Sohvi Kinnula

HOSPITAL-ASSOCIATED INFECTIONS AND THE SAFETY OF ALCOHOL HAND GELS IN CHILDREN
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Oulu, Finland

Abstract

Viral infections are common in childhood and a usual cause for hospitalization. Viruses are easily transmitted among children both in pediatric wards and in other child care facilities, like child day-care centers. Hand hygiene is an important part of prevention of the transmission of viruses. Since hospitalization times are getting shorter, hospital-associated infections often manifest after discharge.

The aim of the study was to evaluate the magnitude of hospital-associated infections during and after hospitalization in pediatric wards with a focus on the effect of the ward structure. Data were collected during two periods of two years in the pediatric infectious diseases ward in Oulu University Hospital; data collection in the latter period was done using electronic follow-up methods. A two-year study period was also carried out in University Children’s hospital in Basel and in North Karelia Central Hospital in Joensuu. Paper questionnaires and electronic questionnaires were compared as methods of doing continuous surveillance of hospital-associated infections during and after hospitalization. The safety of alcohol-based hand gels in children’s use was studied using alcrometer measurements after hand rub. Experiences on the use of alcohol-based hand gels in child day-care centers were collected by interviewing the personnel with questionnaires.

Altogether 5.8 to 17.5% of hospitalized children (N=7046) got a hospital-associated infection; 65 to 93% of the infections became evident after discharge. The number of hospital-associated infections was lowest in wards where single rooms and cohorting based on infection etiology were used. Increased risk for hospital-associated infection was associated with young age, longer hospitalization time and a shared room. A higher response rate was achieved with electronic follow-up compared with questionnaires on paper, 84 vs. 61%. The costs of follow-up were €13.61 and €15.07 per patient in electronic and conventional follow-up, respectively. Electronic follow-up decreased annual expenses by 17.1%. Alcohol-based hand gels were found to be safe in children’s use, as no absorption was detected despite several contacts between hands and mucous membranes. Personnel in child day-care centers were active in using hand rubs and found them useful and easy to use. Earlier, there had been one incident with fire when using matches while hands were still wet with alcohol.

The majority of hospital-associated infections in children become evident after discharge, and electronic follow-up is useful in evaluating their magnitude. The number of hospital-associated infections can be decreased with single room bedding and careful infection control. Alcohol-based hand gels are safe in children’s hand hygiene.

Keywords: child day care centers, cross infection, hand hygiene, hospital-associated infection, infection control, pediatrics, risk factors, virus diseases
Kinnula, Sohvi, Sairaalinfektiot ja alkoholikäsihuuhteiden turvallisuus lapsilla
Oulun yliopiston tutkijakoulu; Oulun yliopisto, Lääketieteellinen tiedekunta, Kliinisen lääketieteen laitos, PL 5000, 90014 Oulun yliopisto
Oulu

Tiivistelmä


Sairaalainfektion sai 5,8-17,1 % sairaalassa hoidetuista lapsista (N=7046). Infektioiden 65-93 % tuli oireiksi kotiutuksen jälkeen. Sairaalinfektioiden määrä oli pienin osastoilla, joissa käytettiin yhden yksinhuoneen ja potilaiden kohortointia taudinaiheuttajana mukaan. Sairaalinfektion riskiä lisäsi lapsen ikä, ja pitkälti sairaalahoidoita ja jaettu potilashuone. Sähköisessä sairaalinfektioseurannassa oli parempi kotiutuksen jälkeinen vastaustasoa kuin paperilomakkeilla, 84 % vrt. 61 %. Potilasta kohden kuluja tuli sähköisessä seurannassa 13,61 euroa ja paperilomakkeilla tehdysissä seurannassa 15,07 euroa. Sähköisessä seurannan käyttö laski vuosikuluja 17,1 %. Alkoholikäsihuuhteiden käyttö todettiin turvalliseksi lapsilla. Useista lampaalatutkimuksesta huolimatta käsihuuhden käytön jälkeen alkoholia ei imeytynyt verenkiertoon. Käsihuuhteen käyttö päiväkodeissa on aktiivista, ja henkilökunta koki sen helpoksi ja hyödylliseksi. Aiemmin oli tapahtunut yksi vaarallinen tapahtuma tulitikkua sytytettäessä käsin ollessa vielä käsihuuhteen määrät.

Lasten sairaalinfektioiden suurin osa ilmenee kotiutuksen jälkeen, ja näiden infektioiden määrää voidaan arvioida sähköisellä seurantajärjestelmällä. Sairaalinfektioiden määrää voidaan vähentää käyttämällä yhden yksinhuoneita ja huolehtimalla hyvästä hygieniasta. Alkoholihuuhteiden käyttö lasten käsihygieniassa on turvallista.

Asiasanat: käsihygienia, lastentaudut, päiväkodit, riskitekijät, sairaalahygienia, sairaalinfektiot, virusinfektiot
Acknowledgements

This study was carried out at the Department of Pediatrics in the University of Oulu, Finland. Part of the data collection was done in collaboration with the University Children's Hospital in Basel, Switzerland, and with the North Karelia Central Hospital in Joensuu, Finland.

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Rovaniemi, June 2012

Sohvi Kinnula
Abbreviations

ACIP  Advisory Committee on Immunization Practices
AHG   alcohol-based hand gel
AIIR  airborne infection isolation room
CDC   Centers for Disease Control and Prevention
CDCC  child day-care center
CI    confidence interval
ESBL  extended-spectrum β-lactamase
HAI   hospital-associated infection
HCW   health-care worker
MRSA  methicillin-resistant *Staphylococcus aureus*
NICU  neonatal intensive care unit
OR    odds ratio
PICU  pediatric intensive care unit
RSV   respiratory syncytial virus
SD    standard deviation
SENIC Study on the Efficacy of Nosocomial Infection Control
sms   short message service
SSI   surgical-site infection
List of the original publications

This thesis is based on the following original articles, which are referred to in the text by their Roman numerals I–IV.


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Abstract

Tiivistelmä

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Abbreviations

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1 Introduction

Hospital-associated infections (HAI) have mainly been discussed in the light of bacterial infections, as bacteria cause most of the HAIs in adult wards. Especially surgical site infections (SSI) lead to severe and expensive consequences, and infection control procedures were first designed to reduce the number of surgical HAIs. Thus, most recommendations on infection control practices in hospitals have been based on experiences and studies on bacterial infections in adult wards. However, the situation in pediatric wards is different, as the majority of HAIs are viral infections (Allen & Ford-Jones 1990). These respiratory and gastrointestinal infections are spread in pediatric wards, but as they are seldom documented their actual number is not known, even though they cause significant morbidity among children. As the hospitalization times in pediatric acute wards are getting shorter, most of the viral HAIs become evident after hospitalization and remain unreported.

According to the Centers for Disease Control and Prevention (CDC) definition, an infection is hospital-associated when there is no evidence that it was present or incubating at the time of hospital admission. Similarly, an infection that is acquired in hospital and becomes evident after discharge is regarded as hospital-associated (Garner et al. 1988). It has been common to set a time limit for the appearance of the symptoms of HAI at 48 hours counting from the admission to hospital and from the time of discharge. However, as the incubation periods for several viruses are longer than 48 hours, HAI in pediatrics is often defined as new signs of infection after 72 hours after admission to hospital or within the first 72 hours after discharge from hospital for the infections becoming evident at home.

Respiratory and gastrointestinal viruses are easily transmitted in child-care facilities such as pediatric wards in hospitals and child day-care centers (CDCC). We wanted both to identify risk factors for the transmission of viruses and to study the safety of hygienic procedures that are used in infection control in child-care facilities. To evaluate the number of HAIs in pediatric wards we have conducted continuous HAI surveillance, which covers the immediate time after hospitalization.
2 Review of the literature

2.1 Epidemiology of hospital-associated infections in children

The main focus in studies for HAIs is on bacterial HAIs, especially on SSI and device-related infections, as these infections are difficult to treat and cause major expenses. In pediatrics the majority of research on HAIs has been done on neonatal wards with intensive care facilities, where bacteria predominate as causes of HAIs. However, viruses cause most of the respiratory and gastrointestinal infections leading to hospitalization in children (Iwane et al. 2004, McIver et al. 2001, Oh et al. 2003), and these viruses transmit easily in health care facilities causing the majority of HAIs in general pediatric wards (Gleizes et al. 2006, Raymond & Aujard 2000). As viral infections with longer incubation periods often manifest themselves after hospitalization, the magnitude of this problem is not known.

2.1.1 Bacterial hospital-associated infections

Reported frequencies of HAIs in pediatric hospitals vary from 2 to 7% during hospitalization (Ford-Jones et al. 1989, Muhlemann et al. 2004, Welliver & McLaughlin 1984). There is variation in HAI rates between different wards in pediatric hospitals. HAI rates are the highest in neonatal intensive care unit (NICU) and pediatric intensive care unit (PICU), and the lowest in general pediatric wards and infectious diseases wards (Ford-Jones et al. 1989). The most common bacterial HAIs in children are bloodstream infections, SSI and lower respiratory tract infections (Muhlemann et al. 2004).

Hospital-associated infections in intensive care

The risk of bacterial HAIs in children is related to intensive care where the use of invasive medical devices is common (Jarvis & Robles 1996). The risk of bacteremia is increased by the presence of intravascular catheters, especially central venous catheters that are used for longer periods. On average 5% of patients get hospital-associated bloodstream infections in PICU (Raymond & Aujard 2000, Urrea et al. 2003). Hospital-associated bloodstream infections are mostly caused by gram-positive bacteria; coagulase-negative staphylococci.

In addition to the use of invasive devices, patients in NICU are prone to infections due to prematurity, low birth weight and immunological immaturity. It is reported that 7 to 13\% of the patients in NICU get a HAI (Jarvis & Robles 1996, Orsi \textit{et al.} 2009, Raymond & Aujard 2000). The most common HAIs in NICUs are bloodstream infections, the rate of which is about 7\%, and pneumonias, the rate of which is about 4\%. Gram-positive bacteria cause most of the bloodstream infections, coagulase-negative staphylococci being the leading pathogen. Pneumonias are mostly due to gram-negative bacteria, especially \textit{Klebsiella pneumonia} (Jarvis & Robles 1996, Orsi \textit{et al.} 2009, Raymond & Aujard 2000, Sarvikivi \textit{et al.} 2008).

\textbf{Surgical site infections}

SSI is an infection that occurs on the operated site within 30 days after operation. If a foreign body is left on the operated site, the time limit is extended to one year (Mangram \textit{et al.} 1999). The frequency of SSIs is 4.4 to 6.6\% in children according to studies with post-discharge follow-up extended to 30 days after operation (Horwitz \textit{et al.} 1998, Uludag \textit{et al.} 2000). The risk of SSI is increased in contaminated and dirty wounds, with operations with longer duration, emergency operations, and operations done on patients with in-patient status. It seems that in children, factors related to the operation affect the risk of SSI more than patient characteristics and physiologic status. \textit{Staphylococcus aureus}, coagulase-negative staphylococci and gram-negative bacilli cause most of the SSIs (Raymond & Aujard 2000).
2.1.2 Viral hospital-associated infections

There is plenty of variation in the reported number of viral HAIs, due to epidemic seasons of viruses and different surveillance methods (Table 1). The comparison shown in Table 1 includes only surveys focusing on viral infections (Muhlemann et al. 2004). In high epidemic season as many as 17% of hospitalized children in a general pediatric ward may get a hospital-associated respiratory infection caused by respiratory syncytial virus (RSV), rhinovirus, parainfluenza virus or influenza viruses (Wenzel et al. 1977). Outbreaks caused by influenza virus, RSV and rhinovirus have taken place in neonatal units (Cunney et al. 2000, Valenti et al. 1982). In addition, coronavirus may be an important pathogen for HAIs in neonatal wards (Sizun et al. 1995). Most studies on respiratory HAIs focus on RSV that transmits easily and carries significant morbidity especially in young children, and children with history of prematurity, congenital heart disease, bronchopulmonary dysplasia or immunosuppression (Berner et al. 2001, Mlinaric-Galinovic & Varda-Brkic 2000). As the incubation periods for respiratory viruses are rather long, varying from 0.6 days for Influenza B virus to 5.6 days for adenovirus (Table 2), respiratory HAIs often become evident after discharge from hospital and remain underreported (Lessler et al. 2009).

Altogether 4.5 to 14% of patients get gastrointestinal HAI during hospitalization (Table 1), and the majority of them are viral infections. Rotavirus has been the leading cause of hospital-associated gastroenteritis in children before the introduction of rotavirus vaccine. Other documented pathogens are astrovirus, norovirus and other caliciviruses, enterovirus and adenovirus. Viral diarrhea outbreaks in hospitals occur during the winter and spring months, when there is an epidemic season for viral gastroenteritis in communities. Young age increases the risk of gastrointestinal HAI (Bennet et al. 1995, Ford-Jones et al. 1990). Viral causes for hospital-associated gastroenteritis in children are more common than bacteria. *Clostridium difficile* is reported to cause HAIs in older children; these diarrhea episodes occurred throughout the year without seasonality (Langley et al. 2002).
<table>
<thead>
<tr>
<th>Study reference</th>
<th>Wards under surveillance</th>
<th>Infection type</th>
<th>HAI frequency</th>
<th>Duration of surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>In hospital (time after admission for defining HAI)</td>
<td>After discharge (time after discharge)</td>
</tr>
<tr>
<td>Ford-Jones et al. 1989</td>
<td>All</td>
<td>Any</td>
<td>6.0%</td>
<td>ND</td>
</tr>
<tr>
<td></td>
<td>Isolation ward</td>
<td>Any</td>
<td>1.3%</td>
<td>ND</td>
</tr>
<tr>
<td>Welliver &amp; McLaughlin 1984</td>
<td>All</td>
<td>Any</td>
<td>4.1%</td>
<td>ND</td>
</tr>
<tr>
<td>Isolation ward</td>
<td>Gastroenteritis</td>
<td>0.68% (&gt;72 hours)</td>
<td>ND</td>
<td>12</td>
</tr>
<tr>
<td>Isolation ward</td>
<td>Respiratory</td>
<td>0.97%</td>
<td>ND</td>
<td>12</td>
</tr>
<tr>
<td>Raymond &amp; Aujard 2000</td>
<td>20 pediatric units</td>
<td>Any</td>
<td>2.5% (2 to 4 days)</td>
<td>ND</td>
</tr>
<tr>
<td>General pediatric wards</td>
<td>Gastroenteritis</td>
<td>0.4% (4 days)</td>
<td>ND</td>
<td>6</td>
</tr>
<tr>
<td>Jusot et al. 2003</td>
<td>31 pediatric/neonatal wards</td>
<td>Gastroenteritis</td>
<td>3.6% (&gt;48 hours)</td>
<td>Not known</td>
</tr>
<tr>
<td>Grassano Morin et al. 2000</td>
<td>All</td>
<td>Gastroenteritis</td>
<td>11.8% (&gt;72 hours)</td>
<td>5.8% (&lt;5 days)</td>
</tr>
<tr>
<td>Bennet et al. 1995</td>
<td>General pediatric, surgical</td>
<td>Gastroenteritis</td>
<td>14% (&gt;72 hours)</td>
<td>ND</td>
</tr>
<tr>
<td>Ford-Jones et al. 1990</td>
<td>3 pediatric wards</td>
<td>Gastroenteritis</td>
<td>4.5% (&gt;72 hours)</td>
<td>ND</td>
</tr>
<tr>
<td>Wenzel et al. 1977</td>
<td>General pediatric</td>
<td>Respiratory</td>
<td>17% (&gt;6 days)</td>
<td>Not known</td>
</tr>
<tr>
<td>Macartney et al. 2000</td>
<td>All</td>
<td>RSV infection</td>
<td>0.098a (&gt;5 days)</td>
<td>ND</td>
</tr>
<tr>
<td>Isaacs et al. 1991</td>
<td>2 medical wards</td>
<td>RSV infection</td>
<td>4.2% (&gt;5 days)</td>
<td>ND</td>
</tr>
<tr>
<td>Ledlair et al. 1987</td>
<td>Medical ward</td>
<td>RSV infection</td>
<td>0.64a (&gt;5 days)</td>
<td>ND</td>
</tr>
</tbody>
</table>

1 ND=not done, 2 per 100 patient days, 3 Surveillance in six-month periods corresponding to RSV season (November-April)
Table 2. Incubation periods for respiratory viruses\(^1\).

