Eur J Clin Microbiol Infect Dis (2012) 31:2481–2490
DOI 10.1007/s10096-012-1611-0

REVIEW

Healthcare-associated infection prevention in pediatric intensive care units: a review

N. Joram · L. de Saint Blanquat · D. Stamm · E. Launay · C. Gras-Le Guen

Received: 9 February 2012 / Accepted: 19 March 2012 / Published online: 1 April 2012

Abstract The objective of this review was to summarize the current knowledge base on the prevention of nosocomial infections in pediatric intensive care units (PICUs). Healthcare-associated infections (HAIs) are a crucial problem in PICUs because of their impact on patient outcome, length of hospital stay, and costs. Studies published between 1998 and 2011 were identified using the MEDLINE and Cochrane databases. Randomized, cohort, case–control studies, and meta-analyses concerning global strategies of prevention, general organization of the wards, general recommendations on antibiotic management, and measures for the prevention of ventilator-associated pneumonia (VAP), bloodstream infections (BSIs), urinary tract infections (UTIs), and surgical site infections (SSIs) were incorporated. Limits of age from 1 month to 18 years were used. When recommendations could not be supported by the pediatric literature, adult studies were also reviewed. This review excludes the neonate population. Specific pediatric data are often lacking so as to establish specific evidence-based pediatric recommendations. This review underlines the absolute necessity of pediatric studies and to harmonize the definitions of HAIs.

N. Joram (✉) · C. Gras-Le Guen
Service de Réanimation Pédiatrique, CHU Nantes,
34 Boulevard Jean Monnet,
44000 Nantes, France
e-mail: nicolas.joram@chu-nantes.fr

N. Joram · E. Launay · C. Gras-Le Guen
CIC Pédiatrique, CHU Nantes,
Nantes, France

L. de Saint Blanquat
Département d'Anesthésie-Réanimation, CHU Cochin—Saint Vincent de Paul, Assistance Publique Hôpitaux de Paris (APHP),
Paris, France

D. Stamm
Service de Réanimation Pédiatrique, CHU Lyon,
Lyon, France

Introduction

Healthcare-associated infections (HAIs) are a major problem in intensive care units (ICUs) because of the severity of the patients and the invasive devices frequently required. The impact of HAIs on patient outcome and length of hospital stay and the underlying economic consequences have been clearly demonstrated [1–3]. Some factors have an overall incidence on HAI rates: length of hospital stay prior to admission to intensive care, workload, staffing level, and blood transfusion rate [4–6]. The Centers for Disease Control and Prevention (CDC) defines an HAI as a localized or systemic condition resulting from the presence of an infectious agent without evidence that the infection was present or incubating at the time of admission to the acute care setting [7]. Criteria for specific types of infection have also been published by the CDC [7]. However, these definitions can differ between countries, making comparisons of incidences and prevalences difficult [8]. In 2000, a European study reported a global prevalence of 23.6 % in pediatric intensive care units (PICUs) and, in 2002, an American study reported a rate of 12 % [9, 10]. Pediatric specificities related to immunological immaturity of the patients and to the difference concerning involved pathogens compared to adult care units [11] make recommendations established for adults inadequate. Pediatric studies are, however, rare and often present a limited power. In this context, the purpose of this report is to review the current knowledge base on the prevention of nosocomial infections in PICUs, reviewing general and specific strategies aimed at

reducing the risk of acquiring HAIs. The neonate population is not concerned by this review. The HAI prevention strategies which have proved or suggested their efficacy in PICUs are summarized in Table 1.

Data source and study selection

Research was performed using the MEDLINE and Cochrane databases using limits of age from 1 month to 18 years. Randomized, cohort, case–control studies, and meta-analyses published in English or French between 1998 and 2011 were incorporated. When recommendations could not be supported by the current pediatric literature, we had to extrapolate from data provided by adult studies.

Global strategies of education for the prevention of HAIs

Some recent pediatric studies have demonstrated the necessity for the introduction of global strategies for the prevention of HAI in PICUs. In a 292-bed tertiary care children's hospital, a stepwise introduction of interventions designed to reduce infection rates, including maximal barrier precautions, transition to antibiotic impregnated central venous catheters, annual hand washing campaigns, and changing the skin disinfectant from povidone–iodine to chlorhexidine, decreased annual rates of bloodstream infections from 9.7/1,000 days with a central venous catheter in 1997 to 3.0/1,000 days in 2005 [12]. In a pediatric cardiac ICU, a multidisciplinary, evidence-based initiative also resulted in a significant reduction in central line-associated bloodstream infections [13]. The efficacy of such educational interventions has also been proved in decreasing ventilator-associated pneumonia (VAP). In a preintervention and postintervention observational study including children and adults from four American hospitals, Babcock et al. found decreased VAP rates from 8.75/1,000 ventilator days in the year prior to the intervention to 4.74/1,000 ventilator days in the 18 months following the intervention ($p<0.001$) [14].

Table 1 Summary of strategies in regard to the prevention of healthcare-associated infections (HAIs) in pediatric intensive care units (PICUs)

Class of interventions	Recommended measures	Not evidence for recommendation
Global strategies of prevention	• Introduction of educational interventions	
General organization of the wards	• Positive pressure and high-efficiency air replacement for immunocompromised patients	Particular architecture of the unit
	• Use of negative-pressure rooms for carriers of pathogens at risk of transmission	
Management of antibiotics	• De-escalation of antibiotics	Antimicrobial cycling
	• Stop empiric antibiotic treatment if infection is not proved	
Prevention of VAP	• Semi-sitting position	• Systematic use of close tracheal suction system
	• Change of the circuits when visibly soiled or malfunctioning	• Heat and moisture exchanger
	• Implementation of protocol to reduce sedation and minimize the duration of mechanical ventilation	• Systematic change of ventilators circuits
	• Reduce the length of treatment for VAP except for non-fermenting Gram-negative bacilli	• Selective decontamination of the selective tract
		• Avoiding stress ulcer prophylaxis
Prevention of CRBSI	• Insertion-site skin disinfection with chlorhexidine solutions	• Prefer a catheterization site
	• Use of chlorhexidine-impregnated dressing	• Continuous infusion of heparin in central venous catheter
	• Administration set replacement every 96 h if no administration of lipid or blood products	• Use of heparin-bonded catheter
	• Administration set replacement 24 h after lipid and blood products perfusion	• Prophylactic continuous administration of antibiotics
Prevention of UTIs	• Early ablation of urinary catheter	
	• Precaution of asepsis during the pose of the catheter	
	• Use of a closed drainage device	
Prevention of surgical site infection	• Close of sternum as soon as possible after cardiac surgery	
	• Avoid ABP beyond 48 h (unclear if thoracostomy tubes not removed)	

VAP, ventilator-associated pneumonia; CRBSI, catheter-related bloodstream infection; UTIs, urinary tract infections; ABP, antibiotic prophylaxis

General organization of the wards

There are no specific pediatric data available concerning the relationship between the architecture of the units and the rate of HAIs. In adult ICUs, no particular ward design (U, square, or line) has demonstrated its superiority in terms of the reduction of HAIs. As described in a review published in 2004, conclusions of studies on the impact of the generalization of one-bed rooms are conflicting [15], with two of them finding a benefit [16, 17] and two others finding no significant difference [18, 19]. In critical care units, the management of air-transmitted infection is more and more crucial because of the increasing rate of immunocompromised patients in these units. This concerns environmental pathogens, in particular, *Aspergillus*. Even though no study has shown any advantage of the specific treatment of air, the use of positive pressure and high-efficiency air replacement systems should be recommended [20]. Concerning patients requiring isolation because of pathogens presenting risks of transmission to others and staff, experts also recommend the use of negative-pressure rooms [21].

