

**SUMMARY**  
**Centers for Disease Control and Prevention**  
**Clinician Outreach and Communication Activity**  
**Clinician Briefing**  
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**Pertussis in Adolescents and Adults**  
**Strategies to Improve Prevention and Control Among All Age Groups**

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***\*\*Please note:** Data and analysis discussed in these presentations were current when presented. Data collection and analysis are ongoing in many cases; therefore updates may be forthcoming elsewhere on this website, through publications such as [CDC's Morbidity and Mortality Weekly Report](#) or other venues. Presentations themselves will not be updated. Please bear this in mind when citing data from these presentations.*

**OVERVIEW:**

As many of you may know, the CDC's Advisory Committee on Immunization Practices met in February 2005. One of the many topics discussed was the **anticipated licensing of two vaccines for adolescents and adults that contain tetanus and diphtheria toxoids and acellular pertussis antigens**. What I'd like to do today is give a brief overview of the consideration for use of these two vaccines.

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As you know, whooping cough, or pertussis is:

- a severe debilitating cough illness that lasts for weeks to months; and it has been termed the "100-day cough" because of its long duration and severity
- Pertussis is caused by a gram-negative bacillus called *Bordetella pertussis*
- The illness is characterized by paroxysms of cough accompanied by vomiting with forceful coughing, and an inspiratory whooping sound when the patient tries to get air after a paroxysm.
- In young babies, the presentation is a series of apneic episodes rather than a cough
- Pertussis is worldwide in its occurrence, can affect people at any age, although
- most deaths and complicated infections are in very young infants.

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## Surveillance

There are many challenges to pertussis. It's primarily a mucosal infection rather than an invasive infection and serum antibody has not directly correlated with protection. That has made developing diagnostic tests difficult. Because "user friendly" diagnostics have not been readily available and culture positive cases represent less than ½ of cases, confirming cases of infection for purposes of surveillance relies in large part on a clinical case definition.

The disease control strategies are driven by a limited number of options for antibiotic prophylaxis, namely the **macrolides: erythromycin, and, more recently, azithromycin and clarithromycin** are the most effective agents. These antibiotics are most effective eradicating *B. pertussis* from the nasopharynx stopping transmission and are very important in that regard. They're less effective modifying the course of the illness unless they're given very early in the illness, a period when pertussis often is not yet recognized.

Current vaccines, as you know, have been targeted for infants and children; the DTaP vaccines are safe. The acellular pertussis DTP vaccines were introduced in the 1991, 1992 for the 4<sup>th</sup> and 5<sup>th</sup> doses, and then in 1996 for the primary series delivered to infants. No pertussis vaccine is licensed for use in adolescents or adults -- anyone over six years of age -- because of past increases in local and systemic reactions associated with the whole cell pertussis vaccines (DTwP).

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## Under-recognition & Clinician Education

Another educational challenge -- and this is probably one of our greatest hurdles—is the perception that pertussis is only a disease of infants and children. **Pertussis, overall, is under-recognized among adolescents and adults.** The burden of disease has been best characterized and recognized in it's classic form among infants. Among adolescents and adults, the disease can be less typical and culture is sensitive after the catarrhal (first) phase of the illness. Suboptimal nasopharyngeal specimens contribute to low yields from specimens obtained for culture. Other tests e.g., serology and PCR remain unlicensed, lack rigorous quality control, validation and population standards. Validated serology using population-based standards is currently available only in one state (Massachusetts) where the test was developed to monitor the effectiveness of vaccine that was manufactured in that state.

Individual morbidity, the symptoms and hospitalizations among adolescents and adults are under-appreciated. **Two per hundred adolescents and three per hundred adults are hospitalized when they have pertussis**, and that represents the tip of the iceberg. High risk groups among adolescents and adults are not well characterized, except in nosocomial outbreaks of infection. We are pleased, that two new pertussis vaccines (tetanus and diphtheria toxoids and acellular pertussis) could be available for adolescents and adults -- perhaps as early as May or June.

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## TDAP Release Timeline

The timeline for licensure of the TDAP is as follows:

- **GlaxoSmithKline** has a version that they submitted the license application in July of last year. The age indication in this application is for 10-18 years of age.
- **Sanofi pasteur** has another version submitted in August of last year, with an intended indication of 11-64 years of age.
- The FDA Vaccine and Related Biological Advisory Committee, or VRBAC, will meet to consider approval of these vaccines on March 15, 2005.