<table>
<thead>
<tr>
<th>Virus</th>
<th>Median incubation period (days)</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenovirus</td>
<td>5.6</td>
<td>4.8 to 6.3</td>
</tr>
<tr>
<td>Coronavirus</td>
<td>3.2</td>
<td>2.8 to 3.7</td>
</tr>
<tr>
<td>Influenza A</td>
<td>1.4</td>
<td>1.3 to 1.5</td>
</tr>
<tr>
<td>Influenza B</td>
<td>0.6</td>
<td>0.5 to 0.6</td>
</tr>
<tr>
<td>Parainfluenza</td>
<td>2.6</td>
<td>2.1 to 3.1</td>
</tr>
<tr>
<td>RSV</td>
<td>4.4</td>
<td>3.9 to 4.9</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>1.9</td>
<td>1.4 to 2.4</td>
</tr>
</tbody>
</table>

\(^1\)Lessler et al. 2009

**Transmission mechanisms of viruses**

There are three basic mechanisms relevant to HAIs describing how microorganisms are transmitted (Siegel *et al.* 2007). Contact transmission can occur via direct and indirect routes. In direct contact transmission a pathogen is transferred via direct physical contact between an infected person and a susceptible host. In indirect contact transmission a pathogen is transferred through the hands of a caregiver or through a contaminated, inanimate object to a susceptible host. Both respiratory and gastrointestinal viruses can survive on a fomite and be transmitted through hands or directly from objects, such as toys or medical equipment (Brady 2005, Coffin & Zaoutis 2005). Respiratory tract infections are also transmitted through large droplets (>10 to 20 μm diameter) produced by coughing and sneezing (Siegel *et al.* 2007). Large droplets contain viral particles and can travel relatively short distances, approximately 1 to 2 meters, inoculating a susceptible host in close proximity. The third mechanism is airborne transmission, where pathogens spread through small-particle aerosols/droplet nuclei that can travel long distances remaining infectious under favorable conditions (Siegel *et al.* 2007, Tang *et al.* 2006). Small-particle aerosols (<5 to 10 μm diameter) are produced by talking, sneezing, coughing and breathing; they are spread by air currents and transmission occurs when they are inhaled. Airborne transmission is difficult to control and carries the potential to cause outbreaks (Tang *et al.* 2006).
Respiratory syncytial virus

RSV is one of the most important respiratory pathogens in infancy and childhood, causing bronchiolitis and pneumonia in young children, which often lead to hospitalization. Older children and adults get milder upper respiratory tract infections. RSV causes the majority of reported pediatric respiratory HAIs (Forster et al. 2004). The epidemic season for RSV occurs during the winter months in the Northern Hemisphere (Berner et al. 2001). Both in Finland and in Switzerland, a major RSV epidemic takes place in the wintertime with two-year periodicity (Duppenthaler et al. 2003, Waris 1991). During the epidemic season 4.2 to 5.3% of patients get a hospital-associated RSV infection (Isaacs et al. 1991, Leclair et al. 1987). The median incubation period of RSV is 4.4 days (Lessler et al. 2009). Young children and those with a history of prematurity are at risk for hospital-associated RSV infection. In addition, mechanical ventilation and nasogastric tube increase the risk of hospital-associated RSV infection in NICU (Valenti et al. 1982).

RSV is an RNA virus that belongs to the paramyxoviridae family. The structure of RSV consists of a nucleocapsid that is enclosed within a lipid envelope (Hall 2004). RSV transmits easily, and almost all children get infected during the first years of life. RSV can remain viable in the environment and be further transferred to hands (Hall et al. 1980). In a clinical experiment it has been shown that RSV transmits through inoculation of large droplets in close contact with a RSV-infected patient and through self-inoculation after touching surfaces contaminated with secretions (Table 3) (Hall & Douglas 1981). No clinical infection occurred after being in the same room at a distance of more than 2 meters from the infected person, suggesting that transmission through small-particle aerosols is unlikely (Hall & Douglas 1981). Later it has been shown that small-particle aerosols containing RSV are unstable in normal indoor air humidity, and under normal conditions airborne transmission does not have a significant role. During acute infection RSV is secreted in large amounts in nasal secretions, more than 10^7 virus particles per milliliter. Secreted viruses remain infectious on countertops for at least 6 hours, and on cloth and paper tissue for 30 minutes (Goldmann 2001, Musher 2003).
Influenza virus

Influenza viruses cause acute respiratory illness that often leads to hospitalization in children and the elderly. Epidemics take place in temperate climates during winter months, and especially during epidemics influenza also transmits in hospitals, with possibly severe consequences (Glezen 2004). The median incubation period is 1.4 days for influenza A and 0.6 days for influenza B (Lessler et al. 2009). During an influenza outbreak in NICU 35% of the neonates were positive for influenza, most of them asymptomatic. One prematurely born infant died. Logistic regression analysis showed that need of mechanical ventilation on admission and twin pregnancy were risk factors for HAI (Cunney et al. 2000).

Influenza viruses belong to orthomyxoviruses, and there are three major types of influenza viruses, A, B and C. They are RNA viruses, covered by a lipid envelope with glycoproteins. Influenza A and B have hemagglutinin and neuraminidase as surface glycoproteins, which are major antigenic determinants defining the subtype and strain of the virus. Influenza C virus is of minor clinical importance. It has a structure with a single glycoprotein with hemagglutinin, esterase and fusion activity (Glezen 2004). Influenza viruses have the ability to transform these antigens by processes called antigenic drift and shift. Antigenic drift is continuous antigenic evolution that occurs through mutation in RNA during the viral replication. Because of antigenic drift there is an influenza epidemic every year, as prior infection does not protect against transformed virus. Antigenic shift is a major change that produces a new subtype of influenza virus. Antigenic shift occurs through transmission of animal virus to humans, or by reassortment of the genes of two viruses of different subtypes that happen to cause a concomitant infection in a host. Antigenic shift happens only in influenza A virus, and produces a novel subtype that has the potential to cause pandemic influenza (Glezen 2004).

Influenza transmits through large droplets when particles produced by coughing or sneezing are inhaled, and through direct contact with secretions (Table 3). At the highest respiratory tract secretions are highly infective containing $10^6$ or more virus particles per milliliter. Spread of influenza can also occur through small-particle aerosols and contaminated hands. However, it is not known what is the main transmission route for influenza virus not known (Brankston et al. 2007, Killingley et al. 2011, Musher 2003). Both influenza A and B viruses can survive on inanimate surfaces 1 to 2 days, depending on temperature and air humidity, and viruses can be transferred from environment to
hands and after that they are shown to remain viable for 5 minutes (Bean et al. 1982). After experimental inoculation of known concentration of H1N1 influenza A virus, it remained culture-detectable in hands at least 60 minutes, which allows indirect transmission through hands (Grayson et al. 2009). Influenza A virus can be detected on environmental surfaces and toys in CDCCs (Boone & Gerba 2005).

Influenza can best be prevented by vaccination, which must be given yearly because of the transformation of viral antigens. Especially children with pulmonary and cardiac diseases and immunodeficiency are at increased risk of hospital-associated influenza if they are not vaccinated (Glezen 2004, Maltezou & Drancourt 2003). As children under six months of age cannot be vaccinated, they are susceptible to hospital-associated influenza (Cunney et al. 2000).

**Rhinoviruses**

Rhinoviruses cause upper respiratory tract infections, wheezing bronchitis and pneumonia. They are probably the most frequent cause of common cold in humans. The epidemic peaks are in the fall and spring, but infections occur throughout the year in temperate climates (Hendley & Gwaltney 1988). The median incubation period for rhinovirus infection is 1.9 days (Lessler et al. 2009). Rhinovirus has been shown to cause HAIs in pediatric and neonatal wards (Valenti et al. 1982, Wenzel et al. 1977).

Human rhinoviruses are divided into three genogroups (A-C). Especially group C rhinovirus is known to cause lower respiratory tract infections and asthma exacerbation in children (Mak et al. 2011, Piralla et al. 2009). Rhinoviruses belong to the family of Picornaviridae. They are small, non-enveloped RNA viruses, with at least 101 serotypes (Atmar 2004). However, the number of rhinovirustypes is greater than this as the classification of viruses is nowadays genetic and new virustypes have been found using PCR technique (Lau et al. 2007, Piralla et al. 2009). Rhinovirus can be transmitted between hands and from an inanimate surface to hands, and further transfer from the hands to conjunctival or nasal mucosa can cause infection (Table 3) (Hendley et al. 1973). In an experimental setting of poker playing with infected and non-infected persons it was shown that rhinovirus transmits through direct contact transmission and through large droplets. No transmission occurred through cards contaminated with secretions when infected persons were not present (Dick et al. 1987). It is
not known which transmission route is predominant, but it seems that prolonged and close contact is needed for transmission of rhinovirus. This is may be related to the rather low viral load, 5 to 2000 infective doses per milliliter, in the nasal secretion of an infected patient (Goldmann 2001, Hendley & Gwaltney 1988, Musher 2003).

Rotavirus

Rotavirus causes gastroenteritis, which may lead to dehydration and hospitalization, especially in young children. The epidemic season for rotavirus is during the winter and spring months in temperate climates. The incubation period for rotavirus infection is 2 to 4 days. Before the start of rotavirus vaccination rotavirus was the most common cause of gastroenteritis that lead to hospitalization in children (Bernstein & Ward 2004, Vesikari et al. 1999). Rotavirus transmits easily in hospitals (Chandran et al. 2006, Fruhwirth et al. 2001b, Gleizes et al. 2006, Lam et al. 1989). Especially children under 2 years of age are afflicted (Pacini et al. 1987). Rotavirus can be transmitted to personnel, and as some of infections in adults are asymptomatic, they can further transmit rotavirus in hospital (Anderson & Weber 2004). Rotavirus has been shown to spread from an outpatient clinic into community causing an outbreak (Li et al. 2011).

Rotavirus belongs to the Reoviridae family, and viral groups A and C are associated with human diseases (Bernstein & Ward 2004). Rotavirus is a non-enveloped RNA virus, the core of which is surrounded by three protein shells. Two outer capsid proteins, glycoprotein (G-protein) and protease-cleavage protein (P-protein), determine the serotype of the virus. The main transmission route for rotavirus is fecal-oral, hands often being the vector in indirect contact transmission (Table 3). In addition, airborne transmission may play some role. During the infection there is high viral load in stools, $10^{12}$ viral particles per gram of stools (Bernstein & Ward 2004). Rotavirus remains infectious on non-porous material (glass, stainless steel and plastic) for several days at room temperature with low to moderate humidity. Survival on cloth is possible for a few days at room temperature and longer at lower temperature (Sattar et al. 1986). Rotavirus can survive at least 4 hours on human hands, and infectious virus can be transferred between hands and between hands and inanimate objects in both directions (Ansari et al. 1988). Direct contact or indirect contact through hands with a contaminated object leads to clinical infection (Ward et al. 1991). During a
rotavirus outbreak in CDCC, virus has been found in environment, the detection rate being the highest in toys (Wilde et al. 1992).

Introduction of rotavirus vaccination into national vaccination programs has reduced the number of severe rotavirus infections. Hospitalization due to rotavirus infection in children has decreased up to 93%, the greatest decline being seen in children younger than 12 months. By national vaccination of young children the number of hospitalizations of older, unvaccinated children has also been shown to decrease, suggesting that there may be an indirect protective effect of rotavirus vaccinations on unvaccinated population (Buttery et al. 2011, Yen et al. 2011). After the first rotavirus vaccine was licensed, there has been a significant decrease in the number of hospital-associated rotavirus infections. The number of rotaviral HAIs has decreased from 0.53 per 1000 patient-days in 2003–2007 to 0.10–0.20 per 1000 hospital-days in 2007 to 2009 (Anderson et al. 2011). Rotavirus vaccination was introduced to Finland in September 2009, after which there has been a decrease in the number of hospitalization due to rotavirus in pediatric wards (Puustinen et al. 2011).

**Norovirus**

Norovirus (previously named Norwalk-like virus and small round-structured virus) causes acute gastroenteritis both in children and adults, and it is the most common cause of gastroenteritis outbreaks worldwide. In children it is estimated that 10 to 15% of severe gastroenteritis is caused by norovirus (Matson 2004). Norovirus infection does not cause long-lasting immunity and re-infections are possible with the same virus strain. There is a peak in norovirus infections during the winter months, but infections occur throughout the year, and some of them can be traced to contaminated food or water. The incubation period ranges from 12 to 48 hours, the mean being 24 hours (Matson 2004). Norovirus transmits both in pediatric and adult wards, infecting typically both patients and personnel (Bennet et al. 1995, Cheng et al. 2006, Ford-Jones et al. 1990, Weber et al. 2005).

Norovirus belongs to Caliciviridae, which are non-enveloped RNA viruses. By their protein structure noroviruses are divided into genogroups GI-GV, and further into several genotypes (Koopmans 2009, Matson 2004). GII.4 genotype has predominated in norovirus outbreaks during the last few decades, and it is known to have caused the majority of endemic infections in Finnish children in 1994–2007 (Puustinen et al. 2012). Norovirus transmits through fecal-oral contact.
transmission (Table 3). Norovirus can remain on a fomite and be further transmitted in indirect contact transmission (Wu et al. 2005). Transmission can also occur through aerosols from viral particles present in vomit (Hall et al. 2011). The peak in viral shedding into stools is 2 to 5 days after infection, when the amount of viral copies can at its highest be $10^{11}$ per gram of stools (Matson 2004). After the inoculation of norovirus viral antigen can be found in stools for a median of 7 days (Atmar et al. 2008). Norovirus is highly contagious; it is estimated that a dose of 18 viral particles is enough to cause an infection (Hall et al. 2011).
<table>
<thead>
<tr>
<th>Virus</th>
<th>Structure</th>
<th>Incubation period (days)</th>
<th>Persistence on dry surfaces</th>
<th>Persistence on hands</th>
<th>Transmission routes</th>
<th>Infectious dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza virus</td>
<td>Enveloped RNA virus</td>
<td>1.4 (IVA&lt;sup&gt;6&lt;/sup&gt;)</td>
<td>1 to 2 days</td>
<td>At least 60 minutes (H1N1)</td>
<td>Direct contact, large droplets, aerosol</td>
<td>2 to 790 TCID&lt;sub&gt;50&lt;/sub&gt;</td>
</tr>
<tr>
<td>RSV</td>
<td>Enveloped RNA virus</td>
<td>4.4</td>
<td>Up to 6 hours</td>
<td>30 minutes</td>
<td>Direct contact, large droplets, fomites</td>
<td>100 to 640 TCID&lt;sub&gt;50&lt;/sub&gt;</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>Non-enveloped RNA virus</td>
<td>1.9</td>
<td>2 hours to 7 days</td>
<td>1 to 3 hours</td>
<td>Direct contact, large droplets, fomites</td>
<td>0.032 to 10 TCID&lt;sub&gt;50&lt;/sub&gt;</td>
</tr>
<tr>
<td>Norovirus</td>
<td>Non-enveloped RNA virus</td>
<td>0.5 to 2</td>
<td>8 hours to 7 days</td>
<td>40 to 60&lt;sup&gt;th&lt;/sup&gt; minutes</td>
<td>Fecal-oral, aerosol, fomites</td>
<td>10 to 100 viral particles</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Non-enveloped RNA virus</td>
<td>2 to 4</td>
<td>6 to 60 days</td>
<td>Over 4 hours</td>
<td>Fecal-oral, fomites, aerosol</td>
<td>10 to 100 TCID&lt;sub&gt;50&lt;/sub&gt;</td>
</tr>
</tbody>
</table>


<sup>4</sup>For respiratory viruses with intranasal inoculation Boone & Gerba 2007, Caul 1994, TCID<sub>50</sub>=tissue culture infective dose

<sup>5</sup>IVA influenza A virus, IVB influenza B virus

<sup>6</sup>IVB influenza A virus, IVB influenza B virus
Other viruses

Also some other viruses have the potential to cause HAIs in pediatric wards. Astrovirus, adenovirus and enteroviruses are known as causes for hospital-associated gastroenteritis (Bennet et al. 1995, Ford-Jones et al. 1990, Langley et al. 2002, Rodriguez-Baez et al. 2002), and coronavirus and parainfluenzaviruses as causes for respiratory HAIs (Ford-Jones et al. 1989, Sizun et al. 1995, Welliver & McLaughlin 1984, Wenzel et al. 1977). Newer respiratory viruses, such as human metapneumovirus, and human bocavirus are reported to cause HAIs among pediatric patients, the clinical significance of which is still unknown (Durigon et al. 2010, Jartti et al. 2012, Kim et al. 2003). Other potential viral causes for pediatric HAIs are varicella and measles (Centers for Disease Control and Prevention (CDC) 2012, Langley & Hanakowski 2000).

2.1.3 Risk factors for hospital-associated infections in children

In children, HAI rates are inversely proportional to age so that young children get HAIs easier, the highest HAI rates being reported in children less than 24 months of age (Ford-Jones et al. 1989). HAI risk increases as the length of hospitalization time increases (Burgner et al. 1996, Jarvis 1987). Comorbidities, particularly neoplasms and congenital illnesses, make children more susceptible to HAIs. Compared to community-acquired RSV infection, hospital-associated RSV infections are more common in children with pre-existing conditions such as prematurity, immunosuppression, and lung or heart disease (Cavalcante et al. 2006, Ford-Jones et al. 1990, Langley et al. 1997). An increased number of roommates increases the risk of hospital-associated diarrhea, and rotavirus is shown to transmit easily to roommates (Ford-Jones et al. 1990, Gaggero et al. 1992, Nakata et al. 1996). On the contrary, roommates are not often documented to be the source for respiratory HAIs; respiratory viruses are transmitted in wards through health care workers, parents and visitors (Slinger & Dennis 2002, Wenzel et al. 1977).

