Prevention of healthcare-associated infections
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Preface

Healthcare-associated infections (HCAIs) are infections that occur while receiving healthcare. Patients with medical devices (central lines, urinary catheters, ventilators) or who undergo surgical procedures are at risk of acquiring HCAIs. HCAIs remain a major clinical problem in terms of morbidity, mortality, length of hospital stay and overall direct and not-direct costs in all regions of the world. Despite guidelines to direct HCAIs prevention strategies, compliance with infection prevention and control is often poor. We hope this manual will draw attention to the need to change practices.

Massimo Sartelli
What are healthcare-associated infections?
What are healthcare-associated infections?

Each year, hundreds of millions of patients around the world are affected by healthcare-associated infections (HCAIs). Although HCAI is the most frequent adverse event in health care, however its true global burden remains unknown because of the difficulty in gathering reliable data.

HCAI is an infection occurring in a patient during the process of care in a hospital or other health care facility which was not present or incubating at the time of admission. HCAI can affect patients in any type of setting where they receive care and can also appear after discharge.

HCAIs can develop either as a direct result of healthcare intervention or from being in contact with a healthcare setting.

Every day, HCAIs result in prolonged hospital stays, long-term disability, increased resistance of microorganisms to antimicrobials, massive additional costs for health systems, high costs for patients and their family, and unnecessary deaths.

The application of appropriate infection prevention and control strategies by the HCWs can reduce the risk of HCAIs, as most of them are preventable.

The preventable proportion of HCAIs may decrease over time as standards of care improve.

A recent systematic review and meta-analysis of studies published between 2005 and 2016 assessing multifaceted interventions to reduce catheter-associated urinary tract infections (CAUTIs), central-line-associated bloodstream infections (CLABSIs), surgical site infections (SSIs), ventilator-associated pneumonia (VAP), and hospital-acquired pneumonia not associated with mechanical ventilation (HAP) in acute-care or long-term care settings suggested a sustained potential for the significant reduction of HCAI rates in the range of 35%-55% associated with multifaceted interventions irrespective of a country’s income level.

Continued progress in healthcare epidemiology and implementation science research has led to improvements in our understanding of effective strategies for HCAI prevention. Despite these advancements, HCAIs continue to affect many hospitalized patients, leading to substantial morbidity, mortality, and excess healthcare expenditures, and there are persistent gaps between what is recommended and what is practiced.

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Out of every 100 hospitalized patients, seven patients in advanced countries and ten patients in emerging countries acquire an HCAI. Other studies conducted in high-income countries found that 5%–15% of the hospitalized patients acquire HCAIs which can affect from 9% to 37% of those admitted to intensive care units. Multiple research studies report that in Europe hospital-wide prevalence rates of HCAIs range from 4.6% to 9.3%. The WHO reports however that HCAIs usually receive public attention only when there are epidemics.

Because HCAIs are a threat to patient safety, many hospitals and healthcare facilities have made the prevention and reduction of these infections a top priority. These resources and interventions have led to an increased focus in prevention efforts, as well as improvements in clinical practice and medical procedures.

The behaviors of HCWs and their interactions with the health care system can influence the rate of HCAIs.

It is well shown that proper education and training of HCWs can increase compliance with and adoption of best practices (e.g., infection control, hand hygiene, attention to safety culture, and antibiotic stewardship) to prevent HCAIs. Examples of best practices by a health care provider include careful insertion, maintenance, and prompt removal of catheters, as well as the careful use of antibiotics.

Poor infection control is the key driver of HCAIs.

Infection control is acknowledged universally as an essential basis towards patient safety and supports the reduction of HCAIs and their consequences.
Healthcare-associated infections and antimicrobial resistance

There is sometimes a false impression that HCAIs are adequately controlled. However, with antimicrobial resistance increasing [Methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE) and carbapenem-resistant Enterobacteriaceae (CRE)...] such infections are more than ever a public health threat. HCAIs show higher resistance rates to antibiotics than community-acquired infections.
Our goal is not to control infections after they happen but to prevent them before they happen!

The most frequent types of infections include central line-associated bloodstream infections, surgical site infections, catheter-associated urinary tract infections, hospital or ventilator-associated pneumonia and *Clostridioides difficile* infection.
First of all
Clean your hands!
Hand hygiene is a simple and effective solution to reduce both the spread of infection and multi-resistant germs, and to protect patients from HCAIs. Hand antisepsis reduces the transmission of health care-associated pathogens and the incidence of HCAI.

Hand hygiene, is simple, low-cost and effective, however it requires staff accountability and behavioral change.
Transmission of health care-associated pathogens from one patient to another patient via HCWs’ hands

The hands of HCWs are commonly colonized with pathogens like methicillin resistant \textit{S. aureus} (MRSA), vancomycin resistant \textit{Enterococcus} (VRE), MDR-Gram Negative bacteria (GNBs), \textit{Candida} spp. and \textit{Clostridioides difficile}, which can survive for as long as 150 h. Approximately $10^6$ skin epithelial cells containing viable microorganisms are shed daily from the normal skin, which can contaminate the gowns, bed linen, bedside furniture, and other objects in the patient's immediate environment. Hand carriage of resistant pathogens has repeatedly been shown to be associated with HCAIs. The highest rates of hand contamination are reported from critical care areas, which also report most cases of cross-transmission. The hands may become contaminated by merely touching the patient's intact skin or inanimate objects in patients’ rooms or during the “clean” procedures like recording blood pressure. Any healthcare worker, caregiver or person involved in direct or indirect patient care needs to be concerned about hand hygiene and should be able to perform it correctly and at the right time.

