Reducing germ transmission paths through sustainable hygiene concepts

An introduction to antimicrobial surfaces

White Paper „Sustainable hygiene concepts for the reduction of germ transmission routes“

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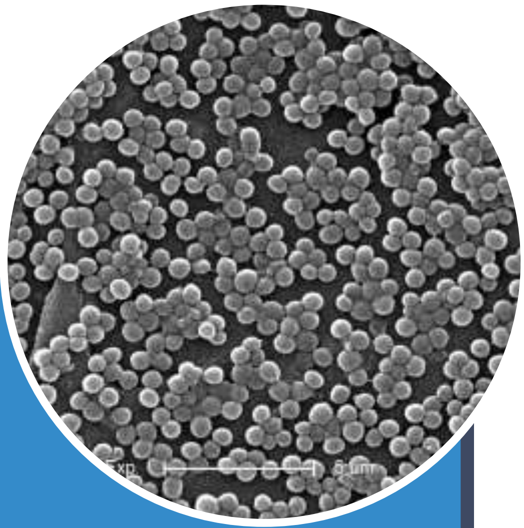


Infectious diseases

are the leading causes
of death worldwide.

15 million people

die annually from the
direct consequences of
infectious diseases.

The causes are germs being transmitted via various routes:

Bacteria
(MRSA, tuberculosis ...),

Viruses
(COVID-19, HIV ...)

Fungi
(candida auris ...).

The challenge of emerging and re emerging infectious diseases. Nature 2004; 430:242–249.

Executive Summary

The history of mankind is accompanied by infectious diseases and pandemics, which repeatedly present modern society with health, social and economic challenges. Therefore, protection against the corresponding dangers has not only been a central topic in the fight against the world of germs since Corona / CoViD-19.

Measures to combat infectious diseases were already used in ancient times and have been continuously developed and optimized ever since. Whether it's silver coins being used in drinking water or copper pipes for water supply: former - mostly superstitiously presumptuous - strategies may appear in a new light thanks to modern findings offering new innovative ways to support the fight against infections. This is also made possible by a better understanding of the transmission routes of infectious germs.

Whereas in the past diseases were seen as divine punishment, today it is well known that they are due to transmission and infection by bacteria, viruses or fungi. Such germs surround us ubiquitously and occur both in nature and in the man-made environment and can be transmitted directly from person to person or indirectly via hands or objects. It is therefore a primary goal of infection research, to understand and to break such chains of infection.

The modern understanding of pathogens as well as the principles of infection and transmission has led, among other things, to the targeted development of new active substances (e.g. polio vaccine) and the optimization of existing hygiene measures. As a result, the first diseases have already been successfully eradicated (smallpox).

Despite this progress, however, pandemics and the discovery of new or previously unknown germs are becoming more frequent. This can be attributed to various factors, such as the high evolutionary strength of viruses, bacteria and fungi on the one hand, but also the increasing modernization and industrialization of society (globalization, demographic change, factory farming, etc.).

The modern healthcare system is facing increasing challenges today as previously effective drugs such as antibiotics, antivirals and antifungals are gradually losing their efficacy. This is mainly due to the increasing resistance of pathogens. At the same time, lack of research activities in the field of drug and antibiotic research hardly provide new effective alternatives.

In view of a rising number of infections that either cannot be treated or are difficult to treat, the further development of additional preventive hygiene concepts is of crucial importance. Yet, for maximum social and economic acceptance, these concepts must complement each other in a meaningful way, efficiently reduce or prevent germ transmission routes and restrict social and economic life as little as possible.

In practice, these different goals often lead to conflicts, for example in the regular and consistent implementation of cleaning and disinfection measures. Though efficient at the time of implementation, these measures do not provide a lasting effect and must be constantly repeated. This is where passive hygiene measures such as antimicrobial surfaces can offer additional, long-term support that contributes to better protection against infectious diseases.

This white paper provides an easy introduction to the topic of antimicrobial surfaces and answers general and specific questions starting with the basic concept, through individual development to the effectiveness testing and the implementation in concrete applications.

For 2019,
the WHO registered

32 antibiotics

in clinical
development,
and potentially
active against
the WHO priority
pathogens

Of those, only

6 antibiotics

were considered
innovative

and only
2 antibiotics
were active against
MDR Gram-negative
bacteria.

https://apps.who.int/iris/bitstream/handle/10665/330420/9789240000193-eng.pdf

A more interconnected world and economy leads to

a faster spread of infectious diseases.

It is time to use this connections to

develop joint solutions to these global challenges!

Infections and hygiene measures

The human immune system is in constant battle with a wide variety of germs (bacteria, fungi and viruses). While many of these are harmless or even useful for the healthy human body (apathogenic and facultative pathogenic), others (so called pathogenic germs) pose a danger. The constitution of the respective immune system largely determines the level of danger and whether non-pathogenic and facultative pathogenic germs may also pose a danger.

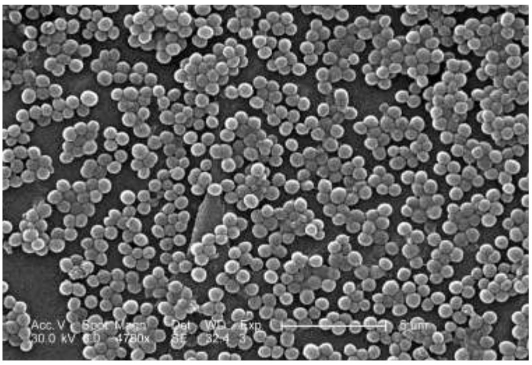
The general rule: the worse the constitution of the immune system, the more risky even otherwise harmless germs can become.

To prevent the transmission of germs and to reduce the risk of potential infections, hygiene measures have a fixed place in modern society. They have been adapted to a wide variety of requirements and situations in many areas of private and public life.

This applies in particular to medical facilities, where a large number of people with weakened immune systems are exposed to potential danger. But hygiene measures also apply in geriatric care, the food industry, in public facilities and means of public transport or in sports facilities.

Causes of rising infection rates...

- Poor socio-economic and hygienic conditions
- Inadequate medical care
- Evolutionary strength of germs
- Decreasing effectiveness of medicines
- Excessive use of antibiotics in human medicine and in factory farming
- Globally increasing life expectancy and demographic change
- Climate change: favoured transmission via living organisms
- Globalization: a more interconnected world and economy leads to a faster spread of infections



Infectious diseases

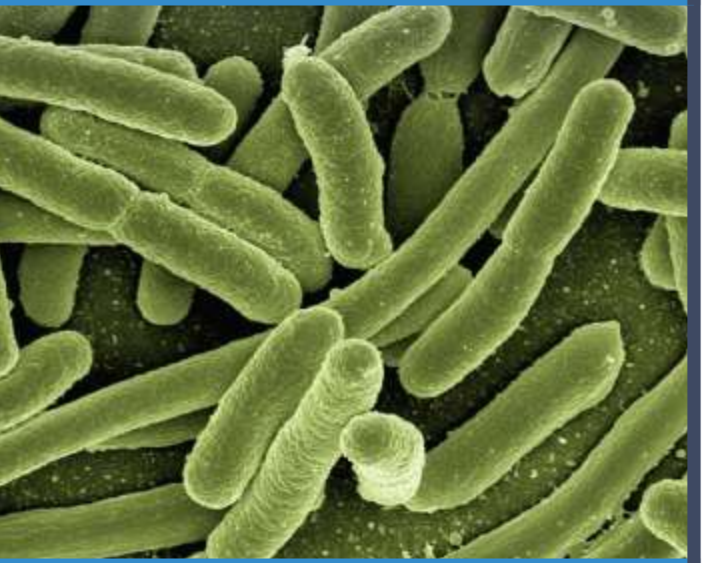
Although hygiene measures are constantly being further developed and awareness of good hygiene practices is generally becoming more present, rising infection numbers can be observed worldwide (incl. multi-resistant germs). In addition, the evolutionary strength of viruses, bacteria and fungi leads to new pathogens being discovered every year.

