that tetanus toxoid may cause adverse reactions,^{3,4} which are usually minor, and that a suitable course of injections of adsorbed toxoid forms an immunity more durable than was previously realized.⁵⁻⁷ Consequently, booster doses of toxoid are required less often.⁸

Because of these developments we have revised our recommendations for the prevention of tetanus in the wounded. The scheme described here does not differ fundamentally from that we described previously¹ and which is still an adequate guide in countries where human tetanus immunoglobulin is not available. Our new recommendations are given in the chart along with explanatory comments.

Surgical Toilet

Surgical toilet is of prime importance, since removal of foreign bodies and of tissues that are dead or likely to die renders the wound less suitable for the growth of tetanus bacilli. Provided careful surgical toilet is practised, patients with wounds that are less than six hours old^{1,9} clean, non-penetrating, and with negligible tissue damage do not need human tetanus immunoglobulin, even if the patient is not actively immune to tetanus. This point requires emphasis since human antitoxin should not be given thoughtlessly to every wounded patient who consults his doctor; the material is expensive and supplies probably cannot be increased indefinitely.

Human Tetanus Immunoglobulin

Human tetanus immunoglobulin provides passive immunity against tetanus. It is generally accepted that immunity requires the maintenance of a serum concentration of antitoxin greater than 0.01 unit/ml until toxin production ceases in a wound.¹⁰ Human antitoxin concentrations in the blood fall at a slower rate than equine antitoxin concentrations; consequently, an intramuscular injection of only 250 units of human tetanus immunoglobulin may be relied on to give a serum concentration of antitoxin which remains above 0.01 unit/ml for about four weeks. There seems to be no risk of an early immune elimination, as sometimes occurs with equine antitoxin, and a 250-unit dose is recommended for all ages. If the wound remains unhealed at four weeks a second dose should be given.

Minor adverse reactions sometimes follow the injection of human immunoglobulin and a few severe reactions, sometimes resembling

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- A Has had a complete course of toxoid or a booster dose within the past 5 years
 B Has had a complete course of toxoid or a booster dose more than 5 and less than 10 years ago
 C Has had a complete course of toxoid or a booster dose more than 10 years ago
 D Has not had a complete course of toxoid or immunity status is unknown

Recommendations for prevention of tetanus in the wounded. Adrenaline injection (B.P.) should be available during prophylactic procedures for treatment of anaphylactic shock (in adults 0.5-1 ml intramuscularly).

anaphylactic shock, have been described.^{11 12} These usually occur in patients given repeated injections for treatment of hypogammaglobulinaemia, but severe reactions are extremely unlikely to occur in healthy patients who receive human immunoglobulin only for tetanus prevention. A trial dose of immunoglobulin to predict the occurrence of anaphylactic shock is therefore unnecessary, just as it is in the case of vaccines used for routine immunization. Nevertheless, as with any immunization procedure, adrenaline should be immediately available whenever immunoglobulin is given.

Toxoid

ACTIVE IMMUNIZATION

For active immunization *adsorbed* toxoid is recommended—that is, toxoid containing an aluminium adjuvant (adsorbed tetanus toxoid B.P.). Adsorbed toxoid is effective when given at the same time as antitoxin (but into a different limb), stimulates a higher, longer-lasting antitoxin response than plain toxoid, and is satisfactory for boosting immunity in wounded people.¹³ Plain toxoid is therefore not recommended.

A complete basic course comprises three spaced doses of toxoid, with, for example, about six weeks between the first and second doses and six to 12 months between the second and third; longer intervals between doses are acceptable, but are less convenient administratively. Routine booster doses are recommended at 10-year intervals unless during this period the patient has received a booster dose at the time of wounding.

The period for which antitoxin is found in the blood of actively immunized people after a complete basic course of adsorbed tetanus toxoid is uncertain, but evidence is accumulating that immunity usually lasts for 10 years, though it is less durable after plain toxoid.^{5-7 13 14} After a booster dose of adsorbed toxoid immunity is believed to last even longer, but until it is established that this is almost invariably the case booster doses are recommended at 10-year intervals.

