Original Paper DOI: 10.5114/biolsport.2017.66001 Biol. Sport 2017;34:243-248

Pertussis outbreak in Polish shooters with adverse event analysis

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ABSTRACT: In addition to different injuries, infections are the most common reason for giving up training altogether or reducing its volume and intensity, as well as a lack of opportunities to participate in sports competitions. Nowadays, a slow but constant re-emergence of pertussis, especially among teenagers and young adults, including athletes, can be observed. This paper describes an outbreak of pertussis among professional Polish shooters, focusing on the transmission of *Bordetella pertussis* infection between members of the national team, its influence on performance capacity and adverse event analysis. From 9 June, 2015 to 31 July, 2015, a total of 4 confirmed and suspected cases of pertussis were reported among members of the Polish Sport Shooting National Team, their relatives and acquaintances. Pertussis significantly decreased exercise performance of the first athlete, a 35-year-old woman, interrupted her training, and finally resulted in failure to win a medal or quota place. Pertussis also significantly decreased performance of the second athlete, a 25-year-old shooter. The other cases emerged in their families. Whooping cough is a real threat to athletes and should be prevented. Preventive measures include appropriate immunization, constant medical supervision, as well as early isolation, diagnostic tests and treatment of all infected sport team members. Regular administration of booster doses of the acellular pertussis vaccine (Tdpa) every 5 years seems reasonable.

CITATION: Skrzypiec-Spring M, Krzywański J, Karlikowska-Skwarnik M et al. Pertussis outbreak in Polish shooters with adverse event analysis. Biol Sport. 2017;34(3):243–248.

Received: 2016-11-04; Reviewed: 2016-12-06; Re-submitted: 2017-01-03; Accepted: 2017-01-20; Published: 2017-02-19.

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Key words:
Bordetella pertussis
Infection
Vaccination
Sports competition
Shooting

INTRODUCTION

The widespread Gram-negative bacterium *Bordetella pertussis* causes whooping cough or pertussis, an acute, potentially serious infectious disease affecting mainly infants and young children in the pre-vaccine era, currently occurring in healthy teenagers and adults including athletes. In the 20th century, before the availability of pertussis vaccine, whooping cough was one of the major causes of mortality in infants. Universal pertussis immunizations while maintaining a high level of vaccination coverage significantly decreased incidence of the disease in infants and young children. Nowadays, we can observe slow but constant re-emergence of pertussis, especially among teenagers and young adults, including athletes. According to the present Polish Immunization Schedule, the routine pertussis immunization includes administration of 4 doses of diphtheria-tetanus-whole cell pertussis vaccine (Diphtheria-Tetanus Pertussis whole cell vaccine – DTPw) in infants at 2, 4, 6 and 16 to 18 months of age and subsequent administration of two booster doses of diphtheria-tetanus-acellular pertussis vaccine (Diphtheria-Tetanus Pertussis acellular vaccine – DTPa) at the ages of 6 and 14 years [1]. Some infants may receive acellular vaccine instead of the whole cell vaccine either as recommended vaccination (fully paid by parents) or free of charge vaccination (provided for children with medical contraindications for DTPa, preterm born infants, etc.) [1]. In Western Europe and the United States recommendations regarding the immunization schedule vary, but generally include the administration of 5-6 doses of the acellular vaccines [2,3]. Despite these differences, immunity to pertussis wanes within 5-10 years after the last dose of the vaccine. Therefore, athletes who do not receive regular booster doses are at risk of pertussis. According to data published by the Polish National Institute of Public Health and Chief Sanitary Inspectorate, in 2014 there were 2101 cases of pertussis reported (5.46/100 000 per year), while in 2015 there were 4956 cases (12.89/100 000 per year) and the majority of cases occurred among teenagers and

adults [4]. The epidemiology of pertussis is similar in Europe: the incidence of pertussis is highest in children aged 10-14 years (13.2% of cases in 2014) and adults older than 30 (47.7%) [5]. One should also remember that epidemics occur every 3-5 years in the natural course of the disease.

