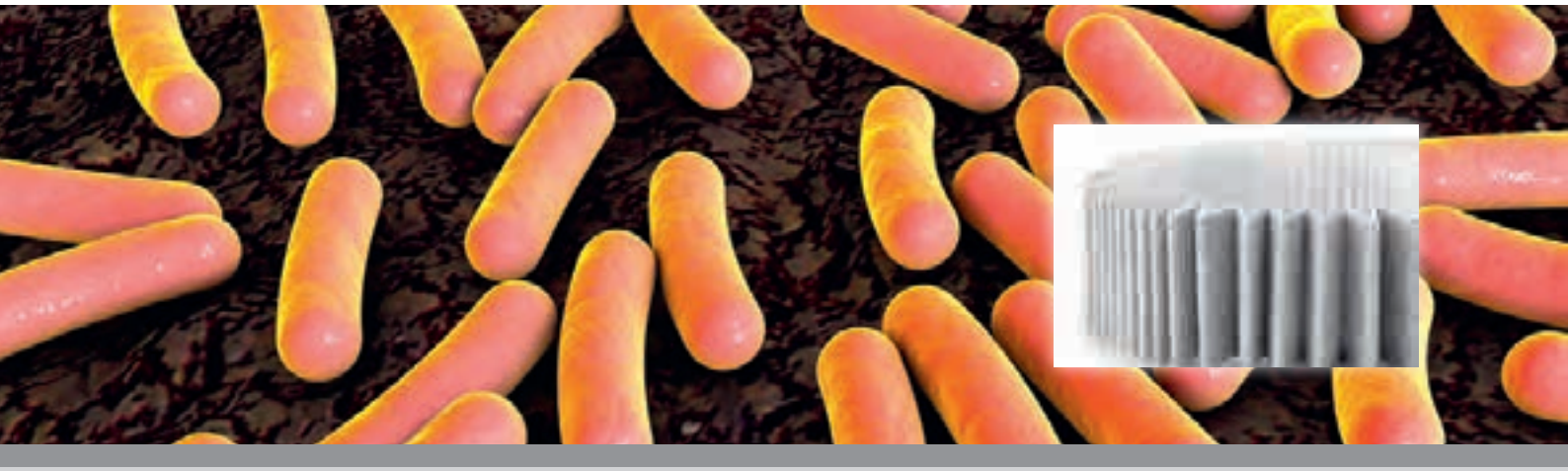
Importance of water and Gram negative microbes in hygiene



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Foreword

Dear professionals,

Water is an important environment for microorganisms. For us humans, water is vital, beneficial and refreshing. It also plays a role in the traditional therapeutic methods of classical naturopathy, helping to maintain our health. In contact with water, we humans are constantly taking in large numbers of these tiny living things when we drink, inhale aerosols or swallow or when water comes into contact with injured skin or mucous membranes.

Most of the pathogens present in water in this region do not cause diseases in healthy people. But things are different when these microorganisms come into contact with people whose immune system or barrier system is weakened. This description encompasses babies, elderly people and those with impaired health. The last of these groups includes those with chronic wounds, hemato-oncological diseases, diseases affecting large areas of skin or mucous membrane, lung diseases or certain metabolic diseases and patients who need one or more catheters (urinary catheters, catheters in blood vessels, feeding tubes etc.).

These populations need special protection that recognizes their risk of becoming infected by pathogens present in water and incurring what is known as a waterborne infection. Because unlike endogenous infections - where the infecting pathogen stems from the patient's own microbiome so that nosocomial occurrence in some cases cannot be prevented with hygiene - waterborne nosocomial infections can usually be prevented by using appropriate measures.

For this reason, intensive monitoring of drinking water quality is especially important to protect patients in health care facilities because these people tend to be at particular risk of contracting waterborne infections.

This booklet provides a glimpse into the complex world of water hygiene, from the formation of biofilms in water systems to the epidemiology and frequency of waterborne diseases. Even now, many nosocomial infections are still caused by pathogens for which water systems act as the main reservoir. For those responsible for the management of infection and hygiene, therefore, an important goal is to recognize the danger points and the potential for spread; their task is to protect the patients by using effective strategies to pursue rigorous prevention of waterborne infections.

Yours

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Nosocomial infections: Statistics and distribution

A look at the statistics

In Germany, the overall prevalence of nosocomial infections in 2016 was 4.6 %. The prevalence of nosocomial infections contracted during the current hospital stay was 3.3 % of all patients treated. This means the current hospital stay was the source of infection for 72.6 % of all nosocomial infections. For large hospitals in particular, and specifically for university hospitals, a high infection rate of 6.6 % was found. **The highest prevalence rate (17.1 %) was found in intensive care units; the prevalence in non-intensive care wards was 3.84 % (2).**

In 2011 the prevalence of nosocomial infections was 5.1 % and in 1994 it was 3.5 %. The prevalence of nosocomial infections in Germany is thus increasing (1). Data from the Robert Koch Institute (RKI) indicate that 400,000 to 600,000 people contract nosocomial infections each year (12). According to Gastmeier et al. (2016), the pathogens S. aureus, E. faecium, E. coli, K. pneumoniae and P. aeruginosa together cause 231,000 nosocomial infections per year. **Of these 231,000 infections, 29,000 are caused by multidrug resistant pathogens (13).**

In a report published by the World Health Organization (WHO) in 2002, the prevalence of nosocomial infections in four WHO regions (Europe, Eastern Mediterranean, South-East Asia and Western Pacific) was reported to be 8.7 % of all hospital patients (4). According to the European Centre for Disease Prevention and Control (ECDC), the point prevalence of nosocomial infections was 19.5 % in intensive care units and 5.2 % for all other wards combined (5).

In 1994 the prevalence of patients receiving antibiotic treatment in Germany was still 17.7 % (1).