Hands should be cleaned by rubbing them with an alcohol-based formulation, as the preferred means for routine hygienic hand antisepsis if hands are not visibly soiled. It is faster, more effective, and better tolerated by your hands than washing with soap and water.

Hands should be washed with soap and water when hands are visibly dirty or visibly soiled with blood or other body fluids or after using the toilet. If exposure to potential spore-forming pathogens is strongly suspected or proven, including outbreaks of \textit{Clostridium difficile}, hand washing with soap and water is the preferred means.

The use of gloves does not replace the need for cleaning hands.
Effective hand hygiene is the single most effective action to reduce health care associated infections. Since Semmelweis’ observation, there have been many studies to confirm the role that HCW hands play in transmission of pathogens in the health care setting. Various organizations, including the CDC and WHO, have published guidelines on appropriate hand hygiene practices for HCWs.

The five moments of hand hygiene outlined by WHO are: Before patient contact; before aseptic task; after bodily fluid exposure; after patient contact; and after contact with patient surroundings.

Clean your hands

Before touching a patient, before clean/aseptic procedures, after body fluid exposure/risk, after touching a patient, and after touching patient surroundings.

Infection prevention and control measures, including hand hygiene, are simple, low-cost and effective, however they require staff accountability and behavioral change.
Hospital hygiene
In a health-care facility, the sources of infection, and of the preceding contamination, may be the personnel, the patients, or the inanimate environment. Two basic principles govern the main measures that should be taken in order to prevent the spread of nosocomial infections in health-care facilities:

- separate the infection source from the rest of the hospital;
- cut off any route of transmission.

The separation of the source has to be interpreted in a broad sense. It includes not only the isolation of infected patients but also all “aseptic techniques”—the measures that are intended to act as a barrier between infected or potentially contaminated tissue and the environment, including other patients and personnel. As the hands of health-care workers are the most frequent vehicle of nosocomial infections, hand hygiene is the primary preventive measure (please, see the previous chapter).

**Isolation of infected patients and standard precautions**

The use of physical barriers and spatial separation in managing patients with an increased likelihood of transmitting infectious agents to other patients or staff members is a key infection control function. The interventions usually include identification of patients and patient care activities at risk for transmission of organisms, geographical separation with isolation or cohorting, use of gloves, gowns and other protective equipment by staff to prevent contamination, and ensuring compliance with these practices by staff, patients, and visitors. Isolation of any degree is expensive, labour-intensive, and usually inconvenient or uncomfortable for both patients and health-care personnel; its implementation should therefore be adapted to the severity of the disease and to the causative agent. Disease-specific precautions should include details of all the measures (private room, wearing of masks or gowns, etc.) to be taken in the case of a specific disease caused by a defined organism.
Cleaning

One of the most basic measures for the maintenance of hygiene, and one that is particularly important in the hospital environment, is cleaning. The principal aim of cleaning is to remove visible dirt. It is essentially a mechanical process: the dirt is dissolved by water, diluted until it is no longer visible, and rinsed off. Soaps and detergents act as solubility promoting agents. The microbiological effect of cleaning is also essentially mechanical: bacteria and other microorganisms are suspended in the cleaning fluid and removed from the surface. The efficacy of the cleaning process depends completely on this mechanical action, since neither soap nor detergents possess any antimicrobial activity. Thorough cleaning will remove more than 90% of microorganisms. However, careless and superficial cleaning is much less effective; it is even possible that it has a negative effect, by dispersing the microorganisms over a greater surface and increasing the chance that they may contaminate other objects. Cleaning has therefore to be carried out in a standardized manner or, better, by automated means that will guarantee an adequate level of cleanliness. Diluting and removing the dirt also removes the breeding-ground or culture medium for bacteria and fungi. Most non-sporulating bacteria and viruses survive only when they are protected by dirt or a film of organic matter; otherwise they dry out and die. Non-sporulating bacteria are unlikely to survive on clean surfaces.

Disinfection

Disinfection describes a process that eliminates many or all pathogenic microorganisms, except bacterial spores, on inanimate objects. Factors that affect the efficacy of both disinfection and sterilization include prior cleaning of the object; organic and inorganic load present; type and level of microbial contamination; concentration of and exposure time to the germicide; physical nature of the object (e.g., crevices, hinges, and lumens); presence of biofilms; temperature and pH of the disinfection process; and in some cases, relative humidity of the sterilization process (e.g., ethylene oxide).

Unlike sterilization, disinfection is not sporicidal. There is no ideal disinfectant and the best compromise should be chosen according to the situation. A disinfectant solution is considered appropriate when the compromise between the antimicrobial activity and the toxicity of the product is satisfactory for the given application.
The principal requirements for a good antiseptic are absence of toxicity and rapid and adequate activity on both the natural flora and, especially, pathogenic bacteria and other microorganisms after a very short exposure time.

