

## **Risk of transmission of vaccine preventable-diseases in healthcare settings**

### **Abstract**

Transmission of infectious agents in healthcare settings is a priority public health problem. While the main burden of healthcare associated infections is commonly caused by Gram negative bacteria and fungi, vaccine preventable diseases represent an additional infectious risk for patients attending healthcare facilities. Hepatitis B, rotavirus gastroenteritis, influenza, measles, pertussis, pneumococcal and meningococcal invasive bacterial infections still represent a threat notwithstanding the presence of universal vaccination programs. For this reason, healthcare worker immunization is an important strategy to limit the risk of VPDs in such fragile population.

**Keywords:** Vaccine preventable disease; healthcare associated infection; outbreak

### **Executive summary**

- Commonly, risk of acquiring a vaccine preventable disease (VPD) in healthcare settings is not perceived to be particularly high;
- Epidemiological and demographic changes make VPDs an additional infectious threat in healthcare settings;
- Preventing VPDs in healthcare settings is important both to improve patient's safety and to avoid that healthcare facilities become a hub of VPDs diffusion;
- Health care workers immunization is an important strategy to limit the risk of VPDs in a fragile population.

## Introduction

Transmission of infectious agents in healthcare settings is a priority public health problem, largely linked to hospital acquired infections with a number of Gram negative (*Pseudomonas* spp, *Acinetobacter* spp, *Escherichia coli*, etc.) and Gram positive bacteria (*Clostridium difficile*, methicillin-resistant *Staphylococcus aureus*) as well as fungi (*Candida* spp, *Aspergillus* spp, etc.) and virus (*Norovirus*) [1,2] Furthermore circulation of infectious agents in healthcare facilities represents one of the most important determinants of antimicrobial resistance[3].

Risk of acquiring a vaccine preventable disease (VPD) following a contact with healthcare settings is not perceived to be particularly high. This is probably due to the fact that VPDs are traditionally associated with childhood diseases that are primarily community spread. On the other hand, during the last decades the list of VPDs has been growing fast and immunization has become a life-long practice. As an example, diseases like rotavirus gastroenteritis – for which nosocomial spread represents a significant burden – recently became vaccine preventable[4].

Community based immunization programs have strongly reduced the burden of VPDs, but risk of acquiring a VPD can be considered close to zero only when disease eradication or elimination is achieved. For this reason, attending healthcare settings still represents an additional risk for susceptible individuals.

This paper is a narrative review of the evidence on risk of transmission of vaccine preventable diseases in healthcare settings.

## Hepatitis B

Despite the considerable improvements in blood supply safety and infection control, nosocomial and iatrogenic HBV transmission is still an issue at least in some EU/EEA countries[5]. Such transmission accounts for 18.6% of all acute HBV cases and for 40.4% of chronic cases reported in EU/EEA in 2016, mostly by Italy and Romania[6], and it may results in outbreaks in healthcare settings [7–12]. While the risk of developing a chronic HBV infection decreases in older childhood and adulthood, acute hepatitis B and fulminant infection is of concern, especially among patients with co-infections, other co-existent diseases and concomitant medications[13]. Case fatalities were reported in few outbreak investigation reports, underscoring the disease burden and the impact of such occurrences[7,8].

Progressive introduction of HBV universal infant vaccination programs (UVP) in Europe since the 1980s has proven to be successful [14], however data on coverage and impact of targeted vaccination for HCWs are hardly available. According to a recent review of published HCW-patient

transmission incidents, cases have been relatively rare and have substantially decreased in frequency over the past four decades due to a combinations of factors, including screening and vaccination of staff and the better infection control practices[15].

Yet, HBV outbreak investigations in North America and Europe point towards failure of health care personnel to adhere to fundamental principles of infection control and aseptic technique. Blood glucose testing was identified as the main putative mechanism of person-to-person transmission in a range of health care settings including community health care facilities, nursing homes, haemodialysis centres[8–10].

## **Influenza**

Influenza poses special hazards inside healthcare facilities and can cause outbreaks of illness.

Person-to-person transmission of influenza-like illness (ILI) and influenza has been described extensively in the literature as occurring in long-term care facilities (LTCF), especially among the frail and the elderly, as well as in acute hospital settings[16–18]. Yet accurate estimates of the burden of nosocomial influenza or ILI are hardly available.