In 2016, 25.9 % of all patients received treatment with antibiotics although only 73 % of these patients exhibited an indication for antibiotic treatment (2). **Thus the number of antibiotic treatments in Germany also increased significantly.**

Gram negative bacteria

The final report of the NRZ (National Reference Center) on nosocomial infections and antibiotic use (2017) states: **In 42.3 % of all nosocomial infections in which the pathogens were identified, Gram negative bacteria were the culprits.** Although the proportion of Gram positive bacteria fell significantly by comparison with 2011, the proportion of Gram negative bacteria remained unchanged in 2016. Escherichia coli (16.6 %), Pseudomonas aeruginosa (5.8 %), Klebsiella pneumoniae (4.5 %), Proteus mirabilis (2.8 %) and Enterobacter cloacea (2.6 %) are particularly frequent Gram negative pathogens (2).
Three of these pathogens were discussed in the ECDC report "Surveillance of antimicrobial resistance in Europe 2016" which was published in 2017. **The study showed that 58.6 % of E. coli isolates were resistant to at least one of the major substances. 4.8 % were resistant to four major substances and <0.1 % were resistant to five major substances.**

34.5 % of the *Klebsiella pneumoniae isolates* showed resistance to at least one of the major substances and 4.4 % were resistant to four major substances.

Of the *Pseudomonas aeruginosa isolates*, 33.9 % demonstrated resistance to at least one major substance. 4.3 % of the isolates were resistant to four major substances and 4.4 % were resistant to five major substances. In the USA it was reported that, between 1999 and 2003, the proportion of fluoroquinolone-resistant *Pseudomonas aeruginosa* bacteria in intensive care units increased from 23 % to 29.5 % (3).

A study at a neonatal intensive care unit in the USA showed that infections due to multidrug resistant pathogens are not restricted to adult patients. The study found that, in the year 2000, ≤4% of the infant patients was infected with MRSA or VRE while 10 – 24 % of babies were colonized by Gram negative bacteria resistant to ceftazidime or aminoglycoside. In addition, <3 % were colonized by β-lactamase-producing Gram negative bacteria (3).

Nosocomial infections: Mortality and resistance

Mortality

In Germany, about 10,000 to 15,000 patients die each year as a result of nosocomial infections (12). 1,000 - 4,000 of these deaths are due to multidrug resistant pathogens. Throughout Europe it is estimated that about 91,000 deaths occur (14). According to Gastmeier et al. (2016), 37,000 people throughout Europe die from nosocomial infections; 25,000 deaths are caused by multidrug resistant pathogens. However, the authors note that about 60 % of the infected people already had severe diseases which would have caused death within a short time even without the additional infection. After excluding these cases, the number of people in Germany dying from nosocomial infections was less than 6,000 (13).

In the USA, the CDC (Centers for Disease Control and Prevention) estimate from the data for 2008 that nosocomial infection leads to 1.7 million infections and 99,000 deaths per year. 1,400 of these deaths are thought to be due to the Gram negative pathogen Pseudomonas aeruginosa alone (6). More recent data indicate that 648,000 people in the USA contract nosocomial infections each year and 23,000 of these infections lead to death as a result of multidrug resistant pathogens (13). Patients with a significantly compromised immune system, such as patients in intensive care units, transplant units and oncology wards, are particularly susceptible to nosocomial infections (7).

A study by Benin, Beson and Besser (2002) showed that the mortality from nosocomial Legionnaire's disease is about 40 % higher than the mortality of patients who become infected with the disease outside hospital.

Classifying the risk

The WHO (2017) classes antibiotic-resistant bacteria as a significant threat to public health. The three bacteria (Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacteriaceae) listed in the Global Priority List of Antibiotic-Resistant Bacteria in the **Priority 1: CRITICAL class are Gram negative bacteria.**

In this publication, the WHO recommends that strategies be developed which tackle the development of new specific antibiotics against multidrug resistant Gram negative bacteria and, at the same time, limit the risk of infection and curb the spread of the pathogens. Actions to curb the spread include increased vaccination and improved hospital hygiene as well as long-term measures to prevent infection (8).

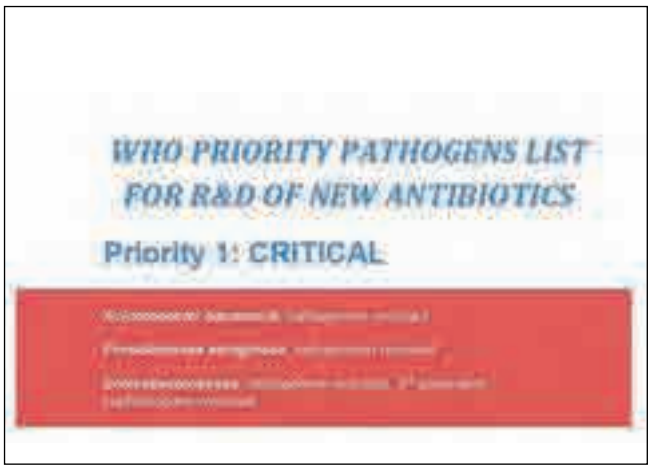


Fig. 1: WHO Priority Pathogens list

Gram negative bacteria and resistance

Gram negative bacteria and their talent for survival

Bacteria living in water or wet environments are usually Gram negative. The pathogenic species among them are increasingly becoming the focus of attention because they demonstrate resistance to antibiotics (especially carbapenem). When dealing with the pathogenic Gram negative bacteria, problems arise as a result of their frugality, their variability with regard to nutrients and their ability to form biofilms. *Pseudomonas aeruginosa* grows best at 30 °C but is able to survive well at any temperature between 4 °C and 42 °C.