**Sterilization**

Sterilization describes a process that destroys or eliminates all forms of microbial life and is carried out in health-care facilities by physical or chemical methods. Sterilization is required with any implement or tool that penetrates intact skin and contacts the vascular (blood) system. Once an item has been sterilized, all microorganisms have been removed. Theoretically, if your sterilizer does its job, nothing survives sterilization. Sterilization is intended to convey an absolute meaning; unfortunately, however, some health professionals and the technical and commercial literature refer to “disinfection” as “sterilization” and items as “partially sterile.”
There are many different germs and infections inside and outside of the healthcare setting. Despite the variety of viruses and bacteria, germs spread from person to person through a common series of events. Therefore, to prevent germs from infecting more people, we must break the chain of infection. No matter the germ, there are six points at which the chain can be broken and a germ can be stopped from infecting another person. The six links include: the infectious agent, reservoir, portal of exit, mode of transmission, portal of entry, and susceptible host.

**Infectious agent** is the pathogen (germ) that causes diseases

**Reservoir** includes places in the environment where the pathogen lives (this includes people, animals and insects, medical equipment, and soil and water)

**Portal of exit** is the way the infectious agent leaves the reservoir (through open wounds, aerosols, and splatter of body fluids including coughing, sneezing, and saliva)

**Mode of transmission** is the way the infectious agent can be passed on (through direct or indirect contact, ingestion, or inhalation)

**Portal of entry** is the way the infectious agent can enter a new host (through broken skin, the respiratory tract, mucous membranes, and catheters and tubes)

**Susceptible host** can be any person (the most vulnerable of whom are receiving healthcare, are immunocompromised, or have invasive medical devices including lines, devices, and airways)

The way to stop germs from spreading is by interrupting this chain at any link. Break the chain by cleaning your hands frequently, following the rules for standard and contact isolation, using personal protective equipment the right way, cleaning and disinfecting the environment, sterilizing medical instruments and equipment, and using antibiotics wisely to prevent antibiotic resistance.
Break the chain of infection

Infectious agent

Susceptible host

Portal of entry

Transmision

Reservoir

Portal of exit
Surgical site infections
Surgical site infections (SSIs)

A surgical site infection (SSI) is an infection that occurs after surgery in the part of the body where the surgery took place. Surgical site infections can sometimes be superficial infections involving the skin only. Other surgical site infections are more serious and can involve tissues under the skin, organs, or implanted material.

The Centers for Disease Control and Prevention (CDC) has defined SSIs to standardize data collection for the National Nosocomial Infections Surveillance (NNIS) program.

SSIs are classified into incisional SSIs, which can be superficial or deep, and organ/space SSIs, which affect the rest of the body other than the body wall layers (see the image below). These classifications are defined as follows:

Superficial incisional SSI - Infection involves only skin and subcutaneous tissue of incision
Deep incisional SSI - Infection involves deep tissues, such as fascial and muscle layers; this also includes infection involving both superficial and deep incision sites and organ/space SSI draining through incision
Organ/space SSI - Infection involves any part of the anatomy in organs and spaces other than the incision, which was opened or manipulated during operation.

SSIs are the most common HCAIs among surgical patients. It is obviously important to improve patient safety by reducing the occurrence of SSIs. Preventing SSIs is a global priority. Bacteria are becoming increasingly resistant to antibiotics, making SSI prevention even more important nowadays.

SSIs are a major clinical problem in terms of morbidity, mortality, length of hospital stay, and overall direct and not-direct costs worldwide. Despite progress in prevention knowledge, SSIs remain one of the most common adverse events in hospitals. SSI prevention is complex and requires the integration of a range of measures before, during, and after surgery.
Both the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) have recently published guidelines for the prevention of SSIs. The 2016 WHO Global guidelines for the prevention of surgical site infection are evidence-based including systematic reviews presenting additional information in support of actions to improve practice.
Surgical care bundles

Numerous clinical interventions with varying levels of supporting evidence have been implemented to reduce SSIs among surgical patients. A recent approach to improving patient outcomes is the use of care bundles. Care bundles were first introduced by the Institute for Healthcare Improvement (IHI) in 2001 to improve clinical outcomes in the critical care population. The concept of a care bundle was developed from evidence documenting that a structured approach to performing 3–5 evidence-based collective interventions could lead to an improved patient outcome. While specific interventions may vary between bundles, it is the bundle approach that ensures consistent implementation of all measures that is claimed to be successful. Surgical care bundles have been developed to reduce SSIs after the success of care bundles in reducing catheter-related bloodstream infections and ventilator-associated pneumonia.
Much progress has been made over recent decades in designing and testing new approaches to infection prevention and control. To achieve substantial and lasting behavioural changes, it is now recognized that these approaches should be grounded in social and implementation science theory. Successful health care improvement projects must be simple enough for frontline staff to understand, sufficiently limited in scope to be accomplished without significant new resources, and relevant enough so as not to require input that participating organizations are fundamentally unable to provide. The most successful improvement projects typically embrace a multimodal approach, which requires a strong understanding of the local context. The WHO five-step approach to Infection prevention and control improvement include:

**Step 1**
Preparation for action: This step ensures that all of the prerequisites that need to be in place for success are addressed, including the necessary resources (human and financial), infrastructures, planning and coordination of activities and the identification of roles and responsibilities (including key opinion leaders and champions). The facility senior managers/leaders play a critical role in this step.

**Step 2**
Baseline assessment: Conducting an exploratory baseline assessment of the current situation, including the identification of existing strengths and weaknesses, is critical for developing a tailor-made action plan that addresses the reality of a health care facility.

**Step 3**
Developing and executing an action plan: The results of the baseline assessment support the development and execution of an action plan based around a multimodal improvement strategy.

