

cvc-partner 3

Catheter Care and Hygiene



Preface

Challenge of modern medicine

For several decades, the prevention of catheter-related infection has been a major challenge of modern medicine; this will continue to be the case for many years to come given the rapid advance of supportive care and the continuing trend toward aggressive and sophisticated critical care techniques.

The handbook series "CVC-partner" has been prepared in consultation with experts in the field of catheter use and health-care associated infection prevention. While volumes 1 and 2 focused on catheter insertion strategy and positioning, the current volume concentrates on the pathogenesis and impact of catheter-associated infections as well as on catheter care and prevention strategies.

Hand hygiene – the basis of infection control

The prevention of catheter-related infections relies first on a strict observation of the basic rules of infection control, particularly hand hygiene practices (1). It is now clearly established that, compared to traditional handwashing with soap and water, the promotion of hand rubbing with alcohol-based solutions may result in significant and prolonged improvement of hand hygiene compliance. This combines the advantages of a rapid action with more potent antimicrobial efficacy at a lower cost. In particular, hand rubbing might bypass the time constraint, the major risk factor for noncompliance in critical care settings with high workload (2). Accordingly guidelines for hand hygiene procedures have been completely reviewed and adapted to these new concepts (3).

Preventive measures include adequate hand hygiene, the use of maximal sterile barriers during insertion, optimal insertion site preparation and technical procedures, and detailed guidelines for maintenance and replacement of the catheters. Defining particular situations in which the use of antiseptic-coated devices might be beneficial is also a relevant issue.

Guidelines – essential tools

Detailed guidelines for the insertion and the care of vascular accesses are regularly published, but data from surveillance programs have repeatedly shown that they are generally not, or insufficiently, applied. A survey of American College of Physicians members published in 1994 indicated that 43% of the physicians believed that guidelines would increase health-care costs, 68% that such guidelines would be used to discipline them, and 34% that they would make medical practice less satisfying. Although evidence has suggested that guidelines could improve both the process and the outcome of patient care, the degree of improvement has varied and may only have been transient. Accordingly, efficient guideline implementation requires their implementation in a manner that effectively communicates best practice to be adopted by healthcare workers.

Education – a recognized way to prevention

Training and educational programs specifically designed to reduce the incidence of catheter-related infections have recently proved to be effective. Based on education of healthcare workers in charge of insertion and handling of vascular accesses in critical care, where almost all patients are equipped with at least one intravenous line, several groups have obtained remarkable results (4,5,6). We evaluated the impact of a global strategy targeted at the reduction of vascular access line infection in 3,154 critically-ill patients consecutively admitted to a medical intensive care unit (6). The program consisted of slide-show-based educational sessions and bedside training of the entire staff, including nurses. Training included specific recommendations for the insertion and handling of vascular accesses. Following the intervention, the incidence of exit-site catheter infection decreased by 64%, and that of bloodstream infection by 67%. Although the overall exposure to central venous catheter did not significantly differ between the control and the intervention

periods, the incidence of bloodstream infection markedly decreased from 22.9 to 6.2 episodes per 1,000 central venous catheter-days due to a reduced incidence of both microbiologically-documented infection (from 6.6 to 2.3 episodes per 1,000 central venous catheter-days) and clinical sepsis (from 16.3 to 3.9 episodes per 1,000 central venous catheter-days). Overall, the incidence of all nosocomial infections was reduced by 35% (from 52.4 to 34.0 episodes per 1,000 patient-days). This corresponded to the prevention of 50 to 104 nosocomial infections over an eight-month period including at least 1 to 11 primary bloodstream infections, 15 to 29 clinical sepsis, and 15 to 32 vascular-access-related infections. When assessed 30 months after the intervention, the incidence of catheter-related infection was decreased further by 25%, suggesting that the integration in the daily practice of the elements included in the prevention strategy was beneficial.

Using a conservative approach, the costs saved following the reduction in nosocomial infections reported after the introduction of education-based prevention programs can be estimated to be at least as effective as those that could be expected if antiseptic-coated catheters would have been introduced in the corresponding wards (4,5,6).

Infection can be prevented

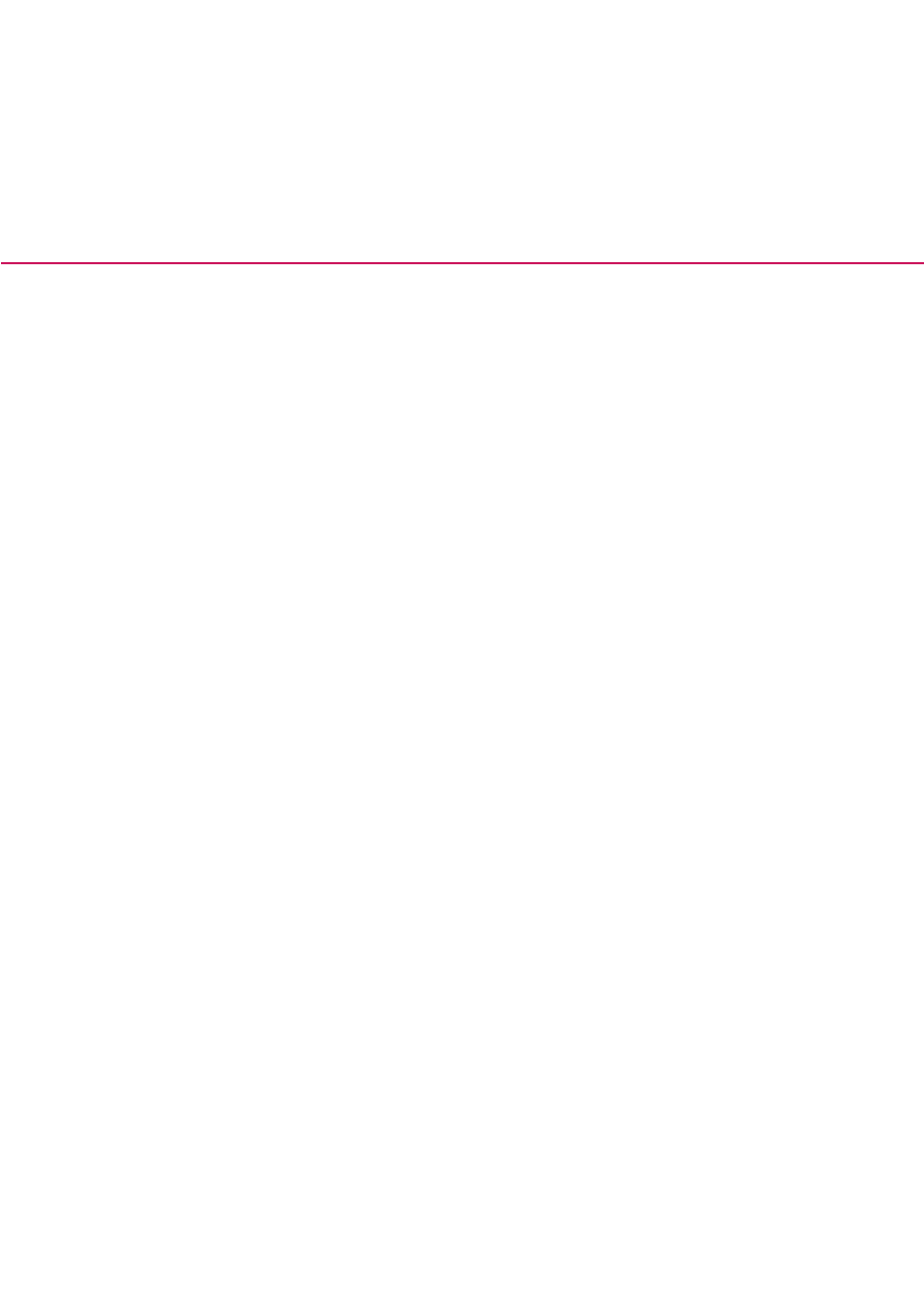
In the absence of other clinical focus of infection, vascular access devices are the leading cause of primary bacteremia and clinical sepsis. Potentially lethal, these infections account for a significant prolongation of hospital stay and associated costs (7,8). However, a large majority are preventable. Thus, vascular device-associated infections should no longer be considered as an inevitable tribute to pay to the technology of medicine. Preventive strategies should be viewed as quality improvement initiatives and based on the introduction of appropriate guidelines and education-based programs.

Didier Pittet, MD, MS
 Professor of Medicine and Preventive Medicine
 Director, Infection Control Program
 University of Geneva Hospitals, Geneva, Switzerland
 and
 Honorary Professor
 Division of Investigative Science and School of Medicine,
 The Hammersmith Hospitals, Imperial College of Science,
 Technology and Medicine, London, UK

Address for correspondence:
 Professor Didier Pittet, MD, MS
 Service Prévention et Contrôle de l'Infection
 Direction médicale
 Hôpitaux Universitaires de Genève
 1211 Geneva 14, Switzerland
 Tel: ++41-22-372.9828
 Fax: ++41-22-372.3987
 E-mail: didier.pittet@hcuge.ch