2.1.4 Surveillance methods for hospital-associated infections

Surveillance of HAIs is an essential part of infection control in hospitals. A program with infection control was first shown to be effective in reducing the number of bacterial hospital-associated infections in the Study on the Efficacy of
Nosocomial Infection Control (SENIC) that was initiated by CDC in the 1970s (Haley et al. 1985). This control program included infection surveillance. The study was conducted among adult patients in medical and surgical wards focusing on bacterial HAIs, namely SSIs, urinary tract infections, pneumonias and bacteremias. According to the infection surveillance, the risk of SSI was reduced by 35% in patients with high infection risk and by 41% in patients with low infection risk. Furthermore, the risk of hospital-associated urinary tract infection was reduced by 31% in high-risk patients and by 41% in low-risk patients, the risk of hospital-associated pneumonia was reduced by 27% in surgical patients and by 13% in medical patients, and the risk of hospital-associated bacteremia was reduced by 35% (Haley et al. 1985). The amount of reduction was related to the components of the infection control program and the risk status of the patient for HAI, such as the use of medical devices and surgical wound classification. In the prevention of SSIs a component that made the program effective was regular reporting of the SSI rates to operating surgeons. With other types of HAIs it was shown that adjacent to other surveillance and control procedures at least one full-time-equivalent infection control nurse per 250 beds increased the effectiveness of the program in reducing the number of HAIs (Haley et al. 1985).

Surveillance programs for HAIs are drawn up to collect data, to carry out data management and data analysis, and to communicate the results to the medical and nursing staff. For the health care institution surveillance provides data to describe the baseline rates of HAIs to detect changes in HAI rates and to investigate the reasons for them, and to evaluate the effectiveness of interventions. Data collection can be done by several methods. The most comprehensive method is hospital-wide data collection, where infection control personnel gather data on HAIs prospectively and continuously by using medical records, microbiology and autopsy reports, and by talking personally with nursing staff and meeting patients (Pottinger et al. 1997). This method is time consuming and expensive. In addition, HAI rates from hospital-wide data collection of this kind are not necessarily valid for comparison between hospitals. Other possibilities to organize surveillance are periodic or prevalence surveillance, where data are gathered during specified time intervals or a specified time period (Pottinger et al. 1997). In pediatrics repeated prevalence surveys are used to collect data on HAIs. They may be useful in evaluating the frequency of bacterial HAIs, but because of the seasonality of viral HAIs, their number is probably better evaluated in longitudinal surveillance (Burgner et al. 1996).
Targeted surveillance can be used in HAI studies. In targeted surveillance selected services, certain populations or other specified areas are followed up for HAIs, and accurate HAI risk is assessed within that area. In HAI surveillance an outbreak threshold can be used to automatically recognize sudden peaks in areas where baseline infection rates are already known. The use of outbreak threshold helps to recognize the problem and respond to it quickly (Pottinger et al. 1997). The method of surveillance is chosen so as to be suitable for the selected population to be followed up and for the outcome of interest. Despite the chosen surveillance method, in order to obtain reliable results through surveillance it is important to maintain the intensity of surveillance at the same level throughout the surveillance period (Lee et al. 1998). The same is true for other elements of surveillance, such as the definitions used and the methods that are used for infection rate calculation, which must be consistent over time to obtain HAI rates that are comparable. External comparison of HAI rates is valid only when the elements and intensity of HAI surveillance are similar in the locations that participate in the comparison (Lee et al. 1998).

HAI surveillance during hospitalization can be done prospectively, i.e. during the time when the patient is under the care of the health care organization. Prospective data collection allows interaction with the patient and caregivers. Another way to collect data from the hospitalization period is retrospective surveillance, where data collection is performed by reviewing patient records after the patient is discharged from hospital (Lee et al. 1998). In both methods of data collection administrative databases, patient records, laboratory reports and other ancillary service reports can be used as a source of information.

**Surveillance after discharge from hospital**

The sources described above provide data concerning the hospitalization time. As the definition of HAI includes the time after hospitalization (Garner et al. 1988), surveillance that covers the time after hospitalization is needed to obtain the true HAI rate. This is especially true for certain types of HAIs, e.g. viral infections with longer incubation periods (Lessler et al. 2009) and SSIs, which are defined to occur within 30 days after operation. There is no single method used for post-discharge HAI surveillance (Mangram et al. 1999).

A possibility for post-discharge follow-up is self-reporting of symptoms that can be done for example using questionnaires or phone calls in data collection. Sands et al. showed that 84% of SSIs in adult patients become evident after
hospitalization, and 63% of them were diagnosed and treated in ambulatory settings. In addition to medical record review to find SSIs, patients filled in a follow-up questionnaire where they were asked about wound recovery. Only 33% of patients returned the questionnaire. The sensitivity of positive patient responses was 68% when unreturned questionnaires were excluded from the analysis. The false-positive results were most often due to reporting of a minor wound complication that did not meet the criteria for SSI (Sands et al. 1996). The accuracy of self-reporting is probably related to the subject and symptoms under study. The presence and severity of colds was assessed in a double-blind setting by patients and by trained clinical observer (Macintyre & Pritchard 1989). In that study there was a high correlation between self-assessment and observer-assessment both in evaluating the presence of cold and its severity. Two methods were used in the assessment of colds for patients, a 5-point ordinal scale with descriptive definitions and a continuous numerical scale. Both showed a statistically significant association between physician’s observations and self-reporting of symptoms (Macintyre & Pritchard 1989).

Post-discharge follow-up for pediatric HAIs has seldom been conducted (Table 1). In a French study, post-discharge follow-up was done with phone calls in order to evaluate the number of hospital-associated gastroenteritis during the winter months (Grassano Morin et al. 2000). Gastrointestinal HAI rate was 11.8% (96 per 817 patients) during the hospitalization. Furthermore, 48 patients got diarrhea within 5 days after hospitalization at home, and thus 33% of HAIs became evident after discharge. Follow-up was done with phone calls to parents, and taking into account those who were re-hospitalized due to diarrhea. Fifty-five per cent of the families were reached by phone. Only patients whose diagnosis on admission was other than gastroenteritis were included in the follow-up (Grassano Morin et al. 2000).

Electronic data collection

A continuous and comprehensive HAI surveillance is expensive to organize, especially if post-discharge follow-up is included. As electronic patient records are now in wide use, it is reasonable to develop a surveillance system that uses computerized databases for surveillance both during hospitalization and after hospital stay (Palumbo et al. 2012). When Asthma Quality of Life Questionnaire was filled in both in paper and electronic form by adults, children, and caregivers
for children with asthma, the results showed a high correlation. In addition, respondents found the use of electronic data collection more convenient than questionnaires on paper. Data were collected using a touch-screen display device (Bushnell et al. 2003). Similar results of electronic questionnaires and questionnaires on paper being equivalent in measuring the quality of life and wellbeing have been found elsewhere (Cook et al. 2004, Kleinman et al. 2001, Pouwer et al. 1998).

2.2 Consequences of hospital-associated infections

2.2.1 Historical aspects

The role of the hands of health-care workers (HCW) in transmitting infections in hospitals was noticed for the first time in the 19th century in transmission of puerperal fever. In 1846, Ignaz Semmelweis observed a mortality rate of 10% among women whose deliveries were taken care of by medical students and physicians, whereas the mortality rate was less than 4% among those whose deliveries were handled by midwives in another clinic (Boyce et al. 2002, Lane et al. 2010). He paid attention to the common practice of physicians and medical students to go straight from an autopsy suite to the obstetric ward. Hand washing was done with soap and water, after which a specific odor was still left in their hands. Semmelweis suspected that puerperal fever was caused by agents that were transferred by hands from the autopsy suite, and he introduced the use of chloride of lime in hand hygiene before entering delivery rooms and between patient contacts. This procedure of introducing hand antisepsis reduced the maternal mortality rate in that clinic dramatically (Boyce et al. 2002, Lane et al. 2010). Some years before Semmelweiss’ observations in Austria, Oliver Holmes made similar conclusions of the role of hand hygiene in transmission of puerperal fever in Boston. His colleague died one week after performing a post-mortem examination to a woman who died of puerperal fever, which prompted Holmes to investigate disease transmission. In 1843 he published a paper arguing that unwashed hands are responsible for transmitting puerperal fever among patients. Both Semmelweiss and Holmes got a hostile response to their findings, which were left without notice at their time (Boyce et al. 2002, Lane et al. 2010).
2.2.2 Economical burden of hospital-associated infections

Even today HAIs cause significant morbidity and mortality in both adults and children. In 2002 there were 1.7 million incidents of HAIs in the USA, and they caused 99,000 deaths (Klevens et al. 2007). In addition to excess suffering and deaths, HAIs cause remarkable costs to the health-care system. Additional costs are caused for example by extended hospital stay, increased use of antibiotics and a need of re-operations. Bacterial HAIs cause a major share of the total costs of HAIs in health-care. The mean direct costs of HAI to health-care system per one HAI case are evaluated to be USD36,000 for bloodstream infection, USD26,000 for SSI, USD10,000 for ventilator-associated pneumonia and USD1000 for urinary tract infection (Stone et al. 2005). In the UK it is estimated that a HAI causes 2.9 times higher total costs of hospitalization, and hospitalization time is 2.5 times longer for patients who get a HAI compared with those who do not. This study was conducted among adults in a hospital with a HAI rate of 7.8% during the study (Plowman et al. 2001). In NICU the total costs of hospital care per patient are almost doubled in the case of a HAI, with evaluated extra costs of €12,000 per patient with a HAI. HAI extends hospitalization time with an average of 24 days in NICU, which makes up 72% of the extra costs of HAI (Mahieu et al. 2001).

Viral HAIs cause extra costs to the healthcare system by extending hospitalization time and increasing the need for diagnostic procedures, laboratory tests and radiological examinations. In addition to these direct costs of HAIs for healthcare systems, there are additional costs for society, especially as viral HAIs often become symptomatic after discharge from hospital. These indirect costs include loss of working days by parents and possible re-visits to healthcare facilities due to HAI. Hospital-associated rotavirus infection prolongs hospital stay by 1.7 to 5.9 days. The direct costs of rotavirus HAI for hospitals in Western Europe are reported to range from €1000 to €2500 per patient (Gleizes et al. 2006). In Austria, the total cost of rotaviral HAI is evaluated to be €2400 per patient. Most of these costs are direct medical costs (€1500), followed by costs for the third party payer (€800) and costs for the family (€120) (Fruhwirth et al. 2001a). Costs of hospital-associated lower respiratory tract infection are €2800, the majority being direct medical costs. HAI of lower respiratory tract extends hospitalization time by seven days (Ehlken et al. 2005). Earlier, direct medical costs for hospital-associated RSV infection were evaluated to be USD9400 using
case-control comparison (Macartney et al. 2000). During one influenza season 11 hospital-associated influenza infections caused additional costs of USD83,000, on average USD7500 per one HAI case (Serwint & Miller 1993).

2.3 Prevention of hospital-associated infections

2.3.1 Isolation practices

Isolation procedures to prevent hospital-associated infections

In patient care isolation procedures are discussed in the light of two categories, as suggested by CDC (Siegel et al. 2007). Standard precautions are used in all medical care, and they are based on the principle that all body fluids, blood, secretions (except sweat), excretions, non-intact skin and mucous membranes may contain infectious agents. Use of gloves is recommended in those contacts. In addition, hand hygiene is recommended before and after every patient contact. Other barrier and protective methods are used based on the anticipated exposure. Transmission-based precautions are used when a patient is known or suspected to have a contagious disease, and they are used in addition to the principles of standard precautions (Siegel et al. 2007). Transmission-based precautions are classified as contact precautions, droplet precautions and airborne precautions, which are carried out with the use of personal protective equipment and patient placement (Table 4). Personal protective equipment - gloves, gowns, masks, goggles and N95 filtering facepiece respirator (N95 respirator, which corresponds to filtering facepiece 3 (FFP3) mask in Europe) - are used to protect HCWs from being infected and contaminated (Siegel et al. 2007). Masks and goggles protect mucous membranes, and particulate respirators protect reliably against inhalation of aerosols. Another part of isolation practices concerns patient placement. If single rooms are not available, cohorting of infected patients to a certain area is an option to limit the spread of pathogens in the ward. HCWs can further be cohorting to work in either clean or contaminated parts (Siegel et al. 2007).
Table 4. Transmission-based isolation precautions.

<table>
<thead>
<tr>
<th>Precaution method</th>
<th>Contact precaution</th>
<th>Droplet precaution</th>
<th>Airborne precaution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gloves²</td>
<td>Recommended</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gowns²</td>
<td>Recommended</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mask²</td>
<td>-</td>
<td>Recommended</td>
<td>If respirator is not available</td>
</tr>
<tr>
<td>N95 respirator</td>
<td>-</td>
<td>-</td>
<td>Recommended</td>
</tr>
<tr>
<td>Single room</td>
<td>Preferred; if not possible, cohering and &gt;2 m separation between beds</td>
<td>Preferred; if not possible, cohering and &gt;2 m separation and curtain between beds</td>
<td>Single bedding in airborne infection isolation room (AIIR)³</td>
</tr>
</tbody>
</table>

When using gowns, masks, and N95 respirators, the separation between beds should be >2 m. Recommended use of gowns is based on the principles of standard precautions in all patients. Use of N95 respirators is recommended if respirator is not available. Single room use is preferred; if not possible, cohorting and >2 m separation and curtain between beds.

³AIIR has monitored negative pressure relative to surrounding area, 6 to 12 air exchanges per hour and air exhausted directly outside or recirculated through high efficiency particulate air filtration.

Efficacy of contact and droplet precautions in preventing pediatric hospital-associated infections

Hospital-associated RSV infection rates have been shown to decrease with high compliance to use of gown and gloves by HCWs while caring for RSV infected patients (Leclair et al. 1987), and by cohorting of patients based on RSV screening on admission (Krasinski et al. 1990, Leclair et al. 1987). In one study a combination of these procedures was needed to reduce hospital-associated RSV infections (Madge et al. 1992). The use of masks and goggles while caring for RSV infected patients reduces the number of RSV infection among HCWs (Agah et al. 1987). Furthermore, an intervention involving informing HCWs and parents of the importance of hand washing, increasing the possibilities to use alcohol containing hand rub, and cohorting of RSV infected patients to a separate unit led to a reduction of a pre-intervention RSV HAI rate of 4.2% to 0.6% and 1.1% after intervention (Isaacs et al. 1991). Preventing RSV transmission in pediatric wards is cost-effective (Macartney et al. 2000). An infection control program with education of HCWs about disease transmission, use of gowns and gloves, cohorting RSV positive patients, cohorting nurses, and regular HAI surveillance reduced the RSV HAI rate by 39% with a cost-benefit ratio of 1:6 (Macartney et al. 2000). Contradictory to these results, it has also been documented that the use of gowns by HCWs is associated with increased risk of RSV transmission (Langley et al. 1997). It has been shown that good compliance with hand hygiene is needed when using gowns, gloves and masks. After removing personal
protective equipment hands and clothes are usually contaminated with virus from this barrier equipment (Casanova et al. 2008).

Single-room bedding is effective in the prevention of hospital-associated gastroenteritis. The risk of hospital-associated gastroenteritis increases as the number of roommates in pediatric wards increases (Ford-Jones et al. 1990). By analyzing rotavirus strains it has been shown that in 81% of hospital-associated rotavirus infection the same rotavirus strain had caused infection in a roommate (Gaggero et al. 1992), but rotavirus spreads also between patients located in different rooms in pediatric wards (Nakata et al. 1996). Keeping the patient room door closed and restricting the patient from moving out of the room are associated with lower risk of hospital-associated diarrhea. The risk was also lower in healthcare units where the number of patients was under 20, compared with units with more patients (Jusot et al. 2003). The rate of hospital-associated gastroenteritis is described to be the lowest in infectious diseases ward and isolation ward in pediatric hospitals (Ford-Jones et al. 1989, Pacini et al. 1987). Cohorting of nurses, and using gowns and chlorhexidine in hand hygiene are effective in preventing bacterial gastroenteritis from spreading in pediatric wards, but rotavirus HAIs were documented despite these precautions (Lam et al. 1989).

There is less evidence on how to effectively prevent norovirus transmission in healthcare settings. Most of the data are from outbreak studies rather than randomized trials (Koopmans 2009). Recommended strategies are cohorting of infected patients, proper hand hygiene and environmental cleaning and disinfection. In addition, contact precautions and the use of gloves and aprons in the care of infected patients is recommended (Chadwick et al. 2000, Dancer 2009, Hall et al. 2011). During a norovirus outbreak restricting infected HCWs from work until they are 48 to 72 hours symptom-free and preventing the movement of HCWs between affected and unaffected areas have been recommended (Chadwick et al. 2000). However, in a recent meta-analysis, which evaluated the efficacy of infection control procedures started during a norovirus outbreak, there was no evidence of the efficacy of infection control measures on the length of the outbreak or attack rates. In the studies that were analyzed intensified hand hygiene, enhanced environmental cleaning, and restriction of infected staff from work were used to prevent the spread of disease (Harris et al. 2010). In addition to other infection control measures, closure of the affected unit may be needed to stop the outbreak (Weber et al. 2005).
Prevention of airborne transmission

Pathogens’ ability to use airborne transmission can be classified as obligate, preferential or opportunistic, describing the importance of airborne transmission in the spread of a disease (Roy & Milton 2004). Obligate airborne transmission refers to diseases that are spread practically only through aerosol, such as tuberculosis. Diseases with preferential airborne transmission can also use other transmission routes, but the spread by small-particle aerosol is predominant (e.g. measles and varicella). Diseases with opportunistic airborne transmission use naturally some other transmission route but are spread through aerosols under favorable circumstances. As contamination of air is more difficult to detect than contamination of hands or environmental surfaces, airborne transmission is often left without notice in cases involving other than well-known airborne transmission (Roy & Milton 2004, Siegel et al. 2007). Pathogens that have some part of their lifecycle in the respiratory tract have the potential for airborne transmission. Under certain conditions aerosols may have a role in transmission of many respiratory pathogens, such as influenza, rhinovirus and RSV, which usually transmit through contact and droplet transmission (Brankston et al. 2007, Goldmann 2001, Siegel et al. 2007). Viruses causing gastroenteritis transmit mainly through fecal-oral contact transmission, where the pathogen is often inoculated through contaminated hands. In addition, gastrointestinal viruses transmit by indirect contact transmission from contaminated environment. Airborne transmission is also a possible route, which can explain the high infectivity of rotavirus and norovirus (Chadwick et al. 2000, Chandran et al. 2006, Goldmann 1992).