The effectiveness of targeted hygiene measures (e.g. vaccination) can be seen in the declining number of deaths resulting from smallpox. While first pathogens have already been completely eradicated, considerable progress has been made for others (e.g. polio).

But: A vaccination option exists only for a few infectious diseases, so that additional protection is necessary.

At least **700,000 people** die each year due to drug resistant diseases.

Forecasts for 2050 expect **ten million deaths per**



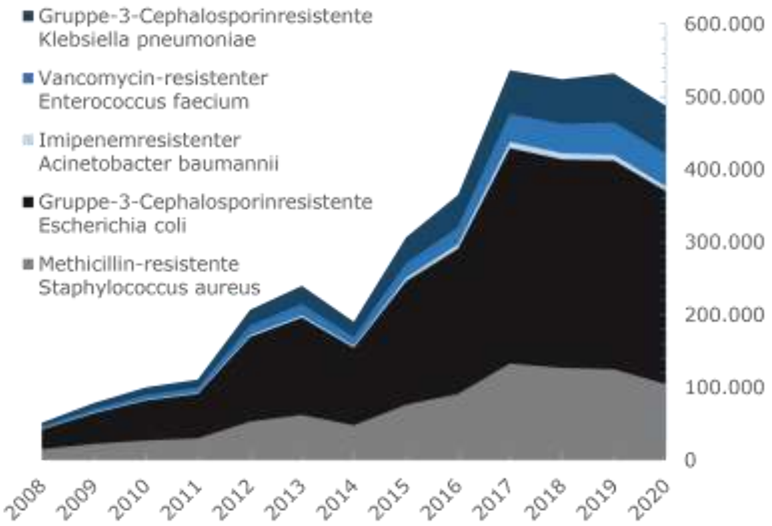
Multidrug resistant Gram-negative bacteria (MDRGN bacteria) show resistance to the antibiotics used as primary bactericidal therapeutics in severe infections

3MDRGN and 4MDRGN refer to rods that are resistant to 3 or 4 of the four antibiotic groups:

- Acylureidopenicilline
- Cephalosporine
- Carbapeneme
- Fluorchinolone

Multidrug resistance (MDR)

Since the 70s/80s, infections with multidrug-resistant pathogens have increasingly occurred in hospitals. These include methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant pathogens and multidrug-resistant gram-negative rod bacteria. Worldwide, the number of deaths from MDR is predicted to reach ten million per year by 2050.



The number of detected infections in intensive care units in Germany is rising sharply. A decline in the number of infections can be observed in the year of the Corona Pandemic 2020. (Source: Robert Koch Institute: ARS, https://ars.rki.de, data status: 01.09.2021)

Economic consequences of MDR infections:

- On average, MDR patients stay in hospital 3 times as long
- an bear additional cost of €17,517.41 each.

Sources:

- *H. Oberdörfer et al. (2014). Mehrkosten bei der Versorgung von Patienten mit multiresistenten Erregern – Eine Analyse aus Sicht einer gesetzlichen Krankenversicherung. Das Gesundheitswesen, 77(11), 854. doi:10.1055/s-0034-1387709*
- *https://de.statista.com/infografik/16910/weltweite-sterbefaelle-durch-ausgewaehlte-infektionskrankheiten/*
- www.who.int/news/item/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis

Nosocomial infections

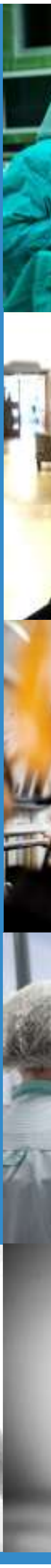
Infections that are causally related to hospitalization are referred to as noscomial infections.

The broader term “health-care associated infections” also includes other health-care facilities (nursing facilities, rehabilitation centres, outpatient clinics, medical practices).

The number of **nosocomial infections** in Germany is about 400,000-600,000 per year (projections).

Of these: about

10,000 - 20,000 deaths.



About **half a million people** worldwide become infected with **multidrug-resistant tuberculosis** every year.

Tuberculosis

Classified as a global emergency by the World Health Organization (WHO) in 1993, tuberculosis poses an enormous challenge, with approximately 10 million new infections and 1.4 million deaths worldwide each year (WHO Global tuberculosis report 2019).

The most common route of transmission is inhalation of infectious droplets, but smear infections also contribute to the spread of the responsible mycobacteria.

The End TB Strategy, adopted in 2014, aims to end the global TB epidemic by 2035. However, corresponding data for 2018 show that the milestones set are far from being achieved. The proportion of TB cases with treatment success after 12 months is 67.6%, significantly below the planned 85%.

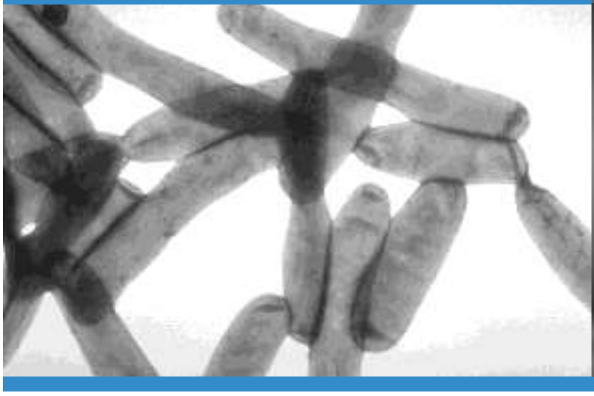
Legionella

Legionella living in water have ideal growth conditions in the temperature range of 20-55 °C and are only effectively killed off above 60 °C. While drinking water containing Legionella does not usually pose a health risk, inhaling it as a bioaerosol (e.g. in showers or air conditioning systems) can result in a life-threatening infection.

A study from 2005 to 2010 showed that one in two hospitals in Berlin was affected by Legionella, and the German Competence Network for Community-Acquired Pneumonia (CAPNETZ) estimates the annual number of Legionnaires' disease cases in Germany at about 15,000 to 30,000. In 2018, the highest ever observed cases in the EU were reported. As in previous years, no large but outbreaks were observed, but rather small and diverse ones.

Legionella was first described in the USA in 1976.

15.000-30.000 cases per year are estimated to be caused by bacteria living in the water.



Sources:

- www.rki.de/DE/Content/Service/Presse/Pressemitteilungen/2019/14_2019.html
- https://www.who.int/en/news-room/fact-sheets/detail/tuberculosis
- https://apps.who.int/iris/bitstream/handle/10665/259636/TBstrat-eng.pdf
- https://www.ecdc.europa.eu/sites/default/files/documents/AER_for_2018_tuberculosis.pdf
- https://www.dvgw.de/themen/wasser/wasserqualitaet/trinkwasserhygiene
- https://www.tagesspiegel.de/berlin/hygiene-im-krankenhaus-legionellen-breiten-sich-in-kliniken-aus/3966494.html
- https://www.ecdc.europa.eu/sites/default/files/documents/AER_for_2018_Legionnaires.pdf

Hygiene measures

In order to effectively prevent the spread of infectious diseases, a sustainable hygiene concept comprises various measures that are applied according to the situation and depending on the germ load.

In addition to the broadly accepted hygiene measures (such as hand washing), statutory hygiene requirements in particular contribute to a reduction of infectious diseases (e.g., in medical facilities and commercial kitchens).

In **drinking water management**, too, statutory hygiene requirements apply, e.g. in large-scale systems for the heating of drinking water (e.g. in residential buildings, hotels, hospitals) and in central water storage facilities. With regard to the risk groups in medical facilities and in nursing homes, the Robert Koch Institute (RKI) therefore recommends, among other things, additional **technical preventive measures** that limit the growth of legionella in water supplying units.

In the optimum scenario, hygiene measures support and complement each other, e.g. in the form of technical designs such as disinfectant and cleaning agents in combination with antimicrobial surfaces.