While HCWs are at risk of acquiring influenza and may serve as a reservoir for the patients, multiple routes of nosocomial transmission are possible, as transmission links between single patients and HCW-patient show[16–18]. A prospective study assessed the risk of hospital-acquired ILI among patients hospitalised in several short-term units of one US hospital. The estimated risk ratio (RR) increased from 5.5 to 17.9 and to 34.7 if the patient had been exposed to one contagious HCW, one contagious patient or one HCW and one contagious patient respectively[17]. A review on the occurrence of outbreaks of ILI in acute health care settings, reports cases in a variety of different wards, including intensive care units (ICU), with attack rates ranging from 25% to 50% [18]. Fatalities during nosocomial outbreaks have also been reported, though mortality rates vary according to the affected patient population and circulating strain[18].

Despite the availability of a number of infection control measures that may be applied in combination, such as treatment of infected patients and patient isolation, the preventive role of HCWs vaccination on virus circulation and influenza incidence among patients may merit further considerations. According to recent studies, vaccine efficacy among vaccinated HCWs was estimated to be above 80%, much higher than that among hospitalised patients in the same setting [19], and was associated with a protective effect on hospitalised patients, at least in LTCFs [20,21]. Yet, the reported coverage of vaccination among healthcare professionals in Europe is low [22] and often perceived as personal protection measure rather than a patient safety one[23]. Several

interventions to increase vaccination uptake have been proposed [24], including compulsory vaccination for HCWs assisting high risk patients [23,24]

### **Rotavirus infection**

Rotavirus (RV) is the leading cause of dehydrating gastroenteritis and is responsible worldwide of the 40% of hospitalizations for diarrhea in children < 5 years[25,26]. RV is highly contagious due to its long survival in the environment, its resistance to antiseptic products, and the low viral load necessary to sustain infection. Pediatric wards are at increased risk of nosocomial transmission because they are an hub for severe RV cases[25,26]. An accurate estimate of incidence of nosocomial rotavirus infection (nRV) is hard to obtain due to the lack of active surveillance and methodological divergences among studies. A recent meta-analysis, however, found that, before UVP, incidence of nRV in Europe and North America was 0.4 case per 100 hospitalizations and 0.7 for children <5 years of age[25]. Availability of live attenuated vaccines against RV and their inclusion in UVP offers new opportunities to prevent nRV infection. UVP is deeply modifying the burden of RV disease. A decline of 62–78% for hospitalizations and 57% for ED visits due to RV has been observed in USA [26]. Two studies reporting data from an American and an Austrian single center found a significant decrease (67% and 92% respectively) for nRV after the implementation of UVP[27,28].

Where RV vaccination levels are still low, another approach to prevent nRV could be the targeted immunization of eligible subjects at increased risk of severe disease (e.g. infants born prematurely, with low birth weight, or with other high-risk medical conditions)[29]. Given the theoretical risk of nosocomial transmission of vaccine-type rotavirus, vaccination is now recommended only at or after discharge from neonatal care settings. A recent study[29] found no vaccine-type rotavirus transmission among unvaccinated age-ineligible infants admitted to an urban academic intensive care unit where eligible infants were vaccinated against RV. This evidence could lead to new opportunities for RV vaccination and prevention of nRV in high risk subjects.

### **Pertussis**

Nosocomial pertussis is a potential threat mostly in pediatric healthcare facilities[30]. HCW, visitors, parents, patients with delayed diagnosis have been identified as sources of nosocomial outbreaks[30]. Several factors may concur to heighten the risk of pertussis transmission in this setting such as the high prevalence of susceptible subjects such as infants too young to be vaccinated or immunocompromised patients; behavioral activities of young children (e.g. sharing of toys) and frequent visits of family members that may be a source of transmission, considering that

colonization with *B. pertussis* may be unrecognized among vaccinated adolescents and adults and may be present among individuals belonging to some religious or ideological groups that refuse vaccinations [30,31]. In addition, pediatric HCWs are at 1.7-fold greater risk for acquiring pertussis compared with the general population due to occupational exposures and waning immunity[30]. While effective prevention of pertussis in healthcare needs multiple concomitant actions (e.g education of HCWs and visitors, limitation of contacts among patients, correct respiratory hygiene, high suspicion in case of persistent whooping cough) immunization is considered the key preventive intervention. Due to the limited and waning effectiveness of pertussis vaccine, the choice of the correct vaccination strategy is essential. Together with vaccination of close contacts of infants (cocoon strategy), vaccination of pregnant women and booster vaccinations in adolescents, vaccination of HCW is emerging as an effective strategy to prevent pertussis in infants[30]. This is confirmed by a recent meta-analysis[32] that found moderate evidence that tetanus–diphtheria acellular pertussis vaccines for healthcare workers were effective in preventing pertussis in all age groups and specifically in infants.

