The emergence of a stronger resistance

According to the World Health Organisation (WHO), the resistance built up by certain bacteria is becoming a growing threat in our modern society and is putting at risk our ability to treat common infections. This issue, called "the superbug crisis", refers to resistance built up by bacteria towards the antibiotics previously used against them. Due to this resistance, some concerns have been raised about the effectiveness of common disinfectant procedures. This paper will go through various bacteria and viruses known to be difficult to prevent, and review the different disinfectant procedures that can be used to prevent them.

Staphylococcus aureus

Staphylococcus aureus is a group of bacteria - not always pathogenic - that can cause a multitude of infections. Often called staphylococcal or staph infections, their impact ranges from minor to life-threatening conditions if and when they become invasive.[1]

Most of the strains of *Staphylococcus aureus* are responsive to antibiotics and can easily be destroyed. Unfortunately, some other strains have developed a stronger resistance enabling them to survive. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a type of *Staphylococcus aureus* which started developing resistance to Penicillin in the late 1940s. To counter this Methicillin was then introduced as a replacement until 1961, when British scientists discovered that *Staphylococcus aureus* had also built up a resistance against it. This resulted in its name: MRSA. It was later discovered that the family of antibiotics known as beta-lactams to which Penicillin and Methicillin belong were all ineffective against the bacteria. In 2002, Vancomycin (another antibiotic) also started to show weaknesses against a few strains of *Staphylococcus aureus*. Based on its multi-resistance, some believe that MRSA should now stand for "Multi-drug resistant *Staphylococcus aureus*" but its original name (Methicillin-resistant *Staphylococcus aureus)* remains widely used today.[2]

When non-invasive, MRSA causes mild skin infections such as boils or impetigo. However, if the bacteria become invasive, they can provoke serious complications such as blood poisoning, urinary tract infection, endocarditis and pneumonia.

According to the Queensland Health, MRSA can either be transmitted via close contact with an infected person or via contaminated surfaces or objects. Know to be especially problematic in hospital environments, MRSA began as a hospital-acquired infection (HA-MRSA).

The risks of outbreaks in medical institutions remain a major concern for the following reasons:

- A large number of patients are gathered within the same infrastructure;
- patients tend to be weakened by their condition and more vulnerable; and
- patients often have injuries or wounds which can lead to invasive MRSA infections.[3]

Today, MRSA is known to be community-acquired (CA-MRSA) as well as hospital-acquired (HA-MRSA). Raising awareness in schools and promoting hand washing for parents and children has become one of the main efforts to prevent the spread of the bacteria.

Clostridium difficile

Clostridium difficile (C. diff.) is another kind of hospital-acquired infection. This gram-positive, spore-forming anaerobic bacterium is the causative agent of *Clostridium difficile* associated disease (CDAD).[4]

Gram-positive defines the characteristic of a bacterium that has a cell wall composed of a thick layer of amino acid and sugar substances, called peptigoglycan. Anaerobic means that the bacteria do not need oxygen to survive and multiply. These properties enable C. diff. to invade the colon and affect the digestive system.

Clostridium difficile infections (CDI) are usually linked to patients who have been treated with broad spectrum antibiotics. Those antibiotics, used against a variety of bacteria, can also destroy the natural bacteria present in the bowel that protect against C. diff. When this happens, C. diff. can multiply and produce toxins resulting in mild to severe inflammation of the colon, known as colitis. This provokes diarrhoea, high temperature and painful abdominal cramps.[5]

As C. diff. produces spores, the bacteria spread easily when leaving the body of an infected person via diarrhoea. The spores which are a much more resistant form of cell can survive on objects and surfaces for many weeks. They can also spread