The bacterium normally lives aerobically but is also able to switch to using nitrate as a substitute for oxygen. Under good conditions it divides every 30 minutes. **This microbe is able to reproduce well even in distilled water (35) and also survives on dry surfaces for up to 16 months (36).** *Acetinobacter spp.* can survive without water for up to five months (36). Antibiotic-resistant *Pseudomonas aeruginosa* also show resistance to chlorine solutions with chlorine concentrations of up to 0.5 mg/l (37).

Resistance to antibiotics – mission impossible in the microscopic world

The situation in Europe is serious. The following illustration shows the resistance of Enterobacteriaceae to carbapenem in Europe (38). It is clearly apparent that they are endemic in Greece and there have already been many other outbreaks.

Even relatively unknown microbes such as *Ralstonia pickettii* and mycobacteria are attracting increasing attention because they cause problems in such contexts as heater-cooler units and demineralized water (used for reprocessing instruments) (34,35). *Ralstonia pickettii* has been found in demineralized water many times and it is suspected that this species can also pass through 0.2 micron filters (39, 40).

Legionella bacteria have long been a focus of attention. As a result of the German Drinking Water Ordinance they are subject to regular monitoring but they nevertheless continue to cause numerous problems.

Fig. 2: Distribution of carbapenem-resistant Enterobacteriaceae in Europe

Exceeding limits

Speed traps for hospitals
Studies involving large numbers of samples (28) indicate that limits, especially those for *Pseudomonas aeruginosa*, are exceeded much more frequently in hospitals than in other public buildings such as schools or hotels. The limit for Legionella bacteria is exceeded in almost 50 % of hospitals. *Pseudomonas aeruginosa* is present in 30 % of water samples from hospitals. The graphic below illustrates this dramatic situation.

The figures show that patients and staff are exposed to Gram negative pathogens in numerous cases. There are many different reasons for this. A look at the German Health Ministry's report (47) shows that 17.9 % of Water Supply Zones take samples less frequently than they should. This means that one Water Supply Zone out of every six is not being adequately monitored. In 2016, 3.4 % of samples exceeded the limit for coliform bacteria and 2.1 % exceeded the limit for enterococci (47). One sample in 30 is not up to standard. And the problem pathogen P*seudomonas aeruginosa* is not monitored at all.

Ageing infrastructure is a further cause for concern. Many hospitals are very old and, thanks to the building of extensions, include a mix of different water supply pipe networks. The documentation of these water networks is often incomplete. Sections of pipe may not have been dismantled completely leaving dead legs; these, along with unused water outlets and old shower hoses or faucets, may be listed among the causes when limits are exceeded. Water treatment equipment such as ion exchangers to reduce the water's hardness and water demineralization plants may be wrongly dimensioned and inadequately maintained.

Especially when *Pseudomonas aeruginosa* is the colonizing organism, it is often impossible to completely eliminate the microbe from the water supply network (28). This organism is known to form biofilms (see p. 12). Once a biofilm is present, the organism can generally withstand water temperature increases and chemical treatment (with chlorine or chlorine dioxide).

Contamination pathways also lead to faucets (see p. 10). This means pathogens in samples taken according to Purpose c) of DIN EN ISO 19458 may come from patients or staff and not from the water supply.

The values indicate that limits are exceeded so often that the problem microbes can be considered to be permanently established in these buildings.

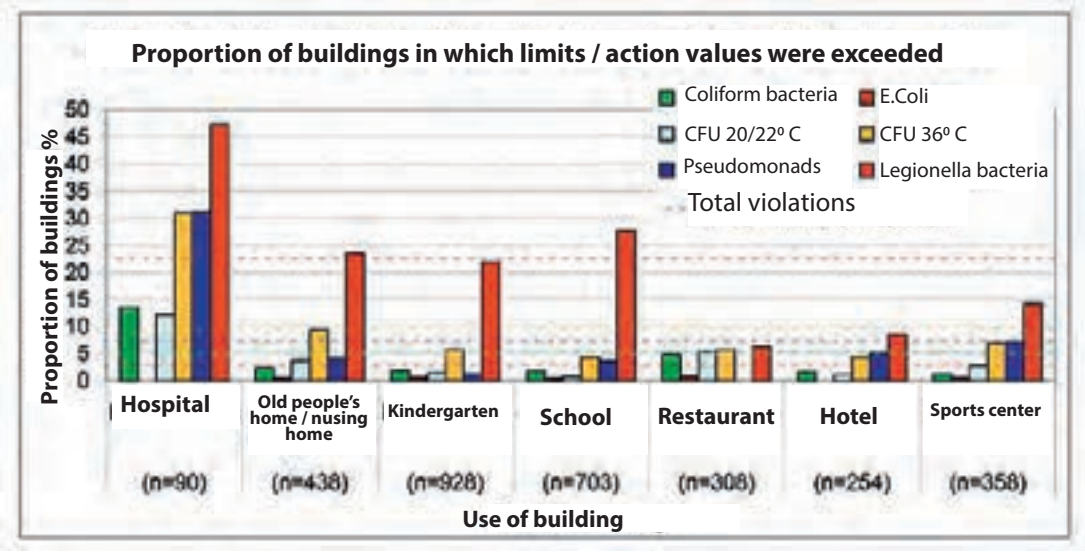


Fig. 3: Violations of the limit / action value at different establishments (28)

Wash me but don't make me ill

Over 70 % of drinking water in Germany is obtained from groundwater or bank filtrate (46). Treatment processes usually begin with the removal of particles, often by flocculation and (sand-) filtration; sometimes pre-oxidation is also carried out. Water treatment is monitored. However, the Health Ministry report (47) reveals that 17.9 % of the Water Supply Zones do not meet the minimum requirement for the frequency of routine monitoring investigations. This means one Water Supply Zone in six was not adequately monitored. If we also consider the frequency with which limits were exceeded in 2016 for coliform bacteria (3.4 %) and enterococci (2.1 %) (47), it can be concluded that one sample in every 30 violated a limit. An overall impression emerges which at least calls into question the frequently-quoted claim that "drinking water is the best-monitored foodstuff in Germany". Furthermore, the pathogenic problem microbe *Pseudomonas aeruginosa*, which is responsible for a huge number of infections, is not separately monitored.