Although athletes are generally believed to have a better health status comparing to the general population, this does not protect them from contracting infectious diseases, e.g. influenza, pertussis or sexually transmitted diseases (STD). Moreover, there has been a significant amount of evidence linking strenuous exercise with increased risk of respiratory tract infections ("open window" hypothesis). It is suggested that while moderate exercise may enhance immune functions, prolonged, strenuous exercise may impair the immune response and foster respiratory infections [6].

Large sports meetings and venues not only give a chance for athletes to win medals but also provide an opportunity for rapidly spreading air-borne infections. Mass gatherings of people – athletes, staff members and fans – as well as shared narrow spaces such as locker rooms, transport vehicles, canteens and hotels create a high risk environment for acquiring pathogens spreading among other team members.

Our article describes an outbreak of pertussis among professional Polish shooters focusing on the transmission of *Bordetella pertussis* infection between members of the national team, its influence on performance capacity and adverse event analysis.

Description of the outbreak

The index case

The index case was 32-year-old female elite shooter, a member of the Polish National Team. She presented with a paroxysmal dry cough, localized upper abdomen pain, loss of appetite and underperformance at the day of departure for the European Games in 2015. The athlete's disease started two weeks earlier from an isolated, recurrent paroxysmal dry cough not accompanied by other symptoms. Previously, she had been healthy, with no chronic conditions, allergy and negative smoking history. The physical examination did not reveal any abnormalities. Her basic laboratory tests were also unremarkable. Because the chronic cough persisted for approximately 3 weeks, a chest x-ray was performed and revealed no abnormalities. The allergy, asthma and atypical respiratory infections caused by *Mycoplasma* or *Chlamydophila* were taken into consideration but the respiratory allergy was regarded as the most probable explanation. The persistent cough also raised a suspicion for *Bordetella pertussis* infection, but a lack of the classic presentation with a characteristic wheezing was one of the arguments against that diagnosis. Empirical therapy with azithromycin in a single daily dose of 500 mg for 3 days was ordered because serologic and microbiological testing was not available at the sport venue. Clinical symptoms partially resolved, but after a few days the frequency of cough paroxysms increased. The cough did not respond to symptomatic antitussive therapy. The extremely strong coughing exhausted the athlete and led to sleep deprivation, markedly decreasing her sport performance. It resulted in her failure to obtain a Quota Place to enter the Olympic Games. The patient returned home and was referred to a pulmonologist 5 weeks after the onset of symptoms. Serologic tests with high antibody titres to pertussis toxin (IgG concentration higher than 200 IU/ml) confirmed the diagnosis of pertussis (no history of pertussis vaccination during the past 10 years was obtained from the patient). The athlete was prescribed oral azithromycin in a dose of 500 mg/day for one week. The paroxysms of coughing decreased in frequency and finally resolved within the next 3 weeks.

Secondary cases and spread of the Bordetella pertussis infection

Two weeks later, the husband of the index case developed a malaise and cough and his serological tests (IgG concentration higher than 200 IU/ml) confirmed *Bordetella pertussis* infection. The next secondary case was a 25-year-old male elite shooter, also a member of the Polish National Team, who developed symptoms of nasal congestion, rhinorrhea, sneezing, malaise, fatigue, and dry cough during the European Championships in 2015. One month previously he had travelled together with the index case by the same plane and bus in close proximity. The athlete was given oral azithromycin in a daily dose of 500 mg for one week without waiting for laboratory confirmation of the disease to prevent spreading. The athlete responded well to the empiric therapy, but the dry cough resolved after the next 3 weeks. Serological tests performed a month after the onset of symptoms revealed markedly elevated IgG and IgA titres to pertussis toxin (IgG and IgA concentrations higher than 200 IU/ml and 14 IU/ml, respectively), making the diagnosis of pertussis highly probable. The epidemiologic investigation revealed that the 64-year-old man, a coach of the Spanish National Team, was probably the source of infection for the index case. Although his diagnosis was not confirmed by serological tests, the presentation of the disease with typical paroxysms of coughing persisting for a few months strongly suggested the diagnosis of pertussis.