There are particular respirators (N95 or higher level) to prevent the inhalation of aerosol. Aerosol production can be contributed to by medical procedures like bronchoscopy, tracheostomy and the use of nebulizers, which set HCWs under greater risk infection (Siegel et al. 2007). In addition to personal protection, architecture and ventilation impact the spreading of contagious aerosols in healthcare facilities (Tang et al. 2006). Airflow directions are dependent on air pressure in neighboring rooms and corridors, which are sensitive to air temperature, opening of windows and doors and the use of mechanical fans. Ventilation ensures that inhaled air is safe and free of infectious particles. Mixing of contaminated air with uncontaminated air reduces the peak concentration of small-particle aerosols in the air, reducing the risk of infection for a certain
amount of time (Tang et al. 2006). Another way to ventilate is to dilute contaminated air with fresh air. The recommended ventilation flow rate in new isolation rooms is at least 12 air changes/hour. For isolation rooms constructed before 2001 ventilation flow rate of 6 air changes/hour is accepted (Siegel et al. 2007). A third aspect in ventilation is to control the airflow to move from HCWs to patient, which is done by placing patients close to exhaust vents. Rooms with air isolation have negative air pressure compared to surrounding area to prevent the contaminated air from flowing out of isolation rooms to clean areas. A minimum of 2.5 Pa negative pressure in relation to corridors is recommended (Tang et al. 2006).

2.3.2 Hygienic procedures

Hand hygiene

Hand hygiene has had a leading role in infection control in healthcare (Boyce et al. 2002). Both hand washing with soap and water and antiseptic agents can be used in hand hygiene. In the late 20th century, non-antimicrobial soap was still recommended to be used in hand hygiene between patient contacts in routine patient care, and antiseptic agents were recommended to be used only in certain circumstances, such as invasive procedures, with patients at high risk for infection, and if water and soap were not available (Larson 1988, Larson 1995). However, hand washing with soap and water between every patient contact is time consuming and leads to skin irritation, and it has now widely been replaced by the use of antiseptic hand gels in healthcare settings (Boyce et al. 2002).

Many common viruses, among them rhinovirus, RSV and rotavirus, are able to survive on human hands and can be further transmitted through them (Sattar et al. 2002). The latest CDC guideline recommends the use of alcohol-based hand gel (AHG) in routine patient care as the first choice for hand hygiene (Boyce et al. 2002). Hand washing with soap and water is recommended before the use of AHG when hands are visibly dirty, soiled or contaminated with protein-containing material. The efficacy of soap and water in hand washing is based on the detergent properties of soap and the mechanical removal of dirt and organic substances from hands, but there is minimal antimicrobial activity. AHGs are now widely used in healthcare facilities as they have been shown to be effective against both against gram-positive and gram-negative bacteria, fungi and many
viruses, especially viruses with lipophilic envelope (Boyce et al. 2002). Besides products containing alcohol, there are other possibilities for antiseptic agents. Chlorhexidinegluconate is effective against gram-positive bacteria and enveloped viruses, but less effective against gram-negative bacteria, non-enveloped viruses and fungi. It has greater residual activity than AHGs. Iodine and iodophores have bactericidal activity against bacteria and they are active against viruses and fungi. In hand hygiene they may cause more problems with skin irritation than other antiseptics used. In addition, hexachlorophene, alkyl benzalkonium chlorides and other quaternary ammonium compounds, and triclosan were earlier used in hand hygiene, but they are no longer recommended because of lack of efficacy or toxic adverse effects (Boyce et al. 2002). Newer water-based hand disinfectant containing polyhexamethylene guanidine is shown to have an efficacy against bacteria that is equal to that of AHGs (Agthe et al. 2009).

The antimicrobial activity of alcohols is based on their ability to cause cell membrane damage and to denature proteins. Alcohol concentration of 60 to 90% is optimal for antiseptics, and both ethanol and isopropanol are used. Viruses with a lipophilic envelope, for example influenza virus and RSV, are more sensitive to AHGs and other antiseptic agents than non-enveloped viruses, such as adenovirus, rhinovirus rotavirus and norovirus (Table 5) (Krilov & Harkness 1993, McDonnell & Russell 1999, Platt & Bucknall 1985). Both AHGs containing ethanol or isopropanol and hand washing with soap and water are effective in reducing H1N1 influenza A virus concentration from contaminated hands. After each hand hygiene protocol no culture detectable virus was found. When assessed by PCR hand washing with soap and water was slightly superior to AHGs (Grayson et al. 2009). Antiseptic agents containing 70% alcohol caused the greatest reduction (mean log₁₀ reduction 2.8 to 3.9 in plaque forming units) in rotavirus titers measured before and after hand rub. Of the other antiseptics triclosan had the best efficacy against rotavirus, followed by chlorhexidine, iodine, parachlorometaxylenol and plain soap (Ansari et al. 1989, Bellamy et al. 1993). AHG containing 60% ethanol is effective against non-enveloped viruses, rotavirus, rhinovirus and adenovirus reducing the infectivity titer by 2.9 to 4.2 log₁₀ (Sattar et al. 2000).

It is not so well known what is the most effective antiseptic against non-enveloped norovirus, as norovirus is difficult to cultivate and there is a lack of in vitro studies. Both feline calicivirus and murine norovirus have been used as surrogates for human norovirus. Murine norovirus is more sensitive to ethanol
than feline calicivirus (Table 5) (Park et al. 2010, Sattar et al. 2011). It has been shown that ethanol has better efficacy than isopropanol against feline calicivirus (Kampf et al. 2005). Furthermore, AHGs with rather low ethanol concentration (50 to 70%) and low pH may have better efficacy reducing the infectivity of feline calicivirus, but it has been questioned whether feline calicivirus is a good model for human norovirus (Park et al. 2010, Sattar et al. 2011). A novel hand rub containing 70% ethanol, polyquaternium polymer and citric acid was reported to have good efficacy against non-enveloped viruses. The infectivity of feline calicivirus was reduced 4.8 log_{10}, and that of murine norovirus was 3.7 log_{10}. This hand rub had good efficacy also against rotavirus and adenovirus (Macinga et al. 2008). GII.4 human norovirus RNA titers were reduced 1.2 and 1.8 log_{10} PCR units/mL by the 5 minutes exposure to 90% concentrations of ethanol and isopropanol, respectively (Park et al. 2010), but the detection of a decrease in RNA titers may not be a reliable method of studying the efficacy of antiseptics. It has been reported that AHG with 62% ethanol was less effective against human norovirus than hand washing with triclosan-containing soap and water when efficacy was evaluated with PCR detection (Liu et al. 2010). Hand washing with soap and water together with the use of ethanol containing AHG is currently recommended for hand antisepsis against norovirus in Finland (Kuusi et al. 2007).
Table 5. Activity of antiseptic agents against viruses.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Structure of the virus</th>
<th>Hand washing with soap</th>
<th>Ethanol (60 to 95%)</th>
<th>Propanol (70% propan-1-ol/propan-2-ol</th>
<th>Chlorhexidine</th>
<th>Triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza virus(^1)</td>
<td>Lipid enveloped</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>ND</td>
</tr>
<tr>
<td>RSV(^2)</td>
<td>Lipid enveloped</td>
<td>ND</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>ND</td>
</tr>
<tr>
<td>Rhinovirus(^3)</td>
<td>Non-enveloped</td>
<td>ND</td>
<td>+++</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Rotavirus(^4)</td>
<td>Non-enveloped</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Feline calicivirus(^5)</td>
<td>Non-enveloped</td>
<td>ND</td>
<td>++ (+++ with pH 2 to 3)</td>
<td>+</td>
<td>-</td>
<td>+++ (pH 3.0)</td>
</tr>
<tr>
<td>Murine norovirus(^6)</td>
<td>Non-enveloped</td>
<td>ND</td>
<td>+++</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

+++ = >3.0 log\(_{10}\) decrease in infectivity  
++  = 2.0 to 3.0 log\(_{10}\) decrease in infectivity  
+=1.0 to 2.0 log\(_{10}\) decrease in infectivity  
-<< 1.0 or no decrease in infectivity  
ND = No data  
\(^2\)Krilov & Harkness 1993, Platt & Bucknall 1985  
\(^5\)Sattar et al. 2011, Kampf et al. 2005, Park et al. 2010  
\(^1,2,3,4,5\)Bloomfield et al. 2007, Boyce et al. 2002, McDonnell & Russell 1999
Improved hand hygiene leads to a decrease in the number of HAIs in pediatric wards. During a hand hygiene intervention with an introduction of AHGs in a pediatric hospital rotaviral HAI frequency decreased from 5.9 to 2.2 per 1,000 discharged patients. With the intervention the overall hand hygiene compliance increased from 62% to 81%, and the use of AHG increased from 4% to 29% of all occasions when hand hygiene was practiced (Zerr et al. 2005). Improved hand hygiene with the availability of AHGs together with cohorting of RSV infected patients is effective in preventing RSV transmission in pediatric wards (Isaacs et al. 1991). Similarly to pediatric wards, viral infections are transmitted in other childcare facilities, such as CDCCs and schools. It has been shown that children attending CDCC are at increased risk for respiratory tract infections and diarrhea (Louhiala et al. 1995, Louhiala et al. 1997). The number of infections among children and personnel in CDCC can be reduced by introducing AHGs into hand hygiene among CDCC personnel together with improving hygiene with food serving, diaper changing and cleaning (Uhari & Mottonen 1999). Use of AHG in the homes of families where children attend CDCC reduces the transmission of gastroenteritis among family members. Transmission of respiratory tract infections can be reduced by active use of AHG in families (Sandora et al. 2005).

In an elementary school the number of influenza A infections decreased after an intervention with recommendation to use AHG in hand hygiene and teaching cough etiquette. There was no effect on influenza B infections. The number of absence episodes from school was lower in the intervention group than in control schools (Stebbins et al. 2011).

One obstacle in reducing the occurrence of HAI is HCWs’ compliance to hand hygiene. Better hand hygiene compliance can be achieved with AHGs compared to hand washing with soap and water, which leads to a decrease in HAI rates including MRSA infections (Pittet et al. 2000). Hand hygiene compliance is documented to be 53% in PICU and 61% in NICU, being higher before patient contact and aseptic tasks than after contact with patient and the surroundings (Scheithauer et al. 2011), whereas hand hygiene compliance of only 22% was documented in adult ICU (Kim et al. 2003). Among HCWs nurses have better compliance to hand hygiene compared to physicians (Costers et al. 2012, Pittet et al. 2000, Scheithauer et al. 2011). To achieve better hand hygiene compliance educational intervention is needed besides the introduction of AHGs as an option for hand hygiene (Harbarth et al. 2002). Hand hygiene campaigns with reminders, HCW education, promotion of AHGs, informing patients and audits with
feedback increase the hand hygiene compliance in health-care settings, part of which is sustained over longer periods (Custers et al. 2012). Better compliance achieved by AHGs is mostly because by bed-side-placing they are easily available, and they are quicker to use than soap and water in hand hygiene (Voss & Widmer 1997). It has been questioned whether commercial alcohol-containing hand gels have as good antimicrobial efficacy as alcohol-containing rinses (Kramer et al. 2002). However, it has later been shown that in clinical use the antimicrobial efficacy of alcohol containing antiseptics is more related to the concentration and type of the alcohol than the form (gel or rinse) of the product (Barbut et al. 2007).

**Environmental disinfection**

Environmental contamination has a role in the transmission of microorganisms in hospitals, especially in that of bacteria with antimicrobial resistance and viruses (Cozad & Jones 2003, Dancer 2009, Sattar 2004). Viruses can remain on a fomite for hours or days, and are further transmitted through contaminated surfaces (Ansari et al. 1988, Boone & Gerba 2007, Kramer et al. 2006, Sattar et al. 1986, Ward et al. 1991, Wu et al. 2005). It is suggested that continuous monitoring of surface contamination to assess cleanliness is beneficial in all healthcare settings (Dancer 2009). Cleaning can be done using detergents that remove organic material, disinfectants that inactivate or kill infectious particles, or using combination of these. Disinfectants are classified as high-level intermediate-level and low-level disinfectants (Hota 2004). Patient care areas are recommended to be cleaned using detergent-disinfectants. “Terminal cleaning” is done in patient rooms after discharge using disinfectant (Hota 2004). Areas in close proximity to patients and hand-touch sites are to be cleaned regularly and with efficient disinfectants (Dancer 2009).

Lipid-enveloped and medium-size viruses are in general sensitive to detergents and they can be inactivated by low-level disinfectants, whereas non-enveloped viruses are more resistant and require intermediate level disinfection (Rutala et al. 2008). Ethanol at concentrations of 60 to 80% is a virucidal disinfectant against enveloped viruses, such as influenza virus and herpes virus, and against many non-enveloped viruses, e.g. adenovirus, enterovirus, rhinovirus and rotavirus. Isopropanol is virucidal against enveloped viruses but it has less efficacy on non-enveloped gastrointestinal viruses (Rutala et al. 2008). Peroxygen
compounds are newer, promising disinfectants, which are effective against many pathogens including viruses and spores (Dettenkofer & Block 2005, Dettenkofer & Spencer 2007). Among peroxygen compounds monopercitric acid was shown to have better efficacy against enveloped vaccinia virus and non-enveloped adenovirus and poliovirus than peracetic acid (Wutzler & Sauerbrei 2004).

Rotavirus, norovirus and rhinovirus are examples of non-enveloped viruses relevant in pediatric settings. Rotavirus survives several days on environmental surfaces in a fomite and even longer if it is suspended in feces (Kramer et al. 2006). Phenolic/ethanol-containing spray is more effective in reducing rotavirus titer from steel disks than sodium hypochlorite or phenol-based products, but all of these products interrupt transfer of rotavirus from disks to fingers in an experimental setting (Sattar et al. 1994). Quaternary ammonium compounds do not have effect greater than water in removing rotavirus (Sattar et al. 1994). Use of phenol/ethanol spray prevents the transmission of clinical infection from rotavirus-contaminated surfaces into humans (Ward et al. 1991). Human norovirus is shown to persist on a contaminated surface up to 7 days (Kramer et al. 2006), and environmental contamination has been found in outbreaks in healthcare settings (Wu et al. 2005). Feline calicivirus, a norovirus surrogate, can be inactivated by sodium hypochlorite, glutaraldehyde and iodone-based products (Sattar 2004, Weber et al. 2010). The efficacy of alcohols against feline calicivirus has not been consistent in experiments. However, human norovirus is thought to be more resistant to disinfectants than feline calicivirus. In a study, where norovirus was detected by PCR after cleaning the contaminated surface, cleaning with detergent followed by disinfection with sodium hypochlorite (chlorine concentration 5000ppm) was the most effective method in eliminating the contamination and preventing further transfer (Barker et al. 2004). Sodium hypochlorite (chlorine concentration of 1000 to 5000ppm) is currently recommended to be used as disinfectant on norovirus-contaminated surfaces (Weber et al. 2010). Phenol/ethanol-containing disinfectant and sodium hypochlorite are effective against rhinovirus preventing the transmission from contaminated disks to fingers, whereas quaternary ammonium- and phenol-based products have significantly less efficacy (Sattar et al. 1993).

It is well documented that certain pathogens, including many viruses, survive on environmental surfaces (Boone & Gerba 2007). However, there is less evidence about the connection of environmental contamination to the number of HAIs (Hota 2004). In few studies done on the effect of routine surface disinfection on HAI rates, there was no significant difference in HAI rates after
the use of disinfectants versus detergents in cleaning (Dettenkofer et al. 2004). Thus, there is no international consensus on the routine disinfection of non-critical surfaces in health-care settings (Daschner & Schuster 2004, Rutala & Weber 2004). An intervention with improved environmental disinfection in a preschool, including the use of disinfectants for cleaning, disinfection of toys and surfaces in the school bus, and improved hand hygiene, decreased the number of respiratory tract and gastrointestinal infections in preschool children (Krilov et al. 1996). Regular washing of toys and cleaning of surfaces together with intensified hand hygiene with AHG reduced the number of infections among children and personnel in CDCCs (Uhari & Mottonen 1999).

2.3.3 Safety of hygienic procedures

Disinfectants have the potential of being harmful both to patients and personnel in health care and to environment. Extensive use of certain disinfectants, (e.g. quaternary ammonium compounds, chlorhexidine, aldehydes) in low concentrations may lead to development of resistance bacteria, and disinfectants cause pollution of water systems (Daschner & Schuster 2004, Dettenkofer & Block 2005). Many disinfectants, aldehydes, quaternary ammonium compounds, triclosan and sodium hypochlorite, are reported to cause skin irritation and allergies (Daschner & Schuster 2004). However, the relevance of these hazards has been questioned (Rutala & Weber 2004). Peroxygen compounds are probably safer for consumer and environment (Dettenkofer & Block 2005, Dettenkofer & Spencer 2007).

