Title
Adult pertussis in the pre- and post-vaccine eras: lifelong vaccine-induced immunity?

Journal
Expert Review of Vaccines, 13(9)

ISSN
1476-0584

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Publication Date
2014-09-01

DOI
10.1586/14760584.2014.935765

Peer reviewed

EXPERT REVIEWS

Adult pertussis in the pre- and post-vaccine eras; lifelong vaccine-induced immunity?

Expert Rev. Vaccines Early online, 1–8 (2014)

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In the pre-vaccine era, there was little information about clinical pertussis in adults, although deaths were noted. Today *Bordetella pertussis* infection in adults is noted to cause a full spectrum of clinical manifestations. If single serum serologic diagnosis becomes routine, the finding of adult cases would increase dramatically. Reported adult pertussis was rare in the pre-vaccine era and it has been increasing markedly in the present era. In the present vaccine era, data on adult pertussis and *B. pertussis* infection have been gathered by studying prolonged cough illnesses, serologic studies determining recent infections and prospective rate of illness studies. These studies suggest that approximately 15% of prolonged cough illnesses are due to *B. pertussis* infections; the yearly rate of infection is approximately 6% and the yearly rate of *B. pertussis* infection with clinical manifestations is >500/100,000. The duration of protection following natural infection or vaccination is relatively short. Therefore, unless new and better pertussis vaccines are developed, lifelong vaccine-induced immunity is not possible.

KEYWORDS: adult • *Bordetella pertussis* • immunity • pertussis • vaccine

There has been a 'resurgence of reported pertussis' in the USA and many other countries [1–13]. For example, in 2012, there were 48,277 cases of reported pertussis in the USA; this is the highest number of cases reported since 1955 [1,14]. The pertussis resurgence has often been attributed to the switch from diptheria and tetanus toxoids and whole cell pertussis vaccine (DTwP) vaccines to diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) vaccines [6,7]. However, this initially was not so because reported pertussis in the USA started its upward climb in 1982–1984, which was approximately 15 years before the universal use of DTaP vaccines was started [15].

In 2005, 2010 and 2012, the rate of reported pertussis in the USA changed rather dramatically. The overall increase in reported pertussis can be mainly attributed to greater awareness [6,7]. During the last decade, the use of PCR for diagnosis contributed to the three recent peaks. In addition, the inferiority of most DTaP vaccines, as compared with most DTwP vaccines, has contributed significantly to the peaks in 2005, 2010 and 2012 [8,16]. Genetic changes in circulating *Bordetella pertussis* strains may also have made a contribution to the resurgence [16–18]. Recent data from studies in the baboon model also suggest that the type of cellular immune response that changed from Th1/Th17 response following vaccination with DTwP vaccines to a Th2 response following DTaP vaccines has contributed to the failure of the vaccine [19,20].

In the pre-vaccine era and much of the vaccine era, reported pertussis was a disease of children. However, during the last decade, the finding of pertussis in adults in some countries has been common. In 2012, 51.5% of reported cases in the USA were noted in persons >10 years of age [1]. Also noted during the last decade is the fact that adults with cough illnesses due to *B. pertussis* infection that have been misdiagnosed as other respiratory illnesses [8,21–24] are the main source of pertussis in infants.

Pre-vaccine era

In the pre-vaccine era, clinical pertussis in children was remarkably similar to the illness seen

 10.1586/14760584.2014.935765 ISSN 1476-0584

today except that death was more common, some findings were more pronounced and complications were more frequent [8,25–27]. In contrast to children, there is relatively little information on clinical aspects of pertussis in adults. In the pre-vaccine era, pertussis was rarely reported in adults [28]. Nevertheless, pertussis deaths in adults were noted in death statistics. For example, in Manhattan and the Bronx, between 1866 and 1915, there were 35 deaths noted in persons ≥15 years of age [28]. In whites in the USA, there were 246 deaths in persons ≥20 years of age during the period between 1917 and 1923 [29].

