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Cocoon Strategy of Vaccinations: Benefits and Limitations

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Abstract

A cocoon vaccination strategy refers to vaccinations in persons from the immediate environment of those patients who might develop an illness (they are susceptible to illnesses) but cannot be vaccinated due to permanent or temporary medical contraindications to a vaccination (e.g. immunosuppressed patients) or are too young to have a vaccination. Most frequently, a cocoon vaccination strategy is associated with vaccinations in adults aimed at preventing the spread of an illness in children (e.g. pertussis vaccination or influenza vaccination), but it is worth considering whether this strategy should not be understood also as vaccinations in children with the view of protecting adults and the elderly against illnesses (e.g. influenza or pneumococcal diseases). The aim of the cocoon strategy is to minimize the risk of the transmission of pathogens in the environment of a patient who is susceptible to an infection. A vaccinated patient is not a source of infection any more for a non-vaccinated patient. The chapter presents a history, current implementation of the strategy in different countries, its benefits and limitations.

Keywords: cocoon, vaccination, influenza, pertussis, strategy

1. Introduction

Immunization methods cover [1]:

1. routine vaccinations in children and adolescents under national immunization programs,
2. vaccinations in adults from risk groups (due to clinical recommendations, e.g. chronic diseases, and epidemiological recommendations, e.g. occupation, scheduled travels),

3. ring vaccination strategy (vaccination of a ring of close contacts of an ill person; it is a strategy used to stop an epidemic, as in the case of smallpox eradication in India) and
4. cocoon vaccination strategy.

A cocoon vaccination strategy refers to vaccinations in persons from the immediate environment of those patients who might develop an illness (they are susceptible to illnesses) but cannot be vaccinated due to permanent or temporary medical contraindications to a vaccination (e.g. patients in immunosuppression) or are too young to have a vaccination [1].

Most frequently, a cocoon vaccination strategy is associated with vaccinations in adults aimed at preventing the spread of an illness in children (e.g. pertussis vaccination or influenza vaccination), but it is worth considering whether this strategy should not be understood also as vaccinations in children with the view of protecting adults and the elderly against illnesses (e.g. influenza or pneumococcal diseases) [1].

The aim of the cocoon strategy is to minimize the risk of the transmission of pathogens in the environment of a patient who is susceptible to an infection. A vaccinated patient is not a source of infection any more for a non-vaccinated patient [1, 2].

2. Cocoon strategy and environmental immunity

The concept of a cocoon vaccination strategy is connected with herd immunity and herd immunity threshold [3].

Herd immunity is a term that was coined as a result of observations which showed that the presence of persons immune to a particular infectious disease in a certain population decreases the probability of developing this disease by other persons in this population who are not immune to this disease. The earliest observation of this phenomenon was made in 1840 by an outstanding British hygienist, William Farr, who wrote in his report on births, deaths and marriages in England and in Wales that “smallpox transmission might be interrupted or sometimes stopped thanks to vaccinations which protect a part of the population” [3]. However, the very term “herd immunity” was used by Topley and Wilson for the first time. In their studies into epizootic in mice under laboratory conditions, they concluded that “immunity understood as a characteristic of a herd should be approached scientifically as a separate issue that is closely related to immunity of particular specimens, but at the same time constitutes a different issue in many aspects” [3]. The essence of herd immunity is that the higher the proportion of specimens immune to a disease in a population, the lower the probability of developing the illness by a specimen with no immunity to the disease. Thus, the term can be used with reference to infectious diseases in which some specimens infect the others [3].

Herd immunity threshold is the proportion of persons who need to be immune in order to stop an infectious disease from spreading in a population. For most diseases, it is over 80% [3]. Herd immunity threshold is influenced by the following factors: transplacental immunity,

patient's age at the time of vaccination, age-related differences in the frequency of contacts or in infection risks (as the result of the decrease in the frequency of contacts, the real herd immunity threshold is lower than the estimated one), seasonal changes in the frequency of contacts (the period of decreased seasonal infectivity decreases the real herd immunity threshold as compared to the estimated threshold), geographical heterogeneity and social structure (irregularities of risk distribution in various social groups) [3]. Herd immunity threshold for pertussis is high, and it amounts to 92–94%. However, considering the decrease in infectivity with age and the seasonality of the disease the estimates indicate 88% [3].

