



Letter to Editor

Emerging Cases of Pertussis Among Early Infants Born to Unvaccinated Mothers, an Infectious Disease Long Absent in Northwestern Greece

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Dear Editor,

Although *Bordetella pertussis* infection is a vaccine-preventable disease, it continues to be a public health concern worldwide with a steadily rising incidence, particularly in small infants, who are at the greatest risk of morbidity and mortality.¹ Possible explanations of this epidemic trend include the waning immunity of pertussis vaccine in adolescents and the diminished efficacy of the current acellular vaccine compared to the previously used whole-cell vaccine.² Other reasons are the widespread use of PCR (polymerase chain reaction) testing that has improved clinicians' ability to confirm the diagnosis, the increased clinician awareness and reporting and genetic alterations in the circulating *Bordetella pertussis* strains.³

In Greece, despite the economic crisis, a high (> 95%) vaccination coverage for pertussis is maintained.⁴ According to the national vaccination schedule, children are immunized compulsory at ages 2, 4, 6 months and with two booster doses at 15–18 months and at 4–6 years with the DTaP vaccine; and with the sixth dose of Tdap at the age of 11. Adults receive Tdap in place of their next Td booster, recommended to be given every 10 years. Furthermore, since 2015, Tdap is recommended in the third trimester of pregnancy, which is a safe option to protect the newborn.⁵ The acellular type has been initiated in the Greek national vaccination schedule since 1997. From 1980 through 2014, the incidence of pertussis declined from 11.2 to 0.1 cases per 100,000.⁶

The Pediatric Departments of the University Hospital of Ioannina and the General Hospital “G. Hatzikosta” are the referral centers for pediatric diseases in Northwestern Greece, with a mean number of 3.450 admissions per year. The last hospitalized case of infantile pertussis was seen at 2000, in a 35-day old boy, with apneic episodes, exaggerated lymphocytosis, pneumonia and acute respiratory distress syndrome (ARDS) who died one day later in the pediatric intensive care unit (PICU).

From January 2016 to January 2017, seven previous healthy infants were admitted because of paroxysms of intense coughing followed by small apneic episodes. The clinical and laboratory data are shown in **Table 1**. The symptoms started two to four weeks before admission. Two infants were already receiving oral dexamethasone and oral salbutamol, prescribed from their pediatrician. From the family history it was interesting that close members of the family had prolonged coughing at that time, mother in 5 cases, father in 4, and grandfather in 1 case. Since there was no laboratory confirmation, we can only assume that they were the possible source of the infection. The siblings were vaccinated and healthy in all cases. Despite the national vaccination guidelines, none of the mothers had received pertussis vaccine at the third trimester of pregnancy. At physical examination, we noted the repetitive coughing and the episodes of apnea, sometimes accompanied by gagging, gasping and eye bulging. The oxygen saturation during the events was low in 3 cases,

Table 1. Clinical and laboratory data of 7 cases of infantile pertussis in Northwestern Greece

Age	52 days	24 days	39 days	11 months	3 months	30 days	36 days
Gestation age (weeks)	34	39	38	38	38	39	38
Year, month	2016, January	2016, May	2016, June	2016, July	2016, August	2016, October	2017, January
Symptoms/Signs	Paroxysmal coughing, rhinitis, wheezing, pneumonia	Paroxysmal coughing, rhinitis, dyspnea, cyanosis	Paroxysmal coughing, rhinitis	Paroxysmal coughing	Paroxysmal coughing, apneas, perioral cyanosis	Paroxysmal coughing, apneas, cyanosis, rhinitis, eye bulging	Paroxysmal coughing, apneas, perioral cyanosis
Days of symptoms	22	18	18	17	21	15	14
Close contact with coughing	Mother, father	Mother, father	Mother	Father	Grandfather	Mother, father	Mother
Leukocytes, x10 ⁹ /L	60.8	38.5	24.3	39.1	18.7	14.3	42.8
Lymphocytes, x10 ⁹ /L	31.2	24.6	19.2	23.8	11.6	9.1	28.3
Serum glucose, mmol/L	4.65	5.22	4.94	6.61	5.32	4.78	5.36
Serum sodium, mmol/L	137	137	132	137	136	134	136
Treatment	Clarithromycin, inhaled salbutamol, i.v corticosteroids, intubation	Azithromycin, i.v hydration, supplemental O ₂	Clarithromycin, i.v hydration	Clarithromycin, i.v hydration	Clarithromycin, i.v hydration	Azithromycin, i.v hydration, supplemental O ₂	Clarithromycin, i.v hydration
Complications	ARDS Pneumomediastinum Subcutaneous emphysema	-	-	-	-	-	-
Admission on intensive care unit	Yes	No	No	No	No	No	No
Days of hospitalization	64	17	8	7	9	16	12
Outcome	Cure	Cure	Cure	Cure	Cure	Cure	Cure

accompanied by signs of respiratory distress, such as tachypnea, cyanosis, retractions, nasal flaring, grunting and use of accessory muscles. One of these infants required admission to PICU due to severe ARDS complicated with pneumomediastinum and subcutaneous emphysema. Increased lymphocyte count was noted in 6 cases, with the highest in the PICU patient.

The suspicion for pertussis was high in all cases due to coughing paroxysms and apneas, lymphocytosis and the family history of coughing. Nasopharyngeal specimens for PCR were all positive for *Bordetella pertussis*. Antibiotics were administered before the PCR results because unvaccinated infants are at increased risk for complications.¹ Azithromycin was preferred in infants younger than one month and clarithromycin in older ones. In all children feeding was stopped due to frequent coughing paroxysms and apneas and intravenous fluids were administered until improvement. The number of

paroxysmal and apneic episodes was gradually reduced, and all children had a good outcome. Clarithromycin was given to affected family members and all close contacts.

In our report, we describe the reemergence of infantile pertussis long absent in hospitals of a large area of Greece. In our country, the policy for Tdap at the third trimester of pregnancy was officially launched at 2015, and therefore the vaccine's coverage among pregnant women remains low. We emphasize the need to reconsider our national strategy towards the enhancement of established pertussis vaccination policy regarding pregnant women and close family members when a newborn is expected. This approach has been recently proven effective to reduce disease in infants.^{7,8} Furthermore, timely vaccination of young infants is essential. Pediatricians, family doctors as well obstetricians have to be informed and work together for this purpose. Furthermore, in response to this small outbreak, we expect increased awareness and reporting of the disease.

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