The pertussis experts during the first half of the 20th century recognized that adult pertussis occurred, but in their discussions, they, for the most part, did not describe severe cases [26,30–33]. In 1916, Luttinger described 'Pertussis Pete,' an adult who had pertussis and was the source patient for pertussis in children in three different families over approximately a 4-week period [28]. In 1934, Mannerstedt noted that adult pertussis was more frequent than generally assumed and that second attacks were also more frequent than commonly believed [33]. He noted that the illness started as an insidious cough 1–3 weeks after exposure. It lasted 5–6 weeks or longer, it was worse at night, gagging and choking were common with the production of thick, white, tenacious phlegm. He also noted that the white blood count was not characteristic of the count seen in pertussis in young children. In 1925, Madsen described 'grandmother's cough' [32]. It represented a second attack of pertussis. He suggested that these second attacks were always light and of shorter duration than first attacks. Friedlander noted that even older adults had pertussis and that the clinical diagnoses in adults were difficult because the paroxysms were mild and there was no definite whoop [30].

Adult pertussis today

In 2000, De Serres *et al.* [34] reviewed clinical pertussis in adolescents and adults who were seen in 1998 in five public health units in Quebec, Canada. There were 280 adolescents and 384 adult cases. Of the total group, 97% had cough for ≥3 weeks duration and 73% had paroxysmal cough for ≥3 weeks duration. Additional findings were: posttussive apnea 87%, posttusive vomiting 65%, whoop 69% and sweating episodes in 32%. Sweating episodes were more common in adults as compared with adolescents. The following complications were noted: sinusitis 13%, pneumonia 4%, otitis media 4%, urinary incontinence 4%, weight loss 3%, rib fracture 2% and fainting 2%. Six percent of adults of ≥50 years of age were hospitalized with a mean duration of stay of 17 days. Eighteen percent of the adult cases had a history of prior pertussis.

In a DTaP vaccine efficacy trial, the author's group in Germany studied 246 adult family members of vaccinees who had cough illnesses [35]. In this group, 64 had laboratory evidence of *B. pertussis* infection. Of these 64 adult patients, when first evaluated, 70% had paroxysms, 38% had whooping, 66% had posttusive phlegm and 17% had posttusive vomiting. The cough was worse at night in 56%. The mean duration of illness prior to the initial evaluation was 4 weeks. Additional findings were: low-grade temperature elevation 13%, coryza 58%, pharyngitis 31% and a history of previous pertussis in 26%.

In another DTaP vaccine efficacy trial, Wirsing von König *et al.* [36] noted pertussis in 84 adult family members. Of these patients, 81% had typical pertussis. Spasmodic cough of >21 days occurred in 65%, sleep disturbed by coughing in 55%, whoops in 11% and posttusive vomiting in 44%. Findings different from those seen in children included: choking episodes 56%, sneezing attacks 23%, sinus pain 17%, headaches 15% and sudden sweating attacks in 15%. These sweating attacks lasted several minutes and occurred mostly during the day. Patients with sweating attacks often experienced multiple episodes over many days. The age range of these adult family members was between 19 and 83 years. Thirty-three percent of these adults had a history of having pertussis previously.

The complications of pertussis in adult patients in this German trial were: otitis media in four; pneumonia in two; pneumonia with hospitalization in one; transient urinary incontinence in three; aspiration in one; one-sided acute hearing loss in one; rib fracture, inguinal hernia and lumbar pain in one and severe weight loss in one patient [37].

In a study of prolonged cough illness in University of California, Los Angeles (UCLA) students during 1986–1989, the student health physicians failed to correctly diagnose pertussis in any of 31 laboratory-confirmed cases [38]. In spite of the fact that the patients had coughing illnesses for 21 days which was paroxysmal and severe in 40%, they called it bronchitis or upper respiratory infection in 84% of the cases.

In a prospective study carried out during 1995–1996, which was designed to study the incidence of pertussis in adolescents and adults, there were 22 cases of laboratory-confirmed pertussis [39]. In this group, 100% had paroxysmal cough, 100% had posttusive gagging, 55.6% had posttusive vomiting and 25.9% had whooping. Unfortunately, only 2% of possible participants were enrolled. Therefore, it is certain that less-severe cases were overlooked.

