



### Clinical Advisory

- 1) Pertussis rates in Massachusetts remain elevated
  - 2) High index of suspicion recommended regardless of vaccination status
  - 3) Tdap during every pregnancy reminder
- August 15, 2013

#### Background

In 2012, over 41,000 pertussis cases were reported nationwide, the greatest number of pertussis cases reported since the late 1950s. During the same time period, Massachusetts experienced a 50% increase in confirmed pertussis cases (from 273 in 2011 to 652 in 2012). **Both the U.S. and Massachusetts continue to see elevated case counts of pertussis in 2013.** An outbreak involving approximately 59 confirmed pertussis cases occurred at a western Massachusetts high school this spring, the largest pertussis outbreak in a school in the Commonwealth in over twenty years. The recent outbreak, consistent with what has occurred nationally, demonstrates that vaccinated individuals may develop pertussis, and that illness may be less severe among vaccinated individuals, as compared to unvaccinated individuals.

In Massachusetts, although the majority of confirmed pertussis cases in 2012 were in adolescents and adults, the highest incidence rates were among infants under the age of one, and there was one pertussis death in an infant. See graph on the next page. Infants are most vulnerable to severe illness, hospitalization and even death from pertussis. This issue, and the importance of vaccinating pregnant women with Tdap during every pregnancy, was examined in detail in a [February 2013 Clinical Advisory](#).

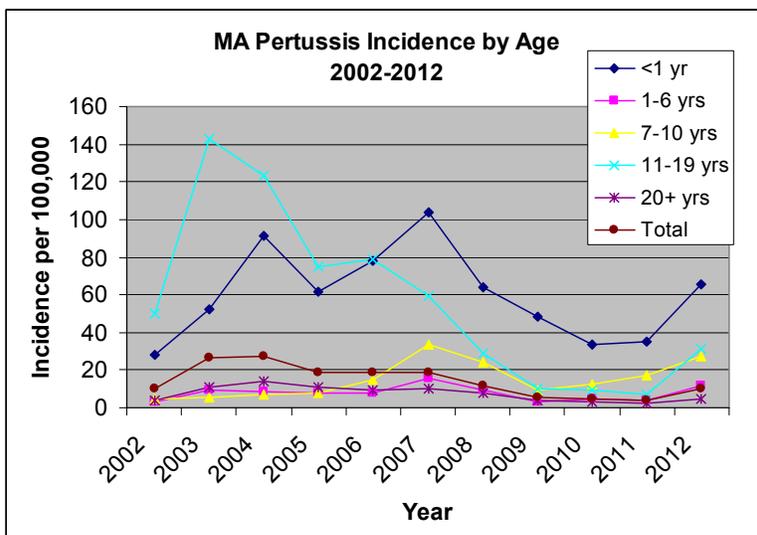
#### MDPH Recommendations

1. Make sure all patients are up-to-date on DTaP and Tdap vaccines. Children < 7 should be up-to-date with DTaP. One dose of Tdap is recommended for all preteens, teens, and adults (only 21% of Massachusetts adults have received a dose of Tdap), except for pregnant women who should receive one dose during each pregnancy.
2. Vaccinate pregnant women during each pregnancy. To maximize the maternal antibody response and passive antibody transfer to the infant, optimal timing for Tdap administration is between 27 and 36 weeks gestation, although Tdap may be given at any time during pregnancy. See the [February 2013 MDPH Clinical Advisory](#).
3. Promote cocooning. Vaccinate everyone who comes into close contact with an infant. Household members are responsible for transmitting pertussis to an infant in over 80% of cases in which a source to infant was identified.
4. Maintain a high index of suspicion and include pertussis in the differential diagnosis for patients in all age groups who present with prolonged cough illness, regardless of vaccination status.
5. Test suspect patients. The appropriate test depends on age, cough duration and Tdap vaccination status. See recommendations below regarding laboratory testing.
6. Initiate treatment promptly. The earlier antibiotics are started, the more effective they are at preventing transmission and possibly modifying illness. This is particularly important for infants whose course of illness may progress rapidly.
7. Call with questions. Call 617-983-6800 and ask to speak with an epidemiologist, or call your local board of health.

## Vaccination Offers the Best Protection

Pertussis vaccines continue to be the best way to protect ourselves from pertussis and its complications. Although pertussis vaccine is not 100% effective in preventing pertussis, vaccination is very effective at preventing serious pertussis disease and hospitalization. In adolescents, vaccine effectiveness within one year of vaccination is approximately 75%, but wanes substantially after one year. Approximately 92% of adolescents in Massachusetts have received a dose of Tdap. **In Massachusetts, the majority of adults have not received a dose of Tdap.** Recent estimates indicate that only 21% of Massachusetts adults have received Tdap.