**Step 4**
Assessing impact: Conducting a follow-up assessment using the same tools as in step 2 is crucial to determine the effectiveness of the plan. The focus is on impact, acceptability and cost-effectiveness.

**Step 5**
Sustaining the programme over the long term: An important step in the cycle of improvement is to develop an ongoing action plan and review schedule to support the long-term impact and benefits of the IPC programme, thus contributing to its overall impact and sustainability.
A proposal for a bundle for the prevention of surgical site infections

- Have the patients take preoperative bathing/showering
- Prescribe appropriate surgical antibiotic prophylaxis
- Do not remove hair or remove hair immediately before surgery by clippers
- Use a correct surgical hand scrub/preparation
- Use a correct skin antiseptic preparation
Antibiotic prophylaxis

Surgical antibiotic prophylaxis (SAP) is one of the most important component of a perioperative infection prevention strategy. The use of AP contributes considerably to the total amount of antibiotics used in hospitals and may be associated with increases in antibiotic resistance and healthcare costs. Although SAP plays a pivotal role in reducing the rate of surgical site infections, other factors such as attention to basic infection-control strategies may have a strong impact on surgical site infections rates. Perioperative surgical AP should be recommended for operative procedures that have a high rate of postoperative wound infection or when foreign material is implanted. Prophylactic antibiotic agents should be nontoxic and inexpensive and have in vitro activity against the common organisms that cause postoperative wound infection after a specific surgical procedure. Therapeutic concentrations of antibiotics should be present in the tissue throughout the all period that the wound is open.
Principles of appropriate antibiotic prophylaxis

1. Antibiotic agents alone are unable to prevent surgical site infections. Strategies to prevent surgical site infections should always include attention to:
   - IPC strategies including correct and compliant hand hygiene practices
   - Meticulous surgical techniques and minimization of tissue trauma
   - Hospital and operating room environments
   - Instrument sterilization processes
   - Peri-operative optimization of patient risk factors
   - Peri-operative temperature, fluid, and oxygenation management
   - Targeted glycemic control
   - Appropriate management of surgical wounds

2. Antibiotic prophylaxis should be administered for operative procedures that have a high rate of post-operative surgical site infection, or when foreign materials are implanted.

3. Antibiotic agents given as prophylaxis should be effective against the aerobic and anaerobic pathogens most likely to contaminate the surgical site—i.e., gram-positive skin commensals or normal flora colonizing the incised mucosae.

4. Antibiotic prophylaxis should be administered within 120 minutes before the incision. Administration of the first dose of antibiotic agents beginning within 30 to 60 minutes before surgical incision, however, is recommended for most antibiotic agents (e.g., cefazolin), to ensure adequate serum and tissue concentrations during the period of potential contamination. Obese patients ≥120 kg require higher doses of antibiotic agents.

5. A single dose generally is sufficient. Additional antibiotic doses should be administered intra-operatively for procedures >2–4 hours (typically where duration exceeds two half-lives of the antibiotic) or with associated significant blood loss (>1.5 L).
6. There is no evidence to support the use of post-operative antibiotic prophylaxis.

7. Each institution is encouraged to develop guidelines for proper surgical prophylaxis.

Hospital-based programs dedicated to improving antibiotic use, commonly referred to as Antimicrobial Stewardship Programs (ASPs), can both optimize the management of infections and reduce adverse events associated with antibiotic use. Therefore, every hospital worldwide should utilize existing resources to create an effective multi-disciplinary team. The preferred means of improving antibiotic stewardship should involve a comprehensive program that incorporates collaboration between various specialties within a healthcare institution including infectious disease specialists, hospital pharmacists, clinical pharmacologists, administrators, epidemiologists, infection prevention and control specialists, microbiologists, surgeons, anesthesiologists, intensivists, and underutilized but pivotal stewardship team members-the surgical, anesthetic, and intensive care nurses in our hospitals. The ASP policies should be based on both international and national antibiotic guidelines and tailored to local microbiology and resistance patterns. Facility-specific treatment recommendations, based on guidelines and local formulary options promoted by the APS team, can guide clinicians in antibiotic agent selection and duration for the most common indications for antibiotic use. Standardizing a shared protocol of antibiotic prophylaxis should represent the first step of any ASP.
Catheter-associated urinary infections
Catheter-associated urinary infections

Urinary tract infections (UTIs) are the most common HCAIs. Most UTIs are attributable to use of an indwelling urethral catheter. Catheter-associated urinary infections (CAUTIs) have received significantly less attention than other hospital–acquired infections probably because CAUTIs present apparent lower morbidity and mortality compared with the other infections, as well as limited financial impact. However, because they are common, their cumulative impact is large.

Among UTIs acquired in the hospital, approximately 75% are associated with a urinary catheter, which is a tube inserted into the bladder through the urethra to drain urine. Between 15-25% of hospitalized patients receive urinary catheters during their hospital stay. The most important risk factor for developing a CAUTI is prolonged use of the urinary catheter. Therefore, catheters should only be used for appropriate indications and should be removed as soon as they are no longer needed.

Many investigations have shown high frequency of inappropriate and unjustified use of urinary catheters, especially in older, female patients. Inappropriate urinary catheter use in acute care hospitals has been reported to range from 21% to greater than 50%.