Basic:
- Hand washing
- Cough and sneeze hygiene

Acute:
- Disinfection
- Cleaning

Situational:
- Barrier measures
- Air purification / Air exchange

Permanent:
- Antimicrobial surfaces
- Vaccination

Sources:

- Pictures: https://commons.wikimedia.org/w/index.php?curid=841034 / https://commons.wikimedia.org/wiki/File:Mycobacterium_tuberculosis_8438_lores.jpg
- https://www.rki.de/DE/Content/InfAZ/L/Legionellose/OEGD/Primaerpraevention_Legionellosen.html

Understanding infection pathways

Depending on the pathogen and its stability and persistence in the environment, there are different possible routes of transmission (i.e. the way pathogens spread and the route by which they enter the body). Transmission occurs either

- **directly**
  (e.g. via droplet infections or via skin contact) or
- **indirectly**
  (e.g. through door handles or food).

However, whether a pathogen transmission ultimately leads to an infection also depends on the infection dose (i.e. the **number of infectious** pathogens, e.g. on a surface).

Investigating the **germ load** on various surfaces in a newly built hospital in the USA identified the hand as an important vector for the room microbiome. After only a few days, the diversity of the microbial composition on frequently touched surfaces increased significantly.

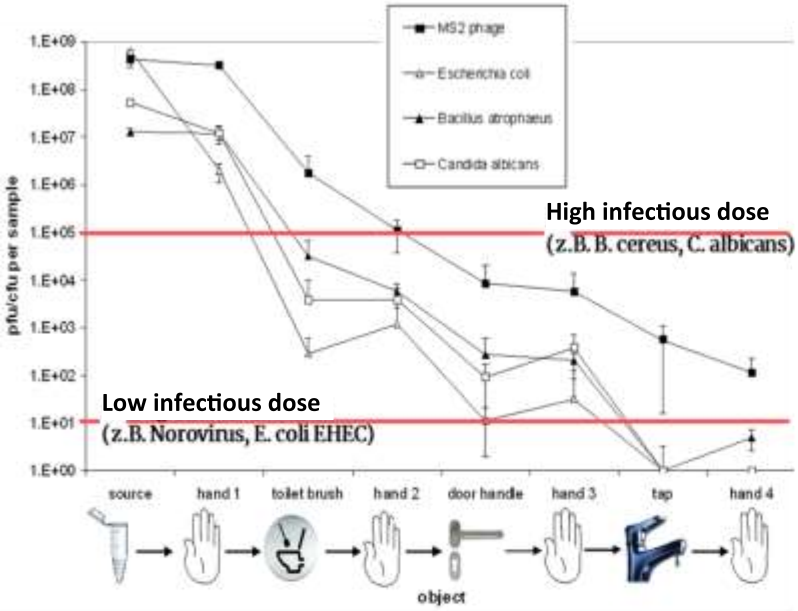
Approx. 20% of nosocomial infections are exogenous in nature (e.g. transmitted via surfaces).

Typical pathogen transmission routes:

- Droplet infection
- Smear infection
- Blood and body fluids
- Insects and parasites
- Surfaces

!

An understanding of the different infection pathways is essential, to prevent infections and to design effective hygiene measures.



So-called transmission models (e.g. artificial skin and stamp systems) can be used to track infection pathways qualitatively and quantitatively. This simulates the transfer of pathogen from surfaces with frequent contact to hands (e.g. door handles, grab handles, operating elements).

These studies can shed light on the relevance of products in transmission routes and the performance antimicrobial products can offer in breaking the chain of infection.

With these studies it is also possible to show how the infection dose (and hence the risk of infection) changes through the different transmission steps.

!

Results: even after several transmission steps the pathogen load on contaminated surfaces remains potentially infectious. Pathogens can be spread over long distances and thus indirectly lead to infections.

Sources:

- S. Lax, B. Stephens, J. A. Gilbert *et al.* (2017) Bacterial colonization and succession in a newly opened hospital. *Science Translational Medicine* 9, 391. Online: https://dx.doi.org/10.1126%2Fscitranslmed.aah6500
- Gerhardts, A. and D. Höfer (2018) A New Approach for a Practical Assessment of Antimicrobial Surfaces Based on a Stamp Assay to Quantify Transfer Routes of Pathogens. *Tenside Surfactants Detergents* 55, 404.
- Gerhardts *et al.* (2012) A model of the transmission of microorganisms in a public setting and its correlation to pathogen infection risks. 112: 614. Online: https://doi.org/10.1111/j.1365-2672.2012.05234.x

Pathogen transmission via surfaces

Even today, generally accepted hygiene concepts take into account the transmission of germs via surfaces (e.g. door handles or handrails). In many cases, disinfection and cleaning measures of surfaces are even prescribed by law.

If these measures are carried out correctly, most germs can be eliminated and removed instantly.

But: The protection only directly exists at the time of the disinfection measure and not between the cleaning and disinfection intervals.

Problem:

If surfaces are touched frequently, they can become contaminated and infectious again at any time.

And: the transmission of pathogens via surfaces can only be traced to a limited extent and is therefore difficult to calculate e.g. in pandemic times. In order to effectively prevent infection chains, surfaces must therefore be given greater consideration and complementary measures must be taken into account.

Public transport

Carsharing

Supermarket

Airport

Handles

Money

Whether a surface is infectious depends on various parameters:

- Type and concentration of the contamination
- Time since last cleaning
- Nature of the material (metal, plastic, porous, absorbent, moist, ...)
- Temperature
- Humidity
- ...

More information:

- *www.virologyj.biomedcentral.com/articles/10.1186/s12985-020-01418-7#Sec7*
- *www.aem.asm.org/content/76/9/2712*