Adverse event analysis

The described outbreak of pertussis among Polish elite shooters (an appropriate timeline is presented in Figure 1) is worth a deeper analysis to prevent similar outbreaks in future. The modern sport is highly competitive, and all factors impairing even slightly the athlete's performance during games reduce the chance of winning. In addition to different injuries, infections are the most common reason for giving up training altogether or reducing its volume and intensity, as well as a lack of opportunities to participate in sports competitions [7-12]. Since pathogens vary in nature and can be transmitted through different routes – inhalation of airborne infectious agents, skin contact or injuries, ingestion of contaminated food or water, via vectors (e.g. tick or mosquito bites) and sexual contacts – infections can be prevented by various measures including the isolation of infectious subjects, hygienic measures, mosquito avoidance, immunization and pharmacological prophylaxis. Simple hygiene measures performed

by athletes may decrease the risk of infecting themselves or others: washing hands, especially before and after preparing food, before eating, and after using the toilet, avoiding touching mucous membranes (eyes, nose or mouth) with hands, staying home when ill (e.g. when vomiting, having diarrhoea or having a fever), practising safe sex with use of condoms especially when the partner has a history of sexually transmitted infections or high-risk behaviour. It is also important not to share personal items such as toothbrushes, combs and razors as well as drinking glasses or dining utensils. Active immunization by vaccines can drastically reduce the risk of contacting many infectious diseases including pertussis. Not only athletes but also their children and other household members may serve as sources for infectious diseases and should be up to date on their recommended vaccinations. One must remember that according to the Polish Immunization Schedule 2016, the acellular pertussis vaccine with a reduced amount of tetanus and diphtheria toxoids (Tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine – Tdpa) is recommended to all adults older than 19 years every 5-10 years. For example, in 2015 the Tdpa vaccine was given to 1768 persons aged 20-29 years and 4377 persons older than 30 years [4]. Although little is known about the pertussis vaccine coverage rates among adults in Poland, it seems to be very low. As the last mandatory pertussis vaccination is given to adolescents who are 14 years old, the majority of Polish adults are susceptible to the disease. Immunization is a prophylactic method of special importance in case of travelling out of the country. Elite athletes are often frequent travellers, and thus they are prone to infections not prevalent in their home countries and may need special vaccinations such as yellow fever, cholera, hepatitis A or typhoid fever as well as malaria chemoprophylaxis. The Tdpa vaccine instead of the tetanus and diphtheria toxoids (Td) vaccine is also recommended for adult travellers, not only as prophylaxis against tetanus (the risk of injuries), but also as prophylaxis against diphtheria (which still occurs, for example, in Eastern European countries) [2,13].

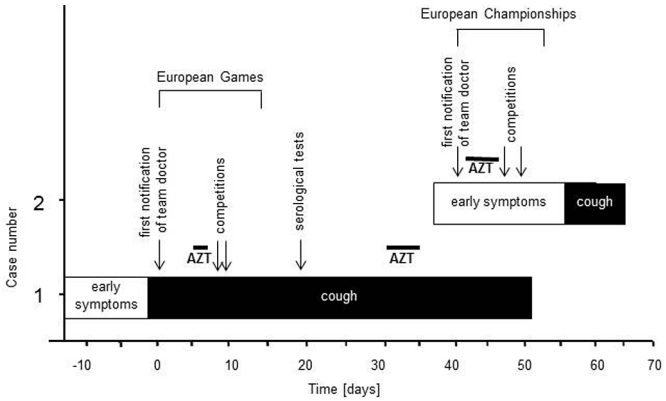

FIG. 1. Timeline of pertussis outbreak in Polish shooters (including the intervals between cases and treatment).