The author has previously presented vignettes of five adult cases of pertussis [40]. These cases (three academic physicians, a college professor and an academic research microbiologist) all had relatively severe long-lasting illnesses. What is more important, however, is that the treating physicians diagnosed the illnesses incorrectly and this led to unnecessary treatment and exposures to others.

In 2006, the Advisory Committee on Immunization Practices [41] reviewed the clinical features and morbidity among adults with pertussis noted in nine different data sets from six countries (this included data from two of the studies mentioned above [34,36]). The median duration of cough in three studies was 8 weeks. Median values for selected complications were as follows: apnea 32%, posttusive vomiting 50%, weight loss 33%, whooping 45%, pneumonia 5%, seizure 0–0.2%, loss of consciousness 0–3% and hospitalization 2–3%. In this report, they also noted a number of anecdotal reports which described other complications. The high pressure generated

doi: 10.1586/14760584.2014.935765

during paroxysms was associated with rib fracture, cough syncope, urinary incontinence, pneumothorax, aspiration, inguinal hernia, herniated lumbar disc and subconjunctival hemorrhage. Also noted were encephalopathy, loss of concentration/memory and angina.

The 71-year-old physician that the author reported described a sweating episode as follows: 'I noticed that I felt faint and was sweating profusely. My wife noticed that I had become drenched with sweat and that I looked gray. After about 20 min, the sensation of lightheadedness and diaphoresis abated' [40].

Mertens *et al.* [42] studied an epidemic of pertussis in elderly people in a religious institution in the Netherlands. Of 41 persons with laboratory-confirmed pertussis, four died from intracranial bleeding. During a 14-year period (1990–2004), five pertussis-associated deaths in adults in the USA were reported to CDC [41]. All these patients had serious underlying medical conditions. In Australia, between 1967 and 2010, there were seven adult pertussis-related deaths [43]. The age range of these patients was 70–93 years. Illness descriptions were not presented. Between 1995 and 1998, in Spain, there were two deaths in adults reported [44].

The laboratory diagnosis of pertussis in adults

In general, adults with pertussis do not usually seek medical care until the 3rd or 4th week of cough illness [8,23,35,36,38] and, therefore, the majority of true cases will be culture and PCR negative. In addition, in spite of the fact that these illnesses are the most common source of infection in infants, they generally shed less bacteria than primary infections in children [45].

The best means of laboratory confirmation of pertussis in adults who are not seen in the first 2 weeks of illness is to measure IgG antibody to pertussis toxin (PT) [8,23,35,38,46–48]. This was routinely instituted in Massachusetts in 1987 and since then, the rate of adolescent and adult pertussis has been higher than in many other states [49,50]. The author's group demonstrated the usefulness of single serum serologic diagnosis during 1986–1989 and demonstrated how the sensitivity and specificity of the test could be established [38]. Single serum serologic diagnosis is routine in much of Europe [47,48,51,52]. In the USA, a number of commercial laboratories offer pertussis serologic diagnosis [46]. However, most of these lack specificity. One company in the USA has a test with a specificity of approximately 95% [46,53,54].

Epidemiology of adult pertussis

Reported pertussis

Pre-vaccine era

In the pre-vaccine era, pertussis in adults was rarely reported [25]. For example, in the USA army during World War I (1917–1919), there were only 109 reported cases among 3,703,191 men (0.27/100,000) [55]. In 1916, Luttinger noted 10,000 pertussis cases in New York City [28]. In this group, only 2.3% occurred in persons ≥15 years of age. In Maryland, between 1908 and 1917, only 2% of all pertussis cases were noted in persons ≥20 years of age [56]. In Massachusetts, between 1918 and 1939, only approximately 1.5% of the reported cases occurred in persons ≥15 years of age [57,58].

