Clinical Clues / *Klinik İpuçları*

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Is it Necessary to Give Pertussis-Contact Prophylaxis in a Child Who Is Fully Vaccinated? Is There a Problem for This Child to Attend Kindergarten?

Aşıları Tam Olan Bir Çocukta, Boğmaca Temaslı Proflaksi Verilmesi Gerekir mi? Bu Çocuğun Kreşe Devamında Sorun Olur mu?

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Question: *The two-month-old brother of a five-year-old child was diagnosed with pertussis (respiratory PCR positive) and started treatment one day ago. Is it necessary to give prophylaxis to a child who received pertussis vaccine (DaBT-IPV vaccine booster dose) three weeks ago and who is fully vaccinated? Is there a problem for this child to attend kindergarten?* **Yasemin Alyay, MD.**

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Answer (Zeynep Gizem Ergün Özdel, MD; Mustafa Kemal Hacımustafaoğlu, MD)

Introduction and general background: Prior to answering the question, it would be useful to discuss concepts such as infection-disease relationship, transmissibility, basic reproductive rates, vaccine protection, sterilizing immunity, pertussis disease immunity, and immune properties associated with acellular and whole cell vaccines.

Pertussis is one of the most contagious childhood diseases. It is also a common disease in both children and adults. It is transmitted by droplet infection. The rate of infectiousness to others (Basic reproductive rate; R0) is considered to be 15-17 (1). In other words, it is assumed that an infectious index case normally infects 15-17 people around him/her. Likewise, it is transmitted to susceptible individuals at a rate of approximately 90% in household contacts and 50-80% in the school environment (2). Therefore, if there is close contact with an index case with pertussis (living in the same house, face-to-face contact <1 m with a symptomatic case, direct contact with respiratory, oral or nasal secretions of a symptomatic patient, sharing a room with a symptomatic case for >1 hour), prophylactic antibiotics are indicated (3). In pertussis, prophylactic antibiotic and therapeutic antibiotic applications are the same. After infection, clinical findings usually start after an incubation period of 9-10 days (6-20 days). Contagiousness is highest in the catarrhal period (4). To a lesser extent, asymptomatic persons or persons with nonspecific mild respiratory tract infection findings (especially vaccinated older children and adults) can also transmit the disease (5). The duration of contagiousness in people receiving treatment is longer compared to many other infectious diseases. Infectiousness disappears after the 5th day of appropriate antibiotic treatment.

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Sterilizing immunity is an high level immunity that is acquired after vaccination or exposure to an infection. And after the microbe is subsequently encountered, not only protecting the disasese, but also it is not expected to infect others. In the presence of sterilizing immunity, once the infectious agent binds to its target site(s), it is effectively neutralized by the host regional immune system. Thus, there will be no effective replication at the first contact site. Therefore, no transmission, colonization or carriage is expected. Lifelong protection and sterilizing immunity are considered to develop after measles, rubella and hepatitis A vaccinations, provided that the vaccination schedule is completed. In the presence of sterilizing immunity, effective and usually very long-lasting complete immunity against the agent is expected; in other words, mild infection or breakthrough infection is not expected after vaccination.

In pertussis, neither natural infection nor vaccination results in lifelong immunity. It is usually accepted that natural infection is protective for an average of 15 years (4-20 years) and vaccination for 10 years (2-12 years). Intervening undocumented infections may affect these durations (3,4,6). The adverse effects of acellular vaccines are lower compared to whole cell vaccines. Although head-to-head evaluations are limited and there are some confounding issues, whole cell vaccines are considered to be more effective than acellular vaccines (4). The clinical efficacy of acellular pertussis vaccines has been reported to be 74-85% (4,7-10). However, in the evaluation of studies on the efficacy of pertussis vaccines, factors such as nature of the country, case definition criteria, follow-up period after vaccination, and antigen content of vaccines should also be taken into consideration. An effective antibody response occurs after pertussis vaccination. However, a serologically measurable, reliable and standardized *immune correlate of protection* against clinical disease has not been determined (4).

