

# The rise of pertussis in Malta in 2011- a case for adolescent and adult pertussis booster vaccination

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## Abstract

Notwithstanding the high rates of pertussis infant vaccination coverage in developed countries, *Bordetella pertussis* infections are manifesting a changing epidemiological pattern of disease. Of notable concern is the rise of pertussis in adolescents and adults. This changing picture is largely attributable to waning immunity after natural infection or vaccination. The belief that pertussis is chiefly a childhood disease is a common misconception. A significant rise of pertussis cases in Malta in older age groups was recorded in 2011. The addition of an adolescent and/or an adult booster dose against pertussis should be strongly considered.

**Key words:** pertussis, infant, vaccination, immunity, adults.

## Introduction

Pertussis (whooping cough) is a highly contagious, acute infection caused by the gram-negative bacterium *Bordetella pertussis*. The classical clinical features of pertussis progress in stages and start with an irritating cough (catarrhal stage) which within 1-2 weeks becomes increasingly paroxysmal. The paroxysmal stage, which lasts for 2 weeks, is characterised by paroxysms of violent coughing that continue uninterrupted and may be followed by the characteristic inspiratory whoop and or post-tussive vomiting. After a period of violent paroxysms, the severity of the cough tapers off with an extensive convalescent period that may range between 2-6 weeks and in some cases may last up to 3 months.<sup>1-2</sup>

Infants have the highest reported rates of illness.<sup>3</sup> However, pertussis may affect persons of all ages<sup>4</sup> and is increasingly being reported in adolescents and adults in many European countries (e.g. Austria, France, Germany) and in the USA irrespective of vaccination status.<sup>5-7</sup> Global incidence of pertussis (mostly in developing countries) has been estimated at 48.5 million cases, with 295,000 deaths, per year.<sup>8</sup>

Transmission of *B. pertussis* occurs from person to person via aerosol or by direct contact with infected respiratory secretions. Secondary attack rates in non-immune households reach up to 90%.<sup>2,8</sup> Even in countries where an effective childhood immunisation programme against pertussis is established, increasing rates of infection among adolescents and adults, as a result of waning of vaccine induced immunity, has been reported.<sup>6,8,9</sup> In these cases, and in contrast to the pre-vaccine era, the manifestations are atypical, may be less severe and may lack the pathognomonic inspiratory whoop and/or post-tussive vomiting<sup>10</sup> (pertussis should be considered in the differential diagnosis of cough illness lasting more than 1-2wks).<sup>11</sup> Furthermore, pertussis infections in adults and adolescents can often be asymptomatic.<sup>12-13</sup>

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Pertussis complications in adolescents and adults include pneumonia, rib fractures, and encephalopathy.<sup>10</sup> One study reported that 31% of adults suffering from acute exacerbations of chronic obstructive pulmonary disease (COPD) were also infected with *B. pertussis*.<sup>14</sup> The socioeconomic burden can be significant: a French study found that half of 77 health-care workers with suspected pertussis missed 5 days of work accounting for 42% loss in productivity.<sup>15</sup>

In spite of the high rates of vaccination coverage in developed countries, the changing epidemiological pattern of pertussis, in particular its rise in adolescents and adults is a cause of concern. The belief that pertussis is chiefly a childhood disease is a common misconception.<sup>10</sup> On the contrary, it is infected adolescents and adults who pose a transmission risk to non-immune infants.<sup>10</sup> In this study we investigated changes in the trends of pertussis in Malta by comparing reported cases of pertussis in 2011 with the previous decade.

## Methods

As a statutory notifiable disease the collection of pertussis data in the Maltese islands were dependent on notifications from hospital and community based medical practitioners. Pertussis data in the Maltese population, from 2001 to 2011, were extracted from the national database of the Directorate for Health Promotion and Disease Prevention (IDCU). The European Centre for Disease Prevention and Control (ECDC) definition criteria for pertussis was used to subdivide cases into confirmed cases (clinical compatible cases with laboratory confirmation), probable cases (clinical compatible cases with an epidemiological link) and possible cases (cases with a clinical compatible nature only). Notified cases that did not confirm with the ECDC definition were excluded from the national data base and not included in the study.

