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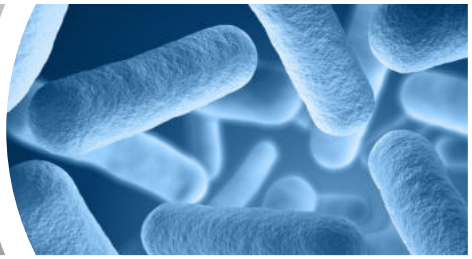

USA: aquatools Inc. – 1 Broadway, 14th floor – Cambridge, MA 02412 United States
Call us: +1 872 261 1554 – sales@aquatools.us
Headquarters: AQUATOOLS – 18, rue du Maréchal Foch – 80130 Friville – France
Tel.: +33 1 39 75 02 20 – www.aquatools.us

Origins, cross-contamination, surveillance, how to protect patients?

HOW FILT'*RAY* POINT-OF-USE FILTERS CAN PREVENT WATERBORNE INFECTION

Pseudomonas and other GRAM negative bacteria in ICUs and neonatal ICUs

Within the classification of gram negative bacilli, the *Pseudomonas* genus has undergone numerous changes and it is now necessary to refer to different sub-classes of *Proteobacteria*:

- *Brevundimonas sp*,
- *Burkholderia sp*, *Ralstonia sp*, etc.,
- *Pseudomonas sp*, *Xanthomonas sp*, *Stenotrophomonas sp*, etc.

It is easier to use the denomination Pseudomonades, described in "Bergey's manual" as straight or slightly curved non-sporulated gram negative bacilli, usually mobile, with one or more polar flagellae. These bacteria develop **aerobiotocally**, with a respiratory metabolism, and are able to exploit carbonated substrates and numerous hydrolytic enzymes. As a consequence, they are able to grow in a variety of different environments, particularly using plastic materials and hydrocarbons. There are now at least 150 species within the *Pseudomonas* genus which can be found in a vast majority of ecosystems with a remarkable ability to survive and multiply even in hostile conditions, in particular in water with limited nutriments.

The main species of interest in hospitals is *Pseudomonas aeruginosa*, a hydrotropic bacterium, able to develop within biofilms, that is resistant to numerous biocides and antibiotics. This allows *Pseudomonas* to colonize water distribution systems, faucets, siphons and any humid environment (surfaces, linen, medical devices, etc.). Including virulence factors, *Pseudomonas aeruginosa* may grow inside numerous animal species and human, who can be healthy or infected carriers.

The species *P. stutzeri* can, sometimes, be associated with human pathology and *Burkholderia* complex *cepacia* and *Stenotrophomonas maltophilia* are increasingly linked to infections in Intensive Care Units (ICUs) and immunocompromised patients, especially in the Neonatal ICUs (NICUs). Each species can easily build biofilms and develop within them: they may also be hosted by free-living amoebae which are highly resistant to disinfectants.

Other gram negative bacteria are increasingly playing a more significant role in waterborne infections in ICUs because of their resistance to antibiotics delivered by different mechanisms. They also thrive in humid environments where they can survive for long periods. Siphons are often contaminated with these antibiotic resistant gram negative bacteria such as *Klebsiella*, *Enterobacter*, *Serratia*, *Acinetobacter*, etc., which are also possibly resistant to disinfectants and able to survive inside Amoebea.

The results of routine analyses at the point-of-use in hospital water distribution systems indicate a low percentage of positive samples. This illustrates that distributed water may distribute this kind of bacterium even after disinfection treatments, both continuous or intermittent, resulting in the need for specific preventive measures.

This is the reason for the dual origin of the strains of *P. aeruginosa* encountered in these ICUs: one that originates in water, linked to the contamination of faucets, shower heads, siphons, and humid surfaces, etc., and one of human origin, linked to patients and healthcare personnel who are healthy carriers (for example, fecal transmission, which explains the importance of hand washing and disinfection). Cross-contaminations may occur between patients and between healthcare personnel and patients, where environmental strains may also be transmitted.

Inside hospital, exposure rarely occurs via oral methods, but via the respiratory route (aerosolization), via injection (contaminated medical device) or via contact or transcutaneous penetration, for example along a catheter. This underlines the importance of a high level of water quality during the patient's care in ICUs and NICUs, or for rinsing medical devices, and is even more important when the patient is immunocompromised or immunosuppressed.