The indwelling urethral catheter is an essential tool for many hospitalized patients. It is placed for a number of reasons, including output monitoring of unstable patients, voiding management for patients with urethral obstruction, and perioperative use for selected surgical procedures. However it may carry predictable and unavoidable risk of UTI perturbing host defense mechanisms and providing easier access of uropathogens to the bladder. Fortunately, most CAUTIs are asymptomatic and do not require antimicrobial treatment.

CAUTI may be extraluminal or intraluminal. Extraluminal infection occurs via entry of bacteria into the bladder along the biofilm that forms around the catheter in the urethra.

Intraluminal infection occurs due to urinary stasis because of drainage failure, or due to contamination of the urine collection bag with subsequent ascending infection. Extraluminal is more common than intraluminal infection. Bacteria can establish colonization of a patient’s bladder within three days of their introduction onto the inner or outer surface of urinary catheters.
The introduction of bacteria with urinary catheter use is often associated with catheter-related biofilms. Biofilms are complex structures that include bacteria, host cells, and cellular by-products. Biofilm formation within invasive medical devices is proposed as a primary mechanism in the development of certain diseases, as well as CAUTI.

The biofilm life cycle illustrated in three steps: initial attachment events, the growth of complex biofilms, and detachment events by clumps of bacteria or by a ‘swarming’ phenomenon within the interior of bacterial clusters, resulting in so-called ‘seeding dispersal.’ Biofilm plays a significant role in the pathogenesis CAUTI. The development of biofilms occurs when free-floating (planktonic) cells come into contact with a surface and become irreversibly attached. Typically catheter surfaces are initially colonized with a thin film of bacteria. As the bacteria continue to produce matrix material (extra-cellular polymeric substances) they are able to develop thick, complex structures. This “slimey coating” may be clearly visible upon catheter removal on indwelling Foleys than have been in place for extended periods of time.

Bacteria living in a biofilm can have significantly different properties from free-floating bacteria, as the dense extracellular matrix of biofilm and the outer layer of cells may protect the bacteria from antibiotics and normal host defense mechanisms of the white blood cells, such as phagocytosis.

Microorganisms may contain or produce toxins and other substances that increase their ability to invade a host, produce damage within the host, or survive on or in host tissue. Characteristics of the specific infecting microorganism, particularly related to virulence as well as the ability to adhere to a foreign object, such as a urinary catheter, play a role in the presentation of infection.

The two most important strategies to prevent CAUTI are not to use a urinary catheter and, if a catheter is necessary, to minimize the duration of use. Catheters should be inserted only when there are valid indications and removed as soon as they are no longer indicated.

Systemic antimicrobial prophylaxis should not be routinely used in patients with short-term or long-term catheterization, including patients who undergo surgical procedures, to reduce catheter acquired bacteriuria or CAUTI because of concern about selection of antimicrobial resistance.
A proposal for a bundle for the prevention of catheter-associated urinary tract infections

- Insert the catheter only if it is absolutely necessary for the patient
- Ensure maximal sterile barrier precautions upon insertion
- Use standard precautions, including hand washing, during any manipulation of the catheter
- Maintain an aseptic continuously closed urinary drainage system
- Remove the urinary catheter as soon as it is no longer needed

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Hospital-acquired pneumonia and ventilator-associated pneumonia
Hospital-acquired pneumonia and ventilator-associated pneumonia

Nosocomial pneumonia including hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) are the second most frequent nosocomial infections and the first in terms of morbidity, mortality, and costs. In recent years two different sets of guidelines for the management of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) were published: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) and (2017) Guidelines of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latino americana del Tórax (ALAT). Nosocomial pneumonia are generally classified into hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP).

Hospital-acquired pneumonia (HAP) is defined as pneumonia occurring at least 48 hours after hospital admission, excluding any infection incubating at the time of admission.

Ventilator-associated pneumonia (VAP) is defined as a pneumonia occurring in patients under mechanical ventilation for at least 48 hours. It is a frequent issue in intensive care units, with a great impact on morbidity, mortality and cost of care. Treating VAP is a difficult task, as initial antibiotics have to be appropriate and prompt.
The term healthcare-associated pneumonia (HCAP) was included in the previous guidelines to identify patients coming from community settings at risk for multidrug-resistant (MDR) bacteria. HCAP referred to pneumonia acquired in healthcare facilities including nursing homes, hemodialysis centers and outpatient clinics or acquired in patients with previous hospitalization within the past 90 days. However HCAP was not included in recent guidelines because there is increasing evidence that aetiology in HCAP patients is similar to that of community-acquired pneumonia and that many patients with HCAP are not at high risk for MDR bacteria.

The pathogenesis of nosocomial pneumonia is multifactorial. The concomitant illnesses of hospitalized patients is a risk for nosocomial infections. In hospitalized patients alterations in immune function make patients more susceptible to invasive infections that would not occur in healthy individuals.