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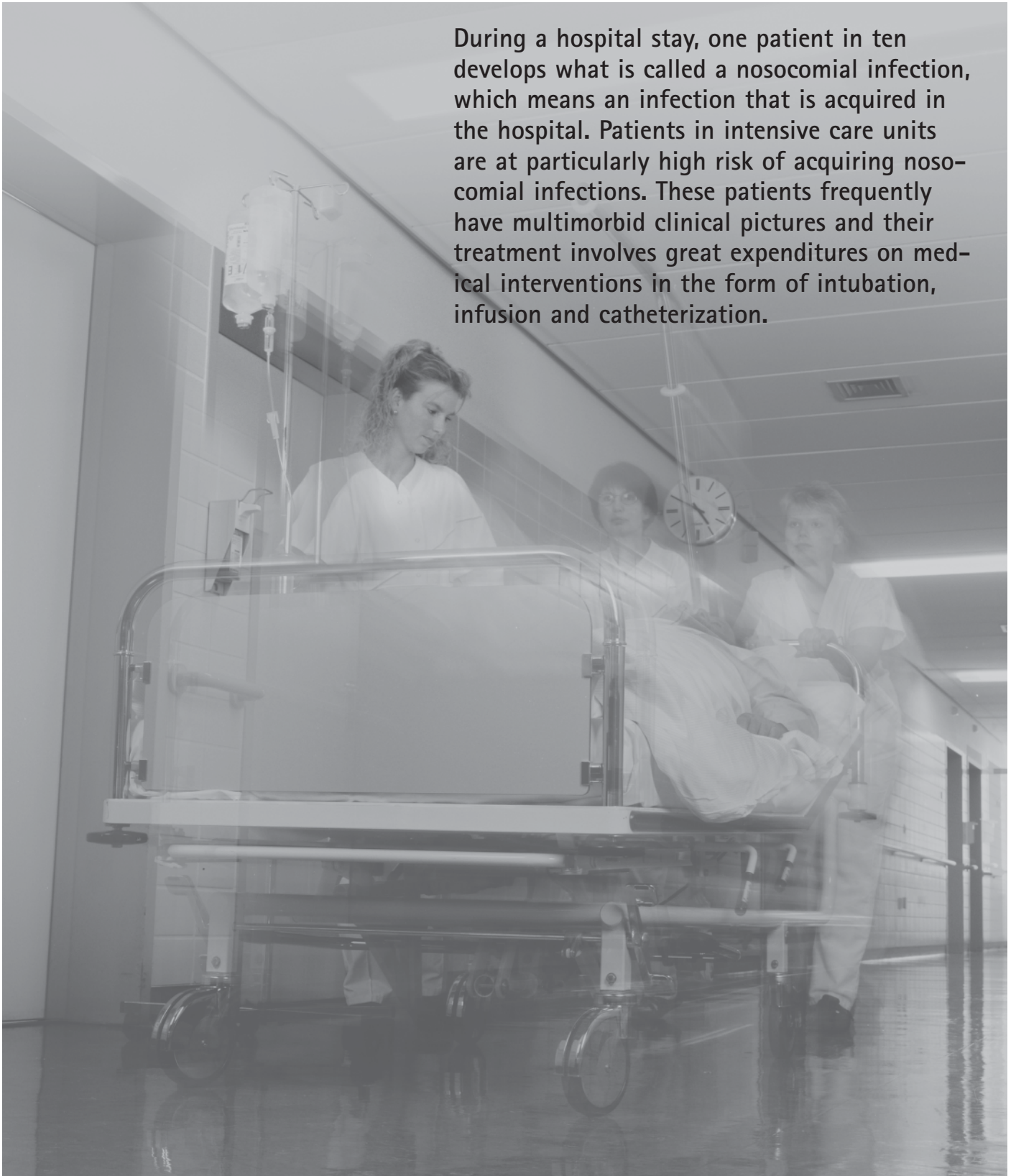
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Hospital-acquired infections

During a hospital stay, one patient in ten develops what is called a nosocomial infection, which means an infection that is acquired in the hospital. Patients in intensive care units are at particularly high risk of acquiring nosocomial infections. These patients frequently have multimorbid clinical pictures and their treatment involves great expenditures on medical interventions in the form of intubation, infusion and catheterization.



No less than 90% of all people who are hospitalized for an acute disease or to undergo elective surgery leave the hospital without suffering any serious complications (1,2). However, ten percent of the patients unintentionally contract an infection from pathogens living in the hospital environment. These infections, called nosocomial infections, prevent a rapid recovery for such patients. In severe cases, the patients' conditions can worsen to the extent that they require intensive medical care.

When cases of nosocomial infection are analyzed retrospectively, it is often very difficult to identify a clearly circumscribed infectious or pathogenic source. Factors that promote the development of nosocomial infections include the great number of manual activities performed on patients and the frequent use of medical devices and equipment for infusion, for stabilizing the airways or for administering intravenous medication.

Even when the administration of care apparently takes a routine course, there is always an inherent risk of infection involved with the treatment of patients. Serious underlying diseases like diabetes, hypertension or COPD (= chronic obstructive pulmonary disease) and/or advanced age increase the risk of nosocomial infection (1). Given that the incidence of these diseases in the overall population has been on the rise in industrial countries, the percentage of hospital patients with these risk factors is also growing steadily.

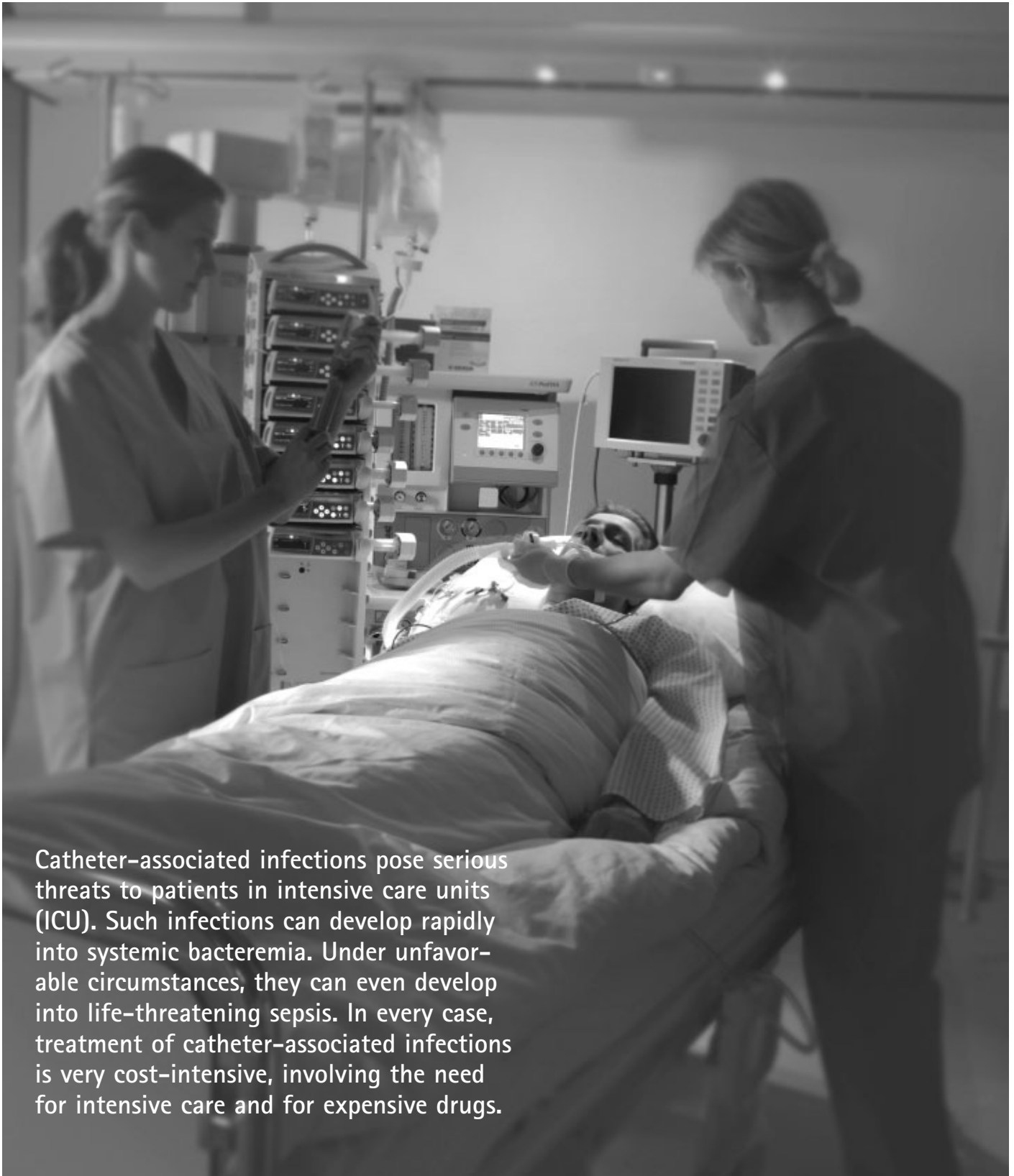
Another important factor that has a major impact on the infection rate in hospitals is the quality of medical and nursing care patients receive. All activities conducted on patients should be performed using aseptic technique to eliminate the potential for inadvertent transmission of bacteria as much as possible.

When hygienic measures are not adequately adhered to, the risk for patients developing nosocomial and particularly catheter-associated infections can increase. The evidence of the past years has proven that the rate of hospital-acquired infections can only be successfully reduced by implementing strict prevention strategies at all levels (for recommendations for the prevention of catheter-associated infections, see page 18 ff). Anesthesia and intensive care medicine have dedicated themselves to tackling this problem.

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Costs and consequences of infections



Catheter-associated infections pose serious threats to patients in intensive care units (ICU). Such infections can develop rapidly into systemic bacteremia. Under unfavorable circumstances, they can even develop into life-threatening sepsis. In every case, treatment of catheter-associated infections is very cost-intensive, involving the need for intensive care and for expensive drugs.

Importance of nosocomial infections

A patient is admitted to a hospital whenever one or more underlying diseases, such as cancer, polytrauma or infection, require inpatient treatment. With a frequency of approx. 10% (1-2), the patient also contracts a nosocomial (hospital-acquired) infection during the hospital stay. Despite this low probability of occurrence, the overall costs incurred by each country's healthcare system add up to huge amounts. In the United Kingdom, it is estimated that the care of patients who develop nosocomial infections costs an additional 1 billion pounds Sterling (2).

The four major types of nosocomial infections are:

- Respiratory tract infections
- Urinary tract infections
- Catheter-associated infections
- Wound infections

Patients in intensive care units (ICUs) are particularly at risk of developing nosocomial infections. This was demonstrated by a pan-European study which found that 30% of all ICU patients develop a nosocomial infection compared to only around 9% of patients on general internal medicine wards or surgery wards (3). The most common source of infection for patients in intensive care units was artificial respiration. Pneumonias and respiratory infections, with a prevalence of 65%, rank highest among the nosocomial infections contracted in intensive care units (see Fig. 1), followed by urinary tract infections (18%), catheter-associated infections (12%) and wound infections (7%) (4).