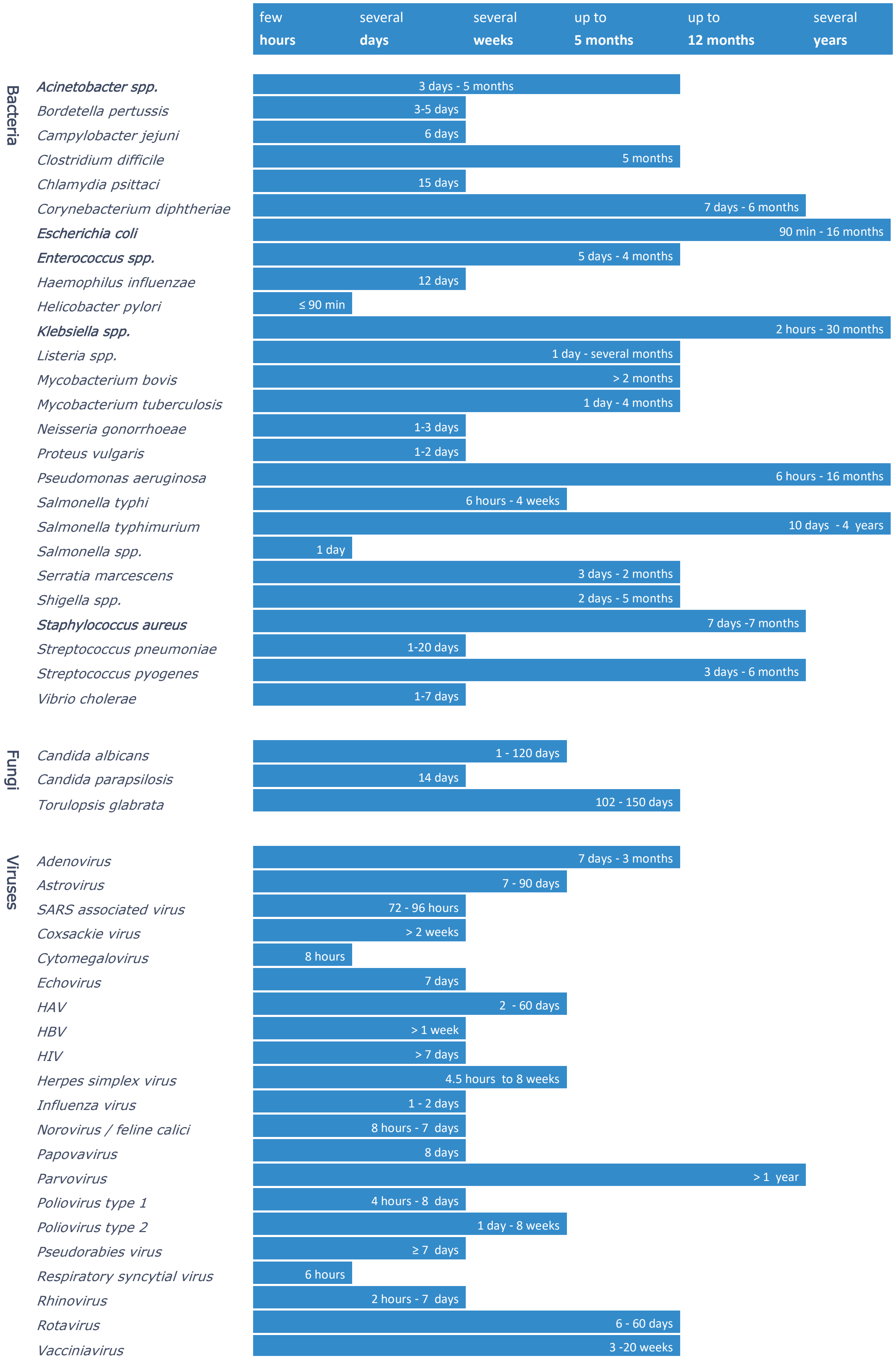
Outlook: Corona viruses on surfaces

Viruses can remain infectious on inanimate surfaces for up to several weeks. Contrary to previous assumptions, this also applies to the human coronavirus. Studies show that SARS-CoV-2 was detectable at 20 °C even after 28 days on surfaces such as glass, stainless steel and paper.

Sources:

- https://doi.org/10.1016/j.jhin.2020.01.022
- https://doi.org/10.1186/s1298 5-020-01418 -7
- https://virologyj.biomedcentral.com/articles/10.1186/s12985-020-01418-7

Persistence of pathogens on surfaces



Antimicrobial surfaces

Complementary hygiene measures

If a surface is contaminated or infectious, properly performed disinfection and cleaning measures can eliminate or remove most germs. However, if the surface becomes contaminated again after cleaning/ disinfection, it may become infectious again until the next interval.

Though efficient, there is no protection between the intervals of cleaning and disinfection. And, there is an even greater risk if the disinfection and cleaning process is not carried out properly or is incomplete.

Long-term hygiene measures (e.g. antimicrobial surfaces) will become more relevant in the future. !

What is an antimicrobial surface?

The term antimicrobial surfaces describes materials and substances that prevent or limit the growth and multiplication of microorganisms. These surfaces are classified according to the underlying mechanism of action (active or passive). Compared to conventional and sometimes highly toxic biocides, antimicrobial surfaces have hardly any side effects, so that they also reduce the burden on humans and the environment.

Many surfaces use the principle of nanotechnology:

"The smaller the particles, the greater the specific surface area and the less material is required."

As a result, even small amounts of the corresponding material are sufficient to achieve an antimicrobial effect.

Furthermore, the reduction of raw materials makes more complex applications become economically viable.

Nanotechnology?

Nanotechnology is the base of many modern applications such as computers, lasers, medical technology. As a cross-sectional technology, it is applied in a wide variety of industries.

Firmly incorporated or fixed into the product or coating, nanomaterials and nanostructures are safe for humans and the environment.

More information:

www.nanoproject.eu/

Do antimicrobial surfaces need to be cleaned? ?

Yes. Standard cleaning and disinfection measures must be carried out. This applies not only to surfaces containing silver or nanosilver, but to antimicrobial coatings in general.

Antimicrobial surfaces have a time period-related effect and improve hygiene in the longer term. I.e. they improve the hygienic situation between cleaning intervals and prevent the growth of pathogens in the corresponding period. The killed pathogens must still be removed by standard cleaning measures.

How do antimicrobial surfaces work?

The functional principle of antimicrobial surfaces can be based on active (drug-releasing or contact-active) and / or passive mechanisms of action (hydrophobic, nano structuring). Depending on the application and germ load, the different mechanisms and materials have specific advantages and disadvantages.

	Silver (nano)	Copper (nano)	Titanium dioxide (nano)	Graphene/ oxide	Hydrophobic	Standard biocides
Description	*Dissolved ions disrupt the metabolism of germs and kill them*	*Dissolved ions disrupt the metabolism of germs and kill them*	*Activation by UV-A radiation and formation of radical oxygen species*	*Sharp edges disrupt the cell membrane and induction of oxidative stress*	*Hydrophobic surfaces prevent germs from adhering to surfaces*	*The antimicrobial effect is due to "poisoning" of the germs*
Effectiveness	*High*	*High*	*Medium*	*Still unknown*	*Medium*	*Very high*
Price	*Medium*	*Medium*	*Cheap*	*Medium*	*Cheap*	*Cheap*
Stability	*Stable and inert*	*Susceptible to oxidation*	*Accelerated aging of plastics*	*Still unknown*	*Sensitive to mechanical stress*	*Low*
Flexibility	*Acts actively*	*Acts actively*	*Requires UV light*	*Still unknown*	*Acts passively*	*Acts acutely*
market approval	*Marketable and approved*	*Not marketable as biocide*	*Marketable*	*Not marketable as biocide*	*Depending on the chemical composition*	*Marketable*
Human toxicity	*None known*	*None known*	*Current testing for carcinogenicity*	*None known*	*None known*	*Highly toxic*
Release of nanoparticles?	*None, when probably bound*	*None, when probably bound*	*None, when probably bound*	*None, when probably bound*	*None, when probably bound*	*No Nanoparticles*
Sustainability / Long-term effect	*High (when firmly bonded)*	*Medium (due to loss of activity by oxidation)*	*High (when tightly bound)*	*Still unknown*	*Medium (weak against mechanical stress)*	*Low (limited life time)*
Applications (examples)	*Door handles, implants, displays, buttons*	*Door handles, handrails (e.g. USA)*	*(Glass) facades, PVC pipes*	*None yet*	*Laquers coatings*	*Disinfectants, cleaning agents*
Availability / "Readiness Level"	*Wide range of applications available; in use for over 100 years in use*	*Few applications in use*	*Wide application in emulsion or wall paints*	*Currently still in development stage*	*Currently still in development stage*	*Triclosan, benzalkonium chloride, isothiazolinone, chlorhexidine*

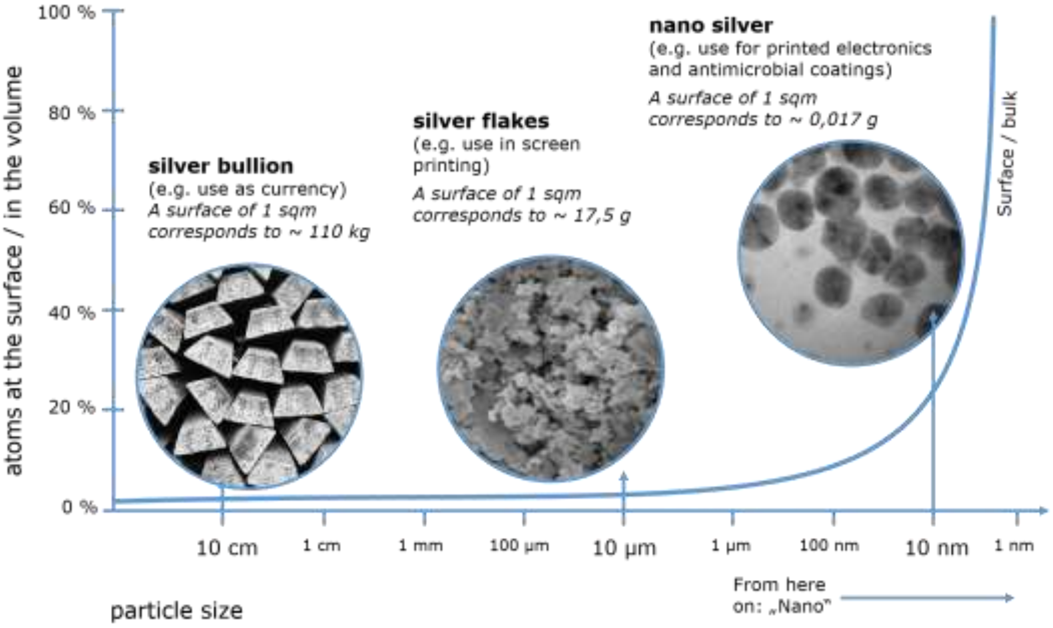
Antimicrobial surfaces with silver

By the way

The ancient Romans placed silver coins in drinking water to keep it "pure" and fresh e.g. when traveling or for storage.