General recommendation on antibiotic management

The protocols for the optimization of the use of antibiotics aim for a de-escalation of antibiotic use in order to reduce their spectrum and for the reduction of the length of treatment. Studies of de-escalation have, above all, demonstrated that this practice is possible in about half of all infections after empiric treatment [22]. Only one study performed in two neonatal ICUs has demonstrated the impact of the reduction of the spectrum of antibiotics in regards to the reduction of HAI and resistance rates [23]. No specific pediatric study has focused on this problem.

Otherwise, there is not enough evidence in adult nor in pediatric studies to recommend the use of antimicrobial cycling for the prevention of HAIs.

Even though pediatric studies are missing, the adult data strongly suggest that too large an antibiotic spectrum and/or excessive length of treatment are associated with negative effects in regards to infections and resistance rates in ICUs. In this context, reasonable and controlled antibiotic use may also be a major objective in PICUs.

Prevention of VAP

Pneumonia is the second most common HAI in the PICU, representing between 20 % [3, 24] and 53 % of HAIs, as found in the European study previously cited [10], and 95 % of nosocomial pneumonia occur in mechanically ventilated patients. The specific incidence of VAP represents 2.9 to 11.6/1,000 ventilator days [25–27]. Pneumonia increases the ICU length of stay and overall care cost, but the influence on mortality is not demonstrated, unlike in adult patients [24, 27]. There are few publications in pediatric populations and, as described in two recent reviews, most guidelines are largely supported by data from adult populations [28, 29]. As in adults, several factors have been implicated in the physiopathology of VAP: aspiration of oropharyngeal secretions, aspiration of gastric fluid, and inhalation of bacteria. In children, the role of gastroesophageal reflux must play a central role because of its incidence in healthy children [30], although its incidence in the ICU population is unknown. In this context, the prevention of VAP with non-medicinal and medicinal means is a high priority.

Non-medicinal means

Neither oral nor tracheal intubation has shown superiority when considering HAIs. However, microaspirations seem to be more frequent with orotracheal intubation, as assessed by a prospective study published by Amantéa et al., reporting that pediatric patients with orotracheal intubation presented a 5-fold increase in tracheal aspiration when compared with nasotracheal intubation [31]. However, this study did not demonstrate any reduction in VAP. As children younger than 1 year of age present anatomical particularities such as large tongue size and frequent sucking motions, nasotracheal intubation should be recommended for these reasons, but not for the prevention of VAP.

Otherwise, even though the reduction of VAP with cuffed endotracheal tubes has not been proved in pediatric populations, it seems to reduce the prevalence of microaspirations, as assessed by Gopalareddy et al. measuring gastric pepsin in tracheal aspirates [32].

Even though closed endotracheal suction systems are usually used in PICUs, their efficacy for the reduction of VAP has never been evaluated in pediatric populations. However, as the physiopathology of VAP does not differ in children and adults and as three meta-analyses comparing open and closed tracheal suction systems did not find any significant difference, there is no evidence-based reason to prefer closed systems more than open systems for the prevention of VAP in PICUs [33–35].

Recent studies of the impact of the humidification system of the airways (heat and moisture exchanger or heated humidifier) on VAP have revealed conflicting results in adult patients [36–39]. In children, the data are insufficient to recommend the use of heat and moisture exchangers.

Concerning the periodic change of ventilator circuits, data are also lacking, but adult studies have demonstrated that systematic change does not reduce the incidence of VAP and, thus, is not recommended. However, the change of the

circuits when visibly soiled or malfunctioning is recommended [40, 41].

Otherwise, the length of ventilation and the number of extubation failures are clearly identified as independent risk factors for VAP in pediatric patients [42]. As the prolongation of ventilation and extubation failure rates are associated with a deep sedation [43, 44], the reduction of sedation administration may be an effective target to reduce VAP. In this context, studies performed in adult populations have demonstrated that daily interruption of sedative infusions or the use of a nurse-implemented sedation protocol could reduce sedation administration, duration of mechanical ventilation, unplanned extubation rate, and VAP incidence [45, 46]. The role of these sedation protocols have been poorly investigated in PICUs, but may offer some potential benefit for the reduction of VAP in this population [47].

The benefit of early enteral nutrition in pediatric critical care has been clearly demonstrated, decreasing morbidity and mortality, but there is no pediatric study comparing the impact of continuous versus discontinuous and gastric versus duodenal enteral feeding on VAP incidence.

In adults, Drakulovic et al. identified supine body position as a risk factor for VAP compared to semi-recumbent position [48], but the best resting angle was not determined [49]. In children, no specific study analyzed the influence of a head-of-bed elevation on the incidence of nosocomial pneumonia, but the interaction between the position and gastroesophageal reflux was described in a meta-analysis in 2004 [50]. The benefit of the semi-sitting position was unclear, but prone positioning, which can be safely performed in critically ill children [51], decreased the reflux index. In conclusion, as in adults, the semi-sitting position is recommended with an unknown angle and prone positioning should have a preventive effect on VAP.

Medicinal means

In the PICU, gastrointestinal bleeding, for which identified risk factors are mechanical ventilation, thrombopenia, and a Pediatric Risk of Mortality (PRISM) score >10 at the time of admission to the acute care setting, concerns about 10 % of patients and is responsible for increased length and costs of hospitalization [52]. This prompts physicians to prescribe stress ulcer prophylaxis to the patients at risk. Two pediatric studies have evaluated the impact of this treatment on VAP incidence. Yildizdas et al. compared three prophylaxis strategies (ranitidine, sucralfate, and omeprazole) to a control group and did not find any significant difference with regards to VAP incidence [53]. Lopriore et al., comparing sucralfate, ranitidine, and a placebo, found similar results [54]. Furthermore, the upper airway colonization rate was not different among the three groups. These results were recently confirmed by a meta-analysis including 132 patients [55]. Thus, as in adults, stress ulcer prophylaxis does not seem to be a risk factor for VAP in PICUs.

