Is now the time for all surgical gloves to be non-pyrogenic?

Ian Mason, Phd, Occupational health and medical author

Poor manufacturing control can increase endotoxin contamination of gloves

- Failing to control and maintain a good water quality during the manufacturing process can increase the amount of Gram-negative bacteria on the gloves.
- Ineffective removal of bacteria later in the manufacturing process such as number of washing cycles and chlorination processes can boost endotoxin levels.
- Unnecessary handling of products may increase the amount of Gram-negative bacteria on the product due to contaminated hands.

Widely used surgical gloves may be putting patients at risk of harm, writes Ian Mason.

It may seem paradoxical, but dead bacteria can sometimes be as dangerous as living bacteria. Take common intestinal bacteria such as Escherichia coli (E. coli). Like all Gram-negative bacteria, these are enclosed in protective outer membrane composed largely of lipopolysaccharide (LPS).

If the bacterium is killed, this outer membrane is disrupted, releasing LPS – more commonly known as endotoxin because LPS is a surprisingly toxic substance. Endotoxins are pyrogens (fever-inducing) – if they get into the bloodstream, they pose a substantial risk to human health, triggering reactions that range from fever through to septic shock and in some cases, death. Because endotoxins and related pyrogens cannot be eliminated by standard sterilisation processes, pyrogen testing has become mandatory for injectable drugs[1].

But what about surgical gloves, sterile medical implants or catheters? It follows from the above that the presence of endotoxin on these, or indeed on any other materials introduced into the human body would be deeply undesirable.

Is this a problem in clinical practice?

Research in many countries has helped clarify the risks associated with endotoxin contamination. The sterilisation method typically used for surgical gloves is Gamma irradiation. Although active against Gram-negative bacteria (which are ubiquitous in water and in the environment) radiation cannot remove the endotoxin residue that remains following bacterial death.

A Reference Laboratory study carried out in the USA found endotoxin to be a 'highly significant' contaminant of some latex gloves (up to 2.8 micrograms/gram of glove)[2]. A Scandinavian study found 'heavy endotoxin contamination'

Mölnlycke®

on the outside of some surgical gloves sold in Sweden[3] – the authors of this study estimated that one type of glove could cause patients to suffer fever, chills, headache and muscle pain if only a tenth of the endotoxin present was absorbed by the patient.

These concerns are far from theoretical; A clinical study found that the incidence of patient febrile reactions in a catheterization laboratory was markedly reduced (from 11.6% to 0.6%) when routine procedure was changed and latex gloves were rinsed using pyrogen-free water prior to patient catheterisation[4]. Some of the potential risks associated with endotoxin contamination are more esoteric – for example it has been suggested that endotoxins may contribute to aseptic loosening of orthopaedic implants, a major problem in joint surgery[5].

Plunging endotoxin-contaminated gloves into a patient's body cavities can clearly be hazardous for the patient, however there are also less significant risks for healthcare workers, for example, contact dermatitis on the hands of healthcare workers has been linked to the presence of bacterial endotoxin in natural rubber latex gloves[6].

Worrying variability

Endotoxin is measured in endotoxin units per millilitre (EU/ml). One EU equals approximately 0.1 to 0.2 ng endotoxin/ml of solution. Studies have identified huge variability in the level of endotoxin in medical gloves – in one study that compared eight types of examination glove, endotoxin contamination of unused gloves ranged almost four thousand-fold (from below 1.5 to 5810 endotoxin units)[7].

Of interest in this study was the finding that gloves drawn from the middle of a box were lower in endotoxin that those from the outside suggesting a role for cardboard packaging in contaminating some gloves.

What about surgical gloves? A recent Japanese study published in the Journal 'Future Microbiology' notes that although strict endotoxin limits have been enforced for medical implants and catheters (see below) – no standard limit has been set for single-use sterile surgical gloves. Sampling gloves from four manufacturers the authors found endotoxin to be present on three types of glove, in the case of one manufacturer, levels exceeded 300 EU. Commenting on their results the authors say that 'strict endotoxin limits need to be established' on surgical gloves[8]. They speculate that the endotoxin source could be inadequate cleaning during manufacture, or use of contaminated cleaning water. They note that until such time as international standards are set for endotoxin residues on gloves, it may be possible to reduce glove endotoxin contamination if healthcare workers wash new gloves in endotoxin-free water – a somewhat impractical suggestion given the added cost of washing every pair of gloves in this relatively expensive product. Of course the problem could be tackled at source, via better manufacturing practice (see box) at suppliers producing endotoxin-contaminated gloves.

Although there is currently no internationally agreed limit for glove endotoxin levels, there have been moves in this direction. For example, the US Food and Drug Administration has set endotoxin limits for medical devices (the limit is 0.5 EU/ml or 20 EU/device for products that directly or indirectly contact the cardiovascular system and lymphatic system. For devices in contact with cerebrospinal fluid, the limit is 0.06 EU/ml or 2.15 EU/device)[9]. There are also North American[10] and European Standards[11] requiring surgical glove manufacturers to monitor endotoxin levels on sterile gloves if they intend to label the gloves as having 'low endotoxin levels'. In this case the level should not exceed 20 EU/per pair of gloves.

These initiatives are to be applauded, however it does seem curious that whilst endotoxin limits have been set for sterile medical devices, gloves worn by surgeons to insert these devices into patients are not covered by the same legislative scrutiny. Perhaps it is time for surgical gloves to be as pristine as the medical products they are used to handle – it would certainly be a step forward for patient safety.

References:

1. Fennrich S et al. More than 70 years of pyrogen detection: Current state and future perspectives. Altern Lab Anim. 2016 Jul;44(3):239-53.
2. Williams PB , Halsey JF, Endotoxin as a factor in adverse reactions to latex gloves Ann Allergy Asthma Immunol 1997 Oct;79(4):303-10 and Zivot JB, Hoffman WD, Pathogenic effects of endotoxin, New Horiz. 1995 May;3(2):267-75.
3. Peiró S et al., Quantitative determination of endotoxins on surgical gloves. The Journal of Hospital Infection 1990 Volume 16, Issue 2, Pages 167-172.
4. Kure R et al., Pyrogens from surgeons' sterile latex gloves. Acta Pathol Microbiol Immunol Scand. 1982 Apr;90(2):85-8.
5. Greenfield EM et al. Does endotoxin contribute to aseptic loosening of orthopaedic implants. J Biomed Mater Res B Appl Biomater 2005 Jan 15;72(1):179-85.
6. Shmunes E, T Darby T, Contact dermatitis due to endotoxin in irradiated latex gloves. Contact Dermatitis. 1984 Apr;10(4):240-4.
7. Thorne PS et al, Surface sampling for endotoxin assessment using electrostatic wiping cloths. Ann.Occup. Hug. 2005, Vol 49, No 5, pp 401-406.
8. Takahashi G et al., Endotoxin contamination of single-use sterile surgical gloves. Future Microbiol Vol 15 No 15. Published Online:6 Nov 2020 https://doi.org/10.2217/fmb-2020-0153.
9. What are the endotoxin limits for medical devices: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-pyrogen-and-endotoxins-testing-questions-and-answers. Accessed 17.12.20. 1
10. American Society for Testing and Materials (ASTM) D7102-17 Standard Guide for Determination of Endotoxin in Sterile Gloves.
11. EN 455-3:2015 Medical Gloves for Single use – Part 3. Requirements and Testing for Biological Evaluation.

Find out more at www.molnlycke.se

Mölnlycke®