Population-based vaccine efficacy depends on a high proportion of the vaccinated individuals in a population. A good example may be measles, a highly contagious disease, which has become a re-emerging disease in countries where the proportion of those vaccinated has diminished (e.g. Germany, Great Britain) [4]. Population protection (herd immunity) resulting from breaking the infection transmission with the use of vaccinations has been observed in Australia for vaccinations against rotaviruses (e.g. after the introduction of common vaccinations against rotaviruses, the frequency of hospitalizations due to acute diarrhea decreased) and vaccinations against human papillomavirus (HPV), as well as in Great Britain for vaccinations against *Haemophilus influenzae* type b and the meningococcal group C [5].

3. Cocoon strategy against pertussis

Pertussis is a contagious bacterial disease of the respiratory system caused by gram-negative rod *Bordetella pertussis*. Infection is transmitted through droplets or contact, and the source of infection is an ill person (there are no carriers) [6]. The disease can be developed in people who have not been vaccinated, fully vaccinated, properly vaccinated or who were vaccinated against pertussis a long time ago, as well as those who have already suffered from it because infection-acquired immunity to pertussis lasts only up to 20 years. The incubation period of the disease ranges from 7–14 to 22 days [6]. In total, the illness lasts up to 3 months, which is why it was called a 100-day cough in the Chinese medicine. The most serious pertussis complications occur most frequently in newborns and infants, and they include pneumonia, other bacterial or viral superinfections, segmental atelectasis and replacement emphysema, pertussis encephalopathy, seizures and encephalitis [6]. Mortality rate amounts to 0.1–4% [7–9].

Since mid-1980s, it has been observed that the epidemiological situation of pertussis in developed European countries, North America, Australia and Japan has been deteriorating. This results from the decrease in post-vaccinal immunity, which is not lifelong, but it lasts for 5–10 years. Currently, the highest incidence of pertussis is reported in adolescents and adults, and the representatives of these age groups are the main known source of infection for newborns and young infants who were not vaccinated against pertussis (in most countries, the first vaccination is given in the 6th week of life), were vaccinated with a delay or did not receive the required number of vaccination doses [7, 8]. It was found that the source of *Bordetella pertussis* infection in 30–75% of disease cases in newborns hospitalized for pertussis was persons from newborns' immediate environment (mothers, fathers or older siblings) (Table 1) [9–12].

Author	Results (source of pertussis)
Bonmarin et al. [9]	Parents 55% Siblings 25% Others 17%
Bisgard et al. [10]	Mother 32% Father 15% Siblings 20% Grandparents 8% Others 25%
Wendelboe et al. [11]	Adults 48–55% Siblings 16–21% Others 18–29%
Kowalzik et al. [12]	Mother 63% Father 13% Siblings 21% Others 30%

Table 1. Adults and adolescents as the main source of *Bordetella pertussis* infection in newborns [9–12].

Currently used strategies for pertussis prevention include [13–15] are listed below:

1. vaccinations in infants and small children, TDPw or TDPa vaccines,
2. booster vaccinations in children of pre-school age, TDPa or Tdpa vaccines, and in children of the school age (adolescents), Tdpa vaccine,
3. booster vaccinations in adults (recommended every 10 years), Tdpa vaccine,
4. vaccinations in pregnant women, Tdpa vaccine and
5. cocoon strategy for protective vaccination, Tdpa vaccine.

TDPw vaccines contain a whole cell pertussis component and may be used in infants older than 6 weeks till 36 months of age. However, due to a higher reactogenicity related to TDPw compared to TDPa vaccines [16, 17], the majority of high-income countries implemented TDPa vaccines into the national immunization schedules. On the other hand, it was reported that the duration of the immunity after TDPa vaccines may be shorter than TDPw vaccines [18]. **Table 2** illustrates differences between TDPa and Tdpa vaccines. Tdpa vaccines contain a reduced antigen content, and they are recommended for individuals older than 4 years of age.