Catheter-associated infections (CAI) pose special problems for patients in ICUs because such infections are difficult to diagnose and can develop into severe sepsis. During their stay in the ICU, the patients' clinical conditions will fluctuate, making it difficult to diagnose catheter-associated infections. It is very difficult to provide the patient with the proper treatment when the diagnosis is uncertain.

Diagnosis of catheter-associated infections

For the first time in 1988, the Center for Disease Control (CDC) in the United States prepared guidelines with definitive criteria for diagnosing catheter-associated infections (5). The general term catheter-associated infections is usually differentiated into three major types (see page 10, Table 1):

- Local infection at the catheter exit site
- Catheter colonization
- Catheter-associated bacteremia (bloodstream infection)

Although each of the three types can occur separately, they frequently tend to occur in combination. A central venous catheter in a patient who has erythema around the exit site (local infection) will usually be determined to have bacteria on the intracutaneous segment (colonization). In some cases the catheter removed from a patient with erythema will show no adherent bacteria on the intracutaneous segment. No matter what the circumstances, though, appropriate measures must be implemented whenever one of these three types is encountered (see page 17, Fig. 11).

In the USA, it is estimated that catheter-associated blood stream infections number around 80,000 annually, incurring additional costs of up to US\$ 2.3 billion (5). In the 1980s, it was found that despite the high standard of care in American hospitals the rate of catheter-associated infections tended to increase rather than decrease (1). Figure 2 illustrates that, at the beginning of the eighties, infections occurred in 0.2 – 3.8 of every 1000 patients discharged, while approx. 10 years later that prevalence rate had risen to 1.2 – 6.0. Large teaching hospitals with more than 500 beds had a six-fold higher infection rate

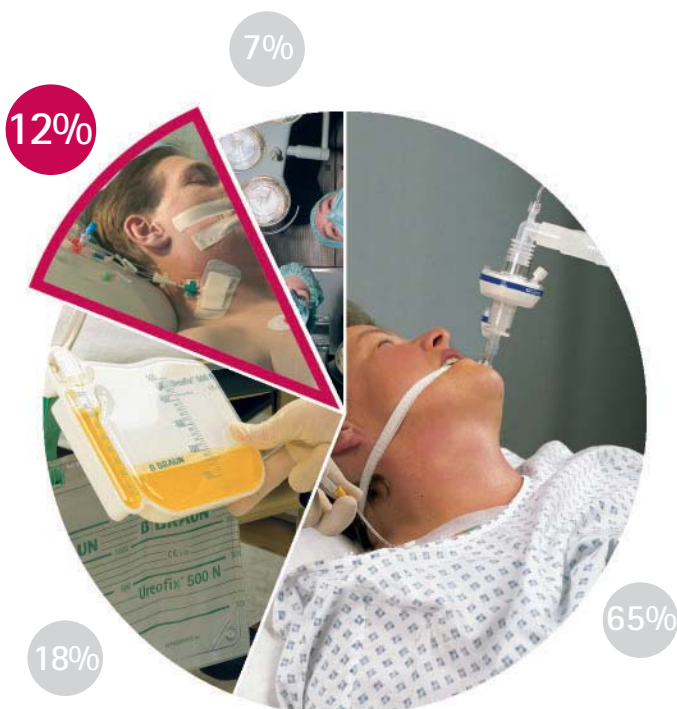


Figure 1: Prevalence of the four major types of nosocomial infections in intensive care units: respiratory tract infection, urinary tract infection, catheter-associated infection and wound infection

Costs and consequences of infections

compared to small hospitals with up to 200 beds; and compared to small teaching hospitals with up to 500 beds, the infection rate was higher by a factor of 1.5. Strikingly, there has been a dramatic increase in the infection rates at small hospitals from approx. 0.2 per 1000 discharges to 1.2 per 1000 discharges. One reason for the increased infection rate is that the number of elderly patients with multiple underlying diseases is growing; another is that the care of patients in hospitals increasingly relies on invasive measures and technological equipment (1).

The risk for a catheterized patient to develop a catheter-associated bacteremia depends on a variety of factors such as age and severity of illness. It is therefore difficult to reach general conclusions. Clinical studies among different patient groups and under different clinical settings have produced numbers ranging between one infection per 100 patients and one infection in 12 patients with a central venous catheter (i.e. infection rates between 1% - 8%) (6).

Implications for the hospital

Outwardly, a catheter-associated infection manifested as a local infection or colonization may seem harmless. It could be treated by thorough disinfection of the puncture site and/or by removing the catheter. In many cases, however, these measures are not sufficient or are taken too late to prevent spreading of bacteria into the bloodstream. A chain of infectious events may develop which is characterized first by bacteremia, followed by systemic inflammatory response syndrome (SIRS), and leading finally to sepsis and multiple organ failure (septic shock). Oftentimes, the final stage of septic shock results in a fatal outcome. Studies have shown that the presence of a catheter-associated bacteremia dramatically increases the mortality risk

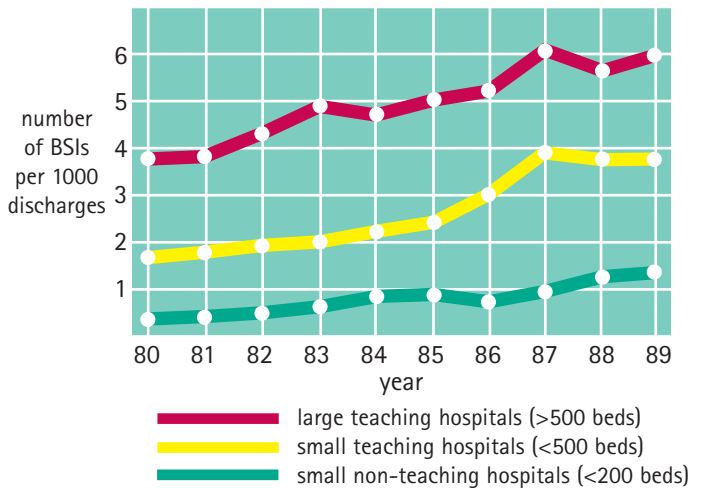


Figure 2: Increase of bloodstream infection (BSI) rate in US hospitals from 1980 - 1989 (adapted from 1)

by up to 35% (7). In the USA, approx. 62,500 deaths annually have a causal association with catheter-related infections (1). Furthermore treatment of catheter-associated bacteremia significantly increases expenditures on patient care. Cost analyses carried out on American ICUs have shown that patients suffering from a catheter-related bacteremia stay on average 7 days longer in the ICU than other intensive care treated patients (7). The additional costs for each patient amounts to at least US\$ 34,000 (5). Critical care efforts should constantly focus on the avoidance of catheter-associated infections and be aimed at preserving the patients' health and promoting the most rapid recovery.

Definition	Criteria
Catheter colonization	Positive bacteria culture isolated from the catheter tip, subcutaneous segment of the catheter, or catheter hub (for details of culture see Chapter 3)
Local infection at the catheter exit site	Clinical signs of infection around the exit site (e.g. erythema, swelling, purulent discharge, tenderness) in the absence of positive blood culture
Catheter-associated bacteremia	<p>After the catheter has been removed: Clinical manifestations of infection, while at the same time a second source of infection (e.g. wound, urinary tract or respiratory tract infection) has been ruled out, and a positive semiquantitative or quantitative culture with bacteria isolated from a previous intracutaneous catheter segment and simultaneous detection of the same organism in blood cultures that were not withdrawn from the catheter.</p> <p>When the catheter remains in place: Clinical manifestations of infection, while at the same time a second source of infection (e.g. wound, urinary tract or respiratory tract infection) has been ruled out, and a positive quantitative blood culture with an at least fivefold higher germ count detected in samples taken from the catheter compared to blood samples from other puncture sites.</p>

Table 1. Definitions of catheter-associated infection (5)

Risk factors

Numerous clinical studies have tried to establish diagnostic criteria that can be used to identify patients at high risk of catheter-associated infections. To date, no strictly defined parameters have been found that are reliable predictors for the occurrence of catheter-associated infections. A number of various risk factors have nevertheless been determined that increase the risk for contracting a catheter-associated infection in individual patients (see Table 2). Obviously, there are several risk factors that cannot be influenced by

the way critical care is administered, such as patient-specific factors like age, concomitant diseases and the nature and severity of the primary disease. However, therapeutic factors like the use of invasive devices, the necessity for admission to the ICU and frequent invasive interventions can be influenced, albeit within limits. Sound knowledge of the pathogenic routes of catheter-associated infections is a prerequisite for implementing adequate measures of infection prevention.