ROLE OF THE BOOSTER DOSE AT INJURY

The recommendation that a booster dose is given at injury to those immunized or boosted between five and 10 years previously is made for three reasons. Firstly, it is desirable to stimulate an increase in the blood antitoxin when the patient may be faced with the challenge of toxin production in a wound. Secondly, there is the possibility that some people may have responded inadequately to the tetanus toxoid given earlier,^{5 7 13 16} and may thus lack circulating antitoxin at the time of injury. This is most likely in those who were immunized with plain toxoid,^{5 13} and since adsorbed toxoid was introduced in the United Kingdom only in 1963, there will still be many such people. Thirdly, it is desirable to take the opportunity of boosting the patient's immunity to ensure that he will remain actively immune for many years.

The booster dose of toxoid for wounded patients immunized more than 10 years earlier is recommended for similar reasons but, owing to the longer time interval, there is a greater possibility that circulating antitoxin may be absent in such patients, particularly since most of them will have been immunized with plain toxoid. Moreover, their booster response may be slow¹⁷—that is, tetanus toxin might be produced in a wound before antitoxin appears in the circulation; for this reason human tetanus immunoglobulin is recommended.

HYPERSENSITIVITY OF TETANUS TOXOID

Hypersensitivity reactions—usually pain at the site of injection—may occur, particularly when tetanus toxoid is given frequently to boost immunity, as for example in factory workers receiving minor wounds.^{3 4} Unnecessary booster doses of toxoid should therefore be avoided.

Immunity Categories

The measures to be recommended for tetanus prevention in a wounded patient depend on whether or not he has been actively immunized and on the degree of immunity he is likely to possess. It is therefore necessary to evaluate the immunity of each patient and we suggest that the following four categories be used.

Immunity Category A.—The patient has had a complete basic course of toxoid or a booster within the past five years. He is adequately immune as a result of active immunization and neither a booster injection of toxoid nor passive immunization with human tetanus immunoglobulin is required for tetanus prevention.

Immunity Category B.—The patient has had a complete basic course of toxoid or a booster more than five and less than 10 years ago. He may not be adequately immune, but is able to respond rapidly to an injection of toxoid. A booster dose therefore suffices for protection, and no human tetanus immunoglobulin is needed.

Immunity Category C.—The patient has had a complete basic course of toxoid or a booster dose more than 10 years ago. The immunity of such patients may be inadequate and some may not respond quickly enough to a toxoid booster. Thus, if the wound is not a minor one human tetanus immunoglobulin should be given. An injection of adsorbed toxoid should also be given simultaneously, but into a different limb.

Immunity Category D.—The patient has not had a complete basic course of toxoid, or his immunization status is not known. He is therefore not actively immune, or is not known to be. Thus, human tetanus immunoglobulin may be needed for immediate protection; it should be given simultaneously (but into a different limb) with a first injection of toxoid, which should be followed later by second and third injections to complete the basic course. Patients who are known to have had only one or two injections of toxoid may also be regarded for practical purposes as falling into this category.

Discussion

The measures to be taken for tetanus prevention in an individual wounded patient are decided on the basis of a knowledge and understanding of the pathological process of tetanus, the mode of action and limitations of the various preventive measures available, and the nature of the patient's wound and his history of tetanus immunization.¹⁸ The recommendations should therefore be regarded not as a set of hard and fast rules but as guidelines since, as with any scheme of general guidance on medical practice, they will not invariably cover the circumstances of all individual patients.

In tetanus prevention it is of basic importance to establish and maintain active immunity. Tetanus immunization is recommended in the infant immunization schedules used in the United Kingdom and every effort should be made to ensure that all infants receive the proper course of injections,¹⁹ usually by means of combined vaccines. Unfortunately, many wounded patients will never have been immunized or do not know their history of immunization. Nevertheless, measures should be taken to ensure that such patients become actively immunized, and it is for this purpose that their recommended treatment at the time of injury includes an injection of toxoid, given as the first of a full course of injections. If this policy is adopted in time fewer and fewer patients should require human immunoglobulin for temporary protection at injury. The doctor should explain the significance of active immunization to his older patients so that increasing numbers of the population will come to realize the advantage of being immunized and of knowing their immunity status.