There are no pediatric data concerning the benefit of oral decontamination for the prevention of VAP. In adult critical care units, selective decontamination of the digestive tract (SDD) is very controversial. This concept is based on the rationale that most cases of VAP are the consequence of the colonization of the oropharynx and the digestive tract by pathogens. SDD associates an antibiotic treatment by local application and a parenteral injection. Even though large studies and a meta-analysis present positive effects of SDD on the incidence of VAP and on mortality [56–58], without an effect on the resistance of bacteria to antibiotics, the medical community remains very hesitant as to its generalization, and these measures are not recommended by the CDC [59]. As a consequence, SDD is not a generalized practice in critical care units. In PICUs, its benefit has been poorly evaluated. One randomized study including 23 severely burned children evaluated the effect of a selective decontamination of the digestive tract by oral treatment and did not reveal any difference in the incidence of infections. Furthermore, colonization rates of the wound, sputum, nasogastric aspirates, and feces were similar. However, patients in the SDD group had a significantly higher incidence of diarrhea [60]. In a prospective, randomized, nonblinded, and controlled clinical microbiology study including 244 critically ill pediatric patients with or without SDD associating a triple therapy with colimycin, tobramycin, and nystatin to an oral decontamination with chlorhexidine, SDD acted as a protective factor of VAP. However, it did not reduce the incidence of other types of nosocomial infection [61]. These controversial data, combined with extrapolated data of adult studies, are not currently sufficient to recommend SDD as an effective measure for the prevention of VAP in children.

Impact of the length of antibiotic treatment of VAP on the risk of recurrent infections and on resistance rates

In a large cohort of adults having developed VAP, Chastre et al. have demonstrated that patients treated for 8 days compared to 15 days had neither excess mortality nor more recurrent infections, but had more antibiotic-free days. Among patients who developed recurrent infections, multiresistant pathogens emerged less frequently in those who had received 8 days of antibiotics. However, when analyzing the specific group of patients with VAP caused by non-fermenting Gram-negative bacilli, including *Pseudomonas aeruginosa*, these patients did not have more unfavorable outcomes when antimicrobial therapy lasted only 8 days, but they did have a higher pulmonary infection–recurrence rate compared with those receiving 15 days of treatment [62]. In a prospective before and after study, Ibrahim et al. demonstrated that the implementation of a standardized antimicrobial guideline for the treatment of VAP could significantly reduce the duration

of antimicrobial treatment and the occurrence of a second episode of VAP [63]. In another study, adult patients were assigned to have the duration of antibiotic treatment for VAP determined by an antibiotic discontinuation policy (discontinuation group) or their treating physician teams (conventional group). There was no difference in regard to the recurrence of a secondary episode nor with resistance rates, but the duration of antibiotic treatment was statistically shorter among patients in the discontinuation group [64].

In this context, some authors have focused on the benefit of the use of inflammatory markers, in particular, procalcitonin (PCT), for the reduction of antibiotic treatment length [65]. Kopterides et al. recently published a meta-analysis of seven randomized, controlled studies including 1,010 adults and the 121 neonates of the previously cited study, but no pediatric patients. They concluded that the implementation of PCT-guided algorithms decreased the duration of antibiotic therapy for the first episode of infection by approximately 2 days and the total duration of antibiotic treatment by 4 days. The comparison between the PCT and the routine practice group was not associated with any apparent adverse clinical outcome: 28-day mortality, ICU length of stay, and relapsed/persistent infection rate [66]. Only one study of this meta-analysis monitored the percentage of emerging multidrug-resistant bacteria without disclosing any significant difference between the PCT and the routine practice group (17.9 % vs. 16.6 %, $p=0.67$) [67].

Prevention of BSIs

The incidence of intravascular catheter-related bloodstream infections (CRBSIs) is not easy to evaluate because of the differences in definitions and because infection rates are expressed differently from one study to another. The American National Nosocomial Infections Surveillance System (NNIS) reports a mean incidence density of 6.6/1,000 days of catheter in PICUs [25]. CRBSIs are associated with an increase of hospitalization length and costs, but also of morbidity and mortality [68], thereby, CDC guidelines were published in 2002 [69]. Risk factors have been described in several studies and reviews [70, 71]: under 2 years of age, neutropenia and tumor pathology represent the most important risk factors. Events linked to hospitalization such as intra-hospital transport, parenteral nutrition, and repeated handlings of the catheter are also predisposing situations. In Europe, bacteria responsible for CRBSIs in PICUs are, in order of frequency, coagulase-negative *Staphylococcus* spp., *Enterococcus* spp., *Staphylococcus aureus*, Gram-negative bacilli, and *Candida* spp. [10].

Contrary to adults, femoral insertion of the catheter is not identified as a risk factor of CRBSI. In a large prospective observational study evaluating 1,092 catheters in 20 Spanish PICUs, the rate of CRBSI was not significantly related to the insertion site [72]. Similar results have been reported in a non-randomized study evaluating 308 catheters [73]. Even in the absence of a randomized study, no recommendation can be made concerning the catheterization site. There is no available pediatric study evaluating the benefit of peripherally placed percutaneous central venous catheters.

Data are also insufficient to recommend the subcutaneous tunnelling of catheters to prevent CRBSIs. One prospective pediatric study reported a decreased colonization of femoral tunnelled versus non-tunnelled catheters, with no difference on the CRBSI rate [74].

Cutaneous disinfection is a crucial factor in the prevention of CRBSIs. As demonstrated by a meta-analysis of eight adult studies, chlorhexidine seems to be more efficient than povidone–iodine solutions in preventing CRBSI. As, in France, the use of povidone–iodine solution is not recommended before 30 months of age because of the risk of hypothyroid, chlorhexidine solutions should be the reference for insertion site skin disinfection. In this context, chlorhexidine-impregnated dressing may also be effective. A prospective randomized, controlled study performed in 145 children after cardiac surgery reported a decrease in catheter colonization with chlorhexidine-impregnated dressing compared to standard polyurethane dressing, but without a difference in the CRBSI rate [75]. A meta-analysis including adult and pediatric data presented the same conclusions [76]. However, in a large study including 1,636 adults also comparing chlorhexidine-impregnated dressing to standard dressing, the rate of CRBSI was significantly reduced with the chlorhexidine-impregnated dressing (6/1,953 catheters, 0.40/1,000 catheter-days vs. 17/1,825 catheters, 1.3/1,000 catheter-days; hazard ratio [HR], 0.24; 95 % confidence interval [CI], 0.09–0.65) [77]. The results of this large study should encourage the undertaking of large pediatric studies and may have a strong impact in the pediatric guidelines.

Otherwise, optimal timing for intravenous administration set replacement has been investigated in a meta-analysis published in 2005, including 13 studies, of which eight were in pediatric populations. It appeared that administration sets that do not contain lipids, blood, or blood products may be left in place for intervals of up to 96 h without increasing the incidence of infection, compared to 24, 48, or 72 h. However, there is no data inciting to increase the delay beyond 24 h after lipid and blood products perfusion sets, as currently recommended [78].