Risk factor	Infection risk	
	HIGH	LOW
Age	older than 65 years, Neonate, infant	2 - 65 years
Concomitant diseases	more than 3	none or up to 3
Primary disease	Burn, Trauma, Cancer, Leukopenia	General surgery, Neurosurgery
Anesthesiological Scoring	APACHE II > 20	APACHE II < 20
Type of ward	Intensive Care Unit	other wards
Devise usage (drain, catheter, ventilation)	high usage rate	low usage rate
Catheter indwelling time	more than 5 days	less than 5 days
Nurse-to-patient ratio	1:2 or less	1:1
Prevalence of pathogens	high incidence	low incidence
Bacterial resistance	multiple-resistant bacteria	Bacteria with no or single resistance

Table 2: Risk factors for catheter-associated infection (1)

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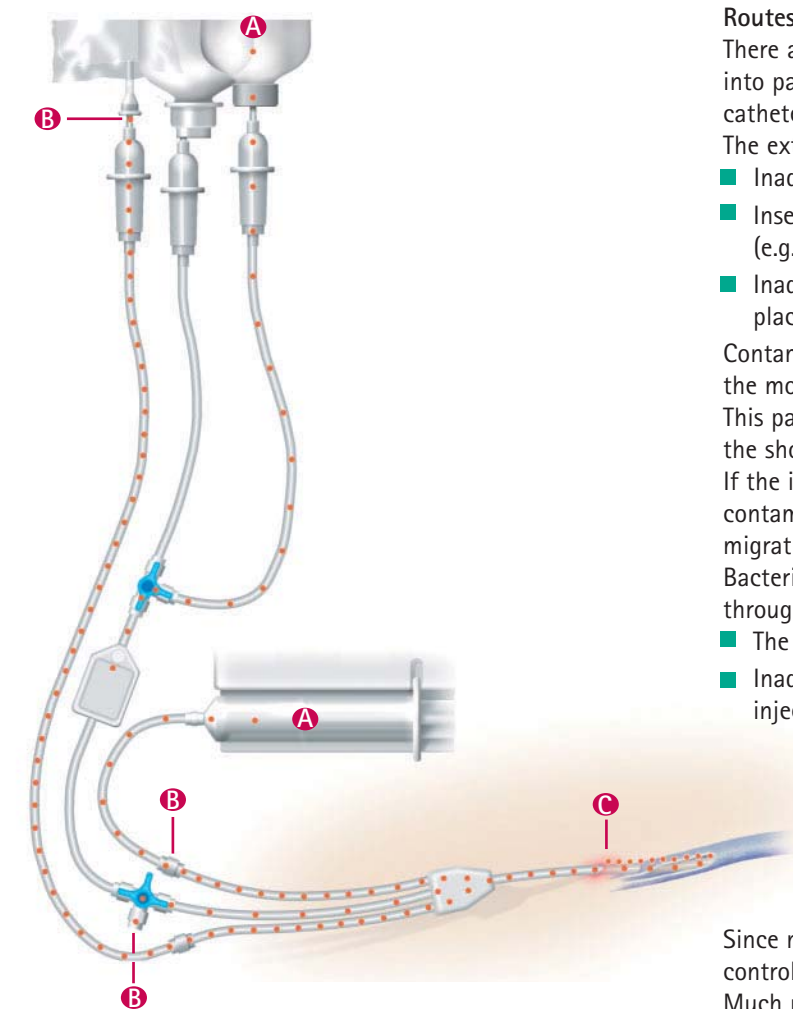
Pathogenesis of catheter-associated infections

Pathogenic bacteria principally use two routes for invading the bloodstream, either migration along the external catheter surface or through the lumen. The former happens as a result of inadequate asepsis during catheter placement, the latter in bedridden patients receiving long-term care. If the patient's immune system is not capable of eliminating bacteria or fungi, the invading germs settle and adhere to the catheter surface, thereby becoming a threatening source of infection. Both constant surveillance and scrupulous monitoring of intensive care patients are imperative to break the chain of contamination – colonization – bacteremia.



Bacteria are widely present in the human environment. While healthy persons can defend themselves against attacks from bacteria, fungi and viruses, hospitalized patients are frequently unable to do so. The immune system of a patient who has just undergone surgery or sustained some other kind of trauma is usually compromised to such an extent that any added threat posed by bacterial contamination cannot be fought off adequately. What otherwise might be considered "harmless" ambi-

ent germs like the *Staphylococcus aureus* or *Staphylococcus epidermidis* bacteria commonly found on the skin can no longer be eliminated once they enter the blood stream and start multiplying rapidly. Plastic devices like central venous catheters that remain in the blood stream for several days provide a surface for invading bacteria to adhere to and grow on. In this way, central venous catheters often contribute to settlement and rapid spread of bacteria in the blood stream (1).



- A** Contaminated infusion solutions
- B** Contaminated hubs, stopcocks and infusion ports
- C** Bacteria on skin and on external surface of catheter

Figure 3: Main sources for bacteria contaminating central venous catheters

Routes of contamination

There are principally two routes by which bacteria can enter into patients through catheters (see Fig. 3): from the external catheter surface (C) or through the catheter lumen (A, B).

The external surface of the catheter gets contaminated by:

- Inadequate skin disinfection at the puncture site
- Inserting the catheter in violation of the rules of hygiene (e.g. hand disinfection)
- Inadvertent contact with a non-sterile environment during placement

Contamination of the external catheter surface is regarded as the most common reason for catheter-related infections (2). This particularly applies when the catheter is only used over the short term.

If the infection develops at a later point in time, not only contamination on the external surface, but also bacterial migration through the catheter lumen play a significant role. Bacteria migrate from the infusion system into the catheter through

- The use of contaminated infusion or drug solutions (A)
- Inadequate hygiene when performing manipulations to the injection ports and/or connections (B)

Since manufacturers are required to comply with strict quality controls, the importance of contaminated solutions is negligible. Much more frequently, connection sites like catheter hubs show a high number of bacteria which could migrate into the catheter lumen and cause an infection. In a clinical study on oncological patients receiving parenteral nutrition, the catheter hub was identified as the source of bacteria in 70% of infected patients (3).

The knowledge that has been gained over the past years about the different routes and sources of infection has been compiled into conclusive recommendations (see Chapter 4). These recommendations all center around the observance of hygienic rules during all phases of the central venous catheter use.

Pathogenesis of catheter-associated infections

Model of catheter colonization

The microbiological colonization of the catheter goes through three stages that ultimately lead to the bacteria becoming irreversibly anchored on the catheter surface (see Fig. 4). In the first stage of **adhesion**, the bacteria (Symbol B) make contact with the catheter surface by means of weak interactive forces (broken arrows). During this phase, the bonds that hold them to the plastic surface are still weak and can be readily broken. In the subsequent phase of **attachment**, bacteria start to increase the number and strength of their bonds to the catheter surface (double arrow). The chemical composition of the plastic material (hydrophobic like Teflon or hydrophilic like polyurethane) and the surface properties (rough or smooth) facilitate or inhibit the formation of stronger bonds (4). Once the microbe has managed to adhere itself to the surface, it is very difficult for the fluids

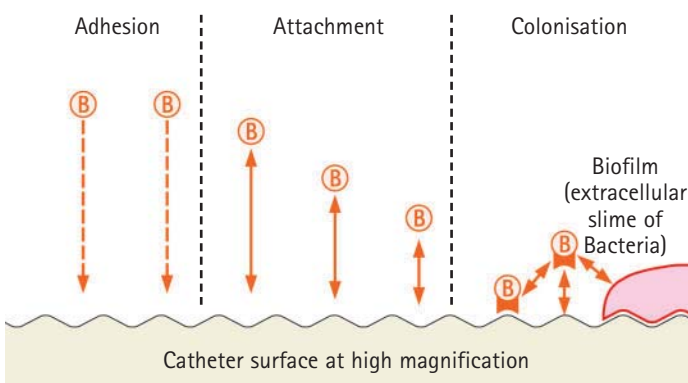


Figure 4: 3-phase model of catheter colonisation by bacteria

flowing past to dissolve this bond. The administration of antibiotic drugs for eradication of bacteria attached to the catheter is the treatment of choice in this phase. Unfortunately, in most cases, the patient shows no clinical sign of infection which means that antibiotic treatment is usually not initiated at this point.

In the final stage of **colonization**, the bacteria start to produce and release special molecules from their surfaces that strengthen their adherence to the catheter surface, but also the adherence of the bacteria to each other. The cohesiveness of the bacteria to each other and to the surface becomes so strong that the fluid flowing past can no longer dissolve the bacterial aggregation. Bacteria and liberated surface molecules form a so called biofilm which is almost impossible for the antibiotics to penetrate. For example, vancomycin must be administered at a 10-times higher dose to kill a biofilm of *Staphylococcus aureus* than when individual colonies are involved (4). Consequently it is virtually impossible to clean catheters with antibiotics once their lumen is coated with a biofilm. Clinical signs of local infection can be, but are not always, noticeable during this phase.

Diagnostics

As explained in Chapter 2, catheter-associated infections can occur in three different forms: local infection, catheter colonization or bacteremia. While it may be relatively easy to diagnose a local infection or bacteremia, catheter colonization can only be established retrospectively after the catheter is removed. The catheter segment that was implanted in the patient's body is rolled out on an agar plate to obtain a sample of all attached bacteria. After incubation of the agar plate the colony forming units (cfu) which represent the colonies of bacteria or fungi are counted.

Maki, who developed the so called roll-plate method in 1977, was able to show that catheter colonization correlated with a clinically relevant local infection or bacteremia (2). In 80% of the cases, catheters from infected patients exhibited more than 15 cfu on the catheter surface. Since that time, a limit of at least 15 cfu on the catheter surface counts as proof of catheter colonization when the roll-plate method is used. The underlying infection is judged to be a catheter-associated infection when no other source of infection is present.

Germs which are widely present in the hospital can be retrieved from catheters of patients suffering from catheter-associated infection. However, the spectrum isolated tends to vary depending on patient population, medical therapy and country. In general, it can be stated that since the 1990s, gram-positive strains are predominant in catheter-associated infections (5).



The bacterial strains listed in the following, which were isolated in a US hospital can certainly be considered representative for other hospitals (cf. Germany, 6).

Gram-positive strains dominate the pathogenic spectrum with a frequency of 54%. These gram-positive strains are subdivided into coagulase-negative Staphylococci, which are involved in 30% of the cases of catheter-associated infections, *Staphylococcus aureus* occurring with a frequency of 13% and Enterococci and Streptococci, which occur with a 7% frequency. Gram-negative bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumonia* contribute to 29% of the outbreaks of infection. Fungi such as *Candida albicans* are found in 7% of the cases. Other bacterial strains are isolated in less than 3% of the infections (5).