In response to the alarming increase in pertussis morbidity in 2001, Global Pertussis Initiative (GPI) consisting of experts from 17 countries was established. In 2005, the organization

Contents of 0.5 ml of vaccine	TDPa	Tdpa
Diphtheria toxoid	>30 IU	>2 IU
Tetanus toxoid	>40 IU	>20 IU
Pertussis antigens:	8.0 µg	2.5 µg
Pertactin	25.0 µg	8.0 µg
Pertussis toxoid	25.0 µg	8.0 µg
Filamentous hemagglutinin		

Table 2. Differences between TDPa and Tdpa vaccines [6].

recommended the increase and extension of the scope of vaccination strategies and the implementation of booster vaccinations against pertussis in adolescents in developed countries. Special attention was drawn to pertussis prevention in newborns and infants who belong to the group, which is subject to the highest risk of severe pertussis. Three vaccination strategies were considered: vaccinations in mothers, vaccinations in newborns and cocoon strategy. On the basis of mathematical modeling, GPI estimated that routine vaccinations in adolescents connected with the cocoon strategy might diminish pertussis morbidity by 50%. These estimates resulted in national and international expert groups' recommendations in 2006 to introduce cocoon strategy in all countries, which have appropriate measures to do this [19].

Cocoon strategy involves administration of Tdpa to persons who have a close contact with newborns and infants (of up to 12 months of age), parents, grandparents, caregivers and older siblings. Optimal time of vaccination is at least 2 weeks before an expected contact with a child [14]. Strategies of vaccinations against pertussis in selected European countries are presented in **Table 3**.

In 2006, the Advisory Committee on Immunization Practices (ACIP) recommended routine Tdpa vaccination in adults who have or are likely to have a close contact with children of up to 12 months of age. In 2011, ACIP decided that this recommendation should be extended and include vaccinations in adults above the age of 65 years, for example, grandparents, nursery and kindergarten employees as well as healthcare facility staff [14]. Currently, cocooning is recommended not only by ACIP but also by American Academy of Pediatrics (AAP) and American Academy of Family Physicians (AAFP) [21].

It is estimated that 605 persons from immediate and distant environments of an infant have to be vaccinated in pertussis epidemiological situation in the USA in order to prevent one disease case, whereas in the case of vaccinations in adolescents, in order to observe the same effect, a four-times bigger group needs to be vaccinated, that is, 2325 persons [14]. This can be explained by the fact that although small children are the source of infection for other population groups in most infection cases (e.g. influenza, pneumococcal infections), in the case of pertussis, an opposite situation can be observed. Common vaccinations in infants and small children have resulted in the transmission of the disease to older age groups and thus household members, parents and adolescents have become the source of infection [6, 14].

Country	Basic vaccination	Booster vaccinations in children and adolescents	Booster vaccinations in adults
Austria	2–4–6 months	12–24 months, 13–16 years	Every 10 years
Belgium	2–3–4 months	15 months 5–7 years, 14–16 years	Cocoon strategy
Finland	3–5–12 months	4 years, 14–15 years	–
France	2–3–4 months	16–18 months, 11–13 years	27–28 years, all healthcare employees (2008) Cocoon strategy
Germany	2–3–4 months	5–6 years, 11–15 years	Cocoon strategy Healthcare employees (2003)
Italy	3–5–11 months	5–6 years, 11–15 years	–
Netherlands	2–3–4 months	11 months 14 years	–
Poland	2–4–6 months	18–18 months, 6 years, 14 years	Healthcare employees who have contact with infants (2015); Adults > 19 years—every 10 years Cocoon strategy (2015)
Switzerland	2–4–6 months	15–24 months 4–7 years (11–15 years, catch up)	–
Luxembourg	12 months	5–6 years, 15–16 years	Every 10 years

Table 3. Strategies of vaccinations against pertussis in particular European countries [20].

Although cocoon strategy against pertussis is accepted by caregivers of young children, its implementation is at a low level. According to the data of 2008, only 5% of adults who had a close contact with infants were given Tdpa vaccinations [14]. Leboucher et al. [22] showed that the idea of cocooning was accepted by 97% of parents of newborns, which resulted in vaccinations in 69% of mothers and 63% of fathers. In 96% of cases, vaccinations were done under the conditions of ambulatory healthcare (at a family doctor) [22]. Decréquy et al. [23] observed that before the cocooning program was implemented on a chosen maternity ward, only 20% of mothers and 13% of fathers had been vaccinated against pertussis, whereas after

the introduction of educational activities, the level of vaccinations increased to 77% in mothers and 57% in fathers. It was indicated that the continuation of vaccinations is necessary, not only at a local but also at a national level [23].