The antimicrobial effect of silver and nanosilver has already been recognized and used in ancient times (e.g. water conservation). Yet, the first scientific research on nanosilver (also called colloidal silver) did not take place before 1889. Since then, (nano)silver has been widely used in industrial applications and products, offering many years of experience in the use and side effects of silver.

As with copper, the primary antimicrobial activity of silver is based on the ionic form of the metal (Ag^+). These ions are dissolved in well defined quantities out of the metal surface and can then intervene in the metabolism of pathogens, killing them in a targeted manner. Compared to conventional and highly toxic biocides, antimicrobial surfaces have hardly any side effects, and can thus reduce the burden on humans and the environment. Various strategies ensure that nanomaterials and nanostructures remain in the product and are not released.



Keep in mind

All silver surfaces do release silver ions. This also applies to so-called macro or micro silver!

However, the amount of silver ions being released directly depends on the specific surface area. Hence, the antimicrobial potency (or activity per mass) is higher for smaller particles.

The smaller the particles:

- the higher the specific surface area and the "surface-to-volume" ratio
- the less silver material is required for a comparable effectiveness

A comparison:

A 5 kg silver bullion has approximately the same surface area as 1 mg silver nanoparticle with an edge length of 10 nm: approx. 5.97 dm^2.

Nano:

Particles with an average size between 1 and 100 nm are called nanoparticles.

(Nano)silver is used in various applications, including electronics, energy storage and conversion, jewellery, as currency and sensor technology.

Where else is (nano)silver used ?

?

Sources:

- G. Broughton, *et al.* (2006) A brief history of wound care. *Plast. Reconstr. Surg.* **117**, 6-11.
- J.W. Alexander, *et al.* (2009) History of the medical use of silver. *Surg. Infect.* **10**, 289-292.
- M.C. Lea, *et al.* (1889) Allotropic forms of silver, *American Journal of Science*, *Series 3 Vol. 37*, 476-491.

Antimicrobial surfaces with silver

The primary effect of firmly bound nano(silver) is based on the release of silver ions. The amount of silver ions can be controlled, among other parameters, by the size of the bound particles and by their specific surface area. Besides silver ions, the accessible (nano)silver surface has an antimicrobial effect, too.

Hence, silver and silver ions interact with proteins on the surface of viruses, bacteria and fungi (e.g. glycoproteins in the case of viruses). In particular, sulfur-sulfur bridges are disrupted, so that the protein structure of the respective pathogens is disturbed and their decomposition is induced.

Keep in mind: A pure silver coating / surface has an antimicrobial effect, too. However, for coating thicknesses greater than 100 nm, the term nanosilver is no longer used.

Silver

Element symbol:	Ag
Melting point:	961,8 °C
Density:	10,49 g/cm³
Boiling point:	2.162 °C
Natural occurrence in the soil:	0.1 mg / kg
Daily intake by food:	0.1 mg
Applications:	Currency, electronics, jewellery, energy storage and conversion, ...

! Important

Safe (nano)silver products firmly bind the antimicrobial (nano)silver particles in or on the respective coating and adapt the antimicrobial activity to the desired application.

Silver ions are only released upon contact with moisture (e.g. through biofilms, water or air humidity from 20%). There is no transition into the air.

? *What is the difference between the various silver coatings?*

Depending on the application different requirements are made on coatings and their antimicrobial activity. Factors influencing the choice of a coating are for example:

- the pathogen load / the required amount of active ingredient,
- range of the antimicrobial activity,
- duration of the antimicrobial activity and the
- release rate.

Also, the **substrate** determines or limits possible coating techniques. Sol-gel layers or direct incorporation and processing in textile yarns are safe, flexible and sustainable ways of coating.

Regulatory: when using particles smaller than 100 nm, the product must also be labelled with "(nano)" in the product description.

By the way:

The most common production method of nanosilver is **chemical reduction of silver salts.**

Other methods applied:

- spark discharge
- electrochemical reduction
- irradiation
- cryochemical synthesis

? *How does (nano)silver differ from conventional biocides?*

The **reduction of health hazards** for humans and the environment are reasons why silver coatings are often used to replace toxic biocides.

Efficacy: proof and duration

Not every antimicrobial surface is equally effective or efficient. Therefore, a wide range of tests were developed to determine the antimicrobial efficacy, taking into account different requirements.

However, the existing normative tests are often impractical and have various deficiencies. The development of new, practice-relevant test methods is therefore crucial in order to be able to compare different surfaces.

Current deficits & possible solutions

So far, existing normative tests do not take into account organic contamination and partly define unrealistic test conditions, which often leads to exaggerated performance expectations in practice. The general trend is therefore towards developing practical modifications of standardized tests, specific test models (e.g. pathogen transmission models), simulations of application-related contamination scenarios with suitable test pathogens (e.g. surrogate viruses) or field studies in order to test the effectiveness in practice.

⇩

The efficacy of antimicrobial surfaces should be tested with at least 5% nutrient content in the inoculum to reflect organic loads in practice.

⇩

Tests should examine shorter exposure times being more relevant in practice (1-2 h). This reflects the fact, that spreading of pathogens via surfaces tends to be short-term.

Not every product containing silver, copper or titanium dioxide shows an antimicrobial activity.

Important !

The right processing of the particles is crucial to ensure a good distribution in the material and an easy accessibility to the active ingredient. Effectiveness and safety must therefore always be proven on a product-specific basis and ideally by means of sampling. This can be done using various tests (see table on the following page).

How long are antimicrobial surfaces effective? ?

The lifetime of the effect depends on various factors. If the antimicrobial activity is based on the release of an active ingredient, the coating gradually loses its antimicrobial protection over time. Still, surfaces such as the sol-gel based coating SANPURE show an effective lifetime of more than 20 years.

Antimicrobial surfaces that do not release an active ingredient theoretically remain permanently antimicrobial active. However, contamination can still hinder antimicrobial protection.

How to determine that the antimicrobial protection is still active? ?

Antimicrobial coatings based on nanosilver generally do not change the optical properties of a product and are therefore difficult to see. Yet, the active ingredient can be labelled with fluorescent particles or dyes, which makes them indirectly visible by means of UV light.