**There is no recommendation for a booster dose of Tdap at this time, except in pregnant women with each pregnancy.** The Advisory Committee on Immunization Practices (ACIP) considered recommending a Tdap booster dose universally at their June 2013 meeting. ACIP concluded that data do not support universal revaccination with Tdap at this time. ACIP will continue to explore the potential need for revaccination of special groups, like healthcare workers and those in close contacts with infants. Source: <http://aapredbook.aappublications.org/site/news#100>



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## Clinical Description

The clinical presentation of pertussis is variable and its diagnosis challenging. Classically, pertussis begins with mild upper respiratory tract symptoms (catarrhal stage, lasting 1–2 weeks) and can progress to severe paroxysms of cough (paroxysmal stage, lasting 2–6 weeks), often with a characteristic respiratory whoop, which may be followed by vomiting. Although children can be exhausted after paroxysms, they usually appear relatively well between episodes. The cough is often worse at night. Cyanosis and apnea may occur; fever is absent or minimal.

Disease in infants younger than 6 months of age may be atypical. Very young infants may present with apnea and no other symptoms. In those with cough, whoop may be absent. Unvaccinated or incompletely vaccinated infants younger than 12 months of age have the highest risk for severe and life-threatening complications, hospitalization and death. Older children and adults also can have atypical manifestations, with persistent cough and no whoop, or they may present with more classic symptoms. **Family members** are the most likely sources of infection of pertussis in infants. In the most recent years, siblings have emerged as an important source.

The differential diagnosis for pertussis often includes infections due to mycoplasma, chlamydia, respiratory syncytial virus (RSV), adenovirus, and other *Bordetella* species (e.g., *B. parapertussis* and *B. holmseii*). Despite increasing awareness and recognition of pertussis as a disease that affects adolescents and adults, pertussis is overlooked in the differential diagnosis of cough illness in this population. Also, adolescents and adults often do not seek medical care until several weeks after the onset of their illness. In addition to the agents listed above, the differential diagnosis may include other causes of chronic cough, such as bronchospasm, gastroesophageal reflux disease, post viral bronchospasm, sinusitis, and chronic lung disease.

## Laboratory Testing

Determining who has pertussis and who does not is often difficult. Laboratory confirmation of pertussis is important because other pathogens can cause symptoms similar to pertussis. Whenever possible, a nasopharyngeal swab or aspirate should be properly obtained for all persons with suspected cases. A [four-minute training video](#) about collection of nasopharyngeal aspirate and swab specimens is available on the CDC website. There are three types of acceptable diagnostic tests for pertussis:

- Culture:** Available at the Hinton State Laboratory Institute (HSLI) and at some diagnostic laboratories. Culture of *B. pertussis* is the most specific diagnostic test. A positive culture for *B. pertussis* in a person with cough illness confirms the diagnosis of pertussis. Isolation of the organism from a nasopharyngeal (NP) swab is most successful during the catarrhal stage (i.e., first 1–2 weeks of cough). Antibiotics decrease the likelihood of recovering the organism; however, patients treated with antibiotics should still be cultured. Although bacterial culture is specific for diagnosis, it is relatively insensitive. Fastidious growth requirements make *B. pertussis* difficult to isolate. Success in isolating the organism declines if the patient has received prior antibiotic therapy effective against *B. pertussis*, if specimen collection has been delayed beyond the first two weeks of illness, and if the patient has been vaccinated.
- Polymerase Chain Reaction (PCR):** Available at commercial laboratories. PCR testing of NP swabs can be an important tool for the rapid diagnosis of pertussis. PCR is less specific than culture, however, and the high sensitivity of the test means false positive results may be obtained, particularly in asymptomatic patients. Therefore, PCR results should be considered presumptive, and isolation of *B. pertussis* by culture should be attempted for confirmation. Only patients with signs and symptoms of pertussis should be tested. PCR is most reliable within the first three weeks after onset of cough and before the initiation of antibiotic therapy. However, treatment should not be postponed for testing.

Although PCR is increasingly used as the sole diagnostic test for pertussis, it is recommended that PCR be used along with culture, rather than as an alternative test.

- Serology:** A single-point serologic assay has been validated at HSLI for persons aged 11 years or older and is used for clinical diagnosis and reporting. **Only those serologic assays performed at the HSLI are acceptable for laboratory confirmation.** Serology (performed at the HSLI) is most sensitive 2–8 weeks after onset of cough. Pertussis serology results from laboratories other than the HSLI and the CDC are **not** interpretable and therefore are not accepted as diagnostic for pertussis by the MDPH or CDC.

Culture and serologic testing are available at no charge at the HSLI. The appropriate pertussis diagnostic test and specimen type is based on patient age and cough duration, as described in the table below. The reliability of each test depends on age and stage of disease.