Absorption of substances from the skin is different in children than in adults, which is especially true in the neonatal period. Hexachlorophene and chlorhexidine were earlier used in bathing of newborn infants to reduce the number of staphylococcal colonization and infections. This was stopped as these antiseptic products were shown to absorb from intact skin into circulation both in term and preterm neonates (Coven et al. 1979, Curley et al. 1971). Hexachlorophene is neurotoxic; spongiform changes in myelinated tracts of the brainstem were found in preterm infants after being bathed with hexachlorophene. The type of myelinopathy was similar to what had been seen after hexachlorophene intoxication in animal experiments (Powell et al. 1973). It is not well known how alcohol is absorbed percutaneously. There are single reports of toxic absorption of alcohol from skin in children when alcohol was used in
antisepsis. The use of methylated ethanol in skin antisepsis in a premature neonate led to hemorrhagic skin necrosis and a rise in blood ethanol and methanol levels (Harpin & Rutter 1982). In a two-year old girl pre-operative use of bandages soaked with ethanol led to skin damage and a rise of blood ethanol level up to 0.8‰ (Puschel 1981). The introduction of AHGs in public places raised discussion in the USA of whether the presence of AHGs should be seen as a fire hazard as alcohol products are flammable (Voss et al. 2003). However, only few cases of fire incidents have been reported during the time with widespread use of AHGs. In Germany seven non-severe cases of fire occurred per 25,038 hospital years of AHG use. Four incidents were related to HCWs’ use of matches or cigarette lighter while hands were still wet with AHG. Two cases were due to vandalism and one caused by a suicidal intention (Kramer & Kampf 2007). After a couple of years of AHG use in healthcare facilities in the USA, no fire incidents related to AHGs were reported (Boyce & Pearson 2003).

Problems with skin are one of the most commonly reported reasons for low compliance to hand hygiene among HCWs. Skin irritation and dryness of hands with the use of AHG and chlorhexidine-containing soap was evaluated in a trial where these products were used for hand hygiene during two study periods (Boyce et al. 2000). Both self-assessment and objective visual assessment of skin irritation and dryness suggested that regular AHG use causes less skin problems than hand washing with antimicrobial soap and water. When epidermal water content was assessed by electrical capacitance measurements, it was shown that hand washing with soap and water decreased the epidermal water content significantly whereas no significant change was seen after the period with regular AHG use (Boyce et al. 2000). There are differences between AHG products from different manufacturers when it comes to skin irritation, which affects HCWs compliance to AHG use (Barbut et al. 2007, Girard et al. 2006). In a double-blinded, randomized setting among nurses in ICU, skin tolerability of AHG was significantly affected by the type of emollient in the AHG; among the AHGs available HCWs preferred that with glycerol. The type of alcohol, ethanol compared to isopropanol, did not affect the skin tolerability of AHG. Other factors that were significantly associated with skin alteration were male sex, fair skin and skin alterations before the study (Pittet et al. 2007).
2.3.4 Current strategies in organizing prevention of hospital-associated infections

Pediatric aspects in organizing prevention

Both isolation policies and hygienic procedures have been shown to have an effect on the spread of infections in pediatric wards. Gastroenteritis transmits easily to roommates (Ford-Jones et al. 1990, Gaggero et al. 1992, Nakata et al. 1996). Isolation precautions, gloves and gowns, and cohorting, reduce the number of HAIs caused by RSV, especially when combined with good compliance with hand hygiene (Isaacs et al. 1991, Leclair et al. 1987, Macartney et al. 2000, Ruuskanen 1995). Both respiratory and gastrointestinal viruses can remain viable on environmental surfaces (Kramer et al. 2006), and unless disinfection is appropriate they can be transferred through HCWs’ hands to patients, or directly from surfaces or inanimate objects, such as toys, to patients. As hands can act as vector for viruses, hand hygiene among HCWs is one of the single most important precautions to prevent the spread of viruses. In pediatric wards, where viruses cause most of the HAIs, AHGs are the first choice for hand hygiene (Boyce et al. 2002). However, hand washing with soap and water may have better efficacy than alcohol against norovirus and influenza virus (Grayson et al. 2009, Hall et al. 2011, Liu et al. 2010).

The lowest HAI rates in pediatric hospitals have been reported in isolation ward and infectious diseases ward (Ford-Jones et al. 1989, Pacini et al. 1987). Pacini et al. described their infectious diseases ward as two-person rooms, where the only difference in the ward structure compared to other wards was an anteroom, a wider space at the entrance to patient room with a sink, hand washing agents, and gowns and gloves available. The authors thought that the main reason for the lower number of rotaviral HAIs in the infectious diseases ward was better compliance with hand hygiene and that isolation policies were better followed, as HCWs were used to caring for patients with infectious diseases. These data suggest that separate wards for infectious diseases are preferable in pediatrics in order to prevent HAIs. Crowding in the ward may be an important risk factor for HAI. Patient density and nursing hours per patient days are associated with the number of HAIs in pediatric wards so that there are more HAIs during the times when patient density is high and there is nurse understaffing (Archibald et al. 1997, Moisiuk et al. 1998, Stegenga et al. 2002). There were a significant
correlation between the monthly patient to nurse ratio and the gastrointestinal HAI rate. During the times that preceded gastrointestinal HAI the mean nursing hours per patient day was 12.5 compared to 13.0 during the time after which there were no HAIs (p<0.05). In the periods with low staffing (nursing hours per patient day less than 10.5) the risk of gastrointestinal HAI was almost three times higher than during other times (Stegenga et al. 2002).

Rotavirus infection can be asymptomatic, and rotavirus has been found in the stools of symptom-free children in hospital (Dearlove et al. 1983, Eiden et al. 1988). This asymptomatic shedding of rotavirus may lead to HAIs unless compliance to infection control procedures is good with all patients. Similarly, adults can have an asymptomatic rotavirus infection with virus excretion (Anderson & Weber 2004). It is documented that HCWs often stay at work while having an upper respiratory tract infection (Cunney et al. 2000). These respiratory viruses can be transmitted from HCWs to patients, which was the case with rhinovirus in a neonatal unit (Valenti et al. 1982).

Vaccinations are one possibility to achieve better infection control in pediatric wards. Introduction of rotavirus vaccination has led to a significant decrease in the number of hospital-associated rotavirus infections (Anderson et al. 2011). In Finland there has been a decrease in the number of rotavirus infections that lead to hospitalization after the introduction of rotavirus vaccine in 2009 (Puustinen et al. 2011). In efficacy studies rotavirus vaccine was 85–98% protective against severe rotavirus infection, and 74–87% protective against rotavirus infection of any severity. Routine rotavirus vaccination is recommended by the Advisory Committee on Immunization Practices (ACIP) starting at the age of 2 months (Cortese et al. 2009). Annual vaccinations are the most effective method to prevent influenza infection. ACIP recommends influenza vaccination to all persons older than 6 months (Fiore et al. 2010). In Finland children from 6 to 35 months of age are recommended to take influenza vaccination. Older children are vaccinated based on their risk profile (Terveyden ja hyvinvoinnin laitos 2011). HCWs are recommended to take influenza vaccination as they are at greater risk of being infected and vaccinating HCWs protects patients against hospital-associated influenza. Especially children under 6 months of age are at increased risk for influenza as they cannot be vaccinated themselves (Advisory Committee on Immunization Practices & Centers for Disease Control and Prevention (CDC) 2011, Maltezou & Drancourt 2003). Still, the coverage for influenza vaccination remains low among HCWs. The vaccination rate among nursing staff for influenza A H1N1 was 15% in a NICU where an outbreak with H1N1 influenza
took place (Tsagris et al. 2012). Increase in the influenza vaccine coverage among HCWs is associated with significant reductions in hospital-associated influenza rate and influenza infections among HCWs (Salgado et al. 2004).

There are some other possibilities to prevent HAIs, especially gastroenteritis. There is some evidence that prophylactic use of probiotics reduces the risk of hospital-associated gastroenteritis in children 1 to 36 months of age. In a placebo-controlled, randomized trial children who got *Lactobacillus* GG had less diarrhea during hospital stay than those in control group, 3 per 45 (6.7%) vs. 12 per 36 (33%). There was no difference in rotaviral shedding in stools between the *Lactobacillus* GG group (9/45, 20%) and controls (10/36, 28%), but the rate of symptomatic rotavirus infection was lower in those who were given probiotics, 2.2% vs. 17% in control group (Szajewska et al. 2001). Probiotics intake reduces the number and length of diarrhea episodes in young infants in CDCCs (Weizman et al. 2005). Being breast-fed protects against hospital-associated rotavirus infection. During a rotavirus epidemic 10.6% of breast-fed children got rotavirus during hospitalization; all infections were asymptomatic. At the same time, the rate of rotavirus infection was 32.4% among non-breast-fed children, of whom 66% were symptomatic (Gianino et al. 2002). It has been suggested that lactadherin, a glycoprotein in human milk, protects against symptoms of rotavirus infection (Newburg et al. 1998).

New, emerging infectious diseases, such as severe acute respiratory syndrome (SARS) and novel influenza viruses, have caused wide public concern during the last decade. Infection control procedures have been re-evaluated in many healthcare settings in order to be prepared for a new pandemic. There are also other threats that may challenge pediatric infection control practices in coming years. Measles has caused epidemics during the last years especially in Western Europe where vaccine coverage has decreased (Centers for Disease Control and Prevention (CDC) 2011, Muscat 2011). Being transmitted through aerosols, measles can spread quickly in healthcare settings if diagnosis is delayed and air isolation is not practiced. A measles outbreak took place in a pediatric emergency department with five secondary cases during a four-hour exposure, one being a HCW (Centers for Disease Control and Prevention (CDC) 2012).
3 Aims of the study

The specific objectives of this study were:

1. To evaluate the magnitude of hospital-associated infections during and after hospitalization in a pediatric ward other than ICU (Study I, Study II).
2. To identify factors that influence infection transmission in pediatric hospitals (Study II).
3. To evaluate the possibility of continuous surveillance for hospital-associated infections during hospitalization and after discharge using electronic data collection (Study III).
4. To evaluate the safety of hygienic procedures (Study IV).
4 Subjects and methods

4.1 Hospital-associated infections in pediatric infectious diseases ward (I)

The data were collected prospectively for two years, from June 2001 to May 2003, in a ward for pediatric infectious diseases in Oulu University Hospital. All the patients hospitalized in the ward during the two years were included. The ward has nine rooms for patients, and they are mostly used as single rooms. Each room has an isolation system of two doors separating it from the corridor, and only one of the doors is opened at a time. In the space between the doors there is a sink with soap and an alcohol hand gel available, and similar facilities are located in each room as well.

We defined HAIs according to the CDC definition, saying that an infection is classified as hospital-acquired when there is no evidence that it was present or incubating at the time of admission (Garner et al. 1988). Similarly, an infection that is acquired in hospital and becomes evident after discharge is regarded as a HAI. We used a time limit of 72 hours after admission to hospital or at home after discharge for HAI based on the incubation periods of acute respiratory and gastrointestinal viral infections (Lessler et al. 2009).

Data concerning the patient’s stay in hospital were collected from the hospital records to a separate sheet (Table 6). When the child was discharged a follow-up questionnaire was given to the parents with a request to fill it in and send it back after 14 days (Table 6). Parents were asked whether the child had shown any symptoms of a new infection and when the symptoms had appeared.
Table 6. Data gathered in the questionnaires concerning the patient's stay in hospital and the two-week period after discharge.

<table>
<thead>
<tr>
<th>Data collected in hospital</th>
<th>Data reported by parents after discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient's age</td>
<td>Time needed for full recovery</td>
</tr>
<tr>
<td>Clinical diagnoses</td>
<td>Appearance and timing of symptoms of new infection</td>
</tr>
<tr>
<td>Etiology of infection</td>
<td>-Fever</td>
</tr>
<tr>
<td>Duration of hospitalization</td>
<td>-Rhinitis</td>
</tr>
<tr>
<td>Number of patients in the room</td>
<td>-Cough</td>
</tr>
<tr>
<td>Treatment with antimicrobials</td>
<td>-Diarrhea</td>
</tr>
<tr>
<td>HAI in hospital</td>
<td>-Vomiting</td>
</tr>
<tr>
<td>Condition at the time of discharge</td>
<td>-Other symptoms</td>
</tr>
<tr>
<td></td>
<td>Medical help sought</td>
</tr>
<tr>
<td></td>
<td>Attendance at child day-care center</td>
</tr>
</tbody>
</table>

The diagnoses of HAI during hospitalization were based on symptoms and clinical findings of respiratory or gastrointestinal infection, the etiology being examined when this was clinically indicated. The diagnoses of HAI after discharge were based on the appearance of new symptoms after discharge reported by parents. Gastroenteritis was defined as the appearance of diarrhea or vomiting within 72 hours after discharge. Respiratory infection was defined as the appearance of rhinitis or cough within 72 hours after discharge.

During hospitalization, fecal specimens were taken to detect rotavirus and adenovirus antigens to identify the etiology of diarrhea. In Finland the annual epidemic season for rotavirus lasts from January to May, while RSV infections have a peculiar seasonal distribution in periods of two years. Every second year (odd numbers: 2001, 2003, etc.) there is first a smaller RSV epidemic in the spring followed by the main epidemic at the end of the year (Waris 1991), continuing into the beginning of the next year, whereas in the years between the epidemics there are practically no cases of RSV in Finland. To cover this variation we extended the survey over two full years.

The HAI frequency during hospitalization was taken to be the number of HAIIs relative to all children included in the study. The post-discharge HAI frequency was calculated relative to the number of children who participated in the follow-up. We assumed that the occurrence of HAIs follows a Poisson distribution and defined 95% CI on this basis. The mean values for continuous variables (age in years, length of hospitalization in days) in each subgroup were calculated and the statistical significances of the differences were tested with one-way ANOVA. Post hoc comparisons between the groups were tested with Tukey’s
test. Proportions were compared using the chi-square and standard deviation tests (SND). Spearman correlation coefficients were calculated between the monthly HAI rate and the number of patient days. Logistic regression analysis was used to find risk factors for HAI. Odds ratios (OR) and their 95% CIs were calculated for age, number of patients in the room and antimicrobial therapy (yes/no). For the risk analysis the data were classified by diagnosis on admission, and that variable was also included in the logistic modeling.

4.2 Hospital-associated infections in four pediatric wards (II)

The survey was performed in three hospitals: Oulu University Hospital, Finland, University Children’s Hospital, Basel, Switzerland, and North Karelia Central Hospital in Joensuu, Finland. Data collection was planned together by the authors prior to the study and similar questionnaires were used in all hospitals (Table 6). Data were collected prospectively for two years in each hospital between the years 2004 and 2008 (Table 7). In the hospital in Joensuu active surveillance of HAIs was started in 2006 when electronic follow-up became available. We anticipated that the two-year follow-up would cover annual respiratory and gastrointestinal virus epidemics as well as one major RSV epidemic in both countries as two-year periodicity of RSV epidemics has been described both in Finland and in Switzerland (Duppenthaler et al. 2003, Waris 1991). All hospitalized patients were included in the survey, as there were no exclusion criteria.

The hospitals in Oulu and Basel offer care up to the tertiary level and the hospital in Joensuu up to the secondary level. Oulu University Hospital has a pediatric department with 103 beds. The survey was conducted in the ward for infectious diseases (Table 7). The University Children’s Hospital in Basel is a pediatric hospital with 131 beds. The survey was carried out in two general wards, a pediatric ward for children older than one year and an infant ward for those younger than one year (Table 7). North Karelia Central Hospital in Joensuu is a secondary care hospital with 27 beds for pediatric patients. The survey applied to a ward with six rooms for 2 to 5 general pediatric or surgical patients each and two isolation rooms (Table 7).
Table 7. Characteristics of the hospitals participating in the survey of HAIs.

<table>
<thead>
<tr>
<th>Ward characteristics</th>
<th>University Hospital Oulu</th>
<th>University Children’s Hospital, Basel</th>
<th>North Karelia Central Hospital, Joensuu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linguistic background²</td>
<td>Mainly Finnish speaking</td>
<td>60% German speaking</td>
<td>Mainly Finnish speaking</td>
</tr>
<tr>
<td>Type of the ward</td>
<td>Infectious diseases</td>
<td>General pediatric</td>
<td>General pediatric</td>
</tr>
<tr>
<td>Patient capacity</td>
<td>9</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>Number of single rooms</td>
<td>9ᵃ</td>
<td>22ᵃ</td>
<td>2</td>
</tr>
<tr>
<td>Area (m²)</td>
<td>605</td>
<td>755</td>
<td>724</td>
</tr>
<tr>
<td>Area of rooms (% of total)</td>
<td>143 (24)</td>
<td>298 (39)</td>
<td>151 (21)</td>
</tr>
<tr>
<td>Average room size (m²)</td>
<td>15.9</td>
<td>13.5</td>
<td>18.9</td>
</tr>
<tr>
<td>Doors to patient rooms</td>
<td>Two doors</td>
<td>One door</td>
<td>One door</td>
</tr>
<tr>
<td>Toilet in patient rooms</td>
<td>Yes</td>
<td>No³</td>
<td>No¹</td>
</tr>
<tr>
<td>Nurses per shift</td>
<td>1.5 to 4</td>
<td>2 to 7</td>
<td>2 to 6</td>
</tr>
<tr>
<td>Use of AHG</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Active cohorting according to the viral etiology</td>
<td>Yes</td>
<td>Yes</td>
<td>No³</td>
</tr>
<tr>
<td>Form of follow-up</td>
<td>Electronic</td>
<td>On paper</td>
<td>Electronic</td>
</tr>
<tr>
<td>Response rate in follow-up</td>
<td>84%</td>
<td>59%</td>
<td>71%</td>
</tr>
</tbody>
</table>

¹Two wards: pediatric ward and infant ward
²Denotes the language used in the questionnaires
ᵃOccasionally more than one patient per room
³Toilets only in single rooms used as isolation rooms.