Many hospitalized patients are in poor nutritional status, increasing their risk of infection. Severe illness and hemodynamic compromise are associated with increased rates of nosocomial pneumonia. Aspiration of oropharyngeal secretions may play a significant role in the development of nosocomial pneumonia. In hospitalized patients the combination of altered immune function, impaired mucociliary clearance of the respiratory tract and oropharynx colonization by enteric Gram-negative pathogens make aspiration an important contributor to pneumonia. Moreover supine positioning contributes greatly to the aspiration risk. Risk factors are also prolonged hospital length of stay, cigarette smoking, increasing age, uremia, prior antibiotic exposure, alcohol consumption, endotracheal intubation, coma, major surgery, malnutrition, multiple organ-system failure, and neutropenia. Importantly, the use of stress ulcer prophylaxis, such as proton pump inhibitors commonly used in critically ill patients, is associated with risk of nosocomial pneumonia. Finally, foreign bodies, such as endotracheal and nasogastric tubes, may provide a source for further colonization allowing migration of pathogens to the lower respiratory.
VAP is one of the most commonly encountered hospital-acquired infections in intensive care units and is associated with significant morbidity and high costs of care. The pathophysiology, epidemiology, treatment and prevention of VAP have been extensively studied for decades, but a clear prevention strategy has not yet emerged.

Any patient who is mechanically ventilated is at risk for VAP. The rate of contracting VAP has been described as 3 per cent per day during the first week of mechanical ventilation, 2 per cent per day during week 2 and 1 per cent per day in the ensuing weeks. The overall incidence of VAP ranges widely, from 5 to 67 per cent depending on the diagnostic criteria used. Mortality that is directly attributable to VAP is estimated to be as high as 30-50 %.

Multiple additional risk factors have been shown to increase the rates of VAP. These are easily divided into non-modifiable and modifiable categories. Non-modifiable risk factors include male gender, increased age (over 60 yr), history of chronic obstructive pulmonary disease, presence of a tracheostomy or cranial trauma, recent neurologic surgery, acute respiratory distress syndrome, multiorgan system failure, and coma. Potentially modifiable risk factors include supine positioning, gastric overdistension, colonization of ventilator circuits, low pressure in the endotracheal tube cuff and repeated patient transfers.

A multidisciplinary strategy for prevention of VAP is recommended. Those interventions that have been shown to have a clinical impact include the following: (i) Respect of infection prevention and control practices, (ii) Non-invasive positive pressure ventilation for able patients, especially in immunocompromised patients, with acute exacerbation of chronic obstructive pulmonary disease or pulmonary oedema, (iii) Sedation and weaning protocols for those patients who do require mechanical ventilation, (iii) Mechanical ventilation protocols including head of bed elevation above 30 degrees and oral care, and (iv) Removal of subglottic secretions. Other interventions, such as selective digestive tract decontamination, selective oropharyngeal decontamination and coating endotracheal tubes, have been tested in different studies.
A proposal for a bundle for the prevention of hospital-acquired pneumonia

- Clean hands and respect infection prevention and control principles
- Perform oral care for the patients
- Prevent aspiration
- Change bed position
- Mobilize early the patient
A proposal for a bundle for the prevention of ventilator-associated pneumonia

- Clean hands and respect infection control and prevention principles
- Perform oral care and aspire subglottic secretions
- Control and maintain cuff pressure
- Avoid elective changes of ventilator circuits and endotracheal tubes
- Reduce the duration of mechanical ventilation when it is possible
Central venous catheter-related bloodstream infections
Central-venous catheter-related bloodstream infections

About half of nosocomial bloodstream infections occur in intensive care units, and the majority of them are associated with intravascular device. Central venous catheter-related bloodstream infections (CRBSIs) are an important cause of healthcare-associated infections. Central venous catheters (CVCs) are integral to the modern clinical practices and are inserted in critically-ill patients for the administration of fluids, blood products, medication, nutritional solutions, and for hemodynamic monitoring. They are the main source of complications in hospitalized patients and therefore should be used only if they are really necessary.

The catheter insertion site affects the risk for catheter-related infection and phlebitis. The risk for catheter infection in part can be related to the risk for thrombophlebitis and the density of local skin flora. Femoral catheters are associated with a higher risk of infection and deep venous thrombosis, than internal jugular or subclavian catheters and should also be avoided, where possible. A subclavian site is preferred in adult patients and factors such as potential for mechanical complications and risk for subclavian vein stenosis, should be considered when determining the catheter insertion site.

Risk factors for CRBSI include patient-, catheter-, and operator-related factors. Several factors have been proposed to participate in the pathogenesis of CRBSI. Hospitalized patients with neutropenia are at high risk. However other host risk factors also include immune deficiencies in general, chronic illness, and malnutrition.

The catheter itself can be involved in 4 different pathogenic pathways: colonization of the catheter by microorganisms from the patient’s skin and occasionally the hands of healthcare workers, intraluminal or hub contamination, secondary seeding from a bloodstream infection, and, rarely, administration of contaminated infusate or additives.
CRBSIs can be reduced by a range of interventions including closed infusion systems, aseptic technique during insertion and management of the central venous line, early removal of central venous lines and appropriate site selection.
A key success factor to the implementation of the central line insertion and maintenance bundles is the adoption of the model of improvement approach involving multidisciplinary process stakeholders.
Different measures have been implemented to reduce the risk for CRBSI, including use of maximal barrier, precautions during catheter insertion, effective cutaneous anti-sepsis, and preventive strategies based on inhibiting micro-organisms originating from the skin or catheter hub from adhering to the catheter. Simultaneous application of multiple recommended best practices to manage CVCs has been associated with significant declines in the rates of CRBSI. Education, and training of health care workers, and adherence to standardized protocols for insertion and maintenance of intravascular catheters significantly reduced the incidence of catheter-related infections and represent the most important preventive measures.
A proposal for a bundle for the prevention of central venous catheter-related bloodstream infections

- Insert the central-line catheter only if it is absolutely necessary for the patient
- Ensure maximal sterile barrier precautions upon insertion
- Select the optimal site (avoid femoral vein in adults)
- Clean hands and respect infection prevention and control principles
- Perform a daily review of central line necessity and remove promptly unnecessary lines

Global Alliance for Infections in Surgery
Clostridioides difficile infection
In the last two decades, the dramatic increase in incidence and severity of Clostridioides difficile infection (CDI) in many countries worldwide, has made CDI a global public health challenge. CDI may be a particular concern in surgical patients, as surgery may predispose patients to CDI and surgery itself needs to treat severe cases of CDI. Optimization of CDI management in the peri-operative setting, has become increasingly necessary to decrease the cost, morbidity and mortality that may result from CDI.