Wounded patients may require an antimicrobial for treatment or prevention of sepsis, and there is evidence that such treatment may sometimes usefully support the action of antitoxin in preventing tetanus.²⁰ But, with the availability of human tetanus immunoglobulin, antimicrobials should now mainly revert to

their former role of dealing with sepsis generally rather than the prevention of tetanus specifically; the use of antimicrobials was therefore not included in our recommendations.

References

- Laurence, D. R., Evans, D. G., and Smith, J. W. G., *British Medical Journal*, 1966, 1, 33.
- Lancet*, 1974, 1, 51.
- White, W. G., et al., *Journal of Hygiene*, 1973, 71, 283.
- British Medical Journal*, 1974, 1, 48.
- White, W. G., et al., *Lancet*, 1969, 2, 35.
- Peebles, T. C., et al., *New England Journal of Medicine*, 1969, 280, 575.
- Trinca, J. C., *Infection and Immunity*, 1974, 10, 1.
- Edsall, G., et al., *Journal of the American Medical Association*, 1967, 202, 17.
- Smith, J. W. G., and MacIver, A. G., *Journal of Medical Microbiology*, 1974, 7, 497.
- Smith, J. W. G., *British Medical Bulletin*, 1969, 25, 177.
- Glaser, J., and Wyss-Souffront, W. A., *Pediatrics*, 1961, 28, 367.
- Mackenzie, D. L., and Vlahcevic, Z. R., *New England Journal of Medicine*, 1974, 290, 749.
- Trinca, J. C., *Medical Journal of Australia*, 1965, 2, 116.
- Scheibel, I., et al., *Acta Pathologica et Microbiologica Scandinavica*, 1966, 67, 380.
- Edsall, G., et al., in *Proceedings of the Third International Conference on Tetanus*, p. 102. Scientific Publication No. 253. Washington, Pan American Health Organisation, 1972.
- MacLennan, R., et al., *Bulletin of the World Health Organization*, 1973, 49, 615.
- King, R. D., et al., *Surgery, Gynecology, and Obstetrics*, 1963, 116, 745.
- Adams, E. B., Laurence, D. R., and Smith, J. W. G., *Tetanus*. Blackwell, Oxford, 1969.
- Department of Health and Social Security, *Immunization Against Infectious Disease*. London, H.M.S.O., 1972.
- Smith, J. W. G., and MacIver, A. G., *Journal of Medical Microbiology*, 1969, 2, 385.

Fibrinogen Uptake Scanning for Diagnosis of Deep Vein Thrombosis: A Plea for Standardization

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British Medical Journal, 1975, 3, 455-458

Summary

From an examination of the factors affecting the diagnostic accuracy of the ¹²⁵I-fibrinogen test for detecting deep vein thrombosis it is concluded that there is a greater possibility of error if postoperative counts are referred to the preoperative baseline rather than counts made immediately after operation. A method is proposed for reducing other errors caused by instrument mishandling.

Introduction

One of the most common hazards of modern surgery is the thrombosis that occurs postoperatively in the leg veins—deep

vein thrombosis (D.V.T.). In assessing the aetiology and techniques of prophylaxis clinical signs alone are an unreliable index and recently the radioisotopic ¹²⁵I-fibrinogen test has been used. Several years' experience of this method has led to a general dissatisfaction with its precision in arriving at a positive diagnosis of thrombosis. This, together with the unjustifiability of denying an effective prophylactic to patients used as controls in clinical trials, prompted a reassessment of the use of ¹²⁵I scanning as a means of diagnosis.

Flancet *et al.*¹ first reported the use of ¹²⁵I-fibrinogen; they used a scintillation counter and referred postoperative counts to preoperative baselines adjusting for both variations in background activity and physical (as opposed to biological) decay of the isotope. Their criterion for diagnosing thrombosis was a change in ratio of >0.56 between the highest and lowest counts on the same calf on any two occasions. They scanned the legs postoperatively and then on the third and sixth days. If counts rose during scanning the legs were scanned on subsequent days—that is, days 1, 2, 4, and 5. Measurements were made at 2-in (5.1-cm) intervals along the leg.

Shortly afterwards Negus *et al.*² published what was to become the standard reference for diagnosis. They referred the radioisotope counts to the precordium and expressed them as a percentage of this count. The scans were also made every day

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