Alcohol hand rub is actively used and the nurse-patient ratio is similar in all wards (Table 7). Type of wards and the number of available single rooms are different in the three hospitals (Table 7). Active cohorting according to specific viral etiology is actively performed based on point-of-care tests for influenza viruses and RSV in Oulu and for rotavirus and adenovirus in Basel. The results of antigen detection tests for respiratory viruses and for gastrointestinal viruses are available during the next office day in Oulu. Results from multiplex PCR for adenovirus, influenza viruses, metapneumovirus, parainfluenza viruses, and RSV are available within 24 hours in Basel. Active cohorting according to viral etiology is not practiced in Joensuu (Table 7).

We used a HAI definition of CDC (Garner et al. 1988), with a 72-hour time limit for infections occurring during hospitalization and after discharge. The diagnosis of a HAI during hospitalization was clinical, performed by the health care personnel working on the wards. The etiology of a HAI was analyzed as
clinically indicated. The data on HAIs during hospitalization were recorded by the health care personnel except in Oulu, where medical records were reviewed from patient records in retrospect.

Data concerning the patient’s stay in hospital were obtained from the hospital records. The patient’s condition at the time of discharge (symptomatic/fully recovered) was recorded in Oulu and Basel but not in Joensuu. The post-discharge follow-up was conducted using a standardized questionnaire (Table 6), this being done electronically in Oulu and Joensuu (e-mail, short message service (sms) or phone call, according to the parents’choice). An information sheet describing the post-discharge follow-up and its questions was given to parents at the time of discharge, and they were asked to return it seven days later. Those who did not answer were contacted by phone. The follow-up in Basel used a paper questionnaire form, which was given to the parents at the time of discharge. They were asked to send it back to the hospital after two weeks, and a reminder letter was sent to those who did not return it on time.

Our post-discharge follow-up was based on new symptoms of a probable viral infection as reported by parents. The viral etiology of new infections was not tested unless the patient was rehospitalized. To avoid counting the continuation of already existing symptoms of infection as HAIs, we defined respiratory HAI as a new symptom of respiratory tract infection in those who were not hospitalized for a respiratory tract infection, unless they had fully recovered and become ill again (Fig. 1). Similarly, gastroenteritis was recorded as a HAI only in patients who had not been hospitalized for gastroenteritis, unless they had fully recovered and become ill again. For patients hospitalized for other infections or non-infectious diseases, all reported symptoms of infection in the relevant time frames were regarded as signs of HAIs (Fig. 1).
To study possible reporting bias, all families in Basel who had not returned the questionnaire two weeks after discharge from hospital were contacted by telephone over a two-month-period. Data on new symptoms of infection were received from 70 families by letter in this way and from 156 families by a telephone interview.

All data were combined and analyzed in the Department of Pediatrics at the University of Oulu. Similar definitions were used for post-discharge HAIs throughout the analysis. Gastroenteritis was defined as the appearance of diarrhea or vomiting within 72 hours after discharge. Respiratory infection was defined as the appearance of rhinitis or cough within 72 hours after discharge. The HAI frequency during hospitalization was taken to be the number of HAIs relative to all children included in the study. The post-discharge HAI frequency was calculated relative to the number of children who participated in the follow-up.
Mean values were calculated for continuous variables (age in years, length of hospitalization in days), and proportions were compared using the chi-square test. As the hospitals differed in infrastructure and settings, ward-specific risk factors for HAIs within each ward were searched by using multivariate logistic regression analysis with the method where all variables were entered to a model at the same time. ORs and their 95% CIs were calculated for age (per year of age), hospitalization time (per day of hospitalization time), shared room (yes/no) and antimicrobial therapy (yes/no). The analyses were performed using SPSS (Chicago, IL, USA) for Windows, version 12.0.1.

4.3 Continuous follow-up for hospital-associated infections (III)

When we started prospective HAI surveillance in the ward for pediatric infectious diseases at Oulu University Hospital in 2001, it was done by collecting data during and after hospitalization with paper questionnaires. Later we were offered a chance to participate in a project in which mobile phones and e-mail were to be used to perform HAI surveillance (Coronaria Ltd, Oulu, Finland). This electronic means of follow-up was used from March 2005 onwards.

In the conventional follow-up, the data were collected using questionnaires on paper in two phases (Table 6). The first questionnaire concerned the time in hospital and the second questionnaire covered the time after hospitalization (Table 6). The data were transferred from the questionnaires to a database by a nurse. All the patients in the ward were included in the surveillance program.

In the electronic follow-up most of the data concerning hospitalization could be taken directly from the hospital database by means of a record linkage, reducing the amount of data entry work. For the post-discharge follow-up, parents were offered the alternatives of sms, e-mail or phone call to be used for answering in seven days after discharge. At the time of the deadline a reminder with the questions was sent to the parents by the chosen data collection method, and if they did not answer in time they were contacted by phone. The questions in the electronic questionnaire were similar to those in the printed questionnaires used earlier except that the answers were coded with numbers or letters to ease management.

We measured the time per patient that HCWs in the ward needed for collecting the data and informing the parents about the HAI follow-up with both methods of surveillance. The costs of the follow-up were then calculated from the time spent on it and the average wages for HCWs in our department. The monthly
costs of employing a nurse were estimated to be €4830 and those for a secretary €2850. Other expenses in the conventional follow-up were two sheets of paper and one envelope with postage for each patient. The cost of the electronic follow-up was €600 per month paid to Coronaria Ltd, who took care of the record linkage and databases. The price also included information sheets for parents, post-discharge data collection and reminders sent to parents. The costs of surveillance were calculated both per patient and per year of follow-up. For comparison, we also calculated the annual costs of a follow-up for 1000 hospitalized patients with both follow-up procedures, this being a figure that came close to the true number of patients that we had in the conventional follow-up (964 per year).

The frequency of HAI during hospitalization was taken as the number of HAI cases relative to all the children monitored, and the post-discharge HAI frequency was calculated relative to the children who participated in the follow-up, i.e., for whom data were received. CDC definition for HAI was used (Garner et al. 1988). Mean values were calculated for continuous variables (age in years, length of hospitalization in days). Standard deviation test (SND) was used to compare the response rates.

4.4 Safety of alcohol hand rubs (IV)

The improvement of infection control practices in CDCCs, including the use of an AHG, was shown to reduce the number of episodes of any infection among children significantly (Uhari & Mottonen 1999), and based on these results, AHGs have been recommended for use by both personnel and children at CDCCs in Oulu. As parents and CDCC personnel have been concerned about children’s use of AHGs, and there have earlier been cases where the use of alcohol in skin disinfection lead to toxic effects (Harpin & Rutter 1982, Puschel 1981), we wanted to make sure that the use of AHGs is safe in children in CDCC environment. We conducted an experimental trial at two CDCCs in February 2006 to evaluate the safety of AHG use among children, and a questionnaire survey among all the CDCCs in Oulu to evaluate the use of AHGs.

Theoretically, a subject’s blood alcohol level would increase significantly after using a hand gel containing 70% ethanol if this were totally absorbed through the skin. Ethanol is equally distributed in all body fluids (De Martinis et al. 2006). Thus the maximum rise in the blood alcohol level of a child weighing
10 kilograms would be about 0.15‰ after using 1.5 mL of AHG and double that if 3 mL were used. These blood alcohol levels are high enough to be both measurable and harmful. Correspondingly, the figure would be 0.075‰ with a 1.5 mL dose for a child weighing twenty kilograms and 0.0375‰ for a child weighing forty kilograms.

Eighty-two children varying in age from 3.5 to 7.2 years (mean 5.7 years, standard deviation (SD) 1.1), 37 of whom were males, participated in the experiment in two CDCCs in Oulu. The children were asked to rub their hands with AHG, and all contacts between the hands and the mucous membranes (eyes, mouth, nostrils) were observed and counted during the first 15 minutes afterwards (Fig. 2). Alcohol concentrations in expiratory air, reflecting the absorption of alcohol through the skin, were measured using an official alcometer as issued to the police (Alco-sensor III, identification number 1062558) before and 15 and 60 minutes after use of the AHG. The measurement threshold of the alcometer was 0.01‰. The dose of AHG used was 1.5 mL at one day-care center and 3.0 mL at the other. Each child’s participation in the trial was voluntary and subject to written consent from the parents.

Fig. 2. Experiment design.

The use of AHGs in CDCCs was evaluated with a questionnaire asking about the frequency of its use, the occasions on which it took place and possible risk situations that had happened. The attitudes of the personnel to the use of an AHG were evaluated using a Likert scale with respect to ease of use (1=easy,
5 = difficult), convenience and usefulness. Medians were used to describe these data as they were not normally distributed. One questionnaire was sent to each of the 70 CDCCs in Oulu and to each member of the staff of six randomly selected ones, so that in the end we received 128 completed questionnaires representing 68 CDCCs. The working experience of the respondents varied from one month to 26 years (mean 10 years, standard deviation (SD) 7.3 years) and the group size from 8 to 28 children (mean 19 children, SD 5.2). The analyses of the results concerning the features of AHG use in each CDCC were performed using only one randomly selected answer from those CDCCs where more than one person had answered. The attitudes and personal practices of the personnel were analyzed using all 128 answered questionnaires.

4.5 Ethical considerations

An ethical committee was consulted about the study protocol for HAI follow-up in pediatric wards during and after hospitalization. All the patients in the wards under study were followed up for HAIs during the hospitalization as part of routine care. Participation in the post-discharge follow-up was offered to all patients, but it was voluntary and participation status did not affect the treatment. According to the Medical Research Decree (Finnish Acts and Decrees 1999) and Declaration of Helsinki, Ethical Committee reviewing was not needed due to the nature of the survey.

We wanted to study the safety of AHGs in children’s use as it is not known whether alcohol from the hand rub is absorbed through skin and mucous membranes in children, especially as children often tend to put their hands into their mouths even though wet with AHG. The use of AHGs in CDCCs is suggested after it has been shown that their use reduces the number of infections in children and personnel (Uhari & Mottonen 1999). It was assumed that their use is safe as AHG is used in small amounts on rather small skin surface, and it evaporates in 15 to 30 seconds. Participation in the experiment was voluntary, and an informed written consent for participation was given by parents. The study protocol for the AHG safety study was approved by the Ethical Committee of Northern Ostrobothnia Hospital District.
5 Results

5.1 Hospital-associated infections in pediatric wards during and after hospitalization (I, II)

5.1.1 Results from the follow-up study in Oulu University Hospital

During the study period from 6/2001 to 5/2003 1927 patients were hospitalized in the infectious diseases ward in Oulu University Hospital. The mean length of hospitalization was 3.0 days (standard deviation (SD) 1.8 days), including the days of admission and discharge as full days. The mean age of patients was 3.0 years (SD 3.5 years). Almost all patients (90%) had a single room. The most common diagnoses were gastroenteritis, 566 cases (30.6%), and wheezing bronchitis, 437 cases (23.6%). A total of 709 patients (38.4%) were treated with antimicrobials.

Twenty-one out of the 1927 patients (1.1%, 95% CI 0.7% to 1.7%) contracted a HAI during their stay in the ward. All of them were cases of gastroenteritis, and seven out of the eighteen tested were rotavirus-positive. The parents of 1175 patients (61%) returned the follow-up questionnaires, and 304 of these patients (26%) were reported as having been taken ill again during the 14 days, including 86 cases (7.3%, 95% CI 5.9% to 9.0%) whose symptoms started within 72 hours of discharge. Thus the total HAI rate was 8.4%, with 80% of these (86/107) occurring at home after discharge. Diarrhea was the most common clinical symptom among those taken ill within the first 72 hours (49%), followed by vomiting (42%), fever (34%), rhinitis (31%) and cough (16%). Rhinitis was the most common symptom among those who got ill 4–14 days after discharge (53%).

The 1927 patients accounted altogether for 5504 patient days during the two-year follow-up for which monthly HAI occurrences were recorded and HAI rate was calculated per 100 patient-days for each month. The epidemic seasons for respiratory and gastroenteric viruses, especially RSV and rotavirus, were reflected in the number of diagnoses on admission to our ward per month, the peaks in the HAI rate being found to coincide with high numbers of respiratory infections with decreases in the rate at times when we had primarily gastroenteric patients (Fig. 3).
Fig. 3. Monthly appearance of hospital-acquired infections (HAI) per 100 patient days and the number of patients cared for because of gastrointestinal (GI) and respiratory tract (RTI) infections at the pediatric infectious disease ward during a two-year follow-up.

The rate of HAIs was associated with the number of patient days spent in the ward, Spearman’s coefficient for the correlation between the monthly HAI rate and patient-days being 0.42 (P=0.04) (Fig. 4).
Fig. 4. Monthly appearance of hospital-acquired infections (HAI) per 100 patient days and the amount of patient days at the pediatric infectious disease ward in a two-year follow-up.

Sixty-one percent of the parents returned adequately filled in follow-up questionnaires. To evaluate possible reporting bias, i.e., to find out if the rate of symptoms after discharge was different between respondents and non-respondents, we pursued an intensified surveillance policy for a three-month period from November 2002 to January 2003, during which there were 185 patients in the ward and 126 (68%) of the parents returned the questionnaires. The 59 non-respondent parents were interviewed by phone after the two-week follow-up. Thirty-three (31.0%) out of the 126 patients whose parents returned the follow-up questionnaire during the intensified surveillance period from November 2002 to January 2003 became ill. Among the patients whose parents were contacted by phone, 13 out of 59 (22.0%) had become ill. Thus, even though the difference between the groups was not significant, we had slightly overestimated the occurrence of HAIs in the data gathered from the respondents during the routine surveillance.
The patients who developed a HAI were younger than those who remained healthy (Table 8). The mean hospitalization time was longer for those who had symptoms of a HAI during their stay at hospital when compared with the other patients (Table 8). Those who developed HAI symptoms on the fourth day or later during the 14 days after the discharge did not differ in their length of stay in hospital from those whose symptoms had started within 72 hours.

Table 8. Appearance of signs and symptoms of a new infection during hospitalization and <72 hours or 4 to 14 days after discharge.

<table>
<thead>
<tr>
<th>Variables</th>
<th>In hospital</th>
<th>&lt;72 hours after discharge</th>
<th>4 to 14 days after discharge</th>
<th>No new symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=21</td>
<td>N=86</td>
<td>N=218</td>
<td>N=831</td>
</tr>
<tr>
<td>Age (years, mean)</td>
<td>1.6</td>
<td>2.4</td>
<td>2.5*</td>
<td>3.4</td>
</tr>
<tr>
<td>Length of hospital stay (days, mean)</td>
<td>6.0**</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Shared room in hospital (N, (%))</td>
<td>4 (20.0)</td>
<td>8 (10.1)</td>
<td>14 (6.8)</td>
<td>70 (9.8)</td>
</tr>
<tr>
<td>Attending a CDCC (N, (%))***</td>
<td>3 (25.0)</td>
<td>15 (18.1)</td>
<td>40 (18.8)</td>
<td>134 (17.1)</td>
</tr>
</tbody>
</table>

*4 to 14 days vs. no, P=0.003
**In hospital vs. any other group, P<0.001
***Comparison between proportions with an overall chi-square test, which gave a non-significant result.

In the logistic regression analysis the patient’s age was the only significant independent variable associated with the risk of contracting a HAI in the whole data, with older age providing protection against HAI with an OR (per year in age) of 0.92 (95% CI 0.85 to 0.99, P=0.02). Among the patients with respiratory infections, a shared room increased the risk of HAI with an OR of 2.3 (95% CI 1.1 to 4.8, P=0.03), as 10 out of the 90 (11.1%) who were in a shared room developed a HAI as against 38 out of the 789 (5.1%) in a single room. Treatment with antimicrobials did not significantly affect the HAI frequency.
5.1.2 Results from the international multicenter follow-up study

Altogether 5119 patients were hospitalized in the three hospitals during the periods concerned, 2838 of whom (55%) were males (Table 8). The most common reasons for hospitalization in Oulu and Basel were gastroenteritis and respiratory infections, while in Joensuu 60% of the patients had surgical, other medical or neurological diseases leading to hospitalization. Altogether 1792 patients (35%) received antibiotics (Table 9).