Vaccine era

In the USA, national age-specific data are not available before 1978. For the period 1978–1981, 6.5% of the cases occurred in persons ≥15 years of age [57]. Between 1983 and 1991, the rate of reported pertussis in the USA in persons ≥15 years of age was <1/100,000 (from CDC yearly summaries of notifiable diseases). From 1992 to 1997, the percentage of reported pertussis cases in the USA in persons ≥15 years of age was approximately 21%. From 1998 until 2002, this percentage increased to approximately 34%, and in the period 2003–2007, the percentage had increased to approximately 45%. Beginning in 2008, the CDC changed the age groups in their reporting. In persons ≥20 years of age, the percentage was approximately 28% between 2008 and 2010. In 2011 and 2012, this percentage was 22%.

Data from Canada and Australia are available from presentations by Scott A. Halperin and Peter McIntyre at a National Pertussis Workshop sponsored by the National Center for Immunization Research and Surveillance in Sydney, Australia, 25–26 August, 2011 [59]. In Australia, the rates in persons aged 20–59 years and ≥60 years were generally <20/100,000 between 1995 and 2007. This changed in 2008, where in both the 20–59 and ≥60 years age groups, the rate approached 50/100,000. In 2009, this increased for both groups to almost 100/100,000. In 2010, the rate in the ≥60-year-old age group was approximately 125/100,000. The percentage of total cases ≥20 years of age was approximately 39% in 1995, approximately 88% in 2006 and approximately 52% in 2010.

In Canada, between 1988 and 2006, the rate of reported pertussis in persons ≥20 years of age was <3/100,000. Throughout the 18-year period, there was virtually no yearly fluctuation in the rate in this adult group. In British Columbia, the percentage of cases ≥20 years of age was approximately 5% in 1993; over the ensuing 13 years, this percentage in persons ≥20 years of age increased to approximately 37% in 2006.

In 1986, in Sweden, there were 7495 cases of laboratory-proven pertussis reported [60]. In this group, 4.5% were persons ≥20 years of age. The percentage of adult pertussis (≥20 years of age) remained relatively constant for about 14 years and then it increased between 2000 and 2012. In 2012, only 209 total cases of laboratory-confirmed pertussis were reported. In this group, 49.8% were ≥20 years of age and 12.3% were ≥60 years of age.

The increasing number of reported pertussis cases in adults in the USA, parts of Canada, Australia, Sweden and other countries is, in the author's opinion, mainly due to increased awareness and the use of PCR and single serum serologic study for diagnosis. Greater awareness resulted from the numerous cough illness studies carried out in adults, the notations that adults were the common source of infant pertussis and many journal editorials.

doi: 10.1586/14760584.2014.935765

Box 1. Summary of pertussis epidemiology.

- *Bordetella pertussis* infections in adolescents and adults are very common and endemic in the present vaccine era
- Data from Germany in the early 1990s when few children were being immunized and pertussis was epidemic, as well as early observations from the USA suggest that infections in adolescents and adults were also common and endemic in the pre-vaccine era
- Rates of reported pertussis are 40–160-fold less common than the actual illness rates
- Asymptomatic infections are 4–22-times more common than symptomatic infections
- Today, symptomatic adolescents and adults are the major source of infection in unvaccinated children

Bordetella pertussis infection

In the pre-vaccine era, no cohort studies to determine *B. pertussis* infection or illness in adults were carried out. In the present vaccine era (and perhaps the immediate pre-vaccine era in Germany), three types of studies have been carried out in an effort to understand *B. pertussis* infection and illness [5,8,23,35,36,39,47,61–64]. These types of studies are: the investigation of prolonged cough illnesses in adults, the determination of significant antibody titer rises to PT in sera from the same subjects (sera collected in other studies) or the demonstration of significant high titers of antibody to PT in a population survey and the study in a defined population of all cough illnesses.