As illustrated by the presented outbreak, pertussis is a real threat to elite athletes. The analysis of adverse events can reveal logistic, systemic and environmental problems, mistakes or failure points to determine their root causes and recovery procedures. The analysis of the outbreak indicates the following problems and failure points:

Poor surveillance of infectious diseases

Infectious diseases among athletes and other members of sport teams should be detected and reported. Based on the local epidemiology, infectious diseases important for the athletes should be identified and prophylactic measures implemented promptly. In the case of pertussis, vaccination is an effective preventive measure, and all athletes and their family members should regularly obtain booster doses. For contacts, pharmacological prophylaxis should be given (azithromycin, clarithromycin or erythromycin doses and duration of the antibiotic courses are the same for prophylaxis and treatment of the disease) [14].

Delayed diagnosis

The etiology of the cough in the index case was determined late – too late for effective treatment with antibiotics. Pertussis is contagious for about 3 weeks if untreated, but only for 5 days with a proper antibiotic therapy. The acute disease in the athlete, especially in team sports, must be diagnosed as soon as possible to avoid or minimize the risk of spreading.

Exposure to infected persons

The index case probably contracted the whooping cough through a direct contact with the symptomatic coach. All symptomatic persons should be excluded from any contact with athletes and other team members as well as auxiliary staff.

DISCUSSION

Despite increasing awareness, pertussis is often overlooked in the differential diagnosis of prolonged coughing in adolescents and adults. This is partially due to the fact that its clinical symptoms in adults are frequently scarce and nonspecific. During the initial, catarrhal (prodromal) phase, patients present with a low-grade fever, rhinitis and fatigue. Non-characteristic symptoms are undistinguishable from common colds and usually treated symptomatically. When paroxysms of the dry cough intensify in the night, that is a classic sign of pertussis development, but it is too late for effective antibiotic treatment [15]. If untreated, paroxysms of coughing can occur for a few weeks, up to three months, then gradually resolve as the patient passes into a convalescent phase. Pertussis should always be taken into consideration as a possible cause of a prolonged cough as adolescents and adults remain a reservoir of infection. It is worth noting that in this age group it can be the only symptom of the disease due to a prior infection or immunization history [16]. Complications of pertussis in athletes may occur as bacterial superinfections (pneumonia, otitis media) but more frequently as repercussions of the severe cough:

sleep deprivation with day sleepiness and difficulty in concentration, less effective training and aiming problems in shooters. More serious complications include urinary incontinence, subconjunctival haemorrhage, abdominal wall hernia and, rarely, rib fractures, intracranial haemorrhage, seizures or encephalopathy (probably due to prolonged hypoxia). Even when those are avoided and the disease course seems to be benign, as in the vast majority of adult athletes, the training plan can be interrupted and competition performance can be significantly affected by inability to train, prolonged recovery, sleep deprivation, and stress.

According to the Centers for Disease Control and Prevention (CDC) case definition for pertussis, all our cases can be classified as *probable* – all patients presented classic symptoms, including paroxysmal coughing lasting more than two weeks, no other more probable diagnosis and proven contact with each other. The diagnosis was confirmed by serologic testing, regarded as inferior to the gold standard techniques of PCR or culture, but many authorities consider serologic testing as sufficient to confirm pertussis. The diagnostic standards involve three different methods: culture, PCR and serology. Each method has its limitations, which can make it difficult to establish the diagnosis of pertussis if based on an incorrectly selected test. Isolation of the *Bordetella pertussis* bacterium remains a gold diagnostic standard, but its basic limitation is that the test can only be performed in the first two weeks of coughing when the bacteria are still present in the nasopharynx, and thus during the unspecific catarrhal phase of the disease. Since initial symptoms can be scanty or absent, the only hint to perform the test at this stage of disease may be recent exposure to pertussis. Early diagnosis is important in the context of preventing spread of the infection as well as reducing the duration of disease symptoms [17]. In the second, paroxysmal phase of pertussis, polymerase chain reaction testing is more sensitive as well as serology. PCR tests can be performed up to 3-4 weeks from the appearance of initial symptoms, and its results are not affected by previous antibiotic treatment [18]. Serologic testing includes measuring titres of specific IgG, IgM and IgA antibodies, mainly to pertussis toxin (PT), and comparing titres from sera taken in the paroxysmal and convalescent phases of infection (2-3 weeks apart). IgG and IgA testing is most specific for diagnosis of *Bordetella pertussis* infection [19]. The best time to perform serologic tests starts 2 weeks after the onset of symptoms, when antibodies rise in the serum. Diagnosis may be established by a single test with a high IgG anti-PT titre greater than or equal to 100-125 EU/ml or a minimum fourfold rise in antibody titres when the test is performed twice – in the acute phase and the convalescent phase [20]. To interpret the results of the serologic tests correctly, the history of pertussis vaccinations should be known, as it may cause elevated levels of IgG and IgM antibodies. According to the Guidelines for the Public Health Management of Pertussis in England, serological testing should only be undertaken when there is a minimum of one year from the primary or booster dose of pertussis vaccine, and the results should be interpreted with caution [21].