Chi-square test was used to analyse any differences between the notifications in 2011 and the previous decade while confidence intervals were calculated. All the yearly notified cases of pertussis in the previous decade of 2001-2010 were reviewed in the national database and reproduced for comparison (table 1).

## Results

In 2011 an increase in the number of pertussis cases in Malta was reported (Figure 1). Four clusters consisting of three clusters of 2 cases each and one cluster of 5 cases making up a total of 11 cases (9 laboratory confirmed, 2 epidemiologically linked)

were reported. In addition 20 single notifications of pertussis were reported. Of the total number ( $n=31$ ) of cases notified five cases were excluded from and 26 were included in the disease register according to the ECDC's definition.

Serologically confirmed cases were those that registered significantly high pertussis toxin IgA and IgG as measured by ELISA. *Bordetella pertussis* culture or PCR were not performed because cases presented outside the necessary window period of two weeks post disease onset. (Tests were performed in Bioscientia Laboratories, Germany).

There was a definite rise in the number of confirmed reported cases in 2011 (14 confirmed cases: four clusters with 9 confirmed cases; while 5 were confirmed sporadic cases) and 12 probable and possible cases ( $14+12: n=26$ ) as compared to the reported cases over the previous ten years (Table 1), that is 2001-2010 ( $n=30$ , with an average notification of 3/year [95% confidence interval: 1.95-4.04]). This means a greater than eightfold significant rise (Chi-square test with Yates correction 16.1,  $p<0.0001$ , 0.5% significance<sup>16</sup>) in 2011 over the average yearly figure of the previous decade. For the calculation the figure of the mid-year population of Malta for the year 2011 was considered as the average population in that year (population 416,110), whereas the mid-year population in 2005 (population 404,962) was considered as the average Maltese population of the previous decade (2001-2010).<sup>17</sup>

The average duration of symptoms at time of notification was 4.35 weeks while the range was 2-8 weeks. Out of all the notified cases (and excluding the epidemiologically linked cases in the clusters) ten cases (mean age 20.1yrs; range 2-40yrs) claimed to have received a pertussis vaccine (full vaccination status could not be verified since the question on previous immunisation was too generic), three were not vaccinated (age range 44-85 yrs) while six cases (mean age 45 yrs; range 20-70yrs) did not know their vaccination status.

All the cases presented between March and September with 69% (18/26) occurring in the three-month period between March-May 2011. Case gender distribution was almost equal (14 M:12 F).

In 2011 pertussis was more common in adolescents (age range: 10-14 years) and adults (age range 20-85). The reported cases in the previous decade (2001-2010) were mainly in children and to a lesser extent, in adolescents<sup>19</sup> (Figure 1).

Table 1: Yearly notified pertussis cases during the period 2001-2010; \*including 3 sporadic cases and two clusters of two persons each in 2005.

Year	2001	2002	2003	2004	2005*	2006	2007	2008	2009	2010
No. of cases	1	4	7	6	7	2	0	1	0	2