Water is distributed through an increasingly elderly infrastructure, which is certainly a further factor in causing the violation frequencies shown in Fig. 3. The photograph below (Fig. 4) shows part of a water pipe taken from a street. Chorine is sometimes added to the water to ensure that parameters remain within limits during distribution.

According to the Drinking Water Ordinance, the limit for chlorine is 0.3 mg/l. However, it has been found that antibiotic-resistant bacteria also demonstrate insensitivity to chlorine at concentrations higher than 0.3 mg/l (5).

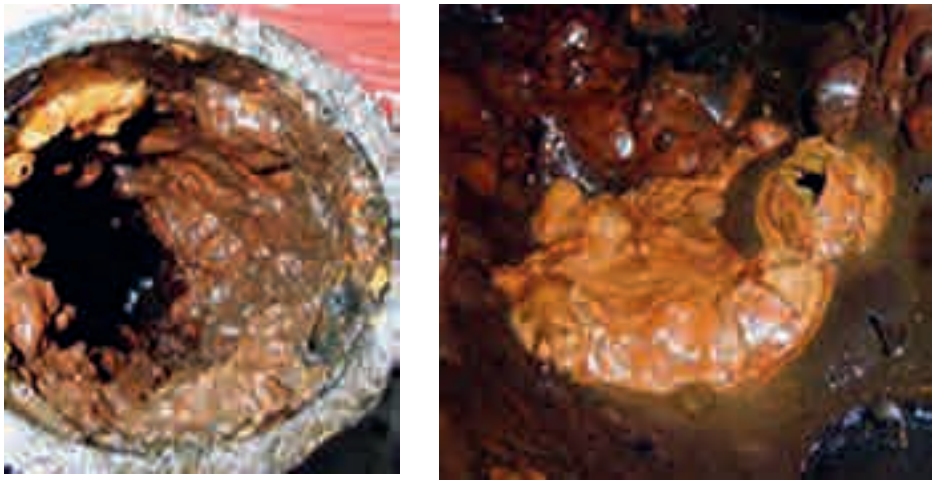


Fig. 4: interior of a drinking water pipe. Kindly authorized by Prof. Flemming, IWW Water Centre, Mühlheim an der Ruhr, 2012

Distilled water

Distilled water is produced by heating (boiling) water and cooling the resulting steam. The water obtained in this way has an extremely low mineral content and is therefore particularly suitable for reprocessing small numbers of instruments in a medical practice. It is often assumed that distilled water is free from microbes. However, that is not the case (48, 49). The problem microbe Pseudomonas aeruginosa is one of those that reproduce in distilled water. The reason for this is not the heating of the water, which reliably kills most microbes, but the containers that catch the distilled water and have not always been handled using sterile techniques.

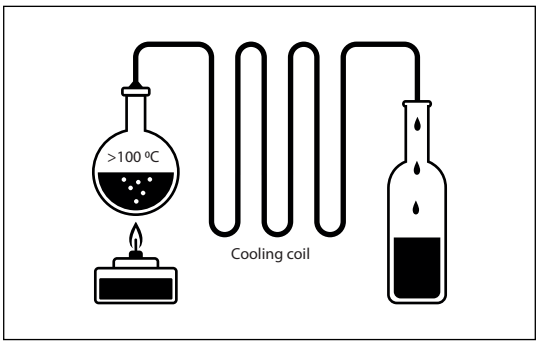


Fig. 5: Destillation

Reverse osmosis

Reverse osmosis is a type of membrane filtration. The pores of the membrane are so small that most salts are not able to pass through. The osmotic pressure naturally ensures that the concentrations are equalized. So if water is to be desalinated, work has to be done to oppose this pressure – hence the name "reverse osmosis". Water molecules are pushed through a membrane under high pressure against the osmotic pressure. The yield (flow per m2 of filter area) is very small so the device is normally in use non-stop (24 hours a day) and catches the filtrate in an expansion tank. This is emptied when water is used and refills itself during periods when water is not being used. The water obtained in this way has a low mineral content but is not free from microbes because of the expansion tank.

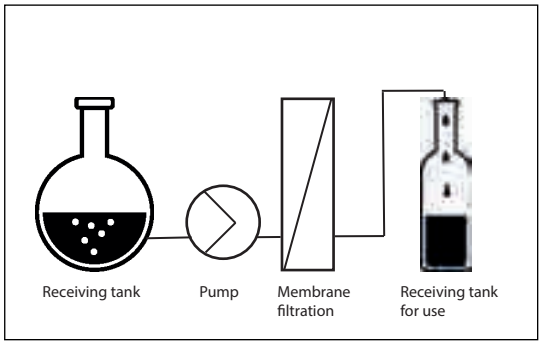


Fig. 6: Reverse osmosis

Ion exchanger

Ion exchangers are granulates with ions bound to their surface; these ions are exchanged for other ions. The granulates used to desalinate water have OH^- and H^+ ions on their surface. These are then exchanged for calcium (Ca^{2+}) or carbonate (CO_3^{2-}) ions. That means calcium carbonate molecules (lime scale) can be exchanged for water molecules (H^+ and OH^- produce H_2O). When all sites have been exchanged, the granulate is regenerated. This involves adding acid (excess of H^+ ions) and alkali (excess of OH^- ions).