Standard tests for checking antimicrobial efficacy

		Description of the test	Strengths	Weaknesses
Bacteria	ISO 22196 (JIS Z 2801)	Measurement of antibacterial activity on plastic and other non-porous surfaces	• quantitative Statement	• hydrophobic samples limited • lower sensitivity • nutrient content in the inoculum too low
	ASTM E 2149	Determining the Antimicrobial Activity of Antimicrobial Agents Under Dynamic Contact Conditions	• hydrophobic specimens possible • free geometry of specimens	• lack of comparability • no zero sample • limited spectrum of activity (only 1 test germ)
	ASTM E 2180	Determining the activity of incorporated antimicrobial agents in polymeric or hydrophobic materials.	• hydrophobic specimens possible • small specimens	• low sensitivity • lack of comparability
	ASTM E 3160	Standard Test Method for Quantitative Evaluation of the Antibacterial Properties of Porous Antibacterial Treated Articles	• quantitative	• limited spectrum of activity (only 1 test germ) • nutrient content in inoculum too low
	DIN EN ISO 11930	Evaluation of the antimicrobial protection of a cosmetic product.		
	DIN EN ISO 20645	Textile fabrics - Determination of antibacterial activity - Agar diffusion plate test	• simple and cheap	• only qualitative • active ingredient must diffuse
	DIN EN ISO 20743	Textiles - Determination of antibacterial activity of textile products	• quantitative • evaluation scale • hydrophobic samples possible	• no activation of TiO2, because of incubation in incubator
	AATCC 100	Antibacterial Finishes on Textile Materials: Assessment	• quantitative	• efficacy stated in %, which often raises false expectations
	DIN EN ISO 16187	Footwear and footwear components - Test method to assess antibacterial activity		
	ISO 27447	Fine ceramics (advanced ceramics, advanced technical ceramics) — Test method for antibacterial activity of semiconducting photocatalytic materials	• detection of photocatalytic effects	• Difficult to evaluate as UV light is per se germ-reducing • complex test apparatus

		Description	Strengths	Weaknesses
Fungi	CEN EN 14119:2003	Testing of textiles - Evaluation of the action of microfungi	evaluation scale	only semi quantitative
	DIN EN ISO 846:2019	Plastics - Evaluation of the action of microorganisms	direct or indirect impact measurable nutrient source, product damage)	no quantitative pathogen analysis draft standard withdrawn
	DIN EN ISO 20150:2019	Footwear and footwear components - Quantitative challenge test method to assess antifungal activity		
Viruses	ISO 18184	Textiles — Determination of antiviral activity of textile products		complex expensive lengthy
	ISO 21702	Measurement of antiviral activity on plastics and other non-porous surfaces		complex expensive lengthy
	ISO 18061	Determination of antiviral activity of semiconducting photocatalytic materials. Test method using bacteriophage Q-betat		draft standard withdrawn

Tests to determine the antimicrobial efficacy take into account:

- differences in antimicrobial activity
- field of application
- properties of the substrate
- different pathogens

Safety

The application of nanotechnologies and the use of nanomaterials have been the focus of critical observations for decades and are subject of numerous toxicity studies.

State of knowledge: Nanomaterials differ greatly in their biological effects on humans as well as on ecosystems. The behaviour and also the hazard potential of nanomaterials is decisively influenced by the factors size, shape, chemical composition as well as surface properties and reactivity.

In general, however:

Generalizing statements on toxicity must always be considered carefully!

A critical examination of toxicity studies shows that many studies investigate unrealistically high concentrations or conditions remote from practice.

!

> "Nanoparticles firmly bound in a material are more likely to be considered safe"
>
> \- Stiftung Warentest

Even though nanomaterials have been used for centuries, and no intrinsic health hazard to humans is known to date, safety research remains an essential component in the development of nano based products.

The safety concept is also reflected in the complex process for market approval:

For example, extensive tests and safety requirements are mandatory.

? *Can silver particles be releases out of the layer?*

The fixation of (nano)silver particles is a decisive factor for the safety of a product. Depending on the product formulation, different interaction mechanisms are used to firmly anchor the (nano)silver particles: e.g. via appropriate binders or via dipole interactions.

For example: even under mechanical abrasion the sol-gel based coating SANPURE, does not show a release of nanoparticles.

? *Is it dangerous for the cells of the skin to touch a coated surface?*

No. (nano)silver is primarily effective against single cells (bacteria, cell cultures, ...), but not against robust multicellular organisms or cells in a cellular network (e.g. skin).

For instance, silver has also been used in wound dressings for burns and no cell damage to the skin has been observed for decades.

Also, a scientific study involving a total of 60 subjects who wore antimicrobial-treated T-shirts over a period of six weeks showed:

"antimicrobial agents (show) no adverse effects on the ecological balance of healthy human skin microflora."

Sources:

- nanoinitiative-bayern.de/nanosilber/kooperationsprojekte/abschaetzung-der-umweltgefaehrdung-durch-silbernanomaterialien-umsicht
- B. Schäfer *et al.* (2012) State of the art in human risk assessment of silver compounds in consumer products: a conference report on silver and nanosilver held at the BfR in 2012. *Arch Toxicol* **87**, 2249–2262. (open Access)
- K. Schwirn, D. Völker (2016) Nanomaterialien in der Umwelt – Aktueller Stand der Wissenschaft und Regulierungen zur Chemikaliensicherheit - Empfehlungen des Umweltbundesamtes. (pdf)
- https://www.test.de/Nanoteilchen-Das-sollten-Sie-wissen-4445980-0/
- D. Hoefer, T. R. Hammer (2011) Antimicrobial Active Clothes Display No Adverse Effects on the Ecological Balance of the Healthy Human Skin Microflora. *International Scholarly Research Notices*. https://doi.org/10.5402/2011/369603.

SANPURE®

- Temperatures:
  up to 200 °C
- Layer thicknesses:
  150 nm - 2.5 µm
- Biocompatibility:
  DIN EN ISO 10993-5
- Abrasion resistant:
  according to DIN EN 60068-2-70
- Scratch resistant:
  DIN EN ISO 1518; ISO 15184
- Adhesion resistant:
  DIN EN ISO 2409

SANPURE®
HYGIENIC
CERTIFIED

Applications:

- Automotive
  (e.g. interior, displays).
- Fittings and handles
  (e.g. door handles, PIN locks)
- Supermarket
  (e.g. shopping cart handles)
- Aviation
  (e.g. lavatory, armrest, luggage cart handles)
- Sanitary
  (e.g. handles, dispenser)
- Public transport
  (e.g. grab rails, knobs)
- Electronics
  (e.g. displays, keypads)
- Furniture industry
  (e.g. table tops, overlays)

Product example:
Nanosilver-containing sol-gel surfaces

SANPURE® is an antimicrobial coating based on silver nanoparticles. The active ingredient agpure® nanosilver is marketable according to EU Biocide Regulation (BPR, EU 528/2012; BAUA Reg. No.: N-79342; CAS No. 7440-22-4).

The sol gel based coating can be flexibly processed on various substrates, even to geometrically complex structures/forms. Further, the thin layer concept allows decorative and additional functional design options.

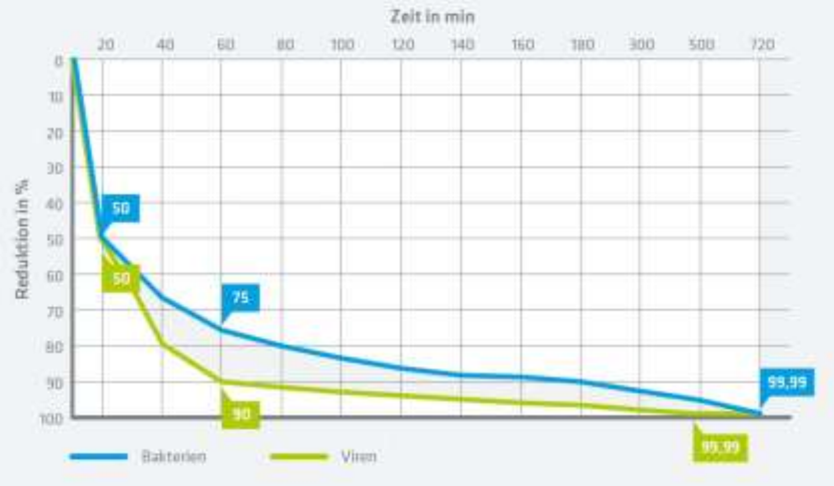
The nanosilver used is manufactured according to medical quality standards (DIN EN ISO 13485) and is also OECD reference material.

- Optics and haptics of the coated substrate are retained even after coating.
- chemically resistant to conventional cleaning agents and disinfection measures
- transparent or coloured, on request also with fluorescent particles
- mechanically flexible
- tested in contact with foodstuffs (TÜV Rheinland test: coated stainless steel plate corresponds to §31 LFGB)

Antiviral and antibacterial activity:

The SANPURE coating was tested against the bovine coronavirus BoCV; strain: S379 Riems in a practical virucidal carrier test in accordance with the RKI guideline (1995) and ISO 21702:2019. A virus reduction of > 90 % after one hour (lg 1.35) and > 99.99 % after 8 hours (lg 4.5) was found.