Table 9. Detailed information on the patients included in the survey of hospital-associated infections in four pediatric wards.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Oulu</th>
<th>Basel</th>
<th>Joensuu</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=2309</td>
<td>N=961</td>
<td>N=799</td>
</tr>
<tr>
<td>Mean length of hospitalization (days (SD))</td>
<td>2.7 (1.4)</td>
<td>5.2 (5.6)</td>
<td>7.4 (13.5)</td>
</tr>
<tr>
<td>Mean age (years (SD))</td>
<td>2.9 (3.2)</td>
<td>5.9 (5.0)</td>
<td>0.6 (0.60)</td>
</tr>
<tr>
<td>Male</td>
<td>1309 (57)</td>
<td>499 (52)</td>
<td>424 (53)</td>
</tr>
<tr>
<td>Single room¹</td>
<td>2258 (98)</td>
<td>806 (97)</td>
<td>617 (89)</td>
</tr>
<tr>
<td>Two-person room¹</td>
<td>48 (2.1)</td>
<td>25 (3.0)</td>
<td>74 (11)</td>
</tr>
<tr>
<td>Three-person room¹</td>
<td>3 (0.1)</td>
<td>1 (0.1)</td>
<td>5 (0.7)</td>
</tr>
<tr>
<td>Room for &gt;3 persons¹</td>
<td>-</td>
<td>1 (0.1)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Main diagnosis on admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory infection (RI)</td>
<td>709 (42)</td>
<td>364 (38)</td>
<td>306 (38)</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>599 (36)</td>
<td>196 (20)</td>
<td>136 (17)</td>
</tr>
<tr>
<td>RI and gastroenteritis</td>
<td>19 (1.1)</td>
<td>26 (2.7)</td>
<td>27 (3.4)</td>
</tr>
<tr>
<td>Other infection</td>
<td>282 (17)</td>
<td>158 (16)</td>
<td>157 (20)</td>
</tr>
<tr>
<td>Non-infectious diseases</td>
<td>71 (4.2)</td>
<td>217 (23)</td>
<td>172 (22)</td>
</tr>
<tr>
<td>Treatment with antibiotics</td>
<td>909 (39)</td>
<td>359 (37)</td>
<td>273 (34)</td>
</tr>
</tbody>
</table>

¹ Only available data are presented for different room types in Basel, i.e., missing data are not shown separately.

The overall HAI frequency was 12.2%, with 80% of cases occurring after discharge from hospital. We found marked differences in HAI frequencies between the wards, the figure being lowest in the general pediatric ward for older children in Basel and highest in the general pediatric ward in Joensuu (Fig. 5).
Altogether 122 out of 5119 patients developed a HAI during hospitalization, giving a HAI frequency of 2.4% (Table 10). The most common in-hospital HAIs in Oulu and in Basel were gastroenteritis, 27% of the cases of which were caused by rotavirus in Oulu and 85% in Basel, the rest being mainly respiratory infections.
Table 10. The number of HAIs in four pediatric wards during hospitalization and within 72 hours of discharge from hospital.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Oulu</th>
<th>Basel</th>
<th>Joensuu</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pediatric ward</td>
<td>Infant ward</td>
<td></td>
</tr>
<tr>
<td>HAI in hospital (N/N1, (%))*</td>
<td>18/2309 (0.8)</td>
<td>10/961 (1.0)</td>
<td>35/799 (4.4)</td>
</tr>
<tr>
<td>HAI after discharge (N/N2, (%))*</td>
<td>218/1941 (11.2)</td>
<td>28/578 (4.8)</td>
<td>37/463 (8.0)</td>
</tr>
<tr>
<td>Gastrointestinal HAI</td>
<td>108 (5.6)</td>
<td>14 (2.4)</td>
<td>19 (4.1)</td>
</tr>
<tr>
<td>Respiratory HAI</td>
<td>98 (5.0)</td>
<td>14 (2.4)</td>
<td>17 (3.7)</td>
</tr>
<tr>
<td>Both respiratory and gastrointestinal HAI</td>
<td>8 (0.4)</td>
<td>-</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Other infection</td>
<td>4 (0.2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total HAI rate</td>
<td>12.0%</td>
<td>5.8%</td>
<td>12.4%</td>
</tr>
</tbody>
</table>

*Significant difference in proportions with the chi-square test (P<0.001)

1Number of patients surveyed for HAIs in hospital
2Number of patients surveyed for HAIs after discharge

Post-discharge follow-up data were received on 3729 (73%) patients (Table 6). Altogether 365 patients (9.8%, 95% CI 8.9% to 10.8%) developed a viral HAI that manifested after discharge from hospital. The overall frequency of gastrointestinal HAI after discharge was 4.8% (N=178) (95% CI 4.1% to 5.5%). Altogether 170 children (4.6%, 95% CI 3.9% to 5.3%) developed a respiratory HAI and a further 17 (0.5%, 95% CI 0.3% to 0.7%) showed symptoms of both respiratory and gastrointestinal HAI (Table 10). In total 464 children out of the 3729 (12%) visited a doctor within the first week after discharge, including 67 who were diagnosed as having gastroenteritis and 75 as having upper respiratory tract infection.

When the cumulative occurrence of hospital-associated gastroenteritis and respiratory infections during the first seven days after discharge in the case of the infectious disease ward in Oulu was plotted against time, the occurrence of gastroenteritis was seen as an accelerated curve after hospitalization, whereas the occurrence of respiratory infections was as expected, i.e., constant in time (Fig. 6). This indicates that hospitalization increased the rate of gastroenteritis above the expected linear pattern. In the general pediatric ward in Joensuu both the occurrence of gastroenteritis and that of respiratory infections exceeded the expected rate, and a similar phenomenon was found in the two general wards in Basel, but with less marked differences (Fig. 6).
Fig. 6. Timing of the appearance of respiratory infection (RI) and gastroenteritis (GE) in children whose symptoms appeared after discharge. Assuming that the general infection rate in a large population over a short cumulative observation time will remain constant, the infection rate would be seen as a straight line when plotted against time in the case of no HAIs. The dotted line in the figure represents this straight expected line (EL) for infections.

The ward-specific risk factors for HAI were analyzed separately for each ward (Table 11). Sharing a room significantly increased the risk of HAI in the infant ward in Basel (OR=5.5, 95% CI 2.4 to 12.2), but this association could not be analyzed in the pediatric ward in Basel or in the infectious disease ward in Oulu, where single rooms were used almost exclusively. Among the HAIs that manifested themselves in hospital a longer hospitalization time was associated with a higher HAI risk in every ward except the general ward in Joensuu. This may be related to the fact that more than half of the patients in this ward had been hospitalized for other than infectious diseases in Joensuu. Treatment with antibiotics was associated with a higher HAI risk in the infant ward in Basel and
in the general ward in Joensuu, while young age increased the risk of HAI after discharge in Oulu and in Joensuu (Table 11).
Table 11. Risk factors for hospital-associated infections (HAIs) occurring during hospitalization and after discharge. Odds ratios (OR) and 95% confidence intervals (CIs) for risk factors are presented for each ward.

<table>
<thead>
<tr>
<th>Variables in logistic regression modeling</th>
<th>Oulu</th>
<th>Basel</th>
<th>Joensuu</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI), P</td>
<td>OR (95% CI), P</td>
<td>OR (95% CI), P</td>
</tr>
<tr>
<td>HAI in hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per year)</td>
<td>0.72 (0.51 to 0.10), 0.048</td>
<td>0.71 (0.51 to 0.98), 0.04</td>
<td>1.44 (0.86 to 2.41), 0.17</td>
</tr>
<tr>
<td>Time in hospital¹</td>
<td>1.42 (1.20 to 1.67), &lt;0.001</td>
<td>1.22 (1.11 to 1.34), &lt;0.001</td>
<td>1.05 (1.03 to 1.07), &lt;0.001</td>
</tr>
<tr>
<td>Shared room</td>
<td>NA</td>
<td>NA</td>
<td>5.45 (2.44 to 12.2), &lt;0.001</td>
</tr>
<tr>
<td>Antibiotic treatment</td>
<td>2.55 (0.88 to 7.39), 0.09</td>
<td>0.93 (0.18 to 4.97), 0.93</td>
<td>3.14 (1.44 to 6.83), 0.004</td>
</tr>
<tr>
<td>HAI after discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per year)</td>
<td>0.93 (0.88 to 0.98), 0.010</td>
<td>0.90 (0.80 to 1.01), 0.076</td>
<td>0.92 (0.50 to 1.69), 0.78</td>
</tr>
<tr>
<td>Time in hospital¹</td>
<td>1.11 (1.02 to 1.21), 0.022</td>
<td>1.05 (0.97 to 1.13), 0.23</td>
<td>1.02 (0.98 to 1.05), 0.33</td>
</tr>
<tr>
<td>Shared room</td>
<td>0.66 (0.23 to 1.85), 0.43</td>
<td>1.67 (0.20 to 14.0), 0.63</td>
<td>0.16 (0.02 to 1.40), 0.098</td>
</tr>
<tr>
<td>Antibiotic treatment</td>
<td>0.98 (0.73 to 1.31), 0.89</td>
<td>2.01 (0.88 to 4.59), 0.098</td>
<td>1.19 (0.57 to 2.48), 0.65</td>
</tr>
</tbody>
</table>

¹Per day of time in hospital

NA not applicable due to a small number of patients treated in a shared room.
When all the families of discharged patients had been contacted over a period of two months in Basel, the total HAI rate within 72 hours after discharge was 7/79 (8.8%) in the children whose follow-up data were obtained by letter and 15/156 (9.6%) in those whose families were contacted by telephone, given that no follow-up questionnaire had been received. This difference was not statistically significant.

5.2 Continuous follow-up for hospital-associated infections (III)

During the follow-up study with paper questionnaires from 6/2001 to 5/2003 in the infectious diseases ward in Oulu 1927 patients were recruited for the conventional follow-up, and 1175 (61%) returned the questionnaires adequately filled in. During the following study period with electronic questionnaires 1940 of the 2309 recruited patients (84%) sent the post-discharge information to us. The difference in response rate was statistically significant (P<0.001). In the electronic follow-up 20% of the parents chose to answer by sms (response rate 74%), 63% by e-mail (response rate 85%), while 17% wanted us to call them in order to collect the data (response rate 92%) (Table 12).
Table 12. Participation in the post-discharge follow-up of HAI using conventional and electronic procedures. The main results obtained in the two periods are presented in the table.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Paper questionnaire</th>
<th>Electronic questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response rate in total (%)</td>
<td>61%</td>
<td>84%</td>
</tr>
<tr>
<td>Response rate in sms¹ follow-up (%)</td>
<td>-</td>
<td>74%</td>
</tr>
<tr>
<td>Response rate in e-mail follow-up (%)</td>
<td>-</td>
<td>85%</td>
</tr>
<tr>
<td>Response rate in phone call follow-up (%)</td>
<td>-</td>
<td>92%</td>
</tr>
<tr>
<td>Time used for data collection by HCWs per patient</td>
<td>33 minutes</td>
<td>13 minutes</td>
</tr>
<tr>
<td>Costs of follow-up per patient</td>
<td>€15.07</td>
<td>€13.61</td>
</tr>
<tr>
<td>Costs of data collection per year (1000 patients²)</td>
<td>€15,070</td>
<td>€12,490</td>
</tr>
<tr>
<td>HAI at home</td>
<td>86 (7.3%)</td>
<td>214 (11%)</td>
</tr>
<tr>
<td>HAI total³</td>
<td>8.4%</td>
<td>12.2%</td>
</tr>
<tr>
<td>Mean age of patients (years)</td>
<td>3.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Mean length of hospitalization (days)</td>
<td>3.0</td>
<td>2.7</td>
</tr>
</tbody>
</table>

*Statistically significant difference between the response rates, P<0.0001

¹short message service
²For comparison, the annual costs were calculated for 1,000 patients per year with both follow-up procedures, since this figure was close to the average number of patients treated during the conventional follow-up (964 per year).
³Sum of HAI rates during hospitalization and the post-discharge period

The time spent by the HCWs on the conventional follow-up was 33 minutes per patient, compared to 13 minutes per patient on the electronic follow-up. Most of the savings in time arose because no data entry procedure was needed. In the case of conventional follow-up a nurse used 20 minutes per patient for collecting data concerning hospitalization and informing parents, and 10 minutes per patient for data entry. A further 3 minutes per patient were used by a secretary for preparing the follow-up questionnaires. The other costs in the conventional follow-up were €0.041 per patient for two sheets of paper and an envelope with postage, making the total cost €15.07 per patient. As we had 964 patients annually over that period, the costs of performing the survey were €14,525 per year.
Fig. 7. Costs of the two follow-up methods.
The costs of the electronic follow-up included the time spent on it by the HCWs and the monthly price of €600 paid to Coronaria Ltd for administering it. On the electronic follow-up 5 minutes per patient were used by a secretary for collecting data concerning hospitalization and 8 minutes per patient were used by a nurse for informing parents about the post-discharge follow-up, making the cost of the time spent by the HCWs €5.29 per patient. As we had an average of 72 patients per month, the total cost of the follow-up per patient was €13.61 during the period concerned and €11,783 per year. When the costs of the two follow-up procedures were calculated for 1000 patients per year, they were €15,070 in the conventional follow-up and €12,490 in the electronic follow-up, so that the latter gave a saving of 17.1% in annual expenses (Table 12), or €2.58 per patient given a total of 1,000 patients per year.

5.3 Safety of alcohol hand rubs (IV)

In the experimental trial 47 children rubbed their hands with 1.5 mL of AHG and 35 with 3.0 mL. All the alcometer results remained below the measurement limit of 0.01‰, suggesting minimal or no alcohol absorption from the hand gel. The number of contacts between the hands and the mucous membranes varied from 0 to 30 per child during 15 minutes (mean 2.4 times, SD 4.3).

According to the questionnaires, AHGs were used in every CDCC, only among adults in 11 of the 68 CDCCs (16%), and also regularly by the children in 50 of them (74%). In the remaining seven CDCCs the children had only used AHGs at times of epidemics. The mean time for which an AHG had been used in the CDCCs was 7.4 years (SD 3.3). The most common occasions for AHG use by the personnel were before serving food and after cleaning secretions, whereas hand washing with soap was most common after going to the toilet (Table 13). The children most often used an AHG before eating, and washed their hands with soap after going to the toilet (Table 13).
Table 13. Use of AHG and hand washing with soap and water in different situations by personnel and children at 68 CDCCs.

<table>
<thead>
<tr>
<th>Data collected in questionnaires</th>
<th>Personnel (N=68)</th>
<th>Children (N=68)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AHG</td>
<td>Soap¹</td>
</tr>
<tr>
<td>At the start of the shift (n, (%))</td>
<td>40 (59)</td>
<td>39 (57)</td>
</tr>
<tr>
<td>Before serving food² (n, (%))</td>
<td>59 (87)</td>
<td>47 (69)</td>
</tr>
<tr>
<td>After serving food² (n, (%))</td>
<td>10 (15)</td>
<td>25 (37)</td>
</tr>
<tr>
<td>Before changing diapers³ (n, (%))</td>
<td>7 (12)</td>
<td>6 (10)</td>
</tr>
<tr>
<td>After changing diapers³(n, (%))</td>
<td>47 (81)</td>
<td>36 (62)</td>
</tr>
<tr>
<td>Before blowing one’s nose (n, (%))</td>
<td>5 (7.4)</td>
<td>5 (7.4)</td>
</tr>
<tr>
<td>After blowing one’s nose (n, (%))</td>
<td>53 (78)</td>
<td>33 (49)</td>
</tr>
<tr>
<td>After cleaning secretions (n, (%))</td>
<td>61 (90)</td>
<td>52 (76)</td>
</tr>
<tr>
<td>After going to the toilet (n, (%))</td>
<td>49 (72)</td>
<td>59 (87)</td>
</tr>
<tr>
<td>At the end of a shift (n, (%))</td>
<td>26 (38)</td>
<td>31 (46)</td>
</tr>
</tbody>
</table>

¹Washing hands with soap and water or with water only
²The questions for the children were ‘Before eating’ and ‘After eating’.
³There were 58 persons taking care of children who wore diapers.

Forty-three out of the 128 respondents (34%) always washed their hands with soap before using an AHG, and the majority, 120 out of 128 (94%), used soap when their hands were visibly dirty. Seventeen (13%) always washed their hands with soap before using the AHG. The day-care workers used an AHG from zero to 50 times per day (mean 6.7 times per day, SD 6.8), and the children from zero to eight times per day (mean 2.4 times per day, SD 1.7).

The personnel found the use of an AHG easy, the median assessment for ease being 1.2 (interquartile range 1.0 to 1.4) and the median for usefulness 1.2 (interquartile range 1.0 to 1.4), given that a score of one on a Likert scale denoted either easy or useful. The median for convenience was 2.4 (interquartile range 1.2 to 3.0).