Thrombosis is a frequent complication of central catheters and its interaction with infection is well known and reciprocal. Even though in neonates with peripherally placed percutaneous central venous catheters continuous heparin administration, compared with saline, decreased thrombosis rates but not CRBSI rates [79], data are lacking to clarify this debate in older children. In a recent single-center, randomized, placebo-

controlled, double-blinded trial including 90 children younger than 1 year old recovering from cardiac surgery, a continuous infusion of heparin at 10 units/kg/h was safe but it did not reduce catheter-related thrombosis formation nor the BSI rate compared to a placebo [80]. In this context, systematic continuous anticoagulation with heparin is not supported by enough data to be recommended. The benefit of heparin-bonded catheters has also been evaluated. A large study including 209 children compared heparin-bonded and standard catheters. The CRBSI rate was significantly decreased in the heparin-bonded catheter group (5.17 vs. 46.96/1,000 days, $p<0.0005$), with a decreased thrombosis rate as well [81]. In a recent pediatric randomized, controlled, blinded, single-center trial, infants younger than 1 year old with congenital heart disease requiring a central venous line for clinical care were randomly assigned to receive either a heparin-bonded catheter or a standard non-heparin-bonded catheter. No advantage in using heparin-bonded catheters was identified [82]. All things considered, the data remain insufficient to recommend the systematic use of either of these catheters.

In adults and children, prophylactic continuous administration of antibiotics is not recommended because of the risk of bacterial resistance emergence. The benefit of antibiotic flush for decreasing the CRBSI rate has been demonstrated in several studies, but particularly in neonatology and oncology, where the populations differ from the PICU [83, 84]. Moreover, the occlusion of the catheter for antibiotics administration in these patients appears to be a limitative problem. Antibiotic-coated central venous catheters, widely studied in adult populations, have been seldomly evaluated in children. One observational study compared catheters coated with minocycline and rifampicin to standard catheters. The authors reported a 3-fold longer median time to infection among children in the antibiotic-coated catheter group (18 vs. 5 days, *p=0.053), but the infection incidence was not different between the two groups (7.53 vs. 8.63/1,000 days of catheter, p= 1) [85]. The authors explained these results by a decreasing activity of the antibiotics over time.*

Prevention of UTIs

Considering their incidence, urinary tract infections (UTIs) are the third most common cause of nosocomial infections in PICUs. In 2001, among 50 children's hospitals in America, Stover et al. reported a median incidence of 5.4 infections for 1,000 days of urinary catheter-days [86]. The incidence of UTI was not dependent on the site of insertion of the catheter (urethra, ureter, nephrostomy, or supra pubic). In a retrospective study including 25 children, Matlow et al. identified cardiac surgery as the only independent risk factor of UTI [87]. The most efficient means of prevention is the early removal of urinary catheters [86, 88]. The impact of a sepsis during the placement of the catheter and of the use of a closed drainage device are only supported by adult data, but should be recommended [89].

Prevention of SSIs

Surgical site infections (SSIs) are known to be closely related with increased morbidity, mortality, hospital length of stay, and additional cost [90]. This term has been chosen by the CDC and concerns several clinical situations such as infections of scars, walls, or prosthesis. Furthermore, a classification corresponding to different localizations has been proposed: superficial incisional SSI, deep incisional SSI, and organ/space SSI. This classification has not always been respected, making the comparison of studies and the interpretation of meta-analyses difficult. Furthermore, specific pediatric definitions do not exist, so those established for adults are used here. There are few data reporting the incidence of SSIs in PICUs. The most recent multicenter study reported by Horwitz et al. and including 846 American operated children prospectively followed for 30 days reported an SSI rate of 4.4 % [91]. In 2003, a prospective incidence study of nosocomial infections in PICUs after cardiac surgery reported a higher incidence rate (15 %), increasing 2.5-fold the PICU length of stay [26]. Risk factors identified in Horwitz et al.'s study were length of surgery and contamination during surgery. In cardiac surgery, cardiopulmonary bypass length, hospital length of stay before surgery, pre-existent pathology, mechanical ventilation, and requirement of an inotropic agent were identified as SSI risk factors [92]. Sternum open on the ward and high PRISM score on PICU admission were also reported as risk factors by Pollock et al. [93].

In a randomized controlled trial in adults, Segers et al. reported that decontamination of the nasopharynx and oropharynx by chlorhexidine gluconate could significantly decrease the incidence of global nosocomial infections and, in particular, lower respiratory tract and deep SSIs [94]. The benefit of universal screening for *Staphylococcus aureus* is unclear. In a prospective study with a crossover design comparing rapid screening for methicillin-resistant *Staphylococcus aureus* (MRSA) on admission plus standard infection control measures versus standard infection control alone in surgical patients, the nosocomial MRSA infection rate was not decreased in the intervention group. However, in a randomized, double-blind, placebo-controlled, multicenter trial, Bode et al. assessed whether the rapid identification of *Staphylococcus aureus* nasal carriers by means of a real-time polymerase chain reaction (PCR) assay, followed by treatment with mupirocin nasal ointment and chlorhexidine soap, could decrease the risk of postoperative infection in adults. They reported a rate 3.4 % (17 of 504 patients) of

Staphylococcus aureus infection in the mupirocin–chlorhexidine group, as compared with 7.7 % (32 of 413 patients) in the placebo group (relative risk of infection, 0.42; 95 % CI, 0.23 to 0.75) [95]. Despite the lack of data in the pediatric population, these results may have a strong impact in pediatric prevention guidelines.

The duration of postoperative antibiotic prophylaxis (ABP) appears as a key point in the prevention of postoperative infections and of the emergence of antimicrobial resistance. In adults, after clean and clean-contaminated surgery, ABP for longer than 24 h raised the risk for intrahospital and posthospital discharge SSI, regardless of the presence of risk factors (odds ratio [OR], 3.39; 95 % CI, 1.11–10.35; p=0.032 and OR, 5.39; 95 % CI, 1.64–17.75; p=0.006, respectively) [96]. This study did not include patients after cardiac surgery. In 2,641 patients undergoing cardiac surgery, after adjustment for possible confounding, prolonged ABP was not associated with a decreased risk of SSI (adjusted OR, 1.2; 95 % CI, 0.8 to 1.6) and was correlated with an increased risk of acquired antibiotic resistance (adjusted OR, 1.6; 95 % CI, 1.1 to 2.6) [97]. However, several controversies still exist in the use of ABP among children. In a non-randomized comparison of two groups of children studied sequentially, controlled perioperative antimicrobial prophylaxis by reducing the length of antibiotic treatment to <48 h and the use of glycopeptides in case of MRSA was associated with a significant decrease in the nosocomial infection rate and was cost-effective [98]. In an adult trial, 838 patients were randomly given a single dose of cefazolin for a 24-h treatment. Single-dose cefazolin was associated with a higher SSI rate than the second regimen [99]. In a retrospective study including 4,000 children after cardiac surgery, antimicrobial prophylaxis continued as long as thoracostomy tubes were present significantly decreased SSIs compared to a protocol where treatment was discontinued 48 h postoperatively regardless of the presence of tubes [100]. According to these results, it appears clear to recommend to not to continue ABP beyond 48 h in most situations. In case of the prolonged presence of thoracostomy tubes after cardiac surgery, the conclusion remains unclear.