C. difficile is an anaerobic, spore forming Gram-positive bacillus, which may form part of the normal intestinal microbiota in healthy newborns but which is rarely present in the gut of healthy adults. The organism is spread via the oral-fecal route and in hospitalized patients may be acquired through the ingestion of spores or vegetative bacteria spread to patients by healthcare personnel or from the environment. Since CDI is a toxin mediated infection, toxins negative C. difficile strains are non-pathogenic.

Risk factors for CDI may be divided into three general categories: host factors (immune status, co-morbidities), exposure to C. difficile spores (hospitalizations, community sources, long-term care facilities) and factors that disrupt normal colonic microbiome (antibiotics, other medications, surgery). Risk factors have included, age more than 65 years, comorbidity or underlying conditions, inflammatory bowel diseases, immunodeficiency (including human immunodeficiency virus infection), malnutrition, and low serum albumin level. Patients with inflammatory bowel disease are at increased risk of developing CDI, they may have worse outcomes, including higher rates of colectomy, and they experience higher rates of recurrence.

It is well known that antibiotics play a central role in the pathogenesis of CDI, presumably by disruption of the normal gut flora, thereby providing a perfect setting for C. difficile to proliferate and produce toxin. Although nearly all antibiotics have been associated with CDI, clindamycin, third-generation cephalosporins, penicillins and fluoroquinolones have traditionally been considered at greatest risk. A controversial risk factor is related to the exposure to gastric acid-suppressive medications, such as histamine-2 blockers and proton pump inhibitors (PPIs). Recent studies have suggested the association between use of stomach acid–suppressive medications, primarily PPIs, and CDI.
The spectrum of symptomatic CDI ranges from mild diarrhea to severe disease or fulminant colitis and as many as 30% of patients may develop recurrent CDI. Diarrhea is the hallmark symptom, however, patients may not present with initial symptoms of diarrhea due to colonic dysmotility either from previous underlying conditions or possibly from the disease process itself. Diarrhea may in fact be absent. This is especially important in surgical patients who may have a concomitant ileus. Therefore it is important to have a high index of suspicion. Diarrhea usually may be accompanied by abdominal pain and cramps and if prolonged may result in altered electrolyte balance and dehydration.

Severe forms of the disease are associated with increased abdominal cramping and pain and signs of systemic inflammation, such as fever, leukocytosis, and hypoalbuminemia. Diarrhea may be absent in some patients with CDI. Sometimes, it may signal the progression of the infection to its fulminant form. The progression to fulminant *C. difficile* colitis is quite infrequent (1%–3% of all CDI); however, mortality in this group of patients remains high due to the development of toxic megacolon and colonic perforation, peritonitis and septic shock, and subsequent organ dysfunction. Prompt and precise diagnosis is an important aspect of effective management of CDI. Early identification of CDI allows early treatment and can potentially improve outcomes. Rapid isolation of infected patients is important in controlling the transmission of *C. difficile*.

This is particularly important in reducing environmental contamination as spores can survive for months in the environment, despite regular use of environmental cleaning agents. Contact (enteric) precautions patients with CDI should be maintained until the resolution of diarrhea, which is demonstrated by passage of formed stool for at least 48 hours. Patients with known or suspected CDI should ideally be placed in a private room with en-suite hand washing and toilet facilities. If a private room is not available, as often occurs, known CDI patients may be cohort nursed in the same area though the theoretical risk of transfection with different strains exists.
Hand hygiene with soap and water and the use of contact precautions along with good cleaning and disinfection of the environment and patient equipment, should be used by all health-care workers contacting any patient with known or suspected CDI. Hand hygiene is a cornerstone of prevention of nosocomial infections, including *C. difficile*. Alcohol-based hand sanitizers are highly effective against non-spore-forming organisms, but they may not kill *C. difficile* spores or remove *C. difficile* from the hands. The most effective way to remove them from hands is through hand washing with soap and water.
A proposal for a bundle for the prevention of *Clostridioides difficile* infection

Enhance antimicrobial stewardship programs

Detect all cases and activate surveillance

Clean hands and use protective equipment

Clean and disinfect the environment

Educate staff and patients/visitors

Global Alliance for Infections in Surgery
Challenges with surveillance of healthcare-associated infections
Challenges with surveillance of healthcare-associated infections

HCAIs and AMR are intrinsically related and may act synergistically within hospitals. Surveillance of HCAIs and AMR are key parts of any control strategy. Infection prevention and control program should be in place to prevent HCAIs in all hospitals worldwide, and one of the main cornerstones is the presence of a formal system to monitor infection prevention and control and ensure that appropriate actions are taken to minimize infection rates. Surveillance of HCAIs is important because studies have demonstrated that many infections can be prevented through having infection and control surveillance programs in place. Surveillance systems are vital for effective prevention and control of HCAIs and are a cost effective approach to reducing disease. Surveillance of healthcare associated infection assists in identifying:

• Whether there is an infection problem
• The magnitude of the problem
• The factors that contribute to infections

Surveillance also allows hospitals and clinicians to measure the effectiveness of strategies that are implemented to decrease infection rates. Infection rate data should be used in a positive way to improve the quality and safety of healthcare.