Figure 5: *Staphylococcus epidermidis* on sheep blood agar
Small, white to grey colored colonies without hemolytic zone



Figure 6: *Staphylococcus aureus* on sheep blood agar
Bright gold-colored, round colonies with clear hemolytic zone due to β -hemolysine (complete lysis of erythrocytes)



Figure 7: *Enterococcus faecalis* on Enterococcosel agar
Small, black colonies with brown-black zone around each colony, strain representative for faecal bacteria



Pathogenesis of catheter-associated infections



Figure 8: Escherichia coli on MacConkey agar
Pink to faint red colored colonies with a zone of precipitated bile acid
(roll-plate method for semi-quantitative analysis)



Figure 9: Pseudomonas aeruginosa on Cetrimid agar
Faint blue-green colored colonies caused by synthesis of pyocyanin with
emit, fluorescent light (roll-plate method for semi-quantitative analysis)

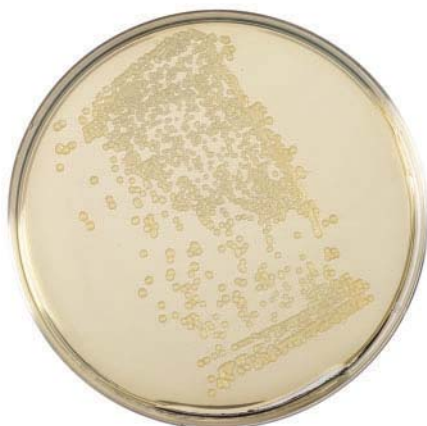


Figure 10: Candida albicans on Sabouraud glucose agar
Bright cream-colored, round colonies with convex surface
(roll-plate method for semi-quantitative analysis)



Catheter management

Bacteria living in the biofilm multiply on the catheter surface and form a reservoir from which bacteria are constantly flooding into the blood stream. A blood sample isolated from a central venous catheter is not appropriate for diagnosing a bacteremia because this blood sample may contain bacteria that were only loosely attached to the catheter surface. Only a blood sample from a peripheral vein will provide conclusive evidence as to whether a source of infection located on the catheter is seeding bacteria into the blood stream. If identical bacterial strains are isolated in blood samples from both the peripheral vein and from the catheter, then this provides conclusive proof of a catheter-associated infection. If no other cause can be identified as the source for the bacterial spread except for the central venous catheter, then it is imperative that the catheter be removed immediately (caution: an alternative vascular access must be available). Figure 11 depicts a decision tree according to Mermel (7) defining the steps to be taken when a patient is determined to have a fever of unknown origin. This flowchart will help health-care workers in their decision-making. Obviously, it is no substitute for hospital-specific instructions or hospital protocols.

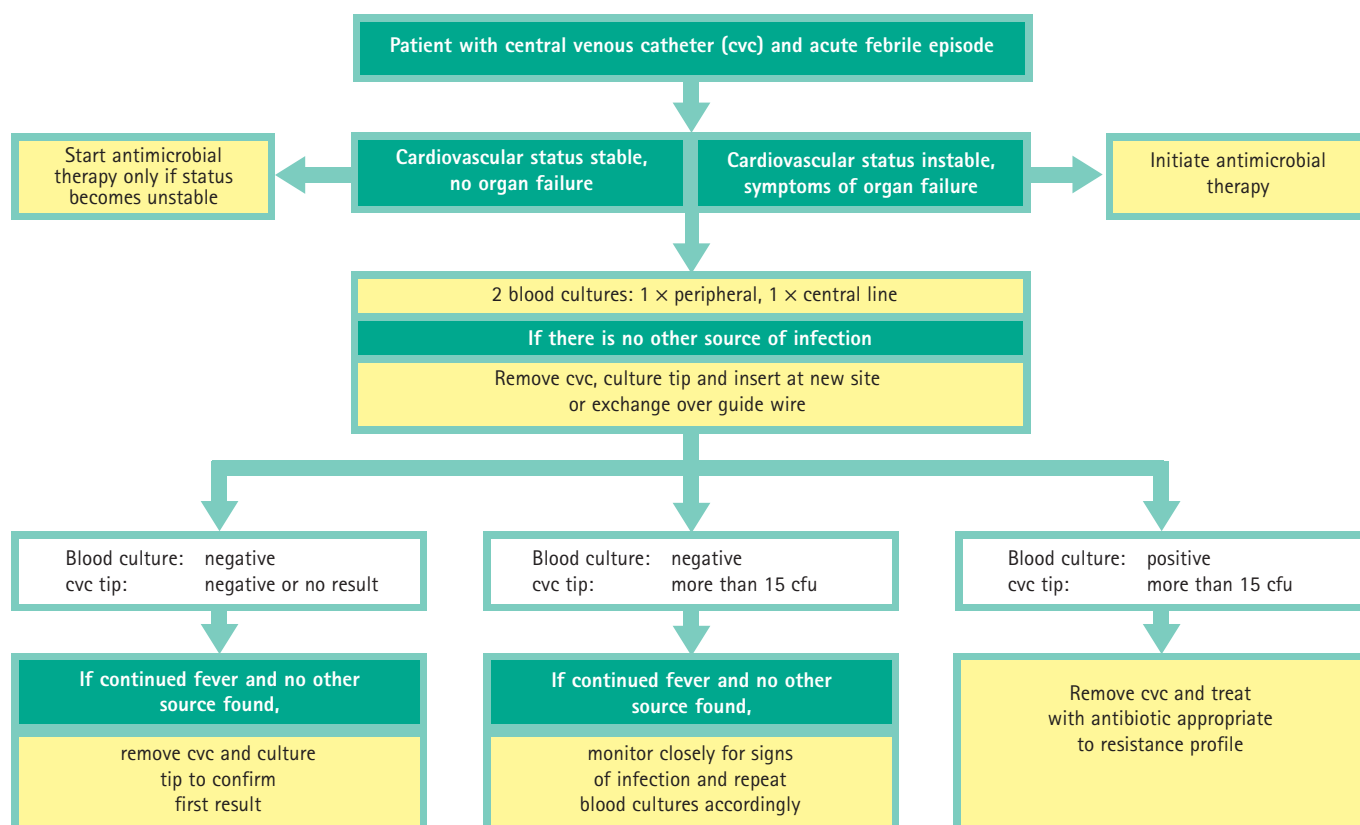
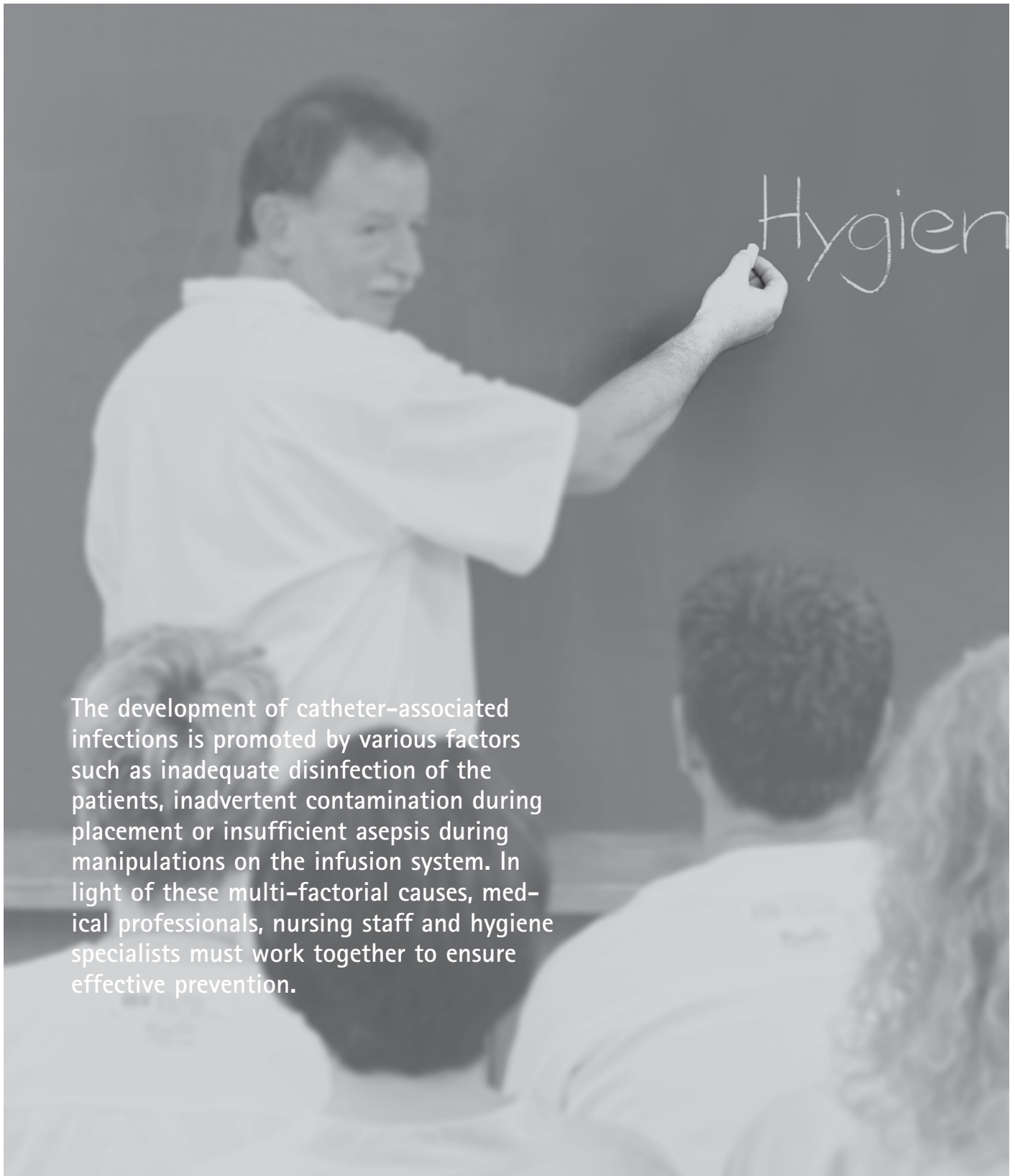


Figure 11: Clinical pathway for patient with central venous catheter and fever of unknown origin

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Prevention strategies



The development of catheter-associated infections is promoted by various factors such as inadequate disinfection of the patients, inadvertent contamination during placement or insufficient asepsis during manipulations on the infusion system. In light of these multi-factorial causes, medical professionals, nursing staff and hygiene specialists must work together to ensure effective prevention.