A few reasons that prevent cocoon strategy against pertussis from being commonly implemented and accepted were identified. It was indicated that to improve the cocooning strategy, it is required to combine parental education with free vaccinations in pediatric or maternal settings [14, 22]. However, implementation of the cocoon strategy on maternity and neonatal wards as well as in pediatric centers requires resources from a doctor to undertaking activities, which go beyond their scope of standard duties, not to mention financial issues related to costs and refunds. Furthermore, implementation of this strategy requires substantial financial resources and the increase in the number of healthcare personnel [6].

Currently, data evaluating the effectiveness of a cocoon strategy are limited. Skowronski et al. [24] suggested that cocooning may not be cost-effective in areas where a disease incidence is low. The authors concluded that it would take 1 million parental immunizations to save one infant death, 100,000 parental immunizations to save one infant's intensive care unit admission and 10,000 parental immunizations to prevent one infant's hospitalization [24]. However, Westra et al. from the Netherlands found that maternal immunization or a cocooning program for both parents was cost-effective and even cost-saving [25] as compared to just an infant immunization program. Healy and Baker [26] found that up to 75% of infant pertussis cases are acquired from a household contact, and cocooning could lead to a 70% reduction in pertussis cases in infants of less than 3 months of age.

The concept of "number needed to treat" to estimate the number of adults that would need to be vaccinated (NNV) to prevent one case of disease, hospitalization and death due to pertussis was used and described by researchers from Ontario (Canada) [2]. After implementation of the cocoon strategy against pertussis, the NNV to prevent one case, hospitalization or death from pertussis was between 500–6400, 12,000–63,000 and 1.1–12.8 million, respectively (after adjusting for under-reporting). Rarer outcomes were associated with higher NNV [2]. The authors also demonstrated that NNV estimates for pertussis vary greatly depending on the frequency of the outcome, including the target age group, the degree of under-reporting believed to be in existence, the assumed vaccine effectiveness (VE) and the estimated proportion of infants infected by the mother and the father. It was concluded that the objectives of implementing a cocoon immunization strategy must be carefully considered if the strategy should be evaluated properly. If the objective of the program is to prevent pertussis in the population in general, a universal strategy should be considered. However, if the objective is to prevent deaths due to pertussis, a large number of adults need to be vaccinated [2]. A similar conclusion was presented by Italian authors [27].

The cocoon strategy against pertussis was implemented in the USA in 2006. Data from two small studies reported conflicting results. One study documented a 50% decline in the incidence of pertussis in hospitals with a post-partum Tdap vaccination policy in 2006 ($n = 48$), while a 20% increase was observed among hospitals that did not have such a policy ($n = 145$) [28]. In contrast, Castagnini et al. [29] found no difference in the rates of illness, length of hospitalization or mortality in infants under 6 months of age when post-partum women were

vaccinated prior to discharge. The authors recommended that all household members and key contacts of newborns should be immunized instead. There is also evidence that immunization coverage of high-risk groups increases when vaccination programs are universal rather than targeted [30, 31].

4. Vaccinations against influenza in cocoon strategy

Influenza is a severe infectious disease caused by *Orthomyxoviridae* viruses. Influenza in child population is an undervalued, not to say underestimated, problem. This might result from the fact that disease symptoms are non-specific and the disease diagnostics is quite difficult, although accessible and feasible both on an outpatient and on an inpatient basis [32]. It is estimated that influenza virus infections cause 10–40% of acute febrile respiratory tract infections in children annually; however, in closed environments this rate might amount even to 50% [33].

In the course of establishing worldwide influenza in children at the age of below 5 years in 2008, Nair et al. [34] estimated, on the basis of an analysis of 43 studies, that in that year there were 90-million influenza cases in the mentioned age group globally. A 13% of cases developed acute lower respiratory insufficiency (ALRI) and 28,000–111,500 cases resulted in death [34].

Occurrence of severe seasonal influenza cases in children and adolescents is described by the number of deaths and the number of hospitalizations in intensive care units. The actual occurrence of influenza in children is underestimated due to the fact that children who suffer from mild influenza are not even consulted on an outpatient basis [32, 33].