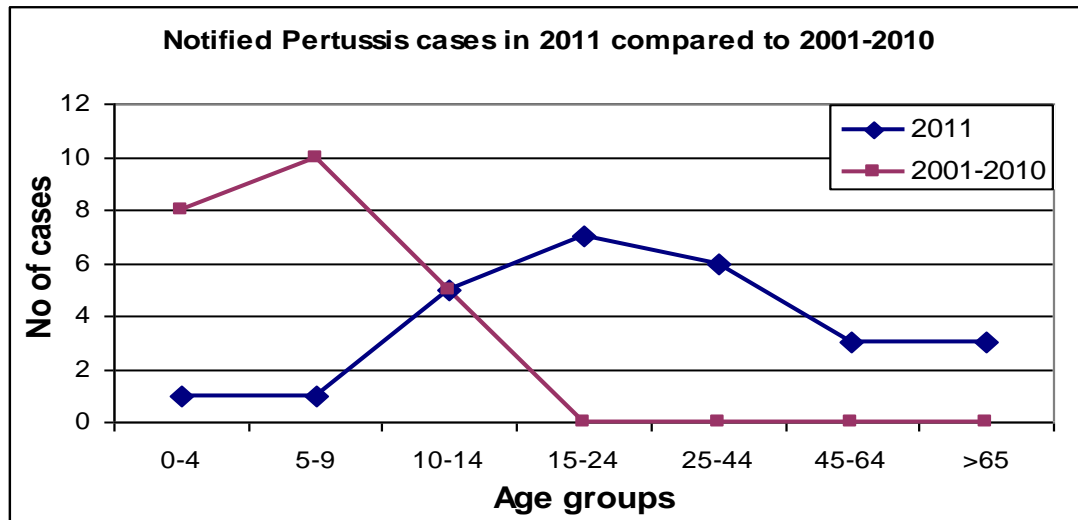


Figure 1: Comparison of the age distribution of the reported pertussis cases 2001-2010 & 2011

The pertussis incidence rate (all cases) in Malta during 2011 was 6.32/100,000 population whereas the average incidence rate in EU/EEA countries was 4.7/100,000 (range 0.2 (Cyprus) – 35.7/100,000 (Estonia)).<sup>20</sup> These contrasting figures are limited by differences in vaccination policies, case definitions, reporting procedures and surveillance systems.

## Discussion

Notable differences in the age groups of the reported cases can be observed (Figure 1). In 2011 pertussis was commoner in adolescents and adults as compared to the reported cases in the previous decade where pertussis occurred predominantly in children.

The reported incidence of pertussis is probably lower than the actual rates as under-reporting and under-recognition or mis-diagnosis in adolescents and adults are common.<sup>5,10,21</sup> This is likely to be due to the altered clinical features of the disease in these age groups - as prolonged cough may be the only clinical feature present. Under-recognition may occur, some may present late while others may not present at all.<sup>22</sup>

The limited local data, the possibility of an increased ascertainment of disease, a change in the diagnostic practice or a change in population characteristics and changes in disease susceptibility<sup>10</sup> all confound the recent rise in pertussis cases in Malta. In addition, although four-yearly epidemic trends of pertussis have been reported elsewhere,<sup>2,11</sup> these have

not been observed in Malta; the national database does not reflect the true epidemiological picture over the years as it relies solely on notification from medical practitioners.

The Maltese National Immunisation Service (NIS) electronic database records National Health Service immunisation data as well as data of reported vaccinations from the private sector. The latter is marked by under-reporting and is thought to result in apparent lower national rates of vaccination as shown by the 3<sup>rd</sup> dose uptake of pertussis vaccine in figure 2.

In September 2010, the whole cell pertussis vaccine formulation recommended by the National Immunisation Schedule was changed to an acellular pertussis containing vaccine, with the first dose being administered at 6 weeks, the 2<sup>nd</sup> at 3 months and the 3<sup>rd</sup> at 4 months of age. Combination vaccines containing acellular pertussis had been previously available on the private market for a number of years. A fourth acellular pertussis vaccine dose was also introduced on the National Immunisation Schedule in 2010 as part of a combination vaccine (Diphtheria, Tetanus, Inactivated Polio, *Haemophilus Influenzae* type b and acellular Pertussis vaccine) for 18 month old toddlers. This explains the higher 4<sup>th</sup> dose vaccination notification rates from 2010 onwards, with the rates reported in previous years being from the private sector.