This is one of the most popular methods of obtaining demineralized water because it is more efficient than reverse osmosis. Both processes can also be used in combination. From a microbiological viewpoint, the disadvantage of using a granulate lies in its very high specific surface area. This favors the formation of biofilm; it is therefore no surprise that demineralized water often contains Gram negative bacteria.

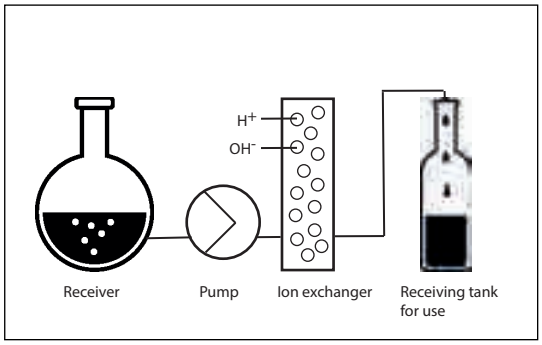
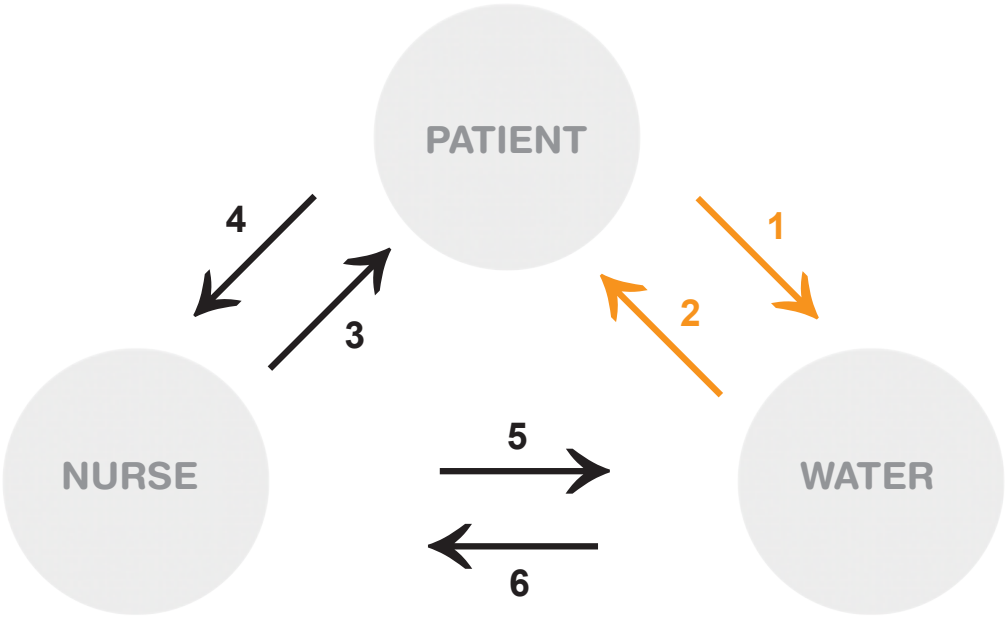


Fig. 7: Ion exchange

Contamination pathways



Studies by Rogues et al. (9) and Trautmann et al. (19) examined the contamination pathways of Pseudomonas aeruginosa in an intensive care unit. With the aid of microbiological surveillance and genetic typing, it was found that the spread of *Pseudomonas aeruginosa* within the unit was multidirectional.

It was shown that contaminated faucets transferred *Pseudomonas aeruginosa* to people (2 and 6) and that contact between nurse and patient can lead to contamination of either by the other (3 and 4). In addition, it was found that infected patients can cause retrograde contamination of faucets.

This contamination pathway from patient to faucet was recorded eleven times; it was recorded more frequently than contamination in the opposite direction from faucet to patient (seven cases).

Water outlets in hospitals are not regularly disinfected. They are therefore a particularly important reservoir of contamination. As a result of contamination coming from the water and caused by staff and patients, water outlets can become established as potential long-term sources of pathogenic Gram negative bacteria. Adequate hand disinfection by nursing staff after patient contact would be a step towards reducing retrograde contamination. The research team emphasizes the importance of further studies to examine the dynamic, multidirectional contamination pathways of nosocomial pathogens and to investigate possible interventions against them (9).

It is apparent that limits can be exceeded as a result of other factors as well as water quality. Water outlets should rather be seen as transit hubs for pathogenic Gram negative bacteria and should also be treated as such.

Hand hygiene

Studies show that hand hygiene is one of the most important interventions for avoiding nosocomial infections. Nonetheless, Kovacs-Litman et al. (2016) demonstrated that there was a lot of room for improvement in the hand hygiene compliance of the medical staff at a hospital in Toronto, Canada. The researchers employed two trained students to observe the hand hygiene behavior of doctors, trainee doctors and nursing staff; their observations were systematic and covert. The data obtained by the students were compared with an official check on hand hygiene that took place during the same period of time as the studies.

The results showed that there was a significant difference between the data obtained secretly and those gathered officially, both for the doctors and for the nursing staff. Hand hygiene compliance by the medical service was 83.7 % during the official check whereas concealed observation found it to be only 50 %. The lowest rate of hand hygiene compliance recorded by secret data collection was found on the emergency ward (43.9 %), followed by the surgical ward (45.7 %).

At the same time, the official audit recorded rates of 73.8 % and 91 % respectively on the same two wards. **The compliance of nursing staff with hand hygiene guidelines was found by the official check to be 85.8 % and by the hidden observers to be 45.1 %.**

The doctors showed overall compliance of 73.2 % in the official audit and 54.2 % in concealed data collection.

The authors emphasize that doctors possess an important function in that they set an example for trainee doctors.

