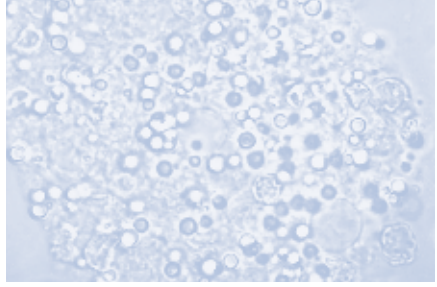


ON THE TRAIL OF HOSPITAL PATHOGENS

Hospital-acquired infections are among the most common infections of all. One of the biggest threats comes from those bacteria that can no longer be effectively treated with antibiotics.

Traces of microorganisms on the skin: a hand print becomes visible on an incubated culture medium

Hands with living organisms

'If a poor servant comes to the hospital with a small wound which would have healed within 14 days under good hospital conditions, he will be on the threshold of death, lies maybe 100 to 150 days seriously ill suffering painfully and when he is finally released from the hospital, thin as a rake and still not able to work, he will be forced to pay from his savings.' This drastic illustration of the faults of hospital hygiene was given by a commentator in the medical journal "Ärztliches Intelligenzblatt" – back in 1875, a time when the most severe wound infections were commonplace in medicine.

The progress achieved since then is enormous: surgical instruments are rendered free of microorganisms by sterilisation procedures, contamination of wards is reduced by means of surface disinfection; and infections that do occur are treated with antibiotics.

Despite this, hospital-acquired infections are some of the most common problems in medicine. An estimated 400,000 to 600,000 people a year catch an infection during a stay in a German hospital. The most common hospital-acquired infections are surgical site infections, urinary tract infections or pneumonia. Hospital-acquired infections frequently increase the length of stay and thus increase the costs of treatment, sometimes they are even life-threatening. It has been estimated that 10,000 to 15,000 deaths are caused by hospital infections in Germany each year.

'At least some of these infections could be avoided by compliance to good hygiene,' notes Mardjan Arvand, head of the unit for Hospital Hygiene, Infection Prevention and Control at the Robert Koch Institute (RKI). The Robert Koch Institute regularly publishes updated guidelines, which are developed by a national advisory board of experts – the Commission for Hospital Hygiene and Infection Prevention at the Robert Koch Institute – and serve as authoritative basis and standard for the necessary prevention measures.

It is thus well proven that pathogens are often transferred from one patient to the next by the hands of health care workers – and the number of hospital infections could be significantly reduced simply by regular hand disinfection. However, surveys reveal that compliance with hand disinfection is still unsatisfactory in German hospitals.

Hygiene training for health care workers in particular needs to be further reinforced, assesses Mardjan Arvand. 'The responsible heads of departments and hospitals should not see hygiene as a necessary evil – but as one of the best and most inexpensive measures of preventing complications in treatment.'

This is precisely the direction followed by the "clean hands campaign", in which the RKI is also a partner. This German-wide programme supported by numerous clinics as well as nursing homes and home care services aims to improve hygiene behaviour, for example by training staff in the organisations concerned.

A further instrument for obtaining an improved grasp of the issue is a recording system especially tailored for hospital infections, known as KISS (Krankenhaus-Infektions-Surveillance-System). A large proportion of German clinics voluntarily record how many of their patients are infected with particular pathogens and provide the data for statistical analysis. In the particularly sensitive area of premature birth medicine all relevant intensive care units take part. KISS – which is operated by the German National Reference Centre for the Surveillance of Nosocomial Infections in co-operation with the RKI – is not only intended to document the extent of the infection situation. It also aims to help resolve specific hygiene issues and to spread awareness of the often hidden infection threat associated with medical procedures.

The number of bacteria colonies growing on test culture mediums is a measure for the effect of disinfectants

Resistant pathogens

In fact, there are several reasons as to why infections are commonplace in hospitals. Patients treated in hospitals are often seriously ill and therefore particularly likely to catch an infection. At the same time, invasive procedures such as respirator tubes and venous or bladder catheters, known to be classic entry portals to the human body for pathogens, and the use of medical equipment and materials is considerable, especially in intensive care units.

Particularly problematic is also the frequent use of antibiotics in hospitals. The intensive use of these drugs creates an environment in which antibiotic-resistant bacteria have a survival advantage over their fellow susceptible strains and are therefore able to spread effectively. Some of these microbes are resistant to multiple drugs – the chemical weapons of infection medicine are being blunted.

A notorious example is that of Staphylococcus aureus, a spherical bacterium that is well known to cause wound infections and blood poisoning. Multiple-resistant strains of this pathogen, MRSA for short, are resistant to important antibiotics and are therefore difficult to treat. The role of MRSA as a pathogen has particularly increased in Germany since the early 1990s. 'Today, about one-sixth of all infections with Staphylococcus aureus are caused by MRSA strains. Happily though, the trend has been downwards in recent years,' says Guido Werner who, together with his team at the RKI site in Wernigerode in the Harz region, is studying the genetic properties of resistant hospital pathogens, particularly MRSA.

'We are now also increasingly concerned about other pathogens,' says Martin Mielke, head of the Department of Infectious Diseases. Some bacteria produce highly potent enzymes – known as ESBL (Extended Spectrum Beta Lactamases) – using these to render the majority of common antibiotics inactive. Such bacteria include strains of Escherichia, Pseudomonas or Klebsiella, pathogens that, for example, can trigger pneumonia and have been increasingly found in hospitals in recent years. If that was not enough, bacteria have also developed defence mechanisms against compounds deployed as "reserve antibiotics". 'There are currently very few possible treatment options for an infection with such pathogens, which are usually so-called gram-negative bacteria residing in the intestines,' states Mielke.