The importance of scrupulous hand disinfection to prevent the transmission of bacteria was proven by the work of Semmelweis, a Hungarian gynecologist, in the mid 19th century. At the Vienna General Hospital in 1847, Semmelweis started to force medical doctors to clean their hands with a disinfectant before touching any woman who was in labor. This precaution succeeded in lowering the post-delivery maternal mortality rate from over 10% down to 1% (1).

Today, meticulous hand hygiene involving handwashing before and after each patient contact still forms the basis of infection prevention. Astonishingly however, compliance with this seemingly simple basic rule does not appear to be very common in routine clinical settings. Depending on the type of ward, only 16% (general ward) or an average of 40% of the healthcare workers (intensive care unit) comply with these hygiene guidelines (1). This means that each patient is exposed to the risk that every second person administering care or treatment is a potential source for the transmission of foreign bacteria.

Such circumstances easily promote the spread of pathogenic bacteria. It has been proven that if medical departments are able to improve hygiene compliance, the rate of nosocomial infection will drop (1). A broad variety of measures such as training programs, the distribution of flyers, notices and bulletins, equipping critical care facilities with sinks for handwashing that the healthcare worker is required to use before leaving the room, the use of hand disinfectants that are gentle to the skin and many more precautions can enhance healthcare workers compliance with hand hygiene (2). Unfortunately, most studies have clearly shown that such improvements are rather short-lived. When training programs are only offered once, a dramatic decline in handwashing frequency is observed within just a week (2). There are only a few hospitals that have succeeded in reducing the infection rate and keeping it low over a period of several years by means of ongoing training sessions, documentation of infection and providing feedback on the results to the staff (e.g. at the Geneva University Hospital, 1).

Prevention strategies



Alongside the compliance with the rules of personal hygiene, it is also important to keep the surroundings as germ-free as possible while placing the central venous catheter. In this way, the inadvertent contamination of the catheter and the migration of bacteria via the external surface of the catheter can be avoided. The scrupulous skin disinfection of the patient lowers the germ count around the puncture site, thereby lowering the risk of infection. For hygienic reasons, a puncture site on the femoral vein is not advisable (3).

Maximal sterile barrier precautions maintained during insertion additionally offer effective protection against contamination of the external surface of the catheter (4). Maximal sterile barrier precautions include wearing cap, mask, sterile gloves, and a long surgical gown for the doctor inserting the catheter along with the use of large sterile drapes to cover the patient. One hospital in the United States managed to reduce the infection rate from

26% to 0.6% just by implementing these protective clothing precautions alone (4).

Luminal colonization of the catheter is a particular problem in bed-ridden patients, who usually have to be fed parenterally (5). Manipulations of the catheter or the infusion system can allow bacteria from the ambient environment (particularly from the staff) to colonize the hubs of the catheter or injection ports. From this point, the bacteria can start colonizing the catheter lumen. Prof. Sitges-Serra of Barcelona is a proponent of the hypothesis that the "hub" is the starting point for catheter-associated infections (6). He advocates the use of a catheter connector containing iodized alcohol that automatically disinfects the connector during connection. Clinical studies showed that this device produced a reduction in the catheter-associated infection rate (7). However, these positive findings have not been confirmed by any other research group so far.



Instead, the generally recognized hygiene recommendations state that the connection device between catheter and infusion line must be disinfected every time before they are connected and the access site of containers must be disinfected before solutions are withdrawn. This will inhibit the inadvertent transmission of bacteria via the lumen of the infusion systems or of the catheter. Compliance with strict aseptic technique when performing manipulations on the infusion system and the catheter not only prevents contamination of lines, but also of the infused solutions. To prevent spoiling of infusion solutions it is additionally recommended to limit the infusion flow times and to change the infusion lines connected to the catheter at regular intervals. This limits the danger of spreading bacteria by contaminated infusion lines or solutions. Expert panels recommend a dwelling time of less than 12h for blood, blood products and lipid-containing solutions, whereas the respective tubing systems can be used for up to 24h. If solutions that do not contain any

amino acids or glucose are infused, the tubing systems can even be used for as long as 72 hours before they must be changed for hygienic reasons (8).

A comprehensive summary of the recommendations published by a panel of American experts in 2002 (8) is presented on the following pages (Tab. 3). The table provides some excerpts from their recommendations. If hospital-specific prevention strategies are to be prepared, the entire publication should be drawn upon. The expert panel has found published clinical studies that support the implementation of preventive measures by very strong or strong arguments respectively. These evidence-based recommendations attest to the great urgency for implementation, and are categorized as Category 1A or 1B respectively. If conclusive clinical data were lacking or a preventive recommendation was based on a consensus of the involved parties, then a recommendation is considered to carry less weight and is therefore categorized as a Category 2 recommendation.

Prevention strategies

Sector	Preventive measure	Importance*
Hand hygiene	Perform hand hygiene before and after inserting, replacing, accessing, repairing, or dressing a catheter	1A
Insertion of the CVC	Maximal sterile barrier precautions: Surgeon: cap, mask, sterile gown, sterile gloves Patient: large sterile fenestrated drape	1A
Selection of catheter insertion site	Hygienically preferred site: subclavian vein Weigh the risk and benefits of placing a device at a recommended site to reduce infectious complications against the risk of mechanical complications (e.g., pneumothorax, air embolism etc.)	1A
Disinfection of insertion site	A 2% chlorhexidine-based preparation is preferred, alternatively tincture of iodine, an iodophor or 70% alcohol can be used. Do not apply solvents (e.g., acetone and ether) to clean the skin	1A
Insertion site care	Monitor catheter sites visually or by palpation through the intact dressing on a regular basis Replace dressings: every 2 days for gauze dressings and at least every 7 days for transparent dressings Replace dressing immediately if the dressing becomes damp, loosened, or visibly soiled Maintain aseptic technique when changing dressing Do not use antibiotic ointment or creams when changing dressing Do not apply acetone and ether when changing dressing When health-care workers are specially trained in catheter care, the risk of infection is lower	1B 1B 1A 1A 1A 1A 1A
Health-care worker education and training	Educate health-care workers regarding the indications for use, insertion and care of catheters Assess knowledge periodically	1A
Catheter		
Catheter care	Clean injection ports with 70% alcohol or an iodophor before accessing the system The routine use of antibiotic lock solutions in unused lumens is not recommended	1A 2
Replacing the CVC	Routine replacement at given intervals is not recommended Routine replacement over guidewire is not recommended Only exchange over guidewire if no infection is evident	1B 1B 1B
Antimicrobial/Antiseptic impregnated catheters	Use in the case of high infection rates after exhausting all conventional hygiene precautions	1B
Needle-free connectors	Disinfect before connecting; only connect sterile products (syringes, lines) Replace at least as frequently as the administration set	1B 2
Single- versus multiple-lumen catheter	Select catheter type so that the number of lumens is appropriate for patient's treatment	1B
Drug delivery/infusion therapy	When a multiple-lumen catheter is used, parenteral nutrition is administered through one lumen only	2

*) Category 1A: Strongly recommended for implementation and strongly supported by well-designed experimental or clinical data
Category 1B: Strongly recommended for implementation and supported by some experimental or clinical data
Category 2: Suggested for implementation and supported by a theoretical rationale or suggestive clinical data

Table 3: Excerpt from the recommendations for the prevention of catheter-associated infections (8)

Sector	Preventive measure	Importance*	
Infusion system			
Disinfection of multidose parenteral medication vials	Cleanse the access diaphragm of multidose vials with 70% alcohol before inserting a device for withdrawal of contents	1A	
	Use a sterile device to access a multidose vial (needles or syringes) for withdrawal of contents	1A	
Admixed infusions	Admix all infusions in the pharmacy in a laminar-flow hood using aseptic technique	1B	
Time for completion of infusion of solutions	Colloidal solutions:	no recommendation to max. time	
	Total parenteral nutrition solution:	max. 24 h	1B
	Lipid solution:	12 h (in exceptional cases up to 24 h)	1B
	Blood products:	max. 4 h	2
Change infusion/transfusion lines after hanging	Colloidal solutions:	within 72 h	1A
	Total parenteral nutrition solution:	within 24 h at the latest	1B
	Lipid solutions:	within 24 h at the latest	1B
	Blood:	within 24 h at the latest	1B