One case of a fire had occurred when a worker had lit a fire while his hands were still wet with AHG. In addition, 25 of the 128 respondents (20%) reported consequences of AHG usage which they believed to be dangerous or harmful. The most common (15 comments) concern was that children put their fingers in their mouths or eyes after using the AHG. Three people mentioned skin problems due to the use of an AHG, while other problems mentioned were splattering of the gel when applying it (6 comments) and children sniffing their hands after using the gel (one comment). The reasons for using alcohol for hand antisepsis were well understood by the personnel, as 98 persons (77%) said it was to prevent the
spread of infectious diseases or to improve hygiene. Four respondents (3%) did not know why an AHG was used.
6 Discussion

We found out that 5.8 to 17.5% of the patients hospitalized in pediatric infectious diseases and general pediatric wards got HAI during hospitalization or within 72 hours after the discharge. The majority of these HAIs became evident at home, the frequency of HAIs during hospitalization varying from 0.8 to 5.6%. Gastroenteritis was the most common HAI during hospitalization, and it was often caused by rotavirus. It has earlier been reported that during the epidemic seasons 3.6 to 14% of children get gastrointestinal HAI and 4.2 to 17% get respiratory HAI during hospitalization (Isaacs et al. 1991, Macartney et al. 2000).

6.1 Post-discharge follow-up in hospital-associated infection surveillance

According to our results, a large proportion of HAIs become evident after discharge, including all the hospital-associated respiratory infections, which is understandable in view of the known incubation period for RSV (4 to 6 days) and the short mean hospitalization time among our patients (3 days). This emphasizes the importance of follow-up after discharge from hospital to avoid underestimating HAIs. Most surveys of HAIs in pediatric settings have not included a systematic follow-up after discharge. In one survey where the follow-up was conducted after discharge by means of phone calls, 144 out of 817 (17.6%) hospitalized children contracted hospital-associated gastroenteritis, one third of which occurred at home, whereas in our study 80% of all HAIs occurred after discharge (Grassano Morin et al. 2000). In our study the parents reported the symptoms as they do in real life, without any special facilities or criteria, which makes it possible to apply the results to an ordinary population. Earlier self-assessing of symptoms of common cold has been shown to be reliable compared to a physician’s observations (Macintyre & Pritchard 1989).

In total, the observed rate of HAIs during hospitalization (1.1%) in our study was rather low as compared to the previously reported frequencies of pediatric HAIs, which vary from 3.6% to 14%. The possible reason for the low rate of HAIs in our study may be the frequent use of disinfection of the hands with AHG by personnel at our ward. Many viruses, including rotavirus, are sensitive to hand hygiene products containing 60% to 90% ethanol (Ansari et al. 1989, Bellamy et al. 1993, McDonnell & Russell 1999, Sattar et al. 2000). The use of alcohol hand gel was recommended for routine decontamination of the hands in the CDC
guideline in 2002 (Boyce et al. 2002, Larson 1995). Even so, hand washing with soap and water is still common in many institutions in comparison to the use of alcohol hand gel, even during a hand hygiene campaign (Zerr et al. 2005).

The use of single rooms for most patients is probably another important part of preventing HAI at our ward. When rooms were shared during our study period, patients with the same symptoms or with the same assumed pathogens were placed in the same rooms in order to prevent the spread of pathogens. In previous studies, a shared room has been shown to be a significant risk factor for the transmission of rotavirus infection (Ford-Jones et al. 1990, Gaggero et al. 1992), but rotavirus also transmits between patient rooms (Nakata et al. 1996). One of the lowest HAI frequencies during hospitalization alongside the results of our present study has been reported by Ford-Jones et al., who observed a rate of 1.3% among patients admitted to an isolation ward, compared to 6.0% in the whole pediatric hospital (Ford-Jones et al. 1989). Similarly, one of the lowest HAI rates was reported in the infectious diseases ward in a pediatric hospital (Pacini et al. 1987). We suggest that those results together with ours show that low HAI rates can be achieved with good compliance to infection control procedures.

The peaks in the HAI rate were found to coincide with high numbers of respiratory infections, with decreases in the rate at times when we had primarily gastroenteric patients. This is in accordance with the findings of Cavalcante et al. and may also reflect the fact that crowding of the ward is one of the most important risk factor for HAI (Archibald et al. 1997, Cavalcante et al. 2006, Moisiuk et al. 1998). Transmission of respiratory viruses can be better prevented with single room bedding than that of enteric viruses. One reason for lower number of HAI during the gastroenteritis epidemics maybe reduced recognition of new gastrointestinal HAIs in patients who had gastroenteritis on admission. In them diarrhea and vomiting after the discharge were counted as HAI only if patient was reported to be symptom-free at the time of discharge.

6.2 Ward structure and the risk of hospital-associated infections

In the multicentre follow-up study we found clear differences in HAI frequencies between the pediatric wards. In all wards most viral HAIs became evident after discharge. The highest HAI frequency was found in the general pediatric ward in Joensuu, where shared rooms were used most often, active cohorting according to
viral etiology was not performed, and where more than half of the patients had been hospitalized for non-infectious diseases. By contrast, the lowest HAI rate was found in the general pediatric ward in Basel, where the patients were older and most of them were treated in a single room. Based on these results we suggest that single room bedding is effective in preventing HAIs. It also seems that treating patients with infectious diseases in a separate unit with active cohorting according to viral etiology is advantageous compared with a general ward.

Our findings are in line with previous findings that a general pediatric ward had a higher rate of gastrointestinal HAIs than specialized non-infectious wards (Ford-Jones et al. 1990), and that the lowest HAI rate in a pediatric hospital was documented in an infectious diseases ward, the majority of the HAIs being gastrointestinal infections (Ford-Jones et al. 1989). Earlier it has been suggested that better compliance with hygienic procedures explains lower number of HAIs in infectious diseases wards compared with other pediatric wards (Pacini et al. 1987). It is also known that an increased number of roommates increases the risk of hospital-associated gastroenteritis (Ford-Jones et al. 1990), whereas cohorting of patients has been reported to reduce the risk of hospital-associated RSV infection (Isaacs et al. 1991, Macartney et al. 2000).

The post-discharge cumulative occurrence of gastroenteritis in an infectious disease ward with isolation rooms in Oulu was seen as exceeding that expected after discharge, whereas the occurrence of respiratory infections was as expected in the general population. In the other wards the occurrence of both gastrointestinal and respiratory HAIs exceeded that expected after hospitalization, this phenomenon being most pronounced in the general ward in Joensuu. With the use of single rooms we could prevent well the spread of respiratory viruses, but gastrointestinal viruses spread despite this precaution. By analyzing rotavirus strains it has been shown that rotavirus spreads between patients located in different rooms in pediatric wards (Nakata et al. 1996). However, cohorting reduces the transmission of RSV (Isaacs et al. 1991, Macartney et al. 2000). Rotavirus survives well on environmental surfaces, making spread via indirect contact possible and infection control more demanding. Another challenge is that asymptomatic children can excrete rotavirus before and after a symptomatic infection (Goldmann 1992). Our findings are in accordance with these spreading mechanisms for infections.

When we analyzed ward-specific risk factors for HAI, young age and longer duration of hospitalization were found to be risk factors in most wards, as seen in previous studies (Bennet et al. 1995, Cavalcante et al. 2006, Ford-Jones et al. 1990).
Young children are at increased risk for HAIs as they are still developing immunity to common pathogens and get viral infections easily. Treatment in a shared room appeared to be associated with an increased risk of HAI during hospitalization in the infant ward in Basel. In the wards that used mainly single rooms, the association was not statistically significant. Another factor associated with the risk of HAI was the use of antibiotics. This may be partly a matter of misinterpretation of the symptoms, as it is not always possible to distinguish gastroenteritis signs and symptoms due to HAI from the side effects of antibiotics.

Alcohol hand rubs play an important role in hand hygiene in hospitals, and besides their efficacy against bacteria, they are effective against common viral pathogens, among them also non-enveloped viruses; adenovirus, rhinovirus and rotavirus (Ansari et al. 1989, Bellamy et al. 1993, Boyce et al. 2002, McDonnell & Russell 1999, Sattar et al. 2000). A lower number of gastrointestinal HAIs has been shown to be associated with the use of alcohol hand rubs (Zerr et al. 2005). Alcohol hand rubs were actively used in each of the wards studied here. Although a high patient-to-nurse ratio has been shown to increase the rate of hospital-associated gastroenteritis (Stegenga et al. 2002), there were no marked differences in this respect between the wards we studied.

The strength of our study was that the follow-up of viral HAIs was done both in hospital and for one week after discharge. The post-discharge follow-up enabled us to observe viral HAIs that were most likely acquired already in hospital but became evident after an incubation period at home. In addition, we collected data prospectively by using similar questionnaires in three different hospitals for two years in order to cover the seasonal variation in infectious diseases and make data comparable between the wards.

The limitation of our study was that we might have overestimated the overall occurrence of HAIs appearing after discharge by calculating all infection symptoms reported by parents within 72 hours after discharge as HAIs. It is impossible to define accurately what proportion of the infection symptoms registered after discharge by the parents were HAIs and which were coinciding viral infections as they occur in the general population. However, we saw an increase in infection symptoms above the expected line of infections in population. The response bias may also have affected the results in different ways in the different wards since those who did not return the questionnaires had more HAIs (as assessed by active follow-up by telephone) than those who returned
them in Basel, whereas we found the opposite earlier in Oulu. In Joensuu, the child’s condition at the time of discharge was not recorded and we assumed that all children were still symptomatic when discharged. Therefore we may have underestimated the occurrence of new symptoms in Joensuu.

Data collection methods were different in the hospitals under study. Electronic questionnaires were used in the two study centers in Finland whereas questionnaires on paper were used in Basel. Electronic questionnaire response rate was higher than those for the paper versions, 81% versus 59%. It has been found earlier that data collected by electronic means are equivalent in content to data collected using paper questionnaires but have less missing data (Bushnell et al. 2003, Junker et al. 2008, Ryan et al. 2002).

6.3 Continuous surveillance for hospital-associated infections

We found out that electronic data collection was a convenient way of performing a continuous post-discharge follow-up for HAIs, as it both yielded a higher participation rate and lowered the costs. The parents accepted the electronic data collection methods well, so that 84% of the parents participated in the post-discharge electronic data collection, whereas the response rate achieved by conventional methods was 23 percentage points lower. Most of the parents in the electronic follow-up chose to answer by e-mail, but all the electronic options showed high participation rates. Electronic follow-up enabled us to send reminders to parents, which may partly explain the higher participation rate.

Earlier, respondents have found electronic questionnaires convenient, and there was a high correlation between the data collected by electronic questionnaires and questionnaires on paper (Bushnell et al. 2003). The use of computers in answering did not cause anxiety even though many of the respondents used computers infrequently (Cook et al. 2004). Patients prefer electronic data collection to paper system when it is done using computers, but data collection with paper to a telephone or interactive voice response system. Using electronic data collection reduces the study costs as no data entry is needed, and electronically collected data are of better quality with fewer lacking answers (Ryan et al. 2002, Velikova et al. 1999, Welker 2007). In daily symptom recording data collected using an electronic or telephone diary has been shown to be more accurate than those in paper diaries, electronic diaries offering the possibility of recording the time the diaries were filled in (Lauritsen et al. 2004).
Data entry was the most laborious part of the conventional data collection procedure, whereas with electronic questionnaires we could take the data directly from the hospital database by record linkage. No additional data entry work was needed for the post-discharge data either, which made the data easily available for showing trends in HAI rates. It has been shown previously that electronic methods can reduce the costs of data collection in clinical trials by as much as 55% (Pavlovic et al. 2009), and that a saving of USD0.63 per patient can be achieved in surgical wound infection surveillance when automated data entry with optical scanning is used (Smyth et al. 1997). In our study the data collection costs decreased by 17% a year with electronic follow-up, implying a saving of €2.60 per patient. These calculations naturally included only the costs in terms of health care facilities. We estimated that the parents spent approximately the same amount of time answering the electronic questionnaire as they did filling in the paper questionnaire.

In this case the electronic surveillance was administered by a private collaborator, and we paid a fixed price of €600 per month for it. In addition, besides normal patient care, nurses spent some time on data collection and informing parents about the arrangements for the post-discharge period, which increased the expenses. The most expensive parts of the electronic data collection were the phone calls made to some parents in order to collect post-discharge data and the reminders sent to parents. Both were included in the monthly price, however, only 17% of the parents chose phone calls as primary method of answering. As the data were collected in an electronic form, no data entry was needed by the private company. Our experience was that electronic data collection is a recommendable way of organizing HAI surveillance. Use of electronic data collection led to reduced costs even when we used a private collaborator to organize it. When electronic means are used for HAI surveillance, an automatic alarm can be used to identify sudden changes in HAI rates to allow quick responses. It is probable that electronic data collection will become more common as time goes by, and most of the costs are caused by following up participation and reminding those who do not answer.

6.4 Use of alcohol hand gels among children

AHGs were shown to be a safe option for hand hygiene in child care facilities. Ethanol was not absorbed when the children at the CDCCs used an AHG for hand
disinfection in the experimental trial, even though there were as many as 30 contacts between the hands and the mucous membranes. There was no sign of any elevated alcohol concentration in the children’s alcometer measurements, although theoretically the amount of alcohol used could have caused a measurable rise in blood alcohol (De Martinis et al. 2006).

Attendance at a CDCC is a significant risk factor for infectious diseases such as diarrhea, common colds, otitis media and pneumonia (Louhiala et al. 1995, Louhiala et al. 1997). It is possible to reduce the number of infections at CDCCs by improving the practices of the personnel in changing diapers, serving food and especially hand hygiene (Uhari & Mottonen 1999), and the most effective way of achieving the latter and preventing the spread of viruses is to use AHGs (Boyce et al. 2002). In our study we found this to be safe in CDCC environment.

Two cases of toxic absorption of alcohol in children have been described earlier, that of a pre-term infant, where this condition may explain the toxic absorption of alcohol and the resulting skin damage (Harpin & Rutter 1982), and that of a two-year-old girl in whom a keloidal scar was exposed overnight to a wrapping containing alcohol (Puschel 1981). Cases of percutaneous absorption of disinfectants have been documented after skin cleaning with hexachlorophene and chlorhexidine in newborn and premature babies (Cowen et al. 1979, Curley et al. 1971, Powell et al. 1973), and this issue has recently been re-evaluated in connection with the wider use of chlorhexidine in obstetrics and neonatal care in developing countries in order to reduce neonatal mortality (Mullany et al. 2006).

A single case of toxic use of AHG by a child in CDCC has been reported in Finland (Lukkarinen & Kujari 2009). A four-year-old girl was brought to emergency room from CDCC because of lowered consciousness and inappropriate behavior. No other cause for the condition was recovered, but blood ethanol was found to be elevated up to 1.9‰. It came out that the girl tended to lick her hands after using AHG, and liked the taste of it. To achieve this high a level of blood ethanol, an intake of an amount of 30 mL of AHG with 70% ethanol was needed for her weight. The results from our trial confirm that when AHG is used with normal dosing (1.5 or 3.0 milliliters), no measurable level of ethanol is absorbed even when there are several contacts to mucous membranes.

The reasons for using AHGs are well understood among CDCC personnel, and their use is taken as a significant improvement. It has been shown earlier that secondary transmission of infections to family members can be reduced by using an AHG at home if there are children who attend a CDCC (Lee et al. 2005, Sandora et al. 2005), and a recent review of the role of AHGs in hand hygiene in
home and community settings has recommended its active use to prevent the transmission of infectious diseases (Bloomfield et al. 2007).

Our study confirmed that the use ethanol containing AHGs is safe in children. There had been one incident of fire in CDCC when matches were used while hands were still wet with AHG. A few similar cases have been reported in Germany; some of the fire incidents were due to vandalism (Kramer & Kampf 2007). In the USA no fire incidents were reported after a couple of years of AHG use in hospitals (Boyce & Pearson 2003). These data suggest that the risk of fire incidents related to AHGs is minimal. Other ingredients used in the hand gels are glycerin and often glycercylcocoate. These skin-conditioning agents are commonly used in cosmetic products and have been found to be safe in animal and clinical test (Johnson Jr 2004).
7 Conclusions

We found that a remarkable number of children get a HAI, the HAI rate being the highest in a mixed pediatric ward where 17% of patients got a new infection. The majority of these infections become symptomatic after discharge and they remain unreported unless HAI follow-up is extended to cover the immediate time at home after hospitalization. Viral HAI frequency was highest in the general pediatric ward, suggesting that patients with contagious diseases should be treated separately. In the wards with lowest HAI rates the majority of patients were in single rooms and active cohorting was done. These isolation practices were especially beneficial in preventing respiratory HAIs.

Electronic follow-up for HAIs is a feasible way of doing HAI surveillance both during hospitalization and after discharge. Post-discharge follow-up is needed to find out the number of viral infections children get after being hospitalized. Main focus in infection control is still on bacterial infections despite the known challenges in prevention of transmission of viruses. Documentation of viral HAIs is important in order to get more focus on the prevention of spread of viruses in health care settings. Based on the experiences of this study both a better response rate and lower costs were achieved with HAI follow-up with electronic questionnaires. With electronic follow-up continuously collected data are easily available, showing the trends in HAI rates, which helps us to identify unexpected peaks in HAI rates so that quick responses can be made. To facilitate this, an automatic alarm can be set to recognize increased HAI rates. Data is also available to be used in giving feedback to HCWs to maintain the motivation for infection control. Continuously collected data will facilitate in measuring the effect of future interventions to reduce HAI rates.

AHGs are important in preventing viruses from spreading both in healthcare settings and other facilities with a high number of viral infections spreading. Use of AHGs was found to be a safe and convenient method for hand hygiene at CDCCs. Based on our results it can be concluded that the use of AHGs at CDCCs can be recommended for the children as well as the staff, as all the alcometer results were below the measurement threshold in children after hand rub.
References


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