Tetanus is a disease caused by tetanus toxin, which is produced by the bacterium Clostridium tetani. This bacterium typically infects penetrating wounds contaminated by foreign material such as soil. In developing countries, poor hygiene after childbirth may cause tetanus in newborn babies. Even though vaccination has dramatically decreased the burden of tetanus, there are still about one million cases per year globally. We found one controlled trial that examined whether 1 gram per day of intravenous vitamin C would help in the treatment of tetanus patients. Vitamin C was used alongside standard treatments for tetanus. Intravenous vitamin C reduced mortality of children aged between 1 and 12 with tetanus by 100% and mortality of 13 to 30 year old patients by 45%. The trial was not properly conducted and therefore great caution is required in the interpretation of the findings. Vitamin C cannot be recommended as a treatment for tetanus on the basis of this single study. Further investigation of the role of vitamin C in tetanus treatment is warranted.
Recently, Thwaites 2006 reported data supporting the possible role of catecholamines (stress hormones) in tetanus. The concentrations of epinephrine and norepinephrine were much higher in tetanus patients than in other critically ill patients and, among the tetanus patients, these concentrations were higher in those who had more severe forms of tetanus.

There is evidence suggesting that vitamin C might influence the course of tetanus infection. Vitamin C is involved in the synthesis of norepinephrine, and the adrenal glands have the highest concentration of this vitamin in the body (Diliberto 1954; Levine 1985; Patak 2004; Rice 2000). Furthermore, various infections and purified bacterial toxins lead to the depletion of vitamin C from the adrenal glands (Hemlí 2006 p 6-7). A few experimental studies have shown that vitamin C improved the functions of phagocytes and the proliferation of T-lymphocytes, indicating that it has a role in the immune system (Hemlí 2006 p 5-6). In dozens of animal studies, vitamin C has been shown to increase resistance against diverse infections and against a few purified bacterial toxins (Hemlí 2006 p 7-9). In trials with humans, vitamin C reduced the duration and severity of the common cold and pneumonia (Douglas 2007; Hemlí 1999; Rice 2000). Imposing that the immune system effects may have clinical importance under certain conditions.

Dey 1966 reported that five rats administered twice the minimal lethal dose of tetanus toxin all died, whereas 25 rats administered vitamin C either before or after the toxin all lived (Hemlí 2006 p 112). Vitamin C also reduced mortality in mice caused by toxins of several Clostridium species (Büller Souto 1939; Hemlí 2006).

Chakrabarti 1955 reported that tetanus patients had lower plasma vitamin C levels than healthy people, and tetanus patients who died had lower levels than those who survived. In trials with humans, tetanus patients had elevated levels of dehydroascorbate, which is the oxidized form of vitamin C. Such changes in vitamin C metabolism provide a rationale for the test of vitamin C in treating tetanus patients. In an early case report, Kenner 1954 described that vitamin C seemed to be beneficial for an unvaccinated six-year-old boy who contracted tetanus. However, vitamin C was used in addition to tetanus antitoxin, penicillin, adrenal cortex extract and Tolserol (mephenesin, muscle relaxant). Although the boy was cured and discharged from hospital on the eighteenth day, the role of vitamin C in the curing process cannot be inferred from the report.

Although vitamin C affects the immune system, it may be important only in particular conditions. For example, it is possible that variation in vitamin C intake does not affect the immune system in the ordinary western population because of their relatively high dietary intake levels, but it may be a limiting factor in populations with low intakes. In the extreme, the prevalence of scurvy (frank vitamin C deficiency) was reported to be up to 44% in refugee camps in Somalia (World Health Organization 1999).

Usually vitamin C is administered as tablets, but it can also be administered intravenously. A recent pharmacokinetic study compared oral and intravenous administration and found substantially higher plasma levels when vitamin C was administered by intravenous route compared with oral administration (Padayatty 2004). The highest dose used in the pharmacokinetic study, 100 g of vitamin C intravenously given over a few hours, increased the plasma concentration peak to 15,000 micromol/L, which is over 100 times the plateau level reached by oral administration (Levine 1996; Padayatty 2004). Vitamin C is safe in high doses. A dose of approximately 10 mg/day prevents scurvy but, according to the USA nutritional recommendations, the ‘tolerable upper intake level’ is 2 g/day for adults (Institute of Medicine 2000). The basis for this upper limit is the appearance of diarrhoea, which is, however, a trivial adverse effect that disappears quickly with a reduction in intake. Several other reviewers have also concluded that vitamin C is safe in doses ranging to several grams per day (Hathcock 2005; Hemlí 2006; Bvers 1987).

Tetanus is a severe infection affecting hundreds of thousands of people annually and vitamin C is a safe and inexpensive essential nutrient. The possibility that vitamin C may have an action on tetanus is therefore worthy of systematic consideration.

Links to the publications cited in this review, for which full text versions are available, can be found at: www.tdk.helsinki.fi/users/hemila/CT/.

**Objectives**

To determine the effects of vitamin C supplementation for:

1. preventing the development of tetanus in vaccinated and unvaccinated individuals; and
2. treating patients with a diagnosis of tetanus.

**Implications for practice**

A single poor quality and poorly reported controlled trial found that 1 g/day intravenous vitamin C significantly reduced death rates in people with tetanus. However the quality of this trial means that routine vitamin C use cannot be recommended on this basis alone. There were no evaluations of vitamin C as a prevention for tetanus.

**Implications for research**

Treatment trials: more research is needed into the effect of vitamin C on mortality in people with tetanus infection. Vitamin C should be studied as an addition to the conventional therapy.

Prevention trials: Because of vaccination, tetanus is nearly non-existent in children and middle-aged people in the developed world. Although vaccination should be a priority in developing countries, the prophylactic effects of vitamin C supplementation might be investigated in populations with a high incidence of tetanus.

**References to studies included in this review**

**Jahan 1984 (published data only)**


* indicates the major publication for the study

**Additional references**

**Balk 2002**


**Bleck 2005**


**Briggs 1984**


**Büller Souto 1939**

Büller Souto A, Lima C. Action de la vitamine C sur la toxine du Bacillus perfringens. Memorias do Instituto Butantan 1939;12:265-95

**Cameron 1976**


**Campbell 1975**


**Cathcart 1981**

StatXact 2008
StatXact. :-.

Stone 1972

Thwaites 2003

Thwaites 2006

Vandelaer 2003

WHO 1999

Maternal and neonatal tetanus elimination by 2005. :-.

WHO 2008
Tetanus. :-.

Graphs

Graphs and Tables

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<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Case fatality rate of tetanus patients</td>
<td>Risk Ratio (M-H, Fixed, 95% CI) Subtotals only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1 aged 1 to 12 years</td>
<td>1</td>
<td>62</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.02 [0.00, 0.34]</td>
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<tr>
<td>1.2 aged 13 to 30 years</td>
<td>1</td>
<td>55</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.55 [0.31, 0.95]</td>
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