The antibacterial efficacy was confirmed according to ISO 22196 / JIS Z 2801:2010.



The SANPURE coating continuously reduces the germ load on surfaces within a few hours.

Product example:
Silver in textile form

Silvertex® is an antimicrobial 3D knitted fabric incorporating silver-plated polyamide yarns. By processing silver as an open-meshed textile it is possible to additionally increase the antimicrobial surface, even without using nanoparticles.

The result is an available silver surface area of 24 m² per square meter of textile surface. This greatly enlarged silver surface enables the protection of even large water reservoirs and water volumes from microbial contamination up to 500 m³.

The defined release of silver ions can be controlled in a customer and application specific manner via the quantity of silver-plated yarns used.

The mesh can be used in a wide range of possible applications: from the treatment of water in small drinking water containers (canisters) to large cooling and process water storage tanks in industry.

Due to the flexible processing, the textiles can also be used for other applications, e.g. for air treatment devices (air humidifiers) or for caravanning.

Silvertex®

- Temperatures:
  up to 60 °C
- 1 m² textile
  = 24 m² silver
- Application range:
  up to 500 m³
- Layer thicknesses:
  500-800 nm
- Biocompatibility certified:
  DIN EN ISO 10993-5

silvertex®

Application:

- Air handling units and systems
- Industrial cooling: cooling towers, air conditioning systems, IT / server systems
- Industrial water disposal, osmosis plant tanks
- Cooling lubricants
- Extruder, granulator, fire water, emergency showers
- Mobile drinking water depots stationary and mobile (caravans, boats)
- Purification of hot and cold drinking water systems (abroad)

Where are antimicrobial surfaces used?

Antimicrobial surfaces in practice

Various surfaces (e.g. plastic, metal or glass) can be functionally coated with (nano)silver to make them antimicrobially active.

These coatings are useful whenever there is a possibility of increased pathogen loads and when different people come into contact with the same surface. Then, these coatings can decisively minimize contamination levels and provide a long-term and permanent protection against pathogens.

In hospitals and nursing

The European Center for Disease Prevention and Control has determined that more than 4 million patients in Europe acquire "healthcare facility associated infections" (HAI) each year. Approximately 10,000 to 30,000 deaths in Germany alone are attributable to nosocomial infections.

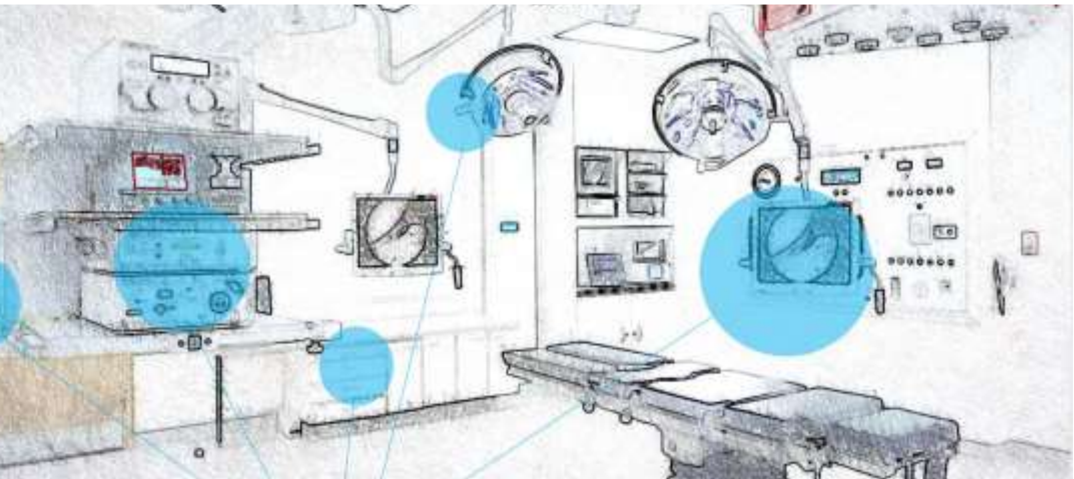
But HAI are not only critical for health reasons. Corresponding infections prolong hospital stays, increase the cost of treatment and are associated with significant additional costs. Hence, there is an urgent need for additional strategies.

Case study

Regensburg: A scientific study conducted by the University Hospital Regensburg and under the direction of a hygienist, investigated various surfaces equipped with a nanosilver coating in different emergency rooms, including touchscreens, handles, keyboards and switches. The researchers examined the respective microbial contamination over a period of more than 9 months.

Previously carried out efficacy tests showed high reduction rates of more than 3 log levels (responds to a killing of more than 99.9% of the pathogens examined) under laboratory conditions and controlled contamination (DIN ISO 22196) with various (multi-resistant) germs. In the long-term practical test, regular swab tests were carried out over a period of one year during ongoing operation of the emergency room and compared with an identically coated room without antimicrobial additives. The double-blind study over a period of 90 days showed:

- Germ resistant surfaces significantly improved the hygiene level in the clinical environment
- An overall lower germ load was observed
- High germ densities were significantly reduced



In Germany **10,000** to **30,000 deaths** per year are attributable to nosocomial infections.

Silver in textiles and masks

(nano)Silver in textiles offers versatile applications, from antimicrobial functionality to complex IOT systems.

Antimicrobial (nano)silver is incorporated into textiles for different reasons:

- Sports textiles for odour control
- Technical textiles (e.g. filters) to avoid fouling processes
- Textiles in health care or in food processing plants (e.g. gowns, towels) to reduce the transmission of pathogens

The technical implementation of silver is done in different ways and depending on the desired application. The processing also has a significant influence on how strongly the particles are bound in or to the textile. The most common processing methods include coating and direct integration into the (synthetic) fibers.

! **Important**

(nano)silver should be incorporated directly into the textile to ensure the greatest possible safety. This also ensures longer lifetimes even with frequent washing.

? *Is the use of nanosilver in masks approved and reasonable?*

In the course of the Corona crisis, masks with nano-silver were increasingly being offered in stores and on the Internet. However, it should be noted that little is known to date about the efficacy of (nano)silver against viruses. Although initial studies show a moderate inactivating effect (A recently published study on SARS-CoV-2, described an inactivating effect resulting from solubilized silver nanoclusters on respirator masks), this effect strongly depends on the type of nanoparticles being used.

Further, one should generally distinguish between a filtering performance (barrier function) and an antimicrobial/antiviral efficacy (killing/inactivating germs). Masks primarily function is to filter and to prevent the inhalation and/or exhalation of germ-containing aerosols. Antimicrobial materials may kill or inactivate pathogens if they remain on the material for a sufficiently long time (incubation period). On masks, this is can be of use if the pathogens are retained by the material for a sufficiently long time due to the filter function.

While the filtering performance of medical face masks and FFP masks need a market approval, no legal requirements for functional parameters apply to community masks. Newly developed guidance documents (e.g., CWA 17553, AFNOR SPEC S76-001) may take into account appropriate testing standards and evaluation criteria, but are still not mandatory.

The French Agency for Nutrition, Environment and Occupational Safety (ANSES) rates textile face masks treated with silver compounds as safe when used correctly, noting that it has not evaluated how effective these treated face masks are.

Sources:

- C. Balagna, S. Perero, E. Percivalle, E. Nepita, M. Ferraris. (2020) Virucidal effect against coronavirus SARS-CoV-2 of a silver nanocluster/silica composite sputtered coating. *Open Ceramics* **1**, 100006. Online

Silver for water conservation

Microorganisms like E. coli/Coliforme, Legionella, fungi and Pseudomonas aeruginosa can cause serious problems in drinking water installations. This includes (among others) cooling towers, hot and cold water systems, air conditioners, spa equipment, fountains, humidifiers, showers, misting devices, ornamental fountains and water features, dental equipment and thermostatic mixing valves.