Otherwise, perioperative factors seem to have a significant impact on postoperative infection rates. Some investigators have hypothesized that supplemental perioperative oxygen could reduce the incidence of surgical wound infections [101]. In a prospective study, adults requiring colorectal surgery were randomized to receive an inspired fraction of oxygen (FiO_2) of 30 or 80 %; Belda et al. demonstrated that an FiO_2 of 80 % was a protective factor of infection [102]. Moreover, in a prospective and randomized study including 103 adults, vasodilatation by active warming was found to decrease the SSI rate (54 vs. 32 %, p=0.02) [103].

Conclusion

The prevention of nosocomial infections remains a crucial problem in pediatric intensive care units (PICUs). This report reviews the published recommendations for their prevention. However, the pediatric data are often missing and many of the pediatric guidelines have to be extrapolated from adult studies and this underlines the urgency to conduct pediatric studies and to establish guidelines in this specific population. Furthermore, the analysis of the literature available on this topic demonstrates the absolute necessity to harmonize the definitions of healthcare-associated infections (HAIs) in order to provide comparable data and standardized pediatric guidelines.

References

1. Abou Elella R, Najm HK, Balkhy H, Bullard L, Kabbani MS (2010) Impact of bloodstream infection on the outcome of children undergoing cardiac surgery. Pediatr Cardiol 31(4):483–489, Epub 2010 Jan 10
2. Foglia EE, Fraser VJ, Elward AM (2007) Effect of nosocomial infections due to antibiotic-resistant organisms on length of stay and mortality in the pediatric intensive care unit. Infect Control Hosp Epidemiol 28(3):299–306, Epub 2007 Feb 20
3. Richards MJ, Edwards JR, Culver DH, Gaynes RP (1999) Nosocomial infections in pediatric intensive care units in the United States. National Nosocomial Infections Surveillance System. Pediatrics 103(4):e39
4. Olaechea PM, Ulibarrena MA, Alvarez-Lerma F, Insausti J, Palomar M, De la Cal MA; ENVIN-UCI Study Group (2003) Factors related to hospital stay among patients with nosocomial infection acquired in the intensive care unit. Infect Control Hosp Epidemiol 24(3):207–213
5. Hugonnet S, Uçkay I, Pittet D (2007) Staffing level: a determinant of late-onset ventilator-associated pneumonia. Crit Care 11(4):R80
6. Taylor RW, O'Brien J, Trottier SJ, Manganaro L, Cytron M, Lesko MF, Arnzen K, Cappadoro C, Fu M, Plisco MS, Sadaka FG, Veremakis C (2006) Red blood cell transfusions and nosocomial infections in critically ill patients. Crit Care Med 34 (9):2302–2308, quiz 2309
7. Horan TC, Andrus M, Dudeck MA (2008) CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 36(5):309–332
8. Dubos F, Vanderborght M, Puybasset-Joncquez AL, Grandbastien B, Leclerc F (2007) Can we apply the European surveillance program of nosocomial infections (HELICS) to pediatric intensive care units? Intensive Care Med 33(11):1972–1977, Epub 2007 Aug 1
9. Raymond J, Aujard Y (2000) Nosocomial infections in pediatric patients: a European, multicenter prospective study. European Study Group. Infect Control Hosp Epidemiol 21(4):260–263
10. Grohskopf LA, Sinkowitz-Cochran RL, Garrett DO, Sohn AH, Levine GL, Siegel JD, Stover BH, Jarvis WR; Pediatric Prevention Network (2002) A national point-prevalence survey of pediatric intensive care unit-acquired infections in the United States. J Pediatr 140(4):432–438
11. Raymond J, Nordmann P, Doit C, Vu Thien H, Guibert M, Ferroni A, Aujard Y (2007) Multidrug-resistant bacteria in hospitalized children: a 5-year multicenter study. Pediatrics 119(4): e798–e803