[1] 'NHS' 'Staphylococcal infections' www.nhs.uk/conditions/Staphylococcal-infections/Pages/Introduction.aspx
[2] 'National Institute of Allergy and Infectious Diseases' 'Methicillin-Resistant *Staphylococcus aureus* (MRSA)' www.niaid.nih.gov/topics/antimicrobialresistance/examples/mrsa/pages/history.aspx
[3] 'NHS' 'MRSA infection' www.nhs.uk/conditions/MRSA/Pages/Introduction.aspx
[4] 'Society for General Microbiology' http://mic.sgmjournals.org/content/journal/micro/10.1099/mic.0.2008/016592-0?crawler=true&mimetype=application/pdf
[5] 'NHS' 'Clostridium difficile' www.nhs.uk/conditions/Clostridium-difficile/Pages/Introduction.aspx

through the air, for example while making the bed, or via the hands of people who come in contact with infected patients or contaminated surfaces. As spores can survive for a long time, the risk of ingesting the bacteria (by touching your nose or mouth after touching a contaminated surface for instance) becomes high unless they are removed by thorough cleaning and repetitive hand-washing.[5]

C. diff. is known to be the biggest cause of infectious diarrhoea in hospitals. According to the Australian Commission on Safety and Quality in Health Care, the country that has been the most successful at reducing C.diff. infections is England. Between 2007 and 2014, England has reduced its number of C.diff. infections from 148.9 to 30.9 per 100,000 bed days.[6]

Although there is no uniform surveillance in Australia, a report published in 2014 in the Medical Journal of Australia revealed the results of a study carried out in 450 public hospitals. At the end of 2012, 4.06 C.diff. infections per 10,000 bed days were recorded. This could be generalised at 40.3 C.diff. infections per 100,000 bed days which is very close to the English numbers.[7]

Norovirus

Unlike MRSA and C. diff. Norovirus is commonly acquired in communities. Norovirus is extremely contagious and can easily be spread in public places such as schools, hotels, cruise ships and other environments.

Sometimes known as Small Round Structured Virus (SRSV), Calicivirus or Norvalk-like virus, Norovirus can also be referred to as stomach flu, food poisoning or winter vomiting bug. It classifies as a non-enveloped virus and although it cannot survive for a very long time in a living body, it does present a higher resistance in outside environments compared to other viruses.[8]

Norovirus is known to be the most common cause of gastroenteritis in Australia. According to the Department of Health of the Australian Government, there are an estimated 1.8 million cases of Norovirus infections each year. The virus is highly contagious because it can survive for many days in the outside world, even in extreme temperatures. People can catch it very easily by touching their nose, mouth or eyes after being in contact with an infected person or touching contaminated surfaces or objects. The virus can also spread through the air, making it very difficult to control. It can also be caught by eating food or drinking water that has been prepared or served by someone who is or was recently ill. Although very unpleasant, it is usually mild and there is no real cure against it. Symptoms can include vomiting, diarhorrea and fever which can lead to dehydration.[9]

Even though Norovirus tends to be less dangerous than MRSA and C. diff. it is far more difficult to prevent. Implementing a proper decontamination procedure including frequent hand washing and high-level disinfection is essential to help keeping the number of infections down. MRSA, C. diff. and Norovirus are known to be difficult to prevent due to their antibiotic resistance, presence of spores, and contagious state respectively. However, there is a concern today that MRSA might evolve to develop a resistance to disinfectants as they did for antibiotics. This concern also extends to other Multidrug Resistant Bacteria (MRB) such as Vancomycin Resistant *Enterococcus* (VRE) and Carbapenemase Producing *Enterobacteriaceae* (CPE). *Enteroccoci* and *Enterobacteriacecae* are bacteria usually present in the human intestines. However they can also lead to infections; as they have developed resistance against strong antibiotics and can survive in the environment for many weeks. One study showed that VRE was still found on surfaces four weeks after an outbreak and was still viable.[10]

The Importance of High-Level Disinfection

Even though it is feared that MRB might develop a resistance towards disinfectant solutions as they did for antibiotics, this is yet to be proven. As far as the industry knows, the appearance of surviving strains after disinfection has nothing to do with a possible resistance and is in fact usually caused by other factors such as inadequate dilutions, wrong proportions and/or insufficient contact times.[11]