**Measles (Rubeola Virus)** Measles (Rubeola Virus) is one the most contagious human disease[33]. Despite the current global effort for its elimination, suboptimal immunization levels still lead to recurrent outbreaks even in industrialized countries[34]. Hospital outbreaks are common, and both cases of transmission from patients to healthcare workers (HCW) and from HCW to patients are described. Measles can, moreover, spread from hospital setting to community. A recent review[35] reporting outbreaks involving hospital found that 22% of total cases could be classified as nosocomial. Nosocomial measles has high mortality and morbidity rates because of the underlying frailty of the subjects involved[35].

Healthcare settings are vulnerable for different reason: 1) Crowded and often inadequately ventilated places such as emergency department, triage wards, waiting rooms and physicians' offices are an ideal setting for the diffusion of airborne diseases 2) Measles can persist in aerosol suspension for at least one hour, so that infection is possible even if the index case has left the hospital 3) Measles is contagious before the onset of the characteristic rash and often requires access to emergency department due to acute but aspecific symptoms such as high fever, conjunctivitis and coryza. This can lead to delayed diagnosis and subsequent delayed adoption of isolation measures 4) Suboptimal immunization increased the mean age of susceptible subjects so that unvaccinated young adults, and the most part of HCW is in this category, are now a pocket of at-risk population[35].

Active offer of two dose vaccination along with recording of the immune status of all workers in the hospital, including hospital personnel not in direct contact with patients[36], and notification of all suspected cases represent the most efficacious preventive measure against measles. In case of outbreak, prompt implementation of respiratory isolation, offer of post-exposure prophylactic vaccination or immunoglobulins, and exclusion from workplace of susceptible HCW can help preventing further spread of the disease[35,37].

Nosocomial transmission represents a real public health threat potentially contributing to the spread of the disease in endemic areas and to reintroduction in regions where it had been previously eliminated[34,35]. It deserves intensive monitoring and prevention.

The use of combined vaccines against measles, mumps, rubella (German measles) and varicella (chickenpox) can help in preventing these diseases that can also cause nosocomial outbreaks and transmission from HCW to patients[21,38–40].

### **Meningococcal and pneumococcal infections**

The burden of nosocomial pneumococcal infections has not been described extensively. A study from Finland indicated a substantial proportion of reported cases of invasive pneumococcal diseases to be hospital-acquired[41]. Likewise reports of meningococcal disease spread in hospital are very rare and risk is considered quite low[42].

Data on coverage and effectiveness of pneumococcal and meningococcal vaccination for HCWs are hardly available in the scientific literature [43] as are policy options. HCWs vaccination has anyway a limited efficacy on patient safety due to suboptimal effectiveness of vaccination on carriage[44,45]. Universal respiratory precautions are generally considered sufficient prevent transmission in healthcare settings..

### **Future perspectives**

Both immunological and epidemiological factors make the risk of spread of VPDs in healthcare settings particularly high and VPD outbreaks are not rare. Universal vaccination programs, by reducing the spread of the infectious agent in the community, limit the risk of healthcare associated outbreaks of diseases like hepatitis B and rotavirus. On the other hand, spread of airborne diseases like influenza, measles, or pertussis is very difficult to prevent if a susceptible population is confined in a closed space like healthcare settings and the infectious agent still circulates in the community. Immunization of HCWs is an important strategy to limit the risk of such VPDs and improving vaccination coverage among HCWs is a priority. The ongoing developments of vaccines targeting other typical nosocomial pathogens such as *Clostridium difficile*, *Staphylococcus aureus*,

*Acinetobacter baumannii*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa* are promising and in a near future may become a valid support to limit the infectious risk in intensive care units [46].

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