Between 1983 and 2008, at least 15 studies of prolonged cough illnesses in adolescent and adults were carried out [5,8,23,35,38,39,61–64]. In an analysis of 14 of these studies, the data suggested that about 25% of these events were due to *B. pertussis* infection [5]. However, in many of these studies, antibody titer rises or high single serum values to filamentous hemagglutinin (FHA) and pertactin (PRN) were used to establish the diagnosis. Since antibody to these two proteins can also be generated by infection with other *Bordetella* sp. and *Mycoplasma pneumoniae*, it is the author's feeling that 25% was an overestimate of the rate. Therefore, the author looked at only antibody to PT (which is specific for only *B. pertussis*) in seven studies [4]. This suggested a rate of 13%. However, this is an underestimate because 10% of adults with infection do not have a titer rise to PT ([Cherry J, Unpublished Data] from the APERT vaccine efficacy study). Therefore, approximately 15% of prolonged cough illnesses in afebrile adults are due to *B. pertussis* infection.

Between 1984 and 1989, in an AIDS-related study, the author's UCLA group had yearly sera from 51 hospital workers [61]. At that time, our published analysis included titer rises to FHA, PRN, fimbriae-2 (FIM-2) as well as PT. The results suggested yearly infection rates between 24 and 40%. Subsequently, the author reviewed the original data and determined the average yearly rate using only a significant rise to PT; the rate was approximately 6%. In an adult acellular pertussis vaccine efficacy trial, the author's study group was able to determine a yearly infection rate in the controls of 1.3% [62].

In another study in adults ≥65 years of age, the author's study group demonstrated a yearly infection rate of 3% [63]. In this study, the author's group had sera from 100 individuals, every 4 months for 3 years. In a population-based study, de Melker *et al.* [47] noted an infection rate of 6.5% per year in persons 25–55 years of age and a rate of 4% per year in those 56–79 years of age. In those 20–24 years of age, the rate of infection per year was 10.8%. The findings in their study support the findings noted in our 1984–1989 study [61]. The data in three of the serologic studies mentioned here indicate the rates of infection, but tell us nothing about infections with clinical manifestations.

In several of the prolonged cough illness studies, attempts were made to determine *B. pertussis* illness rates. In the study conducted by the author's group in UCLA students between 1986 and 1989, they estimated a yearly rate of illness of 69/100,000 [38]. In their study conducted in adults in Germany, they estimated a yearly rate of 133/100,000 [35]. In a prolonged cough illness study in Northern California Kaiser, the incidence of adult pertussis was estimated to be 176/100,000 per year [64]. It seems likely that all three of the above rate estimates are low because population denominators are estimates and whether the patients received all their care at the study location is not known.

What was to be a definitive *B. pertussis* illness rate study was a CDC study in a large health maintenance organization in St. Paul and Minneapolis, Minnesota from January 1995 through December 1996 [39]. The estimated annual incidence of pertussis was 507 cases per 100,000 person years (95% confidence interval: 307–706 cases). There was clearly considerable observer bias [65] in this study because they only enrolled 2% (212 of 8475 patients) of the patients who met the entry criteria. Less severe cases were overlooked, so the incidence of 507/100,000 is clearly an underestimate. In the eight-city adult vaccine efficacy trial of the author's group, they were able to calculate the *B. pertussis* cough illness rate in the controls [66]. This rate was 370 per 100,000 person years. Observer bias was also evident in this trial suggesting that the rate of 370/100,000 is also an underestimate.

The study that members of the author's group did in Cleveland in adults ≥65 years of age also reveals some suggestive rate date [63]. This was originally a respiratory viral/*M. pneumoniae* study in which they subsequently determined *B. pertussis* infections in twelve 4-month time periods. Clinical data were available on all 100 study participants. The rate of cough illness in time periods in which significant PT antibody titer rises occurred was 1.5% per year. If one-third of these coughing illnesses were due to *B. pertussis* infections, the attack rate would be similar to that noted in the Minnesota study.

An epidemiological summary is present in Box 1.

Duration of protection

In 2005, Mattoo and the author extensively reviewed the duration of protection following natural infection and DTwP vaccination [23]. At the same time, Wendelboe *et al.* [67] also evaluated data relating to the duration of immunity following infection or vaccination with DTwP or DTaP. They gathered data from 17 publications; their results suggested that

infection-derived immunity waned after 4–20 years and that immunity following immunization waned in 4–12 years. The difficulty with the data generated in all studies to date is that they rely on the reporting of pertussis which is poor.