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## Advisory Committee on Immunization Practices (ACIP) Working Group

In anticipation of possible licensure of these vaccines, the ACIP convened a working group to consider strategies to achieve better control of pertussis in the U.S. The working group started in June of 2004 and has had more than eleven meetings. The members represent a diverse group of agencies in the federal government, and consultants from many partners including state health departments, industry and academia.

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The charge to the working group was to **consider strategies to improve prevention and control of pertussis in the U.S. using acellular pertussis vaccines formulated for adolescents and adults**. The assumption was that the U.S. childhood program of vaccination with DTaP is fully implemented. This is because vaccination rates for at least three plus doses are ~95%, based on National Immunization Surveys.

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A stepwise approach is being taken by the working group. The **first consideration is Tdap for adolescents**. This is the simplest strategy, because it allows replacing the currently recommended Td vaccine with Tdap.

The next step will be to consider selective or general use of Tdap, e.g., **for healthcare workers**, for adults to better **protect infants, and for adult populations in general**.

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## Rationale for Tdap in Adolescents

The preference for using TDAP first in adolescents is as follows. There are **high rates of endemic pertussis among adolescents**. There's substantial morbidity among adolescents. Tdap is likely to be cost effective from a societal perspective based on several cost benefit analyses, and could even be cost saving depending on the true incidence of disease. Lastly, it is possible that a secondary benefit of vaccinating a large group of adolescents would be to decrease the total burden of endemic (and perhaps epidemic) pertussis.

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### **Adolescent Incidence**

The next slide provides examples of the level of pertussis infections in adolescents. These incidence figures were generated from passive surveillance and thus, are likely to underestimate the true number of cases and incidence of pertussis. Pertussis incidence varies from high to low years with **peaks of disease every three to four years on baseline endemic disease**.

**Some states report 150 to 200 cases per 100,000 in high incidence years among adolescents 10-19 years of age.** In low years, there incidence was still substantial, in the 20s and 30s per 100,000. That contrasts with what passive reporting data overall for the U.S., which usually runs around 6-8 per 100,000 for adolescents. These examples exemplify the problem that arises without adequate diagnostics.

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The next slide shows the age distribution of cases of pertussis among adolescents in Massachusetts. Pertussis incidence **peaks at age 15 years**; 25% of cases have already occurred by 13 years of age. We might speculate from these data that **the current schedule for pre-adolescent Td at 11-12 years of age would be ideal if substituted with Tdap**.

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### **Clinical Complications**

The complications from pertussis among adolescents are shown here. These data are from two series of cases in Massachusetts collected by the Department of Health (Susan Lett and colleagues) in collaboration with the Harvard School of Public Health (Grace Lee and colleagues), and from another series from Quebec (Gaston de Serres et al).

The two series from Massachusetts include a prospectively interviewed group of adolescents, 314 of them, and then a retrospective review of cases reported to the Health Department of almost 1,700 cases. Cough lasted for a mean of 3.4 months at the time of the interview in one series, and greater than a month at the time of diagnosis among 38% of adolescents in the other series. Note that diagnosis was delayed.

In Quebec, 47% of adolescents had more than two months of cough.

**Two out of a hundred adolescents in all of these series had pneumonia; one out of a hundred had a rib fracture from severe coughing paroxysms; one out of a hundred lost consciousness because of the severe cough; hospitalization occurred in about one out of a hundred.**

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This slide shows some of the other morbidity from pertussis in the same 314 adolescents prospectively interviewed in Massachusetts. In terms of medical visits:

- at least 24% had 3 or more visits to a healthcare provider, the range was from 0-15, and the mean was 2 visits
- 83% of students missed a mean of 5 days of school
- 43% of parents or caretakers also missed work, for a mean of 2.4 days, and a second caretaker also missed work for a mean of about 2 days.

This disease in adolescence is significant enough that some schools are closed to control the epidemic. School outbreaks often times are the lead to community outbreaks and sometimes herald state outbreaks.

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### **Wisconsin's Experience**

This slide shows what has happened in one state, Wisconsin, during the last year. This information was shared by Jeff Davis at the Department of Health in Wisconsin. After aggressive case finding and testing (PCR was available in Wisconsin), over 5,000 cases of pertussis were identified in 2004. 111 patients were hospitalized, and about half of them were young infants. Two infants died. 2,000 cases, or 40% of the cases were among adolescents, for a rate of 250 per 100,000. 15 adolescents were hospitalized for pertussis and 33 adolescents developed pneumonia. .