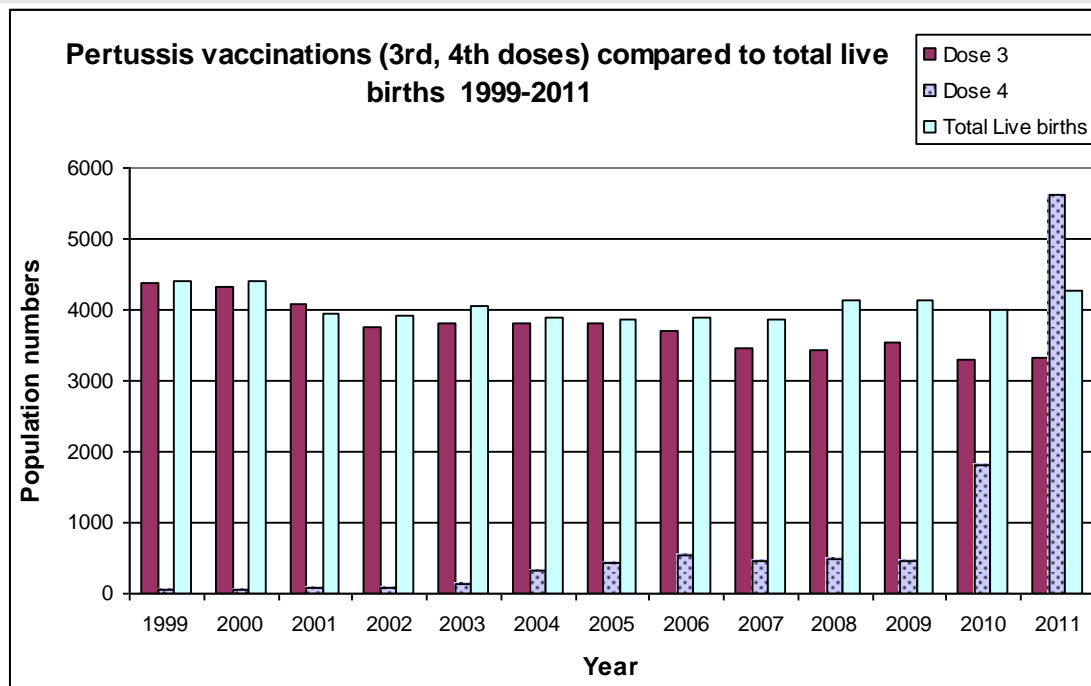


Figure 2: Third & fourth dose pertussis vaccinations registered at NIS (National Immunisation Service) 1999-2011 (NIS data)

Despite high vaccination rates, *B. pertussis* infections have persisted as a consequence of waning vaccine-induced (lasting for 4-12 years) and naturally acquired immunity (lasting for 4-20 years).<sup>23,10</sup> In the absence of further boosting, adolescents and adults (especially mothers) are likely to remain a reservoir of infection and play an important role in transmitting *B. pertussis* infection to incompletely immunised or unimmunised infants.<sup>20,24</sup>

Current literature supports the addition of a single adolescent and/or an adult booster dose of pertussis vaccine.<sup>25-27</sup> In some countries this is already being implemented<sup>28-29</sup> following thorough country-specific evaluations of the epidemiology of pertussis. Other countries have considered administering booster doses to specific target groups such as new mothers, health care workers<sup>30</sup> and adults (e.g. new parents) who are likely to have close contact with a non-immune or incompletely immune infant (<12months) (cocoon vaccination strategy).<sup>10,31</sup>

## Conclusions

The increasing reports of pertussis in Malta in 2011 are of concern. A universal pertussis booster dose for adolescents and perhaps adults as well, is likely to reduce morbidity in adolescents and adults and protect susceptible infants through a reduction in transmission. Other specific groups, such as post-partum mothers can alternatively or concomitantly be targeted prior being discharged from hospital. However, feasibility and cost-effective analyses are essential.

A switch from the low dose diphtheria, tetanus and inactivated polio vaccine (dT-IPV which is administered at 16 yrs of age on the national immunisation schedule) to a similar combination vaccine that includes acellular pertussis (dTap-IPV) for adolescents and adults could be one simple measure. Other authors have recommended a regular dTaP booster vaccine every 10 years for adults; however this poses a substantial resource challenge.<sup>10,30</sup>

There is also the need for introducing more sensitive laboratory methods, like molecular techniques, to improve the diagnosis of pertussis, however late notifications are likely to hinder this. In addition, doctors need to become more aware of the possibility of pertussis amongst adults and adolescents<sup>13</sup> especially in individuals with a persistent cough.<sup>10,11</sup>

Early accurate diagnosis is necessary to control transmission of the disease and enable prompt antibiotic treatment. The atypical presentations indicate that clinical diagnosis is not likely to be enough as it was in the pre-vaccination era and regular laboratory testing is essential.<sup>10,11</sup>

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