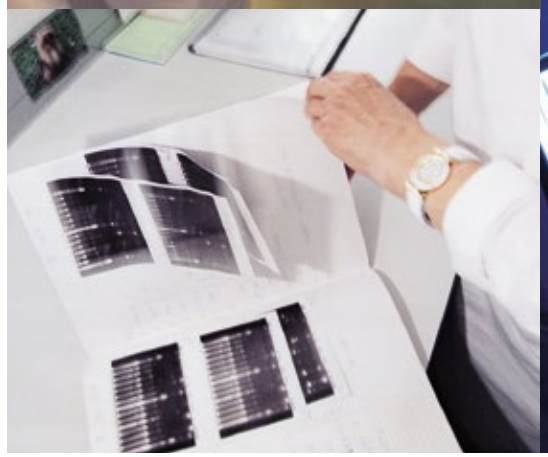
'In order to launch effective countermeasures we need extensive data on where the resistant pathogens occur each time and how the spectrum is changing in the long run,' says Tim Eckmanns of the RKI Department of Infectious Disease Epidemiology. Eckmanns and his colleagues have established a unique nation-wide surveillance system for that purpose – the so called Antimicrobial Resistance Surveillance (ARS). This is part of the German antimicrobial resistance strategy (DART), enacted by the government in 2008, which aims at the containment of the resistance problem.

'As many German hospitals and medical practices as possible should be integrated into the ARS system in the long run,' emphasises Eckmanns. The principle is that microbiological laboratories that conduct resistance testing for health care providers transmit the results online to the RKI. There the data are analysed with special statistical methods for dangerous trends in the resistance spectrum and reports of the results are immediately submitted back to the participating laboratories and health care professionals – in order to promptly contain the spread of the resistant microbes. Moreover, part of the resistance data is also available as an interactive database on the internet, as is a similar database with the results of antibiotic use surveys (AVS).

ANTIMICROBIAL RESISTANCE

Antimicrobial resistance is described as the ability of certain bacteria to resist treatment with antibiotics. Resistant pathogens can degrade the substances, for example with special enzymes. This ability is genetically determined. The resistance genes concerned are often found on mobile genotype elements (plasmids) that can be interchanged between different bacterial strains. If bacteria have multiple resistance genes at the same time, they can no longer be destroyed by conventional drugs. Such bacteria are then referred to as "multi-resistant".

'The spread of antimicrobial resistance is one of the biggest threats for success of modern medicine,' says Martin Mielke, head of the Department of Infectious Diseases



A pathogen can be identified by its genetic pattern – and rendered visible in a special procedure

The tracking of microbes

Today, the ways resistant pathogens are spread can be reconstructed down to the tiniest detail. For example, it is known that the transfer of patients from one hospital to another can result in the distribution of problematic microbes. If e.g. staphylococci of the MRSA type appear in two different hospitals, genetic analysis can be done to identify whether they belong to the same bacterial strain – which then enables conclusions to be drawn regarding the route taken by the pathogen.

For such analyses the RKI experts in Wernigerode use so-called sequence-based typing. Certain parts of the genome of bacterial pathogens which exhibit sequence polymorphisms are analysed in detail – the result is a kind of genetic fingerprint of the respective pathogen strain. Microbiological samples are received from all over Germany where staphylococci bacteria are involved in infections. Moreover, the typing data are now exchanged in international research networks, enabling the spread of resistant strains to be traced even across borders.

Remarkably, bacteria are not only spread by patient transport or by the travel of infected people. The spread of pathogens within and between livestock farms is also a commonly observed phenomenon. For example, MRSA bacteria are often found in livestock, including pigs, fattening poultry and calves. These pathogens are spread within the framework of the international trade in piglets and can also be transmitted to humans.

'Farmers and veterinarians (and, although relatively rare, members of their families) are the principal carriers of MRSA bacteria originating in animals,' reports Guido Werner's colleague Christiane Cuny, who has demonstrated the connection through painstaking investigations of German pig farms. If the individuals carrying resistant pathogens are treated in a hospital, for example, they may introduce infections that are difficult to treat.

As is now known, resistant pathogens are often then transferred from the hospitals to the domestic environments of discharged patients or appear in nursing facilities when patients are moved there.

Molecular-epidemiological studies carried out in Wernigerode in collaboration with scientists in Denmark had already in the 90s demonstrated the transmission of antimicrobial resistance between livestock and humans. Either the resistant bacteria themselves or their genes were being transferred, showing that livestock represent an important reservoir of resistance genes.

It has long been apparent that these multiple transfer chains can only be broken with the cooperation of different stakeholders. For example, the analyses of MRSA bacteria from livestock farming have contributed to the recommendation that people who work in such facilities are systematically examined for pathogens prior to being treated in hospitals. 'Moreover, hospitals, medical practices and nursing facilities have joined together to form regional prevention networks in many regions in Germany in order to exchange information on patients affected and to fight resistant pathogens by means of a coordinated strategy,' explains Martin Mielke.

At a glance

It has been estimated for Germany that each year 400,000 to 600,000 patients suffer a hospital-acquired infection and 10,000 to 15,000 of them die as a consequence. Typical problems for health care providers are surgical site infections, as well as urinary tract infections and pneumonia. Since the early 1990s an increasing role is being played by bacteria with a growing resistance to antibiotics which are therefore difficult to treat. Scientists at the Robert Koch Institute are researching the molecular-genetic properties of the resistant microorganisms. Moreover, they analyse the ways in which the resistant pathogens are spreading and provide data on antimicrobial resistance and antibiotic use online. Regularly updated guidelines are published on how the hospital infections can be avoided with hygiene measures.

In the strain collection at the Wernigerode site, the bacterial strains handled are archived continuously and can be re-cultured at anytime