As mentioned above, antibiotic treatment in the catarrhal phase of infection may shorten the duration of symptoms. Antibiotics administered in the paroxysmal stage will not have an impact on the clinical course of the disease but can reduce the spread of infection. First line therapies include azithromycin and other macrolides, but in the case of allergy or intolerance trimethoprim-sulfamethoxazole can also be used [22,23]. There is no proven symptomatic therapy for severe coughing accompanying pertussis. It resolves spontaneously after a few weeks when respiratory ciliated cells damaged by pertussis toxin are regenerated.

Proper preparation for international competitions such as the Olympic Games needs many years of training and a lot of effort. Infectious diseases such as pertussis directly affect the general condition of the athlete and his or her sport performance and interrupt preparations or even put an end to participation in a sport event. Pertussis may significantly decrease sport performance as well as quality of life due to complications such as sleep disturbance, abdominal and thoracic pain, and subconjunctival haemorrhages, all stemming from intense coughing. The outbreak we have described took place among the National Team members. Competing in sport events such as European or Olympic Games is an experience reserved only for a very few elite athletes and may happen only once in their career. It is crucial not only to be perfectly prepared for the competition but also to undertake all preventive measures to maximize the chance for winning during important events. Infectious disease can have a negative impact on other team members due to the risk of spreading the infection as well as the team's completeness and morale. From the economic point of view, the infected athlete requires special medical care (including diagnostic tests, treatment, possible physiotherapy or rehabilitation) and extra hours of training to improve performance in order to re-establish the previous state. Pertussis is rarely diagnosed in the first days or weeks of symptoms, especially in adults, and a late diagnosis usually has no effect on established paroxysms of coughing. This can rule out an athlete from participation in any training and games for even a few months. The simple and the most effective way to prevent pertussis is to administer regular boosters of Tdpa vaccine to all athletes and their close contacts (e.g. family members, co-workers) according to immunization schedules. Sports medicine professionals should be aware of the necessity of checking the vaccination status of every athlete as well as team staff members. In general, administration of booster doses should start in adolescents (11-18 years old), using Tdpa [24]. Adults aged 19-64 also should receive their Tdpa booster immunization, according to the Advisory Committee for Immunization Practices (ACIP) guidelines. It is known that the effectiveness of Tdpa vaccine in adults wanes after 2-4 years following the booster dose [25]. This is one of the reasons why administration of the next dose to young adults at a 5 to 10 year interval seems to be reasonable [26], although there is no strong evidence that this approach will be economically or epidemically justified [25]. In such a specific group as athletes, who are exposed to many risk factors of acquiring infectious dis-

eases (common travelling, sharing small spaces such as planes, buses, hotels, changing rooms, training halls, participating in large events) it seems to be beneficial to administer additional doses of Tdpa vaccines at regular intervals [27,28]. The risk of a clinically relevant disease is around 1:500 per year, and vaccination reduces this risk by over 90%, at least for the first 2-3 years after vaccination [29].

CONCLUSIONS

Pertussis poses a real risk to the athlete's welfare and optimal performance. Therefore it is reasonable to mitigate this risk with proper anticipatory preventive measures: constant surveillance, early isolation and treatment of infected persons, regularly checking the vaccination status of all team members, and administration of booster doses of Tdpa vaccine every 5-10 years.

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