One method sometimes used in some markets to counter any risk of resistance is called rotational cleaning. Although used by some hospitals, rotational cleaning was originally implemented for the disinfection of cleanrooms. Cleanrooms are used in many industries to produce material and/or equipment sensitive to contamination. The air quality, temperature and humidity need to be constantly regulated. In biotechnology and medicine, cleanrooms are used to ensure an environment free of bacteria, viruses and other pathogens.[12]

Rotational cleaning in cleanrooms is based on the theory that two or more disinfectants need to be used, so that if a few bacteria survive a dose of a certain agent, the second one will be there to kill the remaining strains before they get a chance to multiply and pass on their genetic resistance.[13]

[6] 'Australian Commission on Safety and Quality in Health Care' 'Consultation on surveillance and monitoring of *Clostridium difficile* infection in Australia' April 2015, Page 24
[7] 'The Medical Journal of Australia' 'Increasing incidence of *Clostridium difficile* infection, Australia, 2011-2012' March 2014, Pages 272-276.
[8] 'Health Knowledge' 'Norovirus' www.healthknowledge.org.uk/public-health-textbook/disease-causation-diagnostic/2b-epidemiology-diseases-phs/infectious-diseases/norovirus
[9] 'Australian Government' 'Department of Health' 'Guidelines for the public health management of gastroenteritis outbreaks due to norovirus or suspected viral agents in Australia' April 2010
[10] 'Building Better Healthcare' 'New superbugs threatening UK hospitals' www.buildingbetterhealthcare.co.uk/news/article_page/New_superbugs_threatening_UK_hospitals/102416
[11] 'Institute of Validation Technology' 'Sanitization of Pharmaceutical Facilities' www.ivtnetwork.com/article/sanitization-pharmaceutical-facilities
[12] 'Clean Rooms' 'Consulting, Design and CleanRoom Execution' http://clean-rooms.eu
[13] 'Cleanroom Technology' 'Rotational cleaning: is it necessary' http://www.cleanroomtechnology.com/technical/article_page/Rotational_cleaning_is_it_necessary/94424

Cleanroom disinfection can be very strict. A specific number of particles is established per cubic metre. The number varies based on the cleanroom classification. Environmental surfaces in hospitals are however classified as non-critical items. The disinfection is required to prevent healthcare associated infections (HAI's) and outbreaks. This disinfection process needs to be distinguished from the one used in cleanrooms. Environmental surfaces tend to be in contact with intact skin only. There is no risk of contaminating highly sensitive material as there is in cleanrooms, neither is there a high risk of contaminating internal tissues of the body.[14]

When rotational cleaning is implemented, careful consideration must be given to the disinfectants used. Each disinfectant has a different spectrum of activity, mode of action and efficacy. Healthcare professionals need to make sure that at least one of these disinfectants is strong enough to kill spores, bacteria and Norovirus.

Current guidelines of the Department of Health recommend chlorine-based products (e.g. sodium dichloroisocyanurate - NaDCC) when there is a C.diff. outbreak. Sodium hypochlorite (NaOCl), another oxidising agent is widely used to disinfect environmental surfaces in hospitals. The efficacy of sodium hypocholorite at a concentration of 5,000 ppm has been highlighted in a number of publications. Based on those guidelines and reports, the industry tends to rely on NaDCC and NaOCl when it comes to high-level disinfection. However, it has also often been pointed out that NaDCC and NaOCl are not compatible with all type of surfaces.[15]

NaDCC and NaOCl are known to be corrosive, harmful to users and bad for the environment. Achieving the correct concentration and contact time can also be difficult. These will differ from one manufacturer to another and need to be carefully checked on the product label prior to each use.[16]

Based on the above and regardless of the fact that rotational cleaning is not required for environmental surfaces in hospitals, some believe that the use of two or more disinfectants will prevent the possibility of pathogens developing resistance, while increasing the spectrum of activity of the decontamination process. The use of the stronger sporicidal disinfectant will also become less recurrent which will reduce possible damage on the surfaces, making it safer and easier for the user at the same time.

Chlorine dioxide (ClO_2) is a solution mentioned in various guidelines, which presents similar advantages as rotational cleaning. Chlorine dioxide has been used for water, food, and agriculture disinfection for more than 20 years.