Hand hygiene compliance by trainees was 79.5 % when the doctors disinfected their hands but only 18.9 % when the doctors omitted hand hygiene.

In addition, it was found that adherence to the guidelines was higher (74.8 %) when there was a potential risk to the person in question (e.g. from a patient in isolation). Lastly, it was found that compliance was higher in groups of more than three people than in smaller groups (62.1 % compared to 42 %) (22).

Waterborne *Pseudomonas aeruginosa* infections clearly show that the effects of *Pseudomonas aeruginosa* in particular have up to now been underestimated. This ought to lead to further legally-backed preventive measures in future.

Biofilm formation, the ideal protection from attack by humans

Pseudomonas aeruginosa is a typical biofilm-forming organism. This microbe is able to form what are known as extracellular polymeric substances (EPSs) and thus provide an extremely high level of protection for itself and also other bacteria. The EPSs serve as a barrier against chemical attacks because substances are only able to penetrate them by diffusion (slow transport). But the EPSs also bind nutrients through adsorption so that the bacteria – whose needs are modest anyway – always have access to sufficient nourishment.

Biofilm formation involves two distinct phases.

1. Reversible phase

First of all the surface is conditioned by substances present in the water that alter its charge. The bacteria then settle on this surface and become attached to it by weak interaction forces. This process is reversible. Bacteria can be removed or killed using disinfectant.

2. Irreversible phase

If bacteria remain attached to the surface for a longer period, they begin to form EPSs. The EPSs adhere strongly to the surface and provide very good protection for the organisms forming the biofilm. Now other bacteria can move in as well, although they themselves are not known to form biofilms. They begin to form a biocenosis. Removing these bacteria with the EPS is very difficult and is seldom completely successful.

Attempts to kill Pseudomonas aeruginosa biofilms using antibiotics have shown that the antibiotic needs to be 1,000 times more concentrated than for freely floating (planktonic) bacteria (11). This explains why Gram negative bacteria are hard to remove from medical devices (endoscopes) and water pipes. Experience has shown that using comparatively high concentrations of chemical disinfectants usually has only a short-term effect on an established biofilm.

Exchange of information – bacteria have many friends

Research into the world of communication among bacteria (12) has shown that they carry on lively exchanges with each other. **In this process, it is not only genes that are exchanged; bacteria also "know" how many of their own and other species are present nearby.** It is rather like Facebook. If you constantly send messages to your friends, you receive answers. Bacteria are constantly sending out certain chemical signals (quorum sensing) and they possess receptors with which they are able to receive the signals of others. This means they "know" how many are present and together they are able to trigger an infection, for example, which they would not be able to accomplish alone.

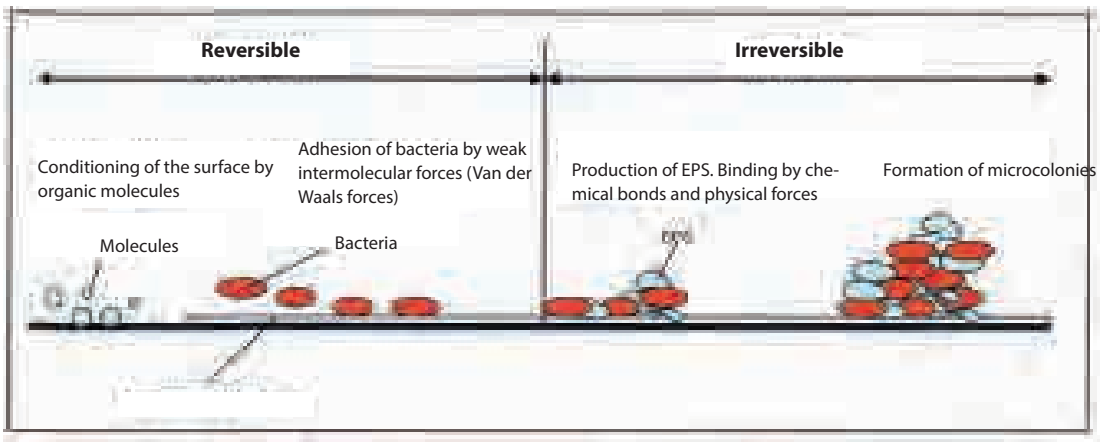


Fig. 8: How biofilms are formed, as described in (9) and (10)

Evidence on point-of-use sterile filters to reduce infection

In the last few decades, the efficiency with which point of use (POU) filters remove pathogens from drinking water has been investigated and documented in detail (6, 23-27 etc.). In recent years, numerous researchers have examined the effectiveness of point-of-use water filters for reducing nosocomial infections in hospitals. In 2006, Vianelli et al. published a paper about the outbreak of *P. aeruginosa* on a hematology ward at the university hospital in Bologna, Italy, between 2002 and 2004. To examine the outbreak, blood cultures were taken from all the patients undergoing treatment on this ward at the time. At the end of 2002, sterile non-returnable filters were installed at all water outlets on the ward. The number of positive blood cultures was significantly reduced by this intervention. 61 blood cultures tested positive for *Pseudomonas aeruginosa* in 2002, whereas only seven blood cultures were positive in 2003 (2002 compared to 2003: p=0.0001 [throat smear] and p=0.0008 [anal smear])(15).

In an intensive care unit in Budapest, Hungary, nosocomial *Pseudomonas aeruginosa* infections were recorded over several years. In 2008, point-of-use filters were installed at all water outlets in the unit for four weeks. The study found that the number of nosocomial infections was reduced from 2.7 cases / 100 patient days to 0 cases / 100 patient days. With the aid of genetic typing of the pathogen *Pseudomonas aeruginosa*, it was also found that five of seven cases of infection had been caused by an identical pathogen type; this type was also found in the unit's water supply (16).