In comparison with adults, children who suffer from influenza, especially infants below the age of 1 year, require a higher number of consultations on an outpatient basis [35]. According to the study, 24% of all outpatient influenza-related visits concerned children [36]. A big number of outpatient visits related to influenza and its complications generates not only direct costs but also indirect costs that are, for example, connected with the child caregivers' absence from work and the loss of earnings [36]. Furthermore, these visits constitute an organizational challenge for medical facilities. The number of hospitalizations related to influenza and its complications in children in the USA is estimated to amount to 0.9/1000 children, and most of them concern children at the age of below 1 year [37]. The risk of influenza-related hospitalizations in children of pre-school age is comparable to the risk that is observed in the group of the elderly above the age of 65 years [37]. The number of hospitalizations for influenza in children at the age of up to 5 years amounts to 5/10,000 children and in adolescents, 1/10,000 persons [37]. A study by Rhim et al. [38] demonstrated that 7.3% of children who reported to admission rooms in pediatric hospitals due to influenza-like symptoms required hospitalization, whereas a study by Irving et al. [39] showed that 5% of outpatients diagnosed with influenza required hospitalizations.

Influenza mortality in children is estimated at <1/100,000 patient-treatment years and unfortunately most deaths (even up to 50%) occur in children with no additional disease burden [40]. Deaths due to influenza in children are rare. In the USA in 2003/2004, mortality in this

group of patients amounted to 2.1/1,000,000 [40]. In the twentieth and twenty-first centuries, influenza can be effectively prevented with vaccinations. It is worth noticing that influenza deaths in children occur also in those children who suffer from no additional burdening diseases that could classify them as patients who are subject to the risk of the severe course of the disease. For example, in 2003/2004 in Great Britain, 17 deaths due to influenza in children and adolescents aged below 18 years were observed and they all occurred in patients who were initially healthy [41]. Furthermore, sudden deaths in children caused by influenza B virus infections were reported. The causes of deaths were determined only in an autopsy (concerning intravital diagnosis, there were no symptoms from the respiratory system but from the digestive system) [42].

Cocoon strategy in influenza prophylaxis was created on the basis of data concerning cocoon strategy in pertussis prevention. Justification of cocoon strategy for influenza is different than for pertussis because no influenza vaccination can be used in infants aged below 6 months due to low immunogenicity in this age group. As mentioned above, the risk of hospitalization in infants due to influenza is particularly high, and the greatest risk concerns children aged below 6 months. The frequency of influenza hospitalizations in healthy infants is similar to the frequency of hospitalizations in adults who are in a high-risk group. Therefore, effective solutions are necessary to provide appropriate protection for this particularly susceptible population group. Influenza prophylaxis includes hand hygiene, avoiding contact with the ill and vaccinations in persons who have a close contact with the ill.

In the first year of their lives, newborns whose mothers were not vaccinated against influenza either have no immunity to influenza viruses or they have low adaptive immunity. Therefore, it is recommended to vaccinate household members and caregivers of infants at the age below 6 months. Such vaccinations should result in the increase in children protection through creating a protective cocoon. Not all adults are aware of the importance of influenza vaccinations in adults and in children. In order to increase the number of vaccinated persons, it is necessary to provide educational activities and develop initiatives addressed not only at the employees of healthcare facilities but also at patients.

Time is another factor that limits the implementation of cocoon strategy in influenza prophylaxis. The strategy can be effective only when all persons from the immediate environment of a newborn, as well as newborn's relatives and caregivers, are vaccinated at least 4 weeks before the child is born because an immunologic response to a vaccination requires time. Gynecologists and obstetricians should propose vaccinations to women on their visits to health centers before they become pregnant or during the pregnancy. After persons from the immediate environment have been vaccinated, another method of infants' protection against influenza is vaccinations in pregnant women. A recent study conducted in Bangladesh, which evaluated vaccinations against influenza in pregnant women, showed that the number of laboratory-confirmed influenza cases in infants of vaccinated mothers decreased by 63% [43].

Cocoon strategy encourages education of patients and employees of healthcare facilities. Educational activities might increase the percentage of the vaccinated population. In families, the main sources of infections for newborns and infants are parents and siblings.

Studies show that providing parents of newborns with information on the benefits of influenza vaccinations, as well as providing free-of-charge vaccines, positively influences implementation of the cocoon strategy. Walter et al. [44] indicated that after such activities had been implemented in one maternity hospital, 54.9% of parents underwent vaccinations (vaccinations were given in maternity units and were free of charge for mothers only). Shah et al. [45] observed even higher indicators (86.9–95% in two consecutive years in parents of newborns in an intensive care unit).