The HCAI surveillance is conventionally conducted by two methods. Passive surveillance (self-reporting of suspected HAI by the treating physicians) is a very poor and inefficient method to track HCAIs as there is a risk of bias and underreporting. Active surveillance, on the other hand, is the systematic collection of data by a designated unbiased surveillance team. This is the method recommended by the main surveillance networks. Following the data extraction, analysis of the collected information should be done. Feedback and reports after analysis should be disseminated by infection control committees, keeping the confidentiality of individuals.
The importance of surveillance systems for HCAI control has been accepted globally and some countries have established national surveillance systems with the aim to prevent HAIs. However, the incidence of healthcare-associated infections in many countries is not known due to the lack of a surveillance system. It was demonstrated that hospitals without surveillance systems had increased HCAI rates. A decrease in the incidence of HCAIs was found in the countries that established surveillance systems.

A change management strategy should be implemented to inculcate and motivate healthcare workers across all levels to consistently collect reliable data that can be used to measure and reduce the burden of HCAIs.
Behavior changes to reduce healthcare-associated infections
Behavior changes to reduce healthcare-associated infections

Despite clear evidence and guidelines to direct HCAIs prevention strategies, compliance is uniformly poor and major difficulties arise when introducing evidence and clinical guidelines into routine daily practice. High rates of inappropriate infection prevention and control (IPC) practices in surgery continue to be reported in the literature. Due to cognitive dissonance (recognising that an action is necessary but not implementing it), changing behavior is extremely challenging.

In hospitals, cultural, contextual, and behavioral determinants influence clinical practice. Improving behavior in IPC practices remains a challenge. Understanding how to implement healthcare workers’ behavior is fundamental to develop effective reduction in HCAIs. There are generally three primary levels of influence related to behavior modification and infection control in healthcare facilities:
1) Intrapersonal factors;
2) Interpersonal factors;
3) Institutional factors.
Including these three levels of influence in IPC interventions may be a key in preventing HAIs.
On an individual level, healthcare workers should have the necessary knowledge, skills, and abilities to implement effective infection control practices. Increasing the knowledge may influence their perceptions and motivate them to change behavior. Education and training represent an important component for accurate implementation of recommendations. Education of all health professionals in preventing HCAIs should begin at undergraduate level and be consolidated with further training throughout the postgraduate years.

Hospitals are responsible for educating clinical staff about IPC programs. Active education techniques, such as academic detailing, consensus building sessions and educational workshops, should be implemented in each hospital worldwide according to its own resources. However, increasing knowledge alone may not be sufficient for effective infection control and may be insufficient to effect sustained change especially considering the multi-factorial nature of the problem of HCAIs.

Accountability is an essential principle for preventing HCAIs. It provides the necessary translational link between science and implementation. Without clear accountability, scientifically based implementation strategies will be used in an inconsistent and fragmented way, decreasing their effectiveness in preventing HCAIs.

Peer-to-peer role modeling, and champions on an interpersonal level have been shown to positively influence implementation of infection control practices.

Many practitioners use educational materials or didactic continuing medical education sessions to keep up-to-date. However, these strategies might not be very effective in changing practice, unless education is interactive and continuous, and includes discussion of evidence, local consensus, feedback on performance (by peers), making personal and group learning plans, etc. Identifying a local opinion leader to serve as a champion may be important because the “champion” may integrate best clinical practices and drive the colleagues in changing behaviors, working on a day to day basis, and promoting a culture in which infection prevention and control is of high importance.
Surgeons with satisfactory knowledge in surgical infections may provide feedback to the prescribers, integrate the best practices among surgeons and implement change within their own sphere of influence interacting directly with IPC team.
Raising awareness of IPC to stakeholders is a crucial factor in changing behaviors. Probably clinicians are more likely to comply with guidelines when they have been involved in developing the recommendations. One way to engage health professionals in guideline development and implementation is to translate practice recommendations into a protocol or pathway that specifies and coordinates responsibilities and timing for particular actions among a multidisciplinary team. There is now a substantial body of evidence that effective team-work in health care contributes to improved quality of care.

Leading international organizations, such as the WHO, acknowledge that collaborative practice is essential for achieving a concerted approach to providing care that is appropriate to meet the needs of patients, thus optimizing individual health outcomes and overall service delivery of health care.

The use of such approaches reinforces the concept that each one brings with them their particular expertise and is responsible for their respective contributions to patient care. In this context the direct involvement of surgeons may be crucial.

Organizational obstacles may influence infection prevention and control implementation. Many different hospital disciplines are typically involved in IPC, making collaboration, coordination, communication, teamwork and efficient care logistics essential. IPC teams have been shown to be both clinically effective improving patients’ outcome, and cost-effective providing important cost savings in terms of fewer HAIs, reduced length of hospital stay, less antimicrobial resistance and decreased costs of treatment for infections.
Interdisciplinary approach to infections in surgery
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