As noted by Fine and Clarkson [68] in England and Wales and also from USA data [57], the epidemic cycles of pertussis did not change with the reduction of reported pertussis due to DTwP immunization. The fact that the interepidemic cycle did not lengthen with the control of reported pertussis in the vaccine era indicated that *B. pertussis* was circulating in the total population in the vaccine era in a fashion similar to that of the pre-vaccine era [23,38]. What we do not know over time is what the variations in clinical expressions in infections in persons who previously had the disease and in persons who previously had been vaccinated [22].

The study of IgA antibody to PT and other *B. pertussis* proteins indicates that the antibody is derived from infection and not vaccination. In one study, the author's Los Angeles group looked at this and found that by 10 years of age, approximately 70% had IgA PT antibody and by age 20, 99% had IgA PT antibody indicating past *B. pertussis* infection [69]. During studies relating to a DTaP vaccine efficacy trial in Germany, members of the author's group had the opportunity to study pertussis in adults and also IgA and IgG antibodies in 21-year-old German and American college students [70]. From these studies, they concluded that lifelong immunity to pertussis did not result from *B. pertussis* infection and that immunity following DTwP immunization was actually better than that following natural infection. At that time, the majority of young adults in Germany had not been vaccinated, but they did have evidence of past infection. The author's group also observed that the adults in Germany with pertussis seemed to have more severe disease than the adults that the author saw in the USA who had been previously vaccinated [35,38]. The author's group was able to look at the IgA and IgG antibodies in the 21-year-old Germans (assumed not to have been vaccinated) and the 21-year-old Americans (assumed to have been vaccinated) [70]. The geometric mean IgA antibodies to PT, FHA, PRN and FIM-2 in the two groups were similar indicating that infections in the Germans and Americans were of similar intensity. However, when the group looked at IgG antibodies to PT, FHA, PRN, FIM-2 and agglutinogens, the results were markedly different. For all five antigens, the titers in the sera from the Americans were significantly higher than the titers in the sera from the Germans. Since IgG antibody to PRN, FIM and PT are associated with protection [71,72], these data suggest to the author that DTwP vaccine protection is better than that induced by infection.

Recent studies suggest that protection wanes more rapidly following DTaP immunization than after DTwP vaccination [73,74]. Recent studies also suggest that protection in adolescents wanes rapidly after tetanus and diphtheria toxoids and acellular pertussis vaccine (Tdap) immunization [75–77].

Lifelong vaccine-induced immunity?

From the data presented in the preceding pages and many recent publications, it is clear that immunity following primary immunization of children has not resulted in long-term immunity. In addition, DTaP vaccines are less effective than good DTwP vaccines and waning of protection occurs faster after DTaP vaccines than after DTwP vaccines [78].

In the APERT vaccine efficacy study of the author's group [66,79], the antibody patters post-immunization suggested to the author that a booster dose every 10 years could be effective in controlling adult pertussis. However, recent studies in both children and adults indicate that protection following either DTaP in children or Tdap in adolescents is of short duration [2–8,73–77]. Therefore, at the present time, repeated Tdap booster immunizations will not control adult pertussis or *B. pertussis* circulation. Present immunization strategy should see that childhood and pre-adolescent immunization is done routinely. In addition, to prevent severe pertussis in young infants, we should see that pregnant women are immunized with Tdap in the later stages of pregnancy, and when possible, cocooning around pregnant women should also be done. The author also believes immunization of infants at birth will also prevent severe disease and deaths.

Box 2. Summary of *Bordetella pertussis* infections in adults.