5. Cocoon strategy for vaccinations in contact with immunosuppressed patients

Patients in immunosuppression resulting from anticancer or anti-inflammatory treatment (inflammatory bowel diseases [IBD], rheumatic diseases) might not achieve appropriate level of protection after the vaccination (vaccines that are considered to be safe for this group of patients are inactivated vaccines). This is why minimizing the risk of disease transmission in those patients' environment is of significant importance. In particular, influenza, pertussis and chickenpox vaccinations are recommended [46]. Unfortunately, vaccinations in the contacts of patients in immunosuppression are at a low level, which proves that education in this group is highly necessary. Waszczuk et al. [47] conducted a self-completed survey among patients with inflammatory bowel disease (IBD) and reported that the use of recommended vaccines in family members of patients was insufficient (22–26%). There was a statistically significant association between the non-reimbursed vaccines coverage level and the educational status of patients [47].

6. Cocoon strategy for vaccinations in healthcare professionals

Due to frequent contact with the ill, high infectivity of the diseases and lack of life-long immunity to diseases, healthcare personnel belong to a group which is highly at the risk of becoming infected with *Bordetella pertussis* or influenza virus.

In the case of pertussis, it is estimated that the risk of developing an illness by healthcare professionals is almost two times higher as compared with the general population. Serological results of one study showed that *Bordetella pertussis* infection in healthcare professionals subject to five-year observations was 2 times higher in 55%, 3 times higher in 17% and 4 times higher in 4% of the personnel [48]. Pertussis might become a hospital infection and its source might be either a patient or a healthcare personnel. Outbreak of the disease in healthcare professionals threatens patients' health, especially infants' health. Activities to stop the outbreak might be costly and disturb the functioning of a healthcare facility. Ward et al. [49] described a pertussis outbreak in a 600-bed general hospital in Paris with 2100 employees. In November 2000, three pertussis cases in the personnel were observed there. An epidemiological investigation showed that the first case was a 51-year-old woman who infected three coworkers. A local committee for hospital infections decided to conduct screenings in all healthcare

employees and patients. Personnel with respiratory symptoms were excluded from work for the first 5 days of antibiotic treatment. Eventually, pertussis was diagnosed in 17 persons, including 15 members of the personnel and 2 patients. The cost of controlling the outbreak, mostly diagnostic tests, treatment and the loss of productivity, amounted to over 46,000 Euro.

Baggett et al. [50] described two pertussis outbreaks in hospitals in King county in the United States of Washington which occurred in 2004:

1. In the first hospital, the source of infection was a 38-year-old doctor who worked on an emergency ward (at that moment when she developed the illness, she was in the 37th week of pregnancy, coughing fits and vomiting after the fits lasted for 37 days, and the doctor associated them with the exacerbation of concurrent bronchial asthma). Epidemiological investigation identified five probable cases, which met the pertussis clinic definition of Centers for Disease Control and Prevention (CDC) at that time, and two cases were confirmed. Disease cases concerned two nurses, a receptionist, a close friend of the infected doctor and the doctor's husband. The woman put 738 persons at risk of infection, including 388 hospital workers, 265 patients and 85 visitors. Among them, 600 persons were examined (80%) and 516 persons were administered antibiotics. Furthermore, one patient who was admitted to the hospital for an emergency appendicitis operation and had contact with the infected doctor in the admission room had a positive polymerase chain reaction (PCR) result without typical clinical symptoms. This resulted in testing 95 persons who had contact with the infected woman (92 persons were given antibiotics) and 29 PCR tests (all results were negative). Hospital pertussis outbreak had significant economic and organizational consequences. The costs included diagnostic tests, antibiotics for all hospital employees with respiratory symptoms who had contact with the persons diagnosed with pertussis and excluding them from work for the first 5 days of treatment and

2. In the other hospital, a 38-year-old physiotherapist working in an intensive care pediatric unit visited a company doctor due to persistent coughing fits which lasted for 22 days. Although the cultivation and testing of the PCR material from nasopharynx were negative and so was the direct immunofluorescence test, an epidemiological investigation was initiated since clinical criteria were fulfilled by the physiotherapist. Pertussis was diagnosed and confirmed in three nurses from the intensive care unit and in one resident doctor who had contact with the ill person. It was estimated that 417 hospital workers, 200 hospital visitors and 120 patients were potentially exposed to the disease. *Bordetella pertussis* infection was confirmed with the PCR method in four members of the hospital personnel. At the expense of the hospital, antibiotics were administered to 343 workers and 70 visitors and patients. Employees with respiratory symptoms were expelled from work for 1 day until obtaining the negative PCR result. The costs of activities connected with controlling the outbreaks exceeded 260,00 US dollars in the first hospital and 120,000 US dollars in the other hospital, and they were connected mostly with the costs of overtime related to expelling persons at risk of pertussis from work and with remuneration for additional work for the hospital infection team.