12. Bhutta A, Gilliam C, Honeycutt M, Schexnayder S, Green J, Moss M, Anand KJ (2007) Reduction of bloodstream infections associated with catheters in paediatric intensive care unit: stepwise approach. BMJ 334(7589):362–365
13. Costello JM, Morrow DF, Graham DA, Potter-Bynoe G, Sandora TJ, Laussen PC (2008) Systematic intervention to reduce central line-associated bloodstream infection rates in a pediatric cardiac intensive care unit. Pediatrics 121(5):915–923
14. Babcock HM, Zack JE, Garrison T, Trovillion E, Jones M, Fraser VJ, Kollef MH (2004) An educational intervention to reduce ventilator-associated pneumonia in an integrated health system: a comparison of effects. Chest 125(6):2224–2231
15. Dettenkofer M, Seegers S, Antes G, Motschall E, Schumacher M, Daschner FD (2004) Does the architecture of hospital facilities influence nosocomial infection rates? A systematic review. Infect Control Hosp Epidemiol 25(1):21–25, review
16. Mulin B, Rouget C, Clément C, Bailly P, Julliot MC, Viel JF, Thouverez M, Vieille I, Barale F, Talon D (1997) Association of private isolation rooms with ventilator-associated *Acinetobacter baumanii* pneumonia in a surgical intensive-care unit. Infect Control Hosp Epidemiol 18(7):499–503
17. Smith G, Smylie HG, McLauchlan J, Logie JR (1980) Ward design and wound infection due to *Staphylococcus pyogenes*. J R Coll Surg Edinb 25(2):76–79
18. Huebner J, Frank U, Kappstein I, Just HM, Noeldge G, Geiger K, Daschner FD (1989) Influence of architectural design on nosocomial infections in intensive care units—a prospective 2-year analysis. Intensive Care Med 15(3):179–183, review
19. Preston GA, Larson EL, Stamm WE (1981) The effect of private isolation rooms on patient care practices, colonization and infection in an intensive care unit. Am J Med 70(3):641–645
20. Société Française d'Hygiène Hospitalière (2000) Prévention du risque aspergillaire chez les patients immunodéprimés (hématologie, transplantation). Conférence de consensus, Paris 2000. Hygiènes 8(6):305–308
21. American Institute of Architects (AIA) Academy of Architecture for Health (AAH) (2001) Guidelines for design and construction of hospital and health care facilities. American Institute of Architects Press, Washington, DC. http://www.aia.org/aah
22. Leone M, Garcin F, Bouvenot J, Boyadjev I, Visintini P, Albanèse J, Martin C (2007) Ventilator-associated pneumonia: breaking the vicious circle of antibiotic overuse. Crit Care Med 35(2):379–385, quizz 386
23. de Man P, Verhoeven BA, Verbrugh HA, Vos MC, van den Anker JN (2000) An antibiotic policy to prevent emergence of resistant bacilli. Lancet 355(9208):973–978
24. Patel JC, Mollitt DL, Pieper P, Tepas JJ 3rd (2000) Nosocomial pneumonia in the pediatric trauma patient: a single center's experience. Crit Care Med 28(10):3530–3533
25. National Nosocomial Infections Surveillance System (2004) National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 32(8):470–485
26. Urrea M, Pons M, Serra M, Latorre C, Palomeque A (2003) Prospective incidence study of nosocomial infections in a pediatric intensive care unit. Pediatr Infect Dis J 22(6):490–494
27. Elward AM, Warren DK, Fraser VJ (2002) Ventilator-associated pneumonia in pediatric intensive care unit patients: risk factors and outcomes. Pediatrics 109(5):758–764
28. Wright ML, Romano MJ (2006) Ventilator-associated pneumonia in children. Semin Pediatr Infect Dis 17(2):58–64
29. Principi N, Esposito S (2007) Ventilator-associated pneumonia (VAP) in pediatric intensive care units. Pediatr Infect Dis J 26 (9):841–843, discussion 843–844
30. Miyazawa R, Tomomasa T, Kaneko H, Tachibana A, Ogawa T, Morikawa A (2002) Prevalence of gastro-esophageal reflux-related symptoms in Japanese infants. Pediatr Int 44(5):513–516
31. Amantéa SL, Piva JP, Sanches PR, Palombini BC (2004) Oropharyngeal aspiration in pediatric patients with endotracheal intubation. Pediatr Crit Care Med 5(2):152–156
32. Gopalareddy V, He Z, Soundar S, Bolling L, Shah M, Penfil S, McCloskey JJ, Mehta DI (2008) Assessment of the prevalence of microaspiration by gastric pepsin in the airway of ventilated children. Acta Paediatr 97(1):55–60, Epub 2007 Dec 10
33. Jongerden IP, Rovers MM, Grypdonck MH, Bonten MJ (2007) Open and closed endotracheal suction systems in mechanically ventilated intensive care patients: a meta-analysis. Crit Care Med 35(1):260–270
34. Subirana M, Solà I, Benito S (2007) Closed tracheal suction systems versus open tracheal suction systems for mechanically ventilated adult patients. Cochrane Database Syst Rev 4: CD004581
35. Vonberg RP, Eckmanns T, Welte T, Gastmeier P (2006) Impact of the suctioning system (open vs. closed) on the incidence of ventilation-associated pneumonia: meta-analysis of randomized controlled trials. Intensive Care Med 32(9):1329–1335, Epub 2006 Jun 21
36. Hess DR, Kallstrom TJ, Mottram CD, Myers TR, Sorenson HM, Vines DL; American Association for Respiratory Care (2003) Care of the ventilator circuit and its relation to ventilator-associated pneumonia. Respir Care 48(9):869–879
37. Kola A, Eckmanns T, Gastmeier P (2005) Efficacy of heat and moisture exchangers in preventing ventilator-associated pneumonia: meta-analysis of randomized controlled trials. Intensive Care Med 31(1):5–11, Epub 2004 Sep 11
38. Boots RJ, George N, Faoagali JL, Druery J, Dean K, Heller RF (2006) Double-heater-wire circuits and heat-and-moisture exchangers and the risk of ventilator-associated pneumonia. Crit Care Med 34(3):687–693
39. Lacherade JC, Auburtin M, Cerf C, Van de Louw A, Soufir L, Rebufat Y, Rezaiguia S, Ricard JD, Lellouche F, Brun-Buisson C, Brochard L (2005) Impact of humidification systems on ventilator-associated pneumonia: a randomized multicenter trial. Am J Respir Crit Care Med 172(10):1276–1282, Epub 2005 Aug 26
40. Dreyfuss D, Djedaini K, Weber P, Brun P, Lanore JJ, Rahmani J, Boussougant Y, Coste F (1991) Prospective study of nosocomial pneumonia and of patient and circuit colonization during mechanical ventilation with circuit changes every 48 hours versus no change. Am Rev Respir Dis 143(4 Pt 1):738–743
41. Lorente L, Lecuona M, Galván R, Ramos MJ, Mora ML, Sierra A (2004) Periodically changing ventilator circuits is not necessary to prevent ventilator-associated pneumonia when a heat and moisture exchanger is used. Infect Control Hosp Epidemiol 25 (12):1077–1082
42. Fontela PS, Piva JP, Garcia PC, Bered PL, Zilles K (2005) Risk factors for extubation failure in mechanically ventilated pediatric patients. Pediatr Crit Care Med 6(2):166–170
43. Kollef MH, Levy NT, Ahrens TS, Schaiff R, Prentice D, Sherman G (1998) The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. Chest 114(2):541–548
44. Sadowski R, Dechert RE, Bandy KP, Juno J, Bhatt-Mehta V, Custer JR, Moler FW, Bratton SL (2004) Continuous quality improvement: reducing unplanned extubations in a pediatric intensive care unit. Pediatrics 114(3):628–632
45. Kress JP, Pohlman AS, O'Connor MF, Hall JB (2000) Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 342(20):1471–1477
46. Quenot JP, Ladoire S, Devoucoux F, Doise JM, Cailliod R, Cunin N, Aubé H, Blettery B, Charles PE (2007) Effect of a nurse-implemented sedation protocol on the incidence of