- *Bordetella pertussis* infections in adolescents and adults are common and endemic
- Immunity after infection or vaccination is not long-lasting
- The outcome of an infection depends upon the time since vaccination or a previous infection
- Endemic adolescent and adult disease is responsible for the cyclic pattern which is most notable in unvaccinated children
- *B. pertussis* circulation cannot be controlled by the present immunization programs
- A universal program with adolescent and adult Tdap boosters with the next generation of these vaccines might possibly decrease the circulation of *B. pertussis* in these age groups
- Since this is unlikely to occur in the near future, the best strategy at present is universal pediatric and adolescent immunization, immunization during pregnancy and vigorous cocooning

Summary & conclusions

Presented in Box 2 are important points relating to adult pertussis. We know that *B. pertussis* was circulating in adults in the pre-vaccine era and also in the present vaccine era. What we do not know is the clinical expression rate in the two different time periods. The outcome of adult exposure depends upon the elapsed time since the last clinical pertussis episode or vaccination. If an adult is repeatedly exposed, he or she is most likely to have an asymptomatic infection. If exposure is less frequent, then clinical disease will occur.

In regard to adult immunization with Tdap, the antibody decay pattern is different from that seen in children following DTaP [78,79]. In children the decay pattern for all vaccine antigens is rapid [78], whereas in adults following Tdap, the decay pattern for FHA and PRN is prolonged suggesting that

doi: 10.1586/14760584.2014.935765

protection should last for years [79]. However, recent studies suggest that protection in adults following Tdap wanes rapidly [75–77]. It is difficult to explain this. Perhaps the antibodies that our ELISA studies detect are cross-reacting antibodies and not very protective in regard to *B. pertussis* infection and illness [16].

Until new vaccines are developed, lifelong vaccine-induced immunity is not possible.

Expert commentary

B. pertussis infection and illness in the pre-vaccine era and early vaccine era in adults were common but overlooked or incorrectly diagnosed. During the last decade, pertussis in adults has been recognized with increasing frequency in many countries. It is my opinion that this upsurge in pertussis in adults is not due to a change in the underlying *B. pertussis* epidemiology. It is mainly due to greater awareness and the addition of PCR and single serum serologic diagnosis. Endemic adult pertussis is the reservoir for the infection of susceptible children. Our present DTaP and Tdap vaccines have significant problems in regard to both short- and long-term efficacy. Therefore, even with a universal use policy in both adults and children, it would not be possible today to interrupt circulation of *B. pertussis*. Therefore, to protect the most vulnerable from severe morbidity and death, it is important to immunize all pregnant women, vaccinate those who will have contact with young infants (cocooning) and lower the start date of infant immunization.

Five-year view

During the next 5 years, there will be an increasing awareness of pertussis in adults. This will occur in countries where PCR and single serum serologic tests are available. In countries without the availability of laboratory diagnostic services, the illnesses in adults with pertussis (prolonged afebrile cough illnesses) will be attributed to other causes such as atypical asthma, bronchitis and gastroesophageal reflux.

New vaccines (both DTaP and Tdap) will be developed and tested, but it is unlikely that these efforts will result in licensed products in this time period. The immunization of pregnant women with Tdap will become universal in most of the developed world and possibly much of the developing world as well.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Key issues

- In the pre-vaccine era, clinical pertussis in adults was rarely reported. Nevertheless, it was recognized by the 'pertussis experts' of the time.
- Clinical pertussis in adults frequently has specific signature findings. These are: an afebrile paroxysmal cough illness which is worse at night; the cough is nonproductive and associated with posttussive apnea, vomiting and whoop; and there are often sweating episodes during non-coughing interludes.
- Laboratory confirmation of pertussis in adults is best done by PCR and single serum serologic study.
- Reported pertussis in adults was uncommon until relatively recently.
- Today *Bordetella pertussis* infection accounts for approximately 15% of prolonged afebrile cough illnesses in adults; infections (mostly asymptomatic) occur in about 6% of adults per year; and the rate of *B. pertussis* illness in adults is >500/100,000 per year.
- The duration of protection following infection on vaccination is relatively short. Contrary to popular belief, studies have shown that protection offered by DTwP vaccination may be better than immunity after natural infection in childhood.
- With our present DTaP and Tdap vaccines, lifelong vaccine-induced immunity is not possible.
- With our present vaccines, we should concentrate on preventing infection in young infants by immunizing pregnant women, cocooning around young infants and lowering the start date of immunization in infants.

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