Calugar et al. [51] focused on cost-effectiveness of pertussis vaccinations in healthcare personnel. They analyzed a pertussis outbreak which occurred in 2003 in a specialist clinic in the USA after a 1-day exposure of healthcare personnel to an infant with a confirmed pertussis

diagnosis [51]. Three hundred and seven members of healthcare personnel were at risk and seven of them had symptomatic pertussis. The authors estimated that vaccinations in healthcare professionals would prevent over 46% of pertussis cases, and from the perspective of the hospital, they would decrease the costs of controlling the outbreak. The authors concluded that pertussis might disturb the functioning of the hospital and that personnel vaccinations could decrease the number of infected workers and could enable the hospital to achieve savings. Members of healthcare personnel who are at the highest risk of developing pertussis are persons who work on pediatric wards and in pediatric centers.

According to ACIP recommendations, it is advisable to promote pertussis vaccinations in healthcare personnel and to facilitate access to these vaccinations (e.g. through facilitating vaccinations at the place of work, providing free-of-charge vaccines, etc.). Activities aiming at performing vaccinations in a vast number of workers should also include educational activities concerning the illness and its consequences (for the personnel and patients), and informative activities regarding the vaccines, their safety and effectiveness. It is not recommended to do serological tests for pertussis before the vaccination and after it. Recovering from pertussis is no contraindication for the vaccination [52].

It was estimated that the costs of including healthcare personnel, who have a direct and close contact with patients, in a pertussis vaccination program in the USA could be two times lower in a 10-year perspective than controlling pertussis epidemics in healthcare facilities [52].

On the basis of serological tests, it can be estimated that even 25% of healthcare professionals have contact with influenza viruses on an annual basis [53]. Interestingly, 25% of persons who had direct contact with patients whose serological tests proved past influenza infections did not provide disease symptoms in the interview [54]. This might indicate a possible mild course of the infection or an infection accompanied with very few symptoms. Nonetheless, these persons can still be a source of infection both for patients and for other members of healthcare personnel [54]. Infectious disease epidemics, including influenza outbreaks, in healthcare facilities might bring measurable and significant consequences for the finance, for example costs of controlling and epidemic outbreaks (patient isolation, implementation of antiviral treatment), costs of temporary termination of medical services due to cancellation of admissions, costs of employing special personnel to care about particular patients suffering from influenza, consequences for the hospital image—loss of trust among patients, impediments in patient visits and legal consequences—and compensation claims [48]. Healthcare professionals are exposed to infections through droplets or contact with influenza viruses at the place of work and they might become the source of infection for patients. Most of them belong to a group which is at a high risk of the severe course of disease and influenza complications due to their age and chronic illnesses, for example, respiratory system diseases (bronchial asthma, chronic obstructive pulmonary disease), cardiovascular diseases or metabolic diseases (e.g. diabetes). According to the studies, 75% of doctors admit that they perform their professional duties despite having disease symptoms, which indicate a current respiratory system infection [52, 53]. Influenza complications, hospitalizations and deaths related to influenza or its consequences occur mostly in chronic patients, infants and young children (aged 2–5 years), senior citizens and pregnant women [54]. Vaccinations in healthcare personnel are particularly