In level III High-Risk Nurseries (HRNs) or Neonatal Intensive Care Units (NICUs), the newborns have a limited immune system linked to their age of gestation and to the limited number of antibodies transferred by the mother. In adults ICUs, immunosupression is possibly brought

on by a pharmaceutical treatment (for example, cortisone or antirejection drugs), or linked to the evolution of the sickness (for example, cancer, cystic fibrosis, burns) or to the age of the patient. This allows the expression of the virulence factors of these bacteria, particularly the extracellular proteolytic enzymes. The clinical symptoms will be diverse and vary according to the infected site: respiratory infections, abscesses, cutaneous or infections in the oropharyngeal sphere, urinary infections, bacteremias and septicemias, endocarditis, etc. The evolution will be more severe if the strain is antibiotic-resistant, limiting the therapeutic possibilities, and also if the patient is immunocompromised.

Numerous epidemiological studies have been dedicated to healthcare associated infections (HCAIs) due to *Pseudomonas aeruginosa* and other Gram-bacteria in ICUs and trauma wards. An excellent synthesis may be found in the articles of Vincent et al., 1995, and Richards et al., 1999.
This bacterium has the second highest levels of incidence, behind *Staphylococcus aureus*, with a prevalence of around 30%. The epidemiological situation is highly variable, depending on the hospital and the control measures they have put in place, but it is reasonable to assume that, globally speaking, half of these ICU infections are endogenous, linked to an original transmission by the patient. The second half of these infections are due to cross-contamination linked to the transmission of a human or environmental strain to the patient; in this case the water distribution system within the ICU is often the source of this strain (Bertrand et al., 2001). Since the 2000's, this has been clearly demonstrated, for example, by Trautmann et al., 2001 (of 17 patients studied, 29% were infected with a strain found in the faucet) and Reuter et al., 2002 (of 45 patients studied, 35% were infected or colonized by tap water strains, and 15% of faucets were retro-contaminated with patients strains).

Multiple papers report HAI cases linked to a contamination of newborns by *Pseudomonas aeruginosa* or other gram negative bacteria. The most famous recent outbreak occurred in Northern Irish neonatal ICUs in 2011, and the subsequent investigations, described by Walker et al. in 2014, reported a strain of *Pseudomonas aeruginosa* isolated from contaminated faucets as the source of infection.

The conclusion is, therefore, that it is essential to secure the water quality at the point-of-use in sensitive hospital wards to prevent waterborne infections. It appears that the first team to use Point-of-Use Filters (PoUFs) was Italian, presented by Ricci and Vianelli during a conference in 2004. Trautmann published the first study in 2005, demonstrating the efficacy of PoUFs in an adult ICU.
In his study, the use of filters delivered germ-free water at all points-of-use and progressively reduced the number of colonizations/infections from 5 - 10 at the beginning of the study, to 0 - 1 per month at the end of the study. **Some researchers highlighted the lack of statistical data to support this study. So, in 2008, following a longer observation period, the group published clearly evidencing the efficacy of the PoUFs**.

Similar findings in a hematological ward were published by Vianelli et al. in 2006 after installing filters on all points-of-use (faucets and showers).

Since then, more and more European ICUs and NICUs are using PoU filters to reduce the bacterial content of water used in healthcare and to comply with the water quality criteria required by French water guidelines (Guide de l'Eau 2005) i.e. "Bacteriologically Controlled Water" (BCW), or the UK 2012 guidelines that requires monitoring for *Pseudomonas aeruginosa* to indicate the water quality in NICUs and ICUs. There are multiple papers which illustrate the excellent results obtained by using PoUFs, both in terms of absence of opportunistic bacteria downstream of the filter which provides a physical barrier, and in terms of clinical results, with a dramatic reduction in colonization and infections (Ortolano et al. 2005). An article by Kerr and Snelling in 2009, focusses on *Pseudomonas aeruginosa* and infection prevention in ICUs and NICUs.

Some "purists" assume that these results need to be supported using epidemiological studies with an undisputable methodology. This is undesirable for ethical reasons, considering the actual results and the official guidelines; exposing a group of "control" patients to the risk of infection by a waterborne pathogen without taking the risk of receiving justifiable complaints from the test-subject's family, and without incurring legal and judicial consequences.

Increased monitoring of water quality control in neonatal wards and in areas where there are patients at risk is covered by the WHO's "Water Safety Plan" framework. Point-of-use filtration of water in NICUs and ICUs, where the most vulnerable patients are cared for, is absolutely essential, and is an example of the indisputable progress experienced over the last few decades. *P. aeruginosa* is considered to be representative of, and an indicator for, the risk of infection from waterborne microorganisms.

Monitoring for the bacterium is required at the point-of-use to ensure that the required level of <1 CFU/100mL is maintained in BCW, and also to ensure high levels of protection during hospitalization. This is now a standard of care in many countries.

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