I have read the Document ‘Risk of Tetanus Following a Male Circumcision Procedure July 2016’ and would like to make the following comments.

**Part 1: Biological Plausibility Mechanism**

Regarding the known mechanism of *Clostridium Tetani* entry: tetanus toxin is an extremely potent neurotoxin and minute doses are required to cause clinical disease (1). In clinical practice approximately 25-40% cases have no identifiable entry site and the majority of patients’ presumed entry sites are minor abrasions which are clean/already healed thus *C Tetani* cannot be cultured from them (2,3). Failure to culture *C Tetani* or to detect a clinically obvious wound therefore cannot disprove the procedure site as the primary site of infection (4,5).

The method of tetanus toxin entry into the central nervous system through retrograde neuronal transport is well established. However, the dissemination of toxin in the body through haematogenous spread prior to neuronal uptake has been demonstrated and is accepted to occur (5,6). Due to the very small amounts of tetanus toxin required to produce tetanus, to prevent disease any device would need to completely eliminate all blood and lymphatic supply from the area to prevent tetanus toxin dissemination. It is not known whether local diffusion of tetanus toxin also plays an important role in tetanus pathophysiology but it should be noted that tetanus usually occurs where entry sites are presumed to be avascular or where scar tissue is present (3,7). In addition direct toxin entry through local membranes may be possible due to minor abrasions. Toxin entry may also be facilitated through the action of cytopathic toxins produced by *C Tetani* and other bacteria present (9,10).

Failure to demonstrate the presence of in *C Tetani* in the experiments examining the microbiome following circumcision does not exclude the possibility of it occurring in clinical practice, especially given the small sample size of this study. Odor may indeed signal increased anaerobic bacteria or the interaction between aerobic and anaerobic microorganisms, and it should be noted that tetanus uncommonly occurs as a single bacterial infection. In cases of tetanus where *C Tetani* has been cultured, the majority of infections are polymicrobial, containing both aerobic and anaerobic bacteria (7). Concomitant infection with the *Staphylococcus Aureus* and *C Tetani* spores has also been shown to increase the severity and speed of onset of tetanus in animal experiments (8).

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References