beneficial for those patients who cannot be given a vaccination, for example patients who are too young (infants at the age 6 months for whom there are no registered vaccines—it needs to be stressed that influenza infections have been observed even in newborns), patients with medical contraindications to vaccinations (e.g. occurrence of a strong anaphylactic reaction after influenza vaccination confirmed allergy to any component of the vaccine), patients who do not respond to vaccination appropriately (e.g. persons aged 85 and more, patients in immunosuppression) and persons who cannot be treated with antiviral medications due to medical contraindications (mostly neuraminidase inhibitors). Thus, influenza vaccinations in health-care personnel constitute an element of cocoon strategy for protective vaccinations [55]. The results of published studies indicate that influenza vaccinations in healthcare professionals in medical facilities ensure a significant decrease in general mortality and flu-like disease morbidity in patients requiring long-term care [56–58]. Carman et al. [56] showed that achieving 50% level of vaccinations in the personnel of a nursing home for the elderly results in the reduction of mortality among the elderly residents by 40%. Individual benefits for the personnel arising from influenza vaccinations are less documented [56–58]; however, it was observed, for example that the number of days absent from work due to respiratory system infections decreased and so did the risk of influenza virus infections (88–89% on average) [59, 60]. A slight decrease in the number of days absent from work (by approx. 0.5 days) was also obtained in the population of vaccinated healthy persons of working age [59, 60]. Salgado et al. [61] showed that the number of laboratory-confirmed influenza cases and the percentage of hospital respiratory system infections diminished from 42 to 9 and from 32 to 3%, respectively, in a group of influenza-vaccinated medical professionals.

Scientific literature gives examples of influenza epidemics in hospital wards which spread in patients requiring special care. In 1998, an epidemic broke out in a neonatal intensive care unit which resulted in disease cases in 19 out of 54 patients and a death of 1 child. Only 15% of the personnel had been vaccinated and 29 persons admitted to taking care of patients while having symptoms of a respiratory system infection [62]. In the same year, 10 patients developed influenza in a bone marrow unit and 1 person died. In this case, 12% of the personnel had been vaccinated and five personnel members were at work with disease symptoms [63]. Influenza virus outbreaks were also observed in liver transplantation, hematological, neonatal and pediatric units (in the last two units, additional risk factors for influenza virus infections were identified: artificial ventilation system and multiple pregnancy) [64–67]. A group of patients who are particularly at risk of hospital epidemics are residents of facilities, which render care and treatment services for patients with chronic illnesses. During the occurrence of an influenza outbreak in a facility whose residents were at the age of above 65 years, the percentage of infected patients in an epidemic season was very high and it could reach even 60% [68]. The facts that influenza vaccinations in the elderly are not as effective as vaccinations in a younger population (30–40% vs 70–90%), and that influenza epidemics occurred in the populations of the residents of nursing homes, where influenza immunization was very high and reached even 90%, prove that it is necessary to perform vaccinations in healthcare professionals in order to protect the patients [69, 70].

Unfortunately, percentage of medical professionals who are vaccinated against pertussis in developed countries is relatively low. According to the studies, although educational activities

result in the increased interest in the vaccinations, only a small group of healthcare personnel are vaccinated despite their initial intentions of undergoing a vaccination. Pertussis education for medical professionals could solve this problem. Tdpa vaccine is safe and effective. Pertussis booster vaccinations for healthcare personnel might be the most effective to diminish the risk of pertussis cases and the occurrence of hospital infections in healthcare facilities.

7. Benefits and drawbacks of the cocoon strategy for protective vaccinations

The main benefit of cocoon strategy is that it decreases the risk of the transmission of an infectious disease in the environment of a patient who might become infected but cannot be vaccinated. A universal adult pertussis program does not only serve to decrease the disease in the overall risk of disease among infants (beyond that which might be achieved with a more focused cocoon strategy) but it also protects adults against the disease.

The main drawback of a cocoon strategy is that it is characterized by a low level of recommendation implementations and a small percentage of vaccinated persons, which impairs the performance of this strategy. It is critical to the success of a universal program to ensure that adequate vaccine coverage is achieved. A comparison of various immunization strategies suggests that the coverage of at least 40% within the adult population is required to achieve herd immunity [2]. In practice, achievement of such high indicators is impossible.

Barriers to receiving vaccines by close contacts include lack of knowledge about the disease and the benefits of vaccination, time and monetary constraints, forgetting about vaccine recommendations if previously received.

Although it is recommended to vaccinate all close contacts under a cocoon strategy, vaccinations are frequently limited to mothers, which also influence negatively the effectiveness of the strategy. Vaccinations should be universal and cover caregivers of all infants instead of being addressed solely to the families of children from risk groups.

To conclude, cocoon strategy for protective vaccinations constitutes a valuable complement to universal vaccination programs. Nonetheless, it should not be the only recommended strategy but it should be an element of a comprehensive strategy for preventing infectious diseases.

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