ventilator-associated pneumonia. Crit Care Med 35(9):2031–2036
47. Popernack ML, Thomas NJ, Lucking SE (2004) Decreasing unplanned extubations: utilization of the Penn State Children's Hospital Sedation Algorithm. Pediatr Crit Care Med 5(1):58–62
48. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogué S, Ferrer M (1999) Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. Lancet 354(9193):1851–1858
49. van Nieuwenhoven CA, Vandenbroucke-Grauls C, van Tiel FH, Joore HC, van Schijndel RJ, van der Tweel I, Ramsay G, Bonten MJ (2006) Feasibility and effects of the semirecumbent position to prevent ventilator-associated pneumonia: a randomized study. Crit Care Med 34(2):396–402
50. Craig WR, Hanlon-Dearman A, Sinclair C, Taback S, Moffatt M (2004) Metoclopramide, thickened feedings, and positioning for gastro-oesophageal reflux in children under two years. Cochrane Database Syst Rev 4:CD003502, review
51. Fineman LD, LaBrecque MA, Shih MC, Curley MA (2006) Prone positioning can be safely performed in critically ill infants and children. Pediatr Crit Care Med 7(5):413–422
52. Gauvin F, Dugas MA, Chaïbou M, Morneau S, Lebel D, Lacroix J (2001) The impact of clinically significant upper gastrointestinal bleeding acquired in a pediatric intensive care unit. Pediatr Crit Care Med 2(4):294–298
53. Yildizdas D, Yapicioglu H, Yilmaz HL (2002) Occurrence of ventilator-associated pneumonia in mechanically ventilated pediatric intensive care patients during stress ulcer prophylaxis with sucralfate, ranitidine, and omeprazole. J Crit Care 17(4):240–245
54. Lopriore E, Markhorst DG, Gemke RJ (2002) Ventilator-associated pneumonia and upper airway colonisation with Gram negative bacilli: the role of stress ulcer prophylaxis in children. Intensive Care Med 28(6):763–767, Epub 2002 Apr 20
55. Reveiz L, Guerrero-Lozano R, Camacho A, Yara L, Mosquera PA (2010) Stress ulcer, gastritis, and gastrointestinal bleeding prophylaxis in critically ill pediatric patients: a systematic review. Pediatr Crit Care Med 11(1):124–132, review
56. Krueger WA, Lenhart FP, Neeser G, Ruckdeschel G, Schreckhase H, Eissner HJ, Forst H, Eckart J, Peter K, Unertl KE (2002) Influence of combined intravenous and topical antibiotic prophylaxis on the incidence of infections, organ dysfunctions, and mortality in critically ill surgical patients: a prospective, stratified, randomized, double-blind, placebo-controlled clinical trial. Am J Respir Crit Care Med 166(8):1029–1037
57. de Jonge E, Schultz MJ, Spanjaard L, Bossuyt PM, Vroom MB, Dankert J, Kesecioglu J (2003) Effects of selective decontamination of digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial. Lancet 362(9389):1011–1016
58. Liberati A, D'Amico R, Pifferi S, Torri V, Brazzi L, Parmelli E (2009) Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care. Cochrane Database Syst Rev 4:CD000022
59. Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R; CDC; Healthcare Infection Control Practices Advisory Committee (2004) Guidelines for preventing health-care-associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. MMWR Recomm Rep 53(RR-3):1–36
60. Barret JP, Jeschke MG, Herndon DN (2001) Selective decontamination of the digestive tract in severely burned pediatric patients. Burns 27(5):439–445
61. Ruza F, Alvarado F, Herruzo R, Delgado MA, García S, Dorao P, Goded F (1998) Prevention of nosocomial infection in a pediatric intensive care unit (PICU) through the use of selective digestive decontamination. Eur J Epidemiol 14(7):719–727
62. Chastre J, Wolff M, Fagon JY, Chevret S, Thomas F, Wermert D, Clementi E, Gonzalez J, Jusserand D, Asfar P, Perrin D, Fieux F, Aubas S; PneumA Trial Group (2003) Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. JAMA 290(19):2588–2598
63. Ibrahim EH, Ward S, Sherman G, Schaiff R, Fraser VJ, Kollef MH (2001) Experience with a clinical guideline for the treatment of ventilator-associated pneumonia. Crit Care Med 29(6):1109–1115
64. Micek ST, Ward S, Fraser VJ, Kollef MH (2004) A randomized controlled trial of an antibiotic discontinuation policy for clinically suspected ventilator-associated pneumonia. Chest 125 (5):1791–1799
65. Stocker M, Fontana M, El Helou S, Wegscheider K, Berger TM (2010) Use of procalcitonin-guided decision-making to shorten antibiotic therapy in suspected neonatal early-onset sepsis: prospective randomized intervention trial. Neonatology 97(2):165–174, Epub 2009 Sep 24
66. Kopterides P, Siempos II, Tsangaris I, Tsantes A, Armaganidis A (2010) Procalcitonin-guided algorithms of antibiotic therapy in the intensive care unit: a systematic review and meta-analysis of randomized controlled trials. Crit Care Med 38(11):2229–2241, review
67. Bouadma L, Luyt CE, Tubach F, Cracco C, Alvarez A, Schwebel C, Schortgen F, Lasocki S, Veber B, Dehoux M, Bernard M, Pasquet B, Régnier B, Brun-Buisson C, Chastre J, Wolff M; PRORATA trial group (2010) Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial. Lancet 375(9713):463–474, Epub 2010 Jan 25
68. Elward AM, Hollenbeak CS, Warren DK, Fraser VJ (2005) Attributable cost of nosocomial primary bloodstream infection in pediatric intensive care unit patients. Pediatrics 115(4):868–872
69. O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, Masur H, McCormick RD, Mermel LA, Pearson ML, Raad II, Randolph A, Weinstein RA (2002) Guidelines for the prevention of intravascular catheter-related infections. The Hospital Infection Control Practices Advisory Committee, Center for Disease Control and Prevention, U.S. Pediatrics 110(5):e51
70. de Jonge RC, Polderman KH, Gemke RJ (2005) Central venous catheter use in the pediatric patient: mechanical and infectious complications. Pediatr Crit Care Med 6(3):329–339, review
71. Yogaraj JS, Elward AM, Fraser VJ (2002) Rate, risk factors, and outcomes of nosocomial primary bloodstream infection in pediatric intensive care unit patients. Pediatrics 110(3):481–485
72. García-Teresa MA, Casado-Flores J, Delgado Domínguez MA, Roqueta-Mas J, Cambra-Lasaosa F, Concha-Torre A, Fernández-Pérez C; Spanish Central Venous Catheter Pediatric Study Group (2007) Infectious complications of percutaneous central venous catheterization in pediatric patients: a Spanish multicenter study. Intensive Care Med 33(3):466–476, Epub 2007 Jan 19
73. Almuneef M, Memish ZA, Balkhy HH, Alalem H, Abutaleb A (2004) Ventilator-associated pneumonia in a pediatric intensive care unit in Saudi Arabia: a 30-month prospective surveillance. Infect Control Hosp Epidemiol 25(9):753–758
74. Nahum E, Levy I, Katz J, Samra Z, Ashkenazi S, Ben-Ari J, Schonfeld T, Dagan O (2002) Efficacy of subcutaneous tunneling for prevention of bacterial colonization of femoral central venous catheters in critically ill children. Pediatr Infect Dis J 21 (11):1000–1004
75. Levy I, Katz J, Solter E, Samra Z, Vidne B, Birk E, Ashkenazi S, Dagan O (2005) Chlorhexidine-impregnated dressing for prevention of colonization of central venous catheters in infants and children: a randomized controlled study. Pediatr Infect Dis J 24 (8):676–679