A team of researchers in China examined the effect of point-of-use water filters on the prevalence of nosocomial infections in a liver transplant ward. According to the authors, this was the first environmental analysis of waterborne pathogens in hospital water supply systems in China. Microbiological investigation showed the presence of *Legionella spp., Pseudomonas aeruginosa, Mycobacterium spp.* and hyphomycetes in the water. During the period between July and November 2010, filters were installed at three taps on the ward. The statistical analysis showed a reduction in the infection/colonization of patients by Gram negative bacteria per 1,000 patient days after using the filters (from 3.2 ± 0.95 to 1.7 ± 1.25; p=0.067). **The number of nosocomial infections / colonizations by Gram negative bacteria was thus reduced by 46.9 % (17).**

Holmes et al. (2010) investigated whether using point-of-use water filters would reduce the number of nosocomial infections caused by *P. aeruginosa* at a subacute care unit (SACU). The investigation, which took place in the USA, showed that the number of infections was significantly reduced after the filters had been in use for five months. The results were reported as number of infections / patient days.

The number of patients with ventilation-related pneumonia was reduced by 90.2 % (p=0.0087), positive cultures with *Pseudomonas aeruginosa* were reduced by 68.3 % (p=0.0004) and a reduction of 58.6 % (p=0.0179) was found in the colonization of the upper airways (nose and sputum) by Pseudomonas aeruginosa (6).

Evidence on point-of-use sterile filters to reduce infection

In 2005, Vonberg et al. published a study to test the effectiveness of water filters for supplying immunosuppressed patients with water free from *Legionella spp.*. The study was carried out in a bone marrow transplant unit at Charité University Hospital in Berlin and in three intensive care units at Hannover Medical School. The results showed that no new nosocomial infections occurred after the installation of water filters (18).

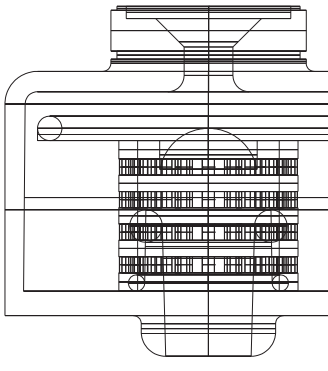
In a large-scale study by Trautmann et al. (2008), several variables were examined in relation to nosocomial infections and the use of point-of-use filters to combat them; the study was carried out at a surgical intensive care unit in southern Germany. This unit had previously had between two and five new *Pseudomonas aeruginosa* infections per month and this epidemic had been in progress for several years. The study investigated the prevalence of *P. aeruginosa* infections in patients and the colonization of water outlets by Pseudomonas aeruginosa. The pathogenic strains were determined using genetic typing. The study also compared the cohorts of patients in the phases before and after the installation of filters and looked at the general variables at the unit (e.g. antibiotic use) which may have contributed to infection with *Pseudomonas aeruginosa*. The investigation went on for two years and the filters were installed for one year. The results show a significant reduction in *P. aeruginosa* colonizations (85 % $p<0.0001$) and invasive infections (56 % $p<0.0003$) but no significant difference was found in the patient cohorts.

Overall, nosocomial infections were reduced by 22 %, which is roughly equivalent to the percentage of all nosocomial infections that are caused by *Pseudomonas aeruginosa*. Genetic typing showed that 100 % of these bacteria isolated in water belonged to clonotype A. In the phase before installation of the filters, 92.6 % of *Pseudomonas aeruginosa* infections were caused by clonotype A. One patient was infected with clonotype B and one with clonotype C (19).

In a hematology and oncology ward that was newly reopened in 2014 after renovation, a large number of nosocomial Legionella infections were recorded. Before the installation of point-of-use water filters, ten cases of infection were recorded; after the installation of filters, no more new cases occurred. Genetic typing showed that the Legionella outbreak had very probably been caused by contamination of the ward's water supply (20). Since the water supply systems of hospitals have repeatedly been identified as the source of outbreaks of nosocomial diseases caused by Gram negative bacteria, Cervia et al. (2009) investigated whether point-of-use water filters could reduce the risk of infection even when no known outbreak was in progress.

The investigation was carried out over a period of nine months in a bone marrow transplant unit at a university hospital in the USA. The pathogens Pseudomonas aeruginosa and Stenotrophomonas maltophilia were identified in water samples. After installation of filters, both the rate of infections caused by Gram negative bacteria (0.4 compared to. 0.09 infections / 100 patient days $p=0.0431$) and the rate of all infections (1.4 compared to 0.18 infections / patient day [$p=0.0068$]) were significantly reduced. All the infections recorded while the filters were in place were caused by non-waterborne pathogens (21).

All the authors of the studies cited above recommend using point-of-use water filters, both when combating acute outbreaks of nosocomial infection caused by bacteria (6, 15, 16, 17, 18, 19, 20) and to prevent nosocomial infections when no acute outbreak is in progress (21).



Requirements of point-of-use sterile filters in medical settings

General requirements

- Sterile filters to prevent nosocomial infections due to waterborne microbes must be CE-marked medical devices [1,2]
- They are subject to the requirements of the German law on medical devices (Medizinproduktegesetz)and the RKI guidelines [2,3,4a-d,5]

Technical product requirements as specified by RKI and DVGW (Germany's water industry body)

- Individually packaged sterile filters with details of minimum durability period [3]
- Nominal pore size of 0.2 µm as required by FDA [6]
- Bacterial retention *(Brevundimonas diminuta)* > 7 log pro cm^2 [6,7]
- Membrane testing of every filter (100 % testing)
- Membrane testing in accordance with ASTM F838-15A (the current standard) [10]
- Filter endures use at temperatures of at least 60 ºC and pressures of at least 5 bar [3]
- Hygienic testing of filter materials in accordance with Trinkwasserverordnung (German Drinking Water Ordinance) 2001 paragraph 17 (KTW, W270) [11]
- Adapter to target the stream of water as recommended by RKI [4a]
- Filter housing with bacteriostatic properties [9]
- Filter resistant to normal surface disinfectants
- Minimum distance of 20 mm must be maintained between filter outlet and maximum water level [3]