### **Conclusion:**

This brief overview gives a flavor of pertussis in the United States, and work to develop strategies for using the new Tdap vaccines when they are available. The ACIP is considering use of TDAP among adolescents as a routine substitute for the recommended Td booster at 11 and 12 years of age, or catching up using Tdap at ages 13-18 years for adolescents who missed Tdap at 11 or 12.

The next step will be to consider Tdap for adults.

I'd like to acknowledge the people who provided their unpublished data for this presentation, and in particular epidemiologists at the Massachusetts and Wisconsin Departments of Health. Thank you.

I'd be delighted to answer any questions.

### **Q&A with Dr. Murphy:**

**Q:** Why is pertussis trending upward in recent years? Is it because of waning immunity from vaccine, or lack of immunization in infancy and preschool years, or maybe increased recognition of pertussis?

**A:** The increases observed in reported cases of pertussis do not appear to represent changes in the number of recently vaccinated infants or children. All evidence to date suggests that the **vaccine effectiveness of currently used DTaP vaccines is at the expected level, about 85% against severe pertussis**, and lower for milder pertussis. It is important to **remind parents that they need to get their baby started on immunization as early as possible**, since the morbidity is highest in that age group and even one dose of DTaP can prevent some deaths from this infection.

**Waning immunity** is likely to be the most important reason for the increase in reported cases of pertussis among adolescents and adults. We know that immunity after pertussis wanes, and although experts vary on how long immunity lasts after natural infection, the number is in the range of 10-20 years. After vaccination with DTwP (whole-cell pertussis) vaccine, and probably after DTaP (acellular pertussis) vaccines immunity also wanes substantially after five years, and probably is gone between 10 and 15 years, leaving adolescents susceptible to pertussis.

Another reason for the rise in reported cases of pertussis is an increase in **PCR testing to confirm pertussis**. During the last five years PCR tests has been developed in many states and hospitals. We believe that recent increases in use of PCR tests account for a substantial proportion of the increased number of cases of pertussis that are now being reported. It is important to culture patients when using PCR tests. False positive PCR tests were recognized to have contributed a large number of cases of pertussis in several outbreak settings. **Culture, although it takes longer to obtain a result is still the gold standard test** serving as a cross check for reliable PCR tests. New PCR tests and standards are being developed.

In summary, it is likely that the increases in reported cases of pertussis are because of waning immunity and greater availability of PCR testing. Nonetheless, the number of cases of pertussis is severely underestimated.

**Q:** Can you elaborate on what strategies are needed to increase awareness of pertussis by physicians so that pertussis will be included in the differential diagnosis when adolescents and adults present to their office with a coughing illness?

**A:** It would be most helpful to have better diagnostics. There is an effort to develop a serologic diagnostic test, as well as guidelines for PCR tests. Lacking sensitive diagnostics, it is **important for physicians to consider pertussis in the differential diagnosis of prolonged cough illness, and especially any cough illness accompanied by vomiting with the cough**.

In suspect cases of pertussis, treatment with a macrolide **antibiotic is best given early to prevent transmission**, particularly to young infants. Antibiotics can modify the course of the illness, but only if given early.

**Q:** In view of the numerous reports of pertussis transmission in hospitals, including the recent MMWR report of pertussis outbreaks associated with hospitals in 2003, what strategies do you suggest to reduce transmission in these hospital settings?

**A:** Until vaccines can be shown to be effective in hospital settings, we must rely on the same precautions that we would for any unknown respiratory infection. **Young infants with pertussis will frequently present with apnea and thus, apnea should be on the list of symptoms that trigger use of large droplet respiratory precautions**. Using

the **appropriate precautions to prevent transmission** will help healthcare workers prevent becoming infected and further transmission in hospitals; this is a great concern right now.

**Q:** Could you elaborate on the groups which currently are under consideration for use of Tdap, the expanded high risk groups?

**A:** Well, there are two that are on the top of the list, one is healthcare workers and the other is adults who are most likely to transmit pertussis to vulnerable infants. These adults would be in households with a very young infant or caretakers of very young infants in other settings, e.g., child day care, teachers. **Mothers and parents are an important source of pertussis infection.**

Additional information is needed to determine the risk of pertussis among adolescents and adults with chronic respiratory or other chronic health problems. At this time there is not much information available. **Morbidity from pertussis appears to be higher with increasing age.**

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