76. Ho KM, Litton E (2006) Use of chlorhexidine-impregnated dressing to prevent vascular and epidural catheter colonization and infection: a meta-analysis. J Antimicrob Chemother 58(2):281–287, Epub 2006 Jun 6, review. Erratum in: J Antimicrob Chemother. 2010 Apr;65(4):815
77. Timsit JF, Schwebel C, Bouadma L, Geffroy A, Garrouste-Orgeas M, Pease S, Herault MC, Haouache H, Calvino-Gunther S, Gestin B, Armand-Lefevre L, Leflon V, Chaplain C, Benali A, Francais A, Adrie C, Zahar JR, Thuong M, Arrault X, Croize J, Lucet JC; Dressing Study Group (2009) Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. JAMA 301(12):1231–1241
78. Gillies D, O'Riordan L, Wallen M, Morrison A, Rankin K, Nagy S (2005) Optimal timing for intravenous administration set replacement. Cochrane Database Syst Rev 4:CD003588, review
79. Shah PS, Shah VS (2008) Continuous heparin infusion to prevent thrombosis and catheter occlusion in neonates with peripherally placed percutaneous central venous catheters. Cochrane Database Syst Rev 2:CD002772, review
80. Schroeder AR, Axelrod DM, Silverman NH, Rubesova E, Merkel E, Roth SJ (2010) A continuous heparin infusion does not prevent catheter-related thrombosis in infants after cardiac surgery. Pediatr Crit Care Med 11(4):489–495
81. Pierce CM, Wade A, Mok Q (2000) Heparin-bonded central venous lines reduce thrombotic and infective complications in critically ill children. Intensive Care Med 26(7):967–972
82. Anton N, Cox PN, Massicotte MP, Chait P, Yasui Y, Dinyari PM, Marzinotto V, Mitchell LG (2009) Heparin-bonded central venous catheters do not reduce thrombosis in infants with congenital heart disease: a blinded randomized, controlled trial. Pediatrics 123(3):e453–e458, Epub 2009 Feb 23
83. Henrickson KJ, Axtell RA, Hoover SM, Kuhn SM, Pritchett J, Kehl SC, Klein JP (2000) Prevention of central venous catheter-related infections and thrombotic events in immunocompromised children by the use of vancomycin/ciprofloxacin/heparin flush solution: a randomized, multicenter, double-blind trial. J Clin Oncol 18(6):1269–1278
84. Safdar N, Maki DG (2006) Use of vancomycin-containing lock or flush solutions for prevention of bloodstream infection associated with central venous access devices: a meta-analysis of prospective, randomized trials. Clin Infect Dis 43(4):474–484, Epub 2006 Jul 11, review
85. Chelliah A, Heydon KH, Zaoutis TE, Rettig SL, Dominguez TE, Lin R, Patil S, Feudtner C, St John KH, Bell LM, Coffin SE (2007) Observational trial of antibiotic-coated central venous catheters in critically ill pediatric patients. Pediatr Infect Dis J 26(9):816–820
86. Stover BH, Shulman ST, Bratcher DF, Brady MT, Levine GL, Jarvis WR; Pediatric Prevention Network (2001) Nosocomial infection rates in US children's hospitals' neonatal and pediatric intensive care units. Am J Infect Control 29(3):152–157
87. Matlow AG, Wray RD, Cox PN (2003) Nosocomial urinary tract infections in children in a pediatric intensive care unit: a follow-up after 10 years. Pediatr Crit Care Med 4(1):74–77
88. Davies HD, Jones EL, Sheng RY, Leslie B, Matlow AG, Gold R (1992) Nosocomial urinary tract infections at a pediatric hospital. Pediatr Infect Dis J 11(5):349–354
89. Pratt RJ, O'Malley B (2007) Supporting evidence-based infection prevention and control practice in the National Health Service in England. The NHS/TVU/Intuition Approach. J Hosp Infect 65 (Suppl 2):142–147
90. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR (1999) Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Am J Infect Control 27:97–132, quiz 133–134, discussion 96
91. Horwitz JR, Chwals WJ, Doski JJ, Suescun EA, Cheu HW, Lally KP (1998) Pediatric wound infections: a prospective multicenter study. Ann Surg 227:553–558
92. Mehta PA, Cunningham CK, Colella CB, Alferis G, Weiner LB (2000) Risk factors for sternal wound and other infections in pediatric cardiac surgery patients. Pediatr Infect Dis J 19 (10):1000–1004
93. Pollock EM, Ford-Jones EL, Rebeyka I, Mindorff CM, Bohn DJ, Edmonds JF, Lightfoot NE, Coles J, Williams WG, Trusler GA, Barker GA (1990) Early nosocomial infections in pediatric cardiovascular surgery patients. Crit Care Med 18(4):378–384
94. Segers P, Speekenbrink RG, Ubbink DT, van Ogtrop ML, de Mol BA (2006) Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate: a randomized controlled trial. JAMA 296(20):2460–2466
95. Bode LG, Kluytmans JA, Wertheim HF, Bogaers D, Vandenbroucke-Grauls CM, Roosendaal R, Troelstra A, Box AT, Voss A, van der Tweel I, van Belkum A, Verbrugh HA, Vos MC (2010) Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. N Engl J Med 362(1):9–17
96. De Chiara S, Chiumello D, Nicolini R, Vigorelli M, Cesana B, Bottino N, Giurati G, Caspani ML, Gattinoni L (2010) Prolongation of antibiotic prophylaxis after clean and clean-contaminated surgery and surgical site infection. Minerva Anestesiol 76 (6):413–419
97. Harbarth S, Samore MH, Lichtenberg D, Carmeli Y (2000) Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. Circulation 101(25):2916–2921
98. Kato Y, Shime N, Hashimoto S, Nomura M, Okayama Y, Yamagishi M, Fujita N (2007) Effects of controlled perioperative antimicrobial prophylaxis on infectious outcomes in pediatric cardiac surgery. Crit Care Med 35(7):1763–1768. Erratum in: Crit Care Med. 2007 Sep;35(9):2240
99. Tamayo E, Gualis J, Flórez S, Castrodeza J, Eiros Bouza JM, Alvarez FJ (2008) Comparative study of single-dose and 24-hour multiple-dose antibiotic prophylaxis for cardiac surgery. J Thorac Cardiovasc Surg 136(6):1522–1527
100. Maher KO, VanDerElzen K, Bove EL, Mosca RS, Chenoweth CE, Kulik TJ (2002) A retrospective review of three antibiotic prophylaxis regimens for pediatric cardiac surgical patients. Ann Thorac Surg 74(4):1195–1200
101. Greif R, Akça O, Horn EP, Kurz A, Sessler DI; Outcomes Research Group (2000) Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. N Engl J Med 342(3):161–167
102. Belda FJ, Aguilera L, García de la Asunción J, Alberti J, Vicente R, Ferrándiz L, Rodríguez R, Company R, Sessler DI, Aguilar G, Botello SG, Ortí R; Spanish Reduccion de la Tasa de Infeccion Quirurgica Group (2005) Supplemental perioperative oxygen and the risk of surgical wound infection: a randomized controlled trial. JAMA 294(16):2035–2042. Erratum in: JAMA. 2005 Dec 21;294(23):2973
103. Wong PF, Kumar S, Bohra A, Whetter D, Leaper DJ (2007) Randomized clinical trial of perioperative systemic warming in major elective abdominal surgery. Br J Surg 94(4):421–426