Numerous projects describe the respective use of silver in the public sector (e.g. drinking water treatment in hospitals). In Germany however, the use of silver is currently only permitted in the private sector or as a pilot project under the supervision of a health authority.

By the way:

The WHO limits the maximum intake of silver to 0.1 mg/l.

Soluble silver compounds are already used in many ways:

- topical antiseptics (15-50 µg/litre)
- bacteriostatic agents (up to 100 µg/litre)
- disinfectants (>150 µg/litre)

More information:

https://www.who.int/water_sanitation_health/dwq/chemicals/silver.pdf

Application example drinking water

Erba, Region of Como, Italy: The local drinking water supply network of the municipality of Erba is fed by alpine springs and stored in a high-altitude intermediate reservoir (700 m³).

The microbial nature of the raw water (E. coli, coliforms, enterococci, clostridia, etc.) requires mandatory disinfection monitored by the competent authority. Traditionally, chlorine dioxide is used as a disinfectant.

With the installation of 25 m² of Silvertex® material, the chlorine dioxide dosage could be significantly reduced (silver content: < 10 µg/L).

Since November 2010, a total of approx. 20,000 m³ of drinking water with officially controlled microbial quality (<1 CFU/100 ml) has been provided during maintenance-free operation.

Sources:

- https://www.dvgw.de/themen/wasser/wasserqualitaet/trinkwasserhygiene

More applications

Eliminating weak points on disinfectant dispensers

A silver coating for disinfectant dispensers was developed in cooperation with the TEMCA. Among other things, the company offers a wide range of products in the field of sanitary hygiene.

The coating now provides a better hygienic protection for the dispenser lever - a weak point that is not considered in many disinfecting systems.

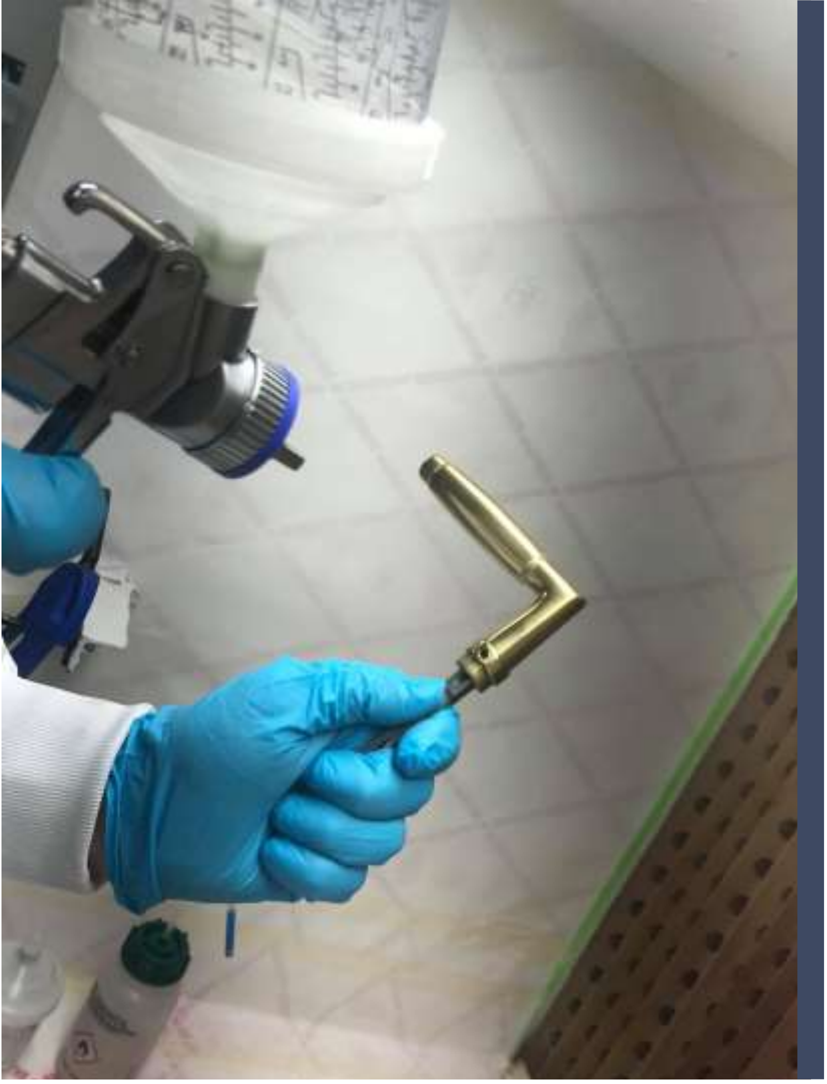
The transparent surface coating can also be made visible under fluorescent light.

Antimicrobial Digital Door Handles, Cylinder, and Panic Bars

To support and facilitate people's new awareness of hygiene, DOM Security has developed antimicrobial surfaces for digital hardware, digital cylinders and panic bars.

The nano-silver coating is used on the metal elements of the Guard family door handles, the metal knobs of the Pro digital locking cylinder, and on the grip surfaces of the panic bars.

Since locks and handles are used by many different people in a short period of time, there is an increased risk of pathogen transmission. The antimicrobial coating thus offers additional protection.



Better hygienic safety in hotels

During the first Corona lockdown, the "Schieferhof" and "Residenz" hotels in the Thuringian Forest had their door handles coated with antimicrobial silver.

The measure is a powerful element of the newly developed hygiene concept and takes account of the fact that hygiene has become a sales argument of enormous importance.

SANPURE® effectively counteracts the risk of infection, particularly in the entrance area and in the catering trade, where many people come into contact with door handles within a short time.

Air treatment

In the private and in industrial sectors, air treatment equipment is used to create a pleasant and clean indoor climate but also to reduce dust generation or to wash/filter certain substances out of the air.

However, under certain conditions (including inadequate cleaning and maintenance of the equipment and insufficient water treatment or exchange), such installations can 1. accumulate pathogens and 2. release them into the environment. This is especially dangerous for asthmatics and allergy sufferers.

Silvertex® was adjusted to significantly reduce the germ load in industrial wet separators or air treatment equipment such as air washers, humidifiers and diffusers.

Summary and conclusion

Today‘s situation

The rising number of infectious diseases and potential transmission routes worldwide poses an increasing threat to modern society.

Future

Specific hygiene measures already play an important role today and will become even more important in the future.

Surface and period-related hygiene measures in particular are increasingly coming into focus.

Problems

Properly implemented hygiene measures, such as disinfection and cleaning, can quickly kill and remove pathogens.

However, protection only exists immediately and only during the disinfection and cleaning process but not between the individual intervals.

Solution

Antimicrobial surfaces (especially (nano)silver-containing coatings) offer an effective, safe, inexpensive and sustainable solution for preventing the transmission of pathogens, even between hygiene intervals.

Antimicrobial surfaces are already being used successfully today and contribute to protection against dangerous pathogens in various areas.

Important:

Conventional hygiene strategies (especially cleaning and disinfection) are not replaced, but rather supplemented and expanded in a meaningful way.

Further information

- www.nanosilber.info
- www.nanoinitiative-bayern.de
- VDI-Statusreport Keimreduzierung im klinischen Umfeld durch Nanotechnologie
- SANPURE: https://sanpure.de/
- GBneuhaus GmbH: https://gbneuhaus.de/de/
- Silvertex: https://silvertex-aqua.de/de/startseite/
- RAS AG: https://ras-ag.com/
- Hohenstein: https://www.hohenstein.de/de/
- Fraunhofer ICT: https://www.ict.fraunhofer.de/

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This white paper was developed and written by an interdisciplinary team of biologists, virologists, chemists and economists from industry and applied research.

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Network NanoSilver

The network NanoSilver connects experts working on joint solutions and products that offer people additional benefits while ensuring high product safety and environmental compatibility.

Focus of the network is the unbiased investigation of opportunities and risks of nanotechnology over the entire product life cycle.

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