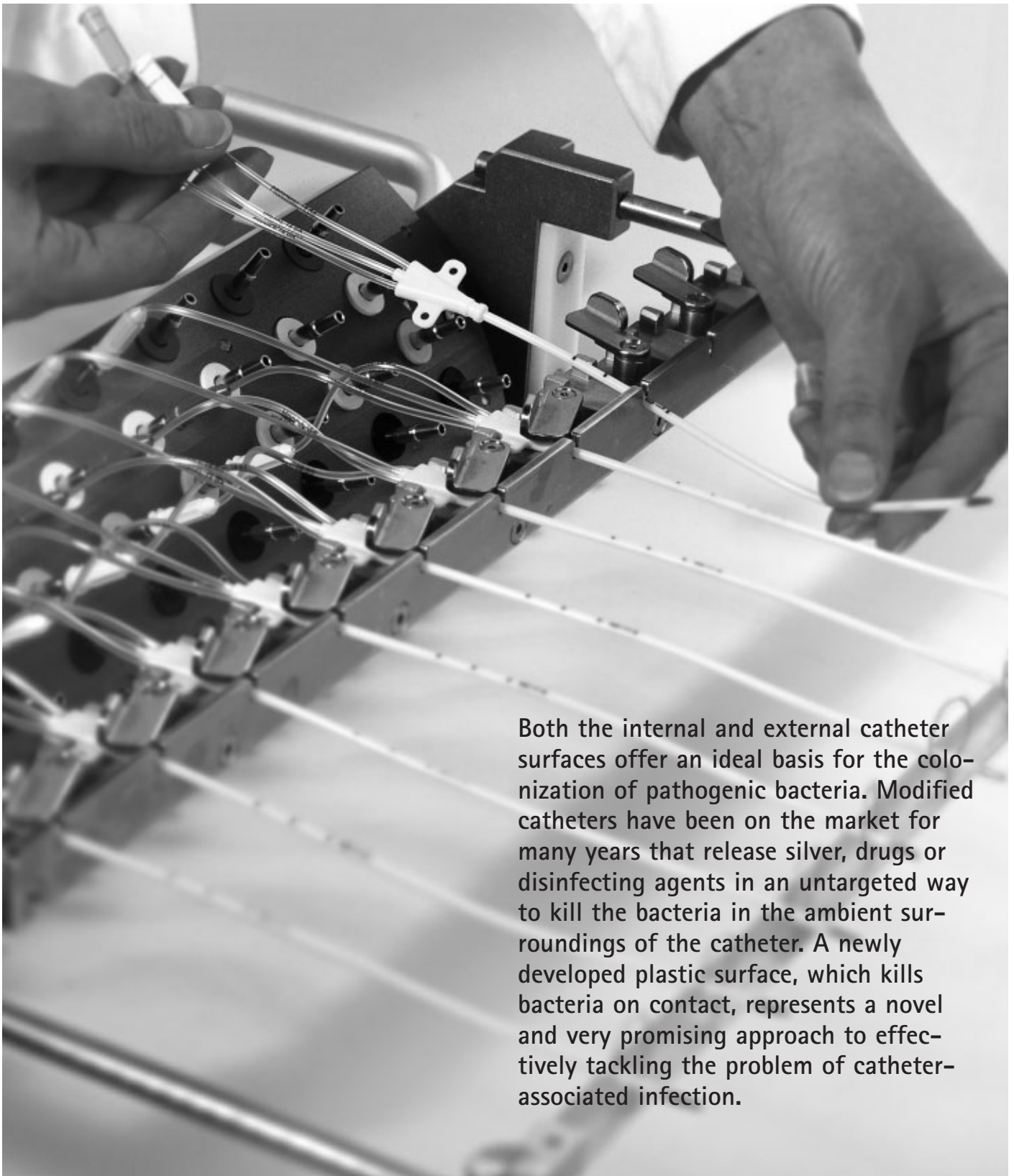
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Table 3: Excerpt from the recommendations for the prevention of catheter-associated infections (8)

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Surface-modified catheters



Both the internal and external catheter surfaces offer an ideal basis for the colonization of pathogenic bacteria. Modified catheters have been on the market for many years that release silver, drugs or disinfecting agents in an untargeted way to kill the bacteria in the ambient surroundings of the catheter. A newly developed plastic surface, which kills bacteria on contact, represents a novel and very promising approach to effectively tackling the problem of catheter-associated infection.

Protection against extraluminal colonization

Researchers have been trying for some 20 years to interrupt the first step in the pathogenesis of infection, namely bacterial colonization on the plastic surface, by means of chemical impregnation of the surface (1). These technical improvements are designed to protect the external surface of the catheter. The aim is to prevent bacteria from adhering and settling on the external surface of the catheter during placement or at a later time. It has not become known until recently that the luminal route of colonization is an equally major source of infection, particularly in patients receiving complex infusion therapies (see page 15, Fig. 3). Current evidence suggests that protection of the external surface of the catheter alone is both inadequate and ineffective.

Preventing migration on external surface

Dressings containing the antiseptically active compounds chlorhexidine or cuffs on tunneled catheters containing silver compounds have been developed to prevent bacteria on the skin from migrating along the external surface of the catheter and entering the blood stream. Both types of devices can at best only block the infection pathway at the skin and the external surface of the catheter. Clinical studies have not been able to demonstrate any significant impact on infection rates by this method (2, 3). Catheters which only possess a coating on the external surface, antiseptic impregnated dressings, or silver cuffs must be classified as unsuitable to reduce infection rates.

Protection through surface modification

A variety of active compounds such as silver, antibiotics or disinfectants have previously been incorporated in the catheter surface to achieve antibacterial protection (4). To date, there has been no clinical testing of catheters whose surfaces release electric current designed to inhibit the adherence of bacteria (5).

The products currently on the market can be classified into 4 groups according to their active principles (cf. figures on pages 28 - 30):

Release of disinfectants like chlorhexidine:	Arrowg ⁺ ard Blue [®]	Arrow
Release of silver from the catheter material: e.g.	Vantex Multicath Expert [™]	Edwards Lifesciences Vygon
Release of antibiotics like the combination of rifampicin and minocycline:	Spectrum [®]	Cook
Contact killing surface without release of drugs	Certofix [®] protect	B. Braun

Surface-modified catheters

Chlorhexidine-releasing catheter

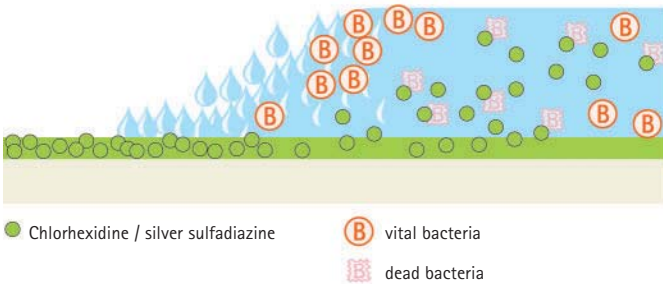


Fig. 12: Release of chemicals from the uppermost catheter coating upon contact with fluid and time-dependent leaching of the coating ingredients

Chlorhexidine catheters contain a mixture of chlorhexidine and silver sulfadiazine in the coating on the external catheter surface. Both agents exert a bactericidal effect. Fluids flowing past the external surface of the catheter (e.g. blood) activate the release of active compounds from the surface. Both chemicals

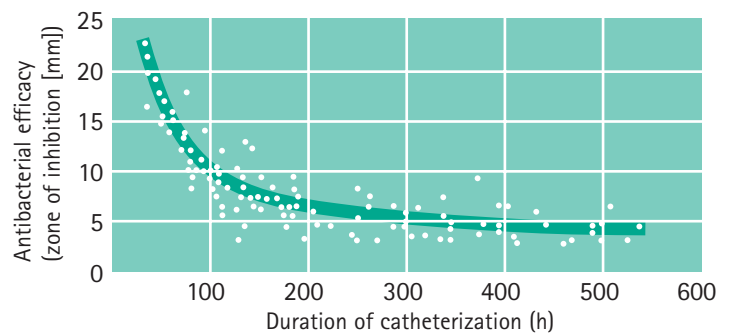


Fig. 13: Loss of efficacy of the chlorhexidine catheter (adapted from 6)

Silver-impregnated catheter

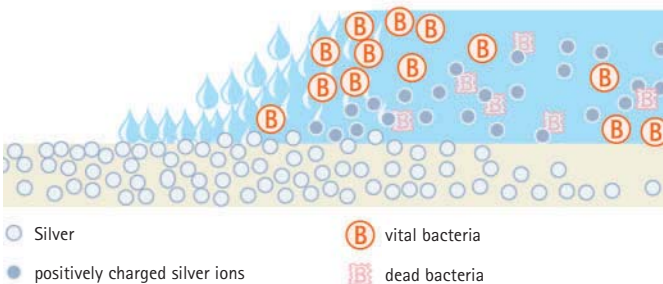


Fig. 14: The silver impregnated in the material is released into the environment and the silver is simultaneously converted into silver ions; time-dependent leaching of the uppermost catheter surface

The two silver-releasing catheters currently on the market differ in terms of how the silver is impregnated in the plastic matrix. The principle of action, however, is the same for both (see Fig. 14). When the catheter comes into contact with fluids (regardless of whether this happens with the internal or external surface) bound silver is released from the plastic and is converted into positively charged silver ions that can kill the bacteria.

This bactericidal effect however starts to dissipate markedly when the catheter is placed in the vein and flushed with infusion solutions. Then, positively charged silver ions will frequently bind with negatively charged counter ions from the infusion solution such as chloride or sulfate. The silver chloride or silver sulfate complexes, however, are not active for germs any more.

Antibiotics-releasing catheter

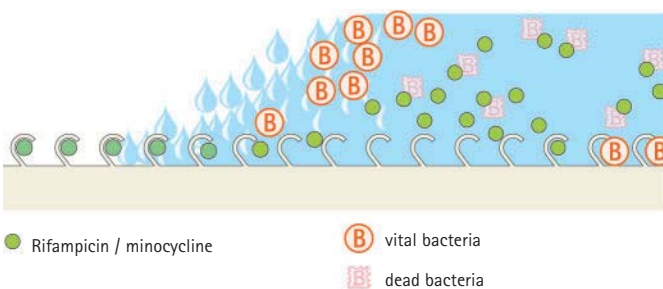


Fig. 15: Release of antibiotics from binding sites on the catheter surface after contact with fluids and time-dependent leaching of the antibiotics

Two different antibiotics, namely rifampicin and minocycline, are released from the surface of the antibiotic-impregnated catheters as soon as the appropriate counter ions are present in the blood stream or in the catheter lumen. Here, like with the chlorhexidine catheter, the antibiotics released into the blood stream are rapidly diluted or flushed out by the infusion solution.

This antibiotic combination was selected due to laboratory tests because its spectrum covers pathogens most commonly found in catheter infections. It should be noted, however, that rifampicin is used in many countries as a reserve antibiotic for tuberculosis since other drugs have become ineffective due to

are effective in killing bacteria in the catheter environment but get rapidly diluted through the blood stream and transported off into the vascular system.

A clinical study on chlorhexidine catheters has shown (6) that the amount of active compounds released drops dramatically once the catheter has been in the patient's body for more than 4 days (cf. Fig. 14). The high blood flow rate in vessels near the heart (with up to 6 l blood flow per minute) causes rapid flooding of active compounds located on the catheter surface.

