Review Question -

Is human tetanus immunoglobulin mandatory in all cases of open fracture?

Section 1: Background-

While in developed countries the incidence of tetanus osteomyelitis after open fractures is extremely rare <.01% the incidence is higher in developing countries with incomplete vaccinations and delayed presentation. This imposes such patients at a significant risk of tetanus osteomyelitis which may progress to generalised tetanus which has very poor outcomes.

Section 2: Data extraction table

S.No	Author, year	Study Design	Sample size,	Population	Intervention	Outcomes , Results

1	O. C. S. Cassell, A. J. Fitton, W. A. Dickson and M. A. E Milling , 2002	Retrospective study	269	269 burns and trauma patients, referred from across South Wales	Questionare regarding past tetanus vaccination history and accordingly tetanus vaccine was given	16 patients had been asked whether they had received a course of tetanus, and 41 patients were not ques- tioned about their tetanus immunisation status
2	MATHIAS TREMP et al, 2020	Case report	2	2 cases of clostridial infection due to contaminate d open injuries. studied follow up till 18m 24 years	Both the patients had undergone prolonged treatment including repeated debridement, excision of bone segment, transport and arthrodesis	Unfavourable outcome.

3	P.-E. Fournier et al, 2014	Case report	1	Single case of tetanus osteomyelitis	The patient had last received vaccination in 1997, the open fracture was sustained in 2011. Despite debridement and antibiotics the patient had to finally undergo amputation.	Unfavourable outcome after clostridium osteomyelitis leading to amputation
4	**Indiran Govender[a*] and Christopher Clark, 2015**	Case report	1	Single case of clostridium infection post open forearm fracture	Patient developed severe neurological symptoms with features of osteomyelitis	Post debridement and 2 week prolonged treatment with anticonvulsants, muscle relaxants and antibiotics tetanus was controlled.

5	**BE Ramasuvha[I]; EJ D'Alton[II]; R Golele, 2010**	Case report	2	2 cases of open fracture treated in Africa	Both. Patients developed severe neurological symptoms requiring ICU admission ventilatory support	Missed tetanus vaccination had led to severe generalised tetanus infection which lead to ICU admission, ventilatory support. The patients finally survived with ICU care and antibiotics.
6	Yasuhito Wakasaya et al, 2009	Case report	1	Case of chronic Tetanus osteomyelitis	Patient developed chronic tetanus osteomyelitis post mandible necrosis after radiation therapy	Despite long term antibiotic cover with metronidazole and tetanus toxoid vaccine the osteomyelitis persisted. This shows the infection can persist in areas of necrosis with anaerobic environment for its growth.

Section 3: Results summary write-up

The above 6 studies highlight that though tetanus osteomyelitis resulting to severe morbidity or generalised tetanus is often missed due to poor history of tetanus prophylaxis (1) taken by patient due to multiple reasons. The musculoskeletal complications are adverse and lead to unfavourable often unsalvageable results (2),(3),(4). The

progression to neurological symptoms may be confused with epilepsy and has a poor outcome in such cases and need ICU care severe patient morbidity and risk of mortality (4),(5). Chronic osteomyelitis can also rarely occur in areas where ischemic bone or muscle remains which would require prolonged antibiotic suppression (6).

Section 4: Discussion

- A history of prior immunisation should not dissuade a physician from making a decision of tetanus vaccination specially with severe contamination, duration of more than 10 years from complete last booster dose.
- Contaminated wounds should receive immunoglobulins irrespective of tetanus vaccination received.
- Adequate debridement must be done on all patients with wounds and if tetanus infection is suspected, wounds must be left open for later closure.
- Always have a high index of suspicion in patients who present with seizures following an open fracture, particularly if there is no history of epilepsy, head injury or history of alcohol abuse.
- The immunity provided by initial tetanus vaccination goes down significantly with time and age after 20 years of booster dose. Such patients or others with associated immunocompromise are at higher risk of tetanus infection.

Section 5: Risk of bias of included studies

MODERATE

Section 5: Response/Recommendation

All open injuries must receive tetanus prophylaxis with tetanus toxoid. Those with inconclusive history of vaccination or at risk of immunocompromise must receive tetanus immunoglobulin.

Section 6: Level/ strength of Evidence:

LOW only 5 case based studies with total of 4 cases have been analysed. One study included is a questionnaire which Based on the number of studies, risk of bias, study design, sample size, and key outcomes.

References.

1. An audit of the tetanus immunisation status of plastic surgery trauma and burns patients ,British Journal of Plastic Surgery (2002), 55, 215-218, O. C. S. Cassell, A. J. Fitton, W. A. Dickson and M. A. E Milling
2. Clostridial infection after open fractures of the lower extrimity- report of 2 cases and discussion of pathomechanism and treatment, In vivo 34:291-298 (2020), Mathias Tremp et al.
3. Genome of a chronic osteitis-causing Clostridium tetani, NEW GENOMES OF MICROORGANISMS AND VIRUSES IN HUMANS 10.1002/2052-2975.27 , P.-E. Fournier et al
4. Tetanus: a patient in a primary healthcare setting, Southern African Journal of Infectious Diseases, 30:3, 85-88, DOI: 10.1080/23120053.2015.1074436 , Indiran Govender & Christopher Clark

5. Is tetanus toxoid still necessary today? , SA orthop. j. vol.9 n.3 Centurion Jan. 2010, Natal et al

6. An Unusual Case of Chronic Relapsing Tetanus Associated with Mandibular Osteomyelitis, Inter Med 48: 1311-1313, 2009 , Yasuhito Wakasaya et al.

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