Pertussis vaccines are protective against *Bordatella pertussis*. They have little or no effect on other pertussis species such as *Bordatella parapertussis*. The genetic targets of commercial kits used in some respiratory PCR tests may target genomes common to multiple Bordatella species. Therefore, interpretation may vary depending on the kit used. For example, *B. parapertussis* may be reported as *B. pertussis*, or vice versa (6,11). Therefore, the routine pertussis vaccination schedule should be completed even in PCR positive cases.

There are some immunologic differences between whole cell pertussis vaccines and acellular pertussis vaccines. Whole cell pertussis vaccines stimulate both Th1 and Th17 responses similar to pertussis natural infection. They also stimulate/generate tissue resident memory (Trm) T cells (CD4+ Trm cells) in the tissue (upper and lower respiratory tract) and Trm T cells induce IL 17 response. Thus, whole cell vaccines have the capacity to generate more effective opsonizing and neutralizing antibodies. In addition, in patients who are administered whole cell pertussis vaccine, the clearance of nasopharyngeal pertussis bacteria increases, colonization and transmission are less in subsequent rechallenge with pertussis bacteria (4,12,13). In acellular pertussis vaccines, a Th2-dominated immune pathway (such as IL-4, IL 9, TGFB) rather than Th1 is primarily activated and Th17 is also increased. Acellular pertussis vaccines elicit lower opsonizing and neutralizing antibody responses than whole cell pertussis vaccines. In acellular pertussis vaccination, although protection from the disease is provided in subsequent challenge with the agent, preventing nasopharyngeal colonization and transmissibility cannot be achieved sufficiently, i.e. sterilizing immunity does not occur (4,12,13). Therefore, it should be kept in mind that acellular vaccines may be insufficient in preventing nasopharyngeal infection, reducing colonization and reducing transmission after subsequent exposure to the microbe (rechallenge). In conclusion, acellular pertussis vaccines are highly effective in preventing disease but have limited effect on transmission. And this efficacy is maximized in the first years after acellular vaccination. High secondary antibody responses are expected within two weeks after booster vaccine doses.

Antibiotic treatment is recommended for whooping cough. The two main aims of the treatment given to the patient; 1) To cure the disease and improve clinical findings, 2) To reduce/eliminate nasopharyngeal microbial load and to reduce transmission. Initiation of treatment as soon as clinical diagnosis is made, facilitates achievement of these goals.

The aims of prophylactic antibiotic treatment in close contacts are to prevent the development of the disease in the individual and to prevent the risk of transmission to others by preventing possible nasopharyngeal colonization. Therefore, antibiotic prophylaxis is given to close contacts regardless of their age and vaccination status (3,14).

Briefly, in pertussis, antibiotic treatment is given to treat the patient and prevent transmission, and antibiotic prophylaxis is given to prevent possible disease and transmission. Acellular vaccination is given to prevent disease and has no significant effect on transmission.

In conclusion, within the framework of the explanations given above, the answers to the question can be summarized as follows:

1) Should a child who is fully immunized and who received pertussis vaccine (DaBT-IPV booster dose) three weeks ago be given prophylaxis? Yes. The main purpose here is not to protect the child from the disease, but to prevent nasopharyngeal

colonization and transmission of the acquired agent and to prevent transmission to others.

2) Is it a problem for this child to attend kindergarten? Considering that education is also very important, it is appropriate to make an individual decision within the framework of compliance with infection control measures. A child who is not ill (cough, cold, increased secretions, etc.) can attend school while continuing prophylactic treatment if he/she can follow standard hygiene rules (secretion control, hand washing, etc.). However, in the presence of clinical signs or illness, or in cases where standard hygienic rules cannot be followed (such as in the presence of neurological disease); at home, standard droplet quarantine measures should continue for the first five days of treatment, and the child should be allowed to go to school after the 5th day of treatment.

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