Chlorhexidine catheters are therefore only effective in patients for a limited time.

As numerous studies have shown the chemical concentration on the catheter surface appears to be sufficient to prevent colonization of the catheter for a dwelling time of 3–4 days (7). However, these studies could not demonstrate any reduction of infection rate. In 14 out of 15 published studies, the infection

rate remained unchanged when a chlorhexidine catheter was used. Only one clinical study in which the catheter dwelling time was short found a significant reduction in the infection rate (8). In all studies in which the antimicrobial catheter was in place for more than 5 days, for example in the publication by Logghe (9), control catheters and chlorhexidine catheters showed similar infection rates. The high number of negative clinical studies and the active compound release that is limited to a maximum of 4 days raise serious doubts about the efficacy of chlorhexidine catheters.

Over the past 5 years, the use of chlorhexidine catheters has often been associated with strong hypersensitivity reactions or even anaphylactic shock (10). The active ingredient chlorhexidine, which is known to have repeatedly caused anaphylactic reactions as a skin disinfectant (11), appears to be responsible for this undesirable side effect.

Laboratory tests have demonstrated that the bactericidal efficacy of a solution containing positively charged silver ions is reduced by a factor of 100 when negatively charged albumin and saline are added (12). The majority of the silver ions released from the catheter are therefore not available to kill the bacteria.

For centuries, medicine has used silver and silver-containing formulations to kill bacteria. Because it is known that the efficacy of silver is greatly diminished by counter ions, it is mostly used in concentrated form. When applied topically, for example in the form of silver-containing ointments to treat burns, the amount of silver must be large in order to achieve a bactericidal effect. For technical reasons, a silver-impregnated catheter can only contain traces of silver. Therefore, the volume of silver released

into the bloodstream is infinitesimally small compared to the quantities that are applied topically.

The low amount of silver ions released from the catheter and the fact that free silver ions bond rapidly to counter ions in the bloodstream both prevent effective levels of active silver from being reached. Hence, positive clinical proof of efficacy is lacking for the silver-impregnated products currently on the market (13).

resistant pathogens (14). The use of a rifampicin-releasing catheter essentially increases the risk that resistant bacteria on the patient will be cultivated and can spread rapidly in the hospital environment (7). Laboratory tests as well as one prospective study demonstrated bacteria that showed a resistance to rifampicin soon after the use of the rifampicin/minocycline impregnated catheter (15, 16).

To date, four clinical studies with antibiotics-coated catheters have been published which paint an inconsistent picture, similar to the chlorhexidine catheter (7, 16). In two publications authored by the inventors of the antibiotic catheter Raad and Darouiche, there was a significant decline in both the coloniza-

tion and infection rate. It was remarkable that in a direct comparison between chlorhexidine and antibiotics catheter, the latter proved to be more effective with a lower infection and colonization rate than the former (17). By contrast, a prospective study by Wright et al., found no difference in the colonization rate and no effect on the infection rate after introducing the use of antibiotic-coated catheters into an intensive care unit. Three times as many *Candida* strains and four times as many rifampicin-resistant strains were detected on the catheter surface after the use of the modified catheter (16).

Surface-modified catheters

Catheter with contact killing surface

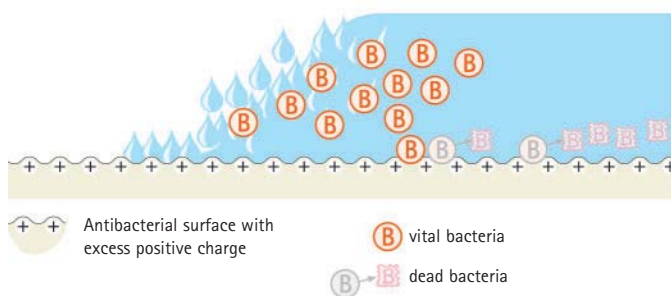


Fig. 16: Excess positive charge of the catheter surface destabilize the bacterial cellwall and prevent bacterial colonization.

Unlike other surface-modified catheters, this novel catheter releases no active compounds into the ambient environment. The bactericidal effect of the catheter surface does not unfold until pathogenic bacteria try to adhere to the surface. Positively charged chemical structures on the internal and external catheter surfaces cleave the bacteria cell wall by shifting the ionic charge. The bacteria lose their adherence capabilities and are ultimately killed. The new catheter surface acts by contact killing without release of potentially toxic chemicals. Thereby, the potential for adverse side effects such as hypersensitivity or the development of resistant bacteria is reduced dramatically.

Previously conducted laboratory tests have proven the long-term efficacy of the antibacterial surface (18). The antimicrobial efficacy of the modified catheter from B. Braun remains consistently effective over 14 days compared to that obtained with an uncoated control catheter (see Fig. 17). The chemical structures on the catheter surface were effective against gram-positive as well as gram-negative bacteria and specifically offered protection against MRSA (18).

This newly developed catheter can be considered the first representative of a new generation of catheters with antibacterial efficacy. The new catheter type is associated with significantly lower risk during use since there is no release of active compounds. The protection it offers has no impact whatsoever on the medical therapy and remains effective over long periods of time.

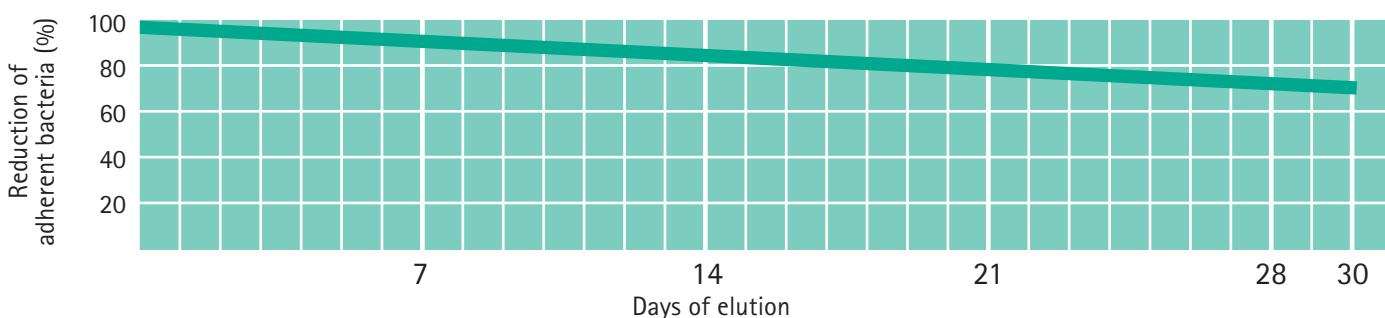


Fig. 17: Efficacy of the antibacterial surface maintained after over a 30 days period

The invention of antimicrobial catheters stems from the desire of physicians to minimize as much as possible the adverse effects associated with the increasingly technological degree of medical science. The advantages gained by the use of an invasive product that enables quick and targeted infusion therapy come at a cost, because the skin, the natural frontline barrier between the body's interior and the outside environment, between the circulatory system and exogenous germs, has to be penetrated. The associated danger of bacterial colonization can be effectively eliminated by intelligent modification of the catheter surface with a bacteria-repellent coating – exactly what B. Braun accomplished with their antimicrobial catheter Certofix® protect.

100% efficacy and the fullest benefit can be derived from an antimicrobial catheter when it is used in conjunction with the hygiene recommendations outlined and discussed in Chapter 4. The disinfection of the patient and medical staff plays a particularly important role, as a recently published study conducted at a university hospital has confirmed (19). The authors tested puncture needle, dilatator and guidewire for microbes and compared the microbiological findings with those found on the catheter tip right after the catheter was removed. In five out of seven catheters that had to be removed due to a catheter-associated infection, the bacterial strains identified were the same as on the catheter tip and the puncture instruments. This suggests that the bacteria that were later localized on the catheter surface and caused the clinical symptoms of infection had already been introduced at the time of puncture. Observance of the hygiene recommendations and the use of an antimicrobial catheter can effectively break the chain of bacterial migration. The antibacterial surface of Certofix® protect acts like a second defensive barrier that shields the catheter surface from any germs that may have penetrated the frontline. The combination of both measures, hygiene and antibacterial catheters, affords maximum protection. Obviously, nobody wants a patient undergoing a routine surgical intervention to end up in the intensive care unit with a bacteremia or even sepsis.

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Glossary

bacteremia	occurrence of vital bacteria in the bloodstream
bactericidal	killing of bacteria
bacteriostatic	inhibition of proliferation of bacteria
catheter-associated infection	(CAI) clinical symptoms of fever, chill, and/or hypotension and identification of bacteria on the catheter and from blood culture and no other apparent source of infection; synonyms: catheter-associated bacteremia, catheter-related bloodstream infection
catheter-associated bacteremia	(CAB) synonym: catheter-associated infection
catheter colonization	growth of organisms from a catheter segment by either semiquantitative (more than 15 colony forming units) or quantitative culture (more than 1000 colony forming units)
catheter-related bloodstream infection	(CRBI) synonym: catheter-associated infection
community-acquired infection	infection which has been developed in the community and needs hospital admission
exit site infection	signs of infection (erythema, tenderness, induration, or purulence) within 2 cm of the exit site of the catheter
hospital acquired infection	see nosocomial infection
nosocomial infection	infection which isn't present at admission to the hospital but develops during stay; four types: wound infection, urinary tract infection, catheter-associated infection or pneumonia (opposite: community-acquired infection)
pathogenic	Greek: causes illness; for example: bacterial, fungal or viral infection
sepsis	systemic response on confirmed bacterial infection accompanied by at least two of the SIRS criteria
septicaemia	synonym: sepsis
systemic inflammatory response syndrome	(SIRS) systemic inflammation reaction to diverse stimuli like bacterial invasion or major surgical operation characterized by at least two of the following: increased or decreased temperature, increased rhythmia, increased breathing frequency and increased or decreased number of leukocytes

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B. Braun Melsungen AG

Postfach 11 20
D-34209 Melsungen
Tel (05661) 71-0
Fax (05661) 71-27 32

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