Documentation and quality assurance requirements

- Quality management system of the manufacturer is certified according to DIN EN ISO 13485:2016 [1,2,8]
- Product is individually identifiable and traceable due to serial numbering [1,3,8]
- Clear and practical instructions for use [1,2]
- Guidance regarding the use and application of filters
- Management of water outlets / documentation [1,8]
- Clinical trials of the defined duration of use (product validation) [1,2,3]
- CE-marked Class I medical device [1,2]

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[2] Medizinproduktegesetz (BRD): Medizinproduktegesetz in der Fassung der Bekanntmachung vom 7. August 2002 (BGBl. I S. 3146), das zuletzt durch Artikel 16 des Gesetzes vom 23. Dezember 2016 (BGBl. I S. 3191) geändert worden ist"

[3] DVGW, Temporärer Einsatz endständiger Filter in mikrobiell kontaminierten Trinkwasser-Installationen. Twin Nr. 12, März 2017

[4a] RKI-Empfehlung: 'Anforderungen an die Hygiene bei der medizinischen Versorgung von immunsupprimierten Patienten' - Bundesgesundheitsbl. 2010 • 53:357-388 (S. 371/3.8)

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[5] Infektionsschutzgesetz (IfSG)-"Infektionsschutzgesetz vom 20. Juli 2000 (BGBl. I S. 1045), das zuletzt durch Artikel 4 Absatz 20 des Gesetzes vom 18. Juli 2016 (BGBl. I S. 1666) geändert worden ist"

[6] FDA, Guidance for Industry Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice, 2004

[7] ASTM-Methode F838-15A mit (*Brevundimonas diminuta* ATCC 19146)

[8] DIN EN ISO 13485:2016 Medizinprodukte - Qualitätsmanagementsysteme - Anforderungen für regulatorische Zwecke

[9] ISO 22196-2007: Messung von antibakterieller Aktivität auf Kunststoffoberflächen mit *Staphylococcus aureus* DSM 799/ATCC 6538 und *Escherichiacoli* DSM 1576/ATCC 8739

[10] ASTM F838 - 15a: Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration

[11] DVGW twin Nr. 12 - Informationen des DVGW zur Trinkwasser-Installation: Temporärer Einsatz endständiger Filterin mikrobiell kontaminierten Trinkwasser-Installationen

Current specifications

The current specifications for investigation parameters and frequency of sampling have been established by the Federal Environment Agency (UBA) and DVGW (TWIN) and are laid down in Germany's Drinking Water Ordinance (TrinkwV) (50). These parameters are given in the following table. In addition, the UBA specifications dated 13 June 2017 (51) require testing of cold water for *Pseudomonas aeruginosa* at the following establishments:

- schools
- hostels, youth hostels
- other educational establishments
- sport centers
- other group accommodation (e.g. homes, accom modation for homeless people, homes for asylum seekers).

The frequency depends on the requirements of the local health authority (usually annually).

Parameter	Volume examined (ml)	Limit (CFU)
Escherichia coli	100	0
Coliform bacteria	100	0
Enterococci	100	0
CFU at 22 °C and 36 °C	1	100
*Legionella spp.**	100	100
Legionella in high risk areas**	100	0
*Pseudomonas aeruginosa***	100	0

Fig. 9: Parameters investigated
*: Technical action value **: According to UBA recommendation dated 13 June 2017

TrinkwV specifies these frequencies for routine testing (50):

- **in hot water in hospitals when testing for Legio nella: annually**
- **in cold water in hospitals at the frequency speci fied by the local health authority, usually annually**

The DGKH (German society for hospital hygiene) recommends much stricter limits; these are given in the table below. The Robert Koch Institute (RKI) recommends the installation of point-of-use water filters on neonatal wards whenever the required microbiological water quality cannot be guaranteed. The use of point-of-use filters is recommended in particular for use in personal hygiene andwound irrigation for highly immunosuppressed patients (risk groups 2 and 3). To prevent food-related diseases it is recommended that water and ice be treated with 0.2 µm filtration. The frequency of water quality testing can be reduced if point-of-use filters have been installed (30).

Location	Limits, DGKH guideline levels and action values	Measures to be taken if DGKH value is exceeded
Transfer point	- < 20 CFU/ml - < 1 *E. coli*/100ml - < 1 coliform/100ml - < 1 *P. aeruginosa*/100ml	- Report to health authority - Repeat sampling - Assessment by physician specializing in hygiene - Involve water supply company - Point-of-use filters if necessary - Investigation as far as central water supply network to establish cause
Cold drinking water installation	- < 20 KbE/ml - < *E. coli*/100 ml - < Coliforme/100 ml - < *P. aeruginosa*/100 ml	- Report to health authority - Repeat sampling; point-of-use filters in areas used by patients if necessary
Hot water installations for normal wards	- < 100 CFU Legionella/100 ml - < 1 CFU *P. aeruginosa* /100 ml	- Evaluation by physician specializing in hygiene - Report to health authority
Water for high risk wards such as intensive care units, hemato-oncology wards, burns units	Cold water: - < 1 CFU coliforms/100 ml - < 1CFU non-fermenting bacteria/100 ml Hot water: - < 1 CFU *Legionnella spp.*/100 ml	- Evaluation by physician specializing in hygiene - Point-of-use filters

Fig. 10: Limits, guideline levels and action values for bacterial indicators including P. aeruginosa in different locations with details of methods, frequency and procedures (28)

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