In England, the Revised Healthcare Cleaning Manual of the NHS states that chlorine dioxide is more effective than chlorine. The required concentration of chlorine dioxide is lower. The efficacy of chlorine dioxide against spores and other pathogens is proven, and it is safer and quicker to use compared to hypochlorite products.[17]

The Tristel for Surfaces range is based on Tristel's proprietary chlorine dioxide chemistry. Tristel Fuse, Jet and Duo are all sporicidal, mycobactericidal, virucidal, fungicidal and bactericidal. They have been tested against a wide range of microorganisms and achieve a $\rangle 3$ $\log_{10}$ reduction against C.diff, a $\rangle 4$ $\log_{10}$ against Norovirus and a $\rangle 5$ $\log_{10}$ against MRSA, CRE and VRE. The contact times required to achieve the biocidal efficacy differ from one product to another:

Tristel Fuse

Tristel Fuse for Surfaces is a high-level sporicidal disinfectant designed for large surface areas. Delivered in sachets, the solution needs to be diluting into 5L of cold water and will achieve sporicidal efficacy in only 5 minutes.

Tristel Jet

Available in a gel or liquid spray format, Tristel Jet will achieve sporicidal efficacy in 30 and 60 seconds respectively.

Tristel Duo

Tristel Duo for Surfaces is a sporicidal disinfectant foam which destroys harmful micro-organism with a contact time of only 30 seconds.

Tristel's proprietary chlorine dioxide chemistry is based on two components: Organic acids (citric acid) and sodium chlorite (salt). Tristel's chlorine dioxide chemistry has an exceptional health and safety record. As well as being a safer and more effective alternative to NaDCC and NaOCl, pathogens cannot develop resistance towards it. Chlorine dioxide is a cell destroyer, meaning there is no chance of any microorganism adapting.

In a recent study, the Healthcare Infection Society compared thirty-two disinfectants against spores of C.diff. The disinfectants included chlorine dioxide, hypochlorite solutions, triamine, quarternary ammonium compound-based mixtures and peracetic acid. They were tested in a suspension test based on the European Standard BS EN 13704:2002, with contact times of 1 and 60 min in clean and dirty conditions. This study identified chlorine dioxide as the only agent able to remove C.diff. from the membrane filter under all the test conditions.[18]

Tristel's proprietary chlorine dioxide chemistry has helped many hospitals around the world to prevent outbreaks and improve disinfection procedures.

[14] 'Centers for Disease Control and Prevention' 'Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008'
www.cdc.gov/hicpac/Disinfection_Sterilization/3_4surfaceDisinfection.html
[15] 'Torbay and Southern Devon Health and Care' 'Clostridium Difficile'
www.sdhct.nhs.uk/uploads/g0914-c-diff-protocol.pdf
[16] 'Staph Infection Resources' 'How to disinfect, clean and kill MRSA' www.staph-infection-resources.com/prevention/infection-control

[17] The Revised Healthcare Cleaning Manual, NHS, Pages 159-160 – Dual function hypochlorite cleaner/disinfectants
[18] Journal of Hospital Infection, Volume 79, Issue 1, September 2011, Pages 18-22 – Evaluation of the sporicidal activity of different chemical disinfectant used in hospitals against Clostridium difficile

In August 2012, University Hospitals Coventry and Warwickshire (UHCW) NHS Trust set out a challenge to achieve 100 days free of C.diff. in all its hospital departments in Coventry and Rugby. Today all wards have achieved 100 days free of C.diff., with 70% of them now over a year and six of those achieving an amazing 1,000 days free of C.diff.[19]

For chlorine to reach Tristel sporicidal efficacy, 25 tablets would have had to be diluted into 5L of water, resulting in a solution that is toxic for staff and corrosive for surfaces. Innovative delivery systems ensure that Tristel's chlorine dioxide chemistry is delivered in a quick and effective way at one concentration for each application.

Picture 1: *Tristel for Surfaces range.*

[19] The Clinical Services Journal, Why disinfect when you can Tristel? August 2015, Pages 6-7