Time Since Cough Onset	Patients <11 Years of Age	Patients ≥11 Years of Age
<14 days	NP swab for culture and PCR.  Serologic testing is not valid in children <11 years of age.	NP swab for culture and PCR
14 – 28 days		Serology at SLI <sup>1</sup> -OR Serology at SLI, and consider NP swab for culture and PCR
29 – 56 days		Serology at SLI

<sup>1</sup>**Serologic results for patients ≥11 years of age who have received a pertussis-containing vaccine (Tdap) within the past 3 years are not interpretable.** Detected antibodies in these individuals may be the result of either past vaccination and/or recent infection. Instead, consider submission of an NP swab for pertussis PCR and culture testing if within the appropriate time interval relative to cough onset. As more data become available about the persistence of antibody after receipt of Tdap, this interval for interpretation may be adjusted.

**Test kits:** NP kits for pertussis culture can be ordered from the HSLI Kit Room at (617) 983-6640. Because NP test kits have a short shelf life (two months), only the quantity to be used immediately should be ordered. All specimens must be accompanied by a fully completed HSLI [Specimen Submission Form](#). Instructions for specimen collection are included in the kits.

## Treatment

The earlier antibiotics are started, the more effective they are in preventing disease transmission from the case to contacts, as well as from contacts to others. The symptoms of pertussis may be ameliorated if treatment is begun early, during the catarrhal stage. If begun later in the course of illness, treatment will decrease the infectious period but may not decrease the duration of cough or severity of disease. The recommendations for treatment of cases and prophylaxis of close contacts to cases are identical. Because pertussis in young infants may progress rapidly, treat suspected unconfirmed cases promptly.

A reasonable guideline is to treat persons aged >1 year within 3 weeks of cough onset and infants aged <1 year and pregnant women (especially near term) within 6 weeks of cough onset. The antimicrobial agents of choice for treatment or chemoprophylaxis of pertussis in persons ≥1 month of age are azithromycin, clarithromycin, and erythromycin.

**Treatment of infants < 1 month of age:** Infants < 1 month require special consideration. An association between orally administered erythromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants younger than one month of age. Although substantial use of azithromycin in infants younger than one month of age without IHPS has been reported, some cases of IHPS in such infants following use of azithromycin have been identified (Red Book 2012). Until additional information is available, azithromycin is the drug of choice for treatment or prophylaxis of pertussis in infants <1 month of age, for whom the risk of developing severe pertussis and life-threatening complications outweighs the potential risk of IHPS that has been associated with azithromycin. For persons ≥2 months of age, an alternative to macrolides is trimethoprim-sulfamethoxazole (TMP-SMZ).

**Note:** Physicians who prescribe any macrolide antibiotics, including azithromycin, to infants <1 month of age should:

- 1) Monitor patients for the development of IHPS during and for one month after completing the course. Parents should be informed about the potential risks of IHPS and the signs of IHPS, such as projectile vomiting or excessive irritability, and
- 2) Report cases of pyloric stenosis following use of macrolides to MedWatch via telephone at (800) FDA-1088, via fax at (800) FDA-0178, or through the FDA website at [www.fda.gov/medwatch](http://www.fda.gov/medwatch). Cases should also be reported to the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or toll-free at (888) 658-2850.

### Summary of Oral Macrolide Treatment and Prophylaxis for Pertussis by Age Group<sup>1</sup>

Drug	Age			
	Adults	Children and Infants ≥6 months	Infants 1–5 months	Infants <1 month
<b>Azithromycin (5-day course)</b>	500 mg given as single dose on Day 1, then 250 mg per day on Days 2–5.	10 mg/kg/day in single dose on Day 1, then 5 mg/kg/day on Days 2–5.	10 mg/kg/day in single daily dose, for 5 days. <sup>2</sup>	Recommended agent. 10mg/kg/day in single daily dose for 5 days. (Only limited safety data are available.) <sup>2</sup>
<b>Clarithromycin (7-day course)</b>	500 mg 2 times per day for 7 days.	15 mg/kg/day in 2 divided doses (maximum 500 mg/dose) for 7 days.	Same dosage as noted for ≥6 months of age. <sup>3</sup>	Not recommended. <sup>3</sup> (Safety data unavailable.)
<b>Erythromycin (14-day course)</b>	500 mg 4 times per day for 14 days.	40–50 mg/kg/day in 4 divided doses (maximum 2 gm/ day) for 14 days.	Same dosage as noted for ≥6 months of age (estolate preparation preferred, if available).	Use as alternate drug in doses as noted for ≥6 months of age. Drug use is associated with elevated risk of infantile hypertrophic pyloric stenosis (IHPS).

<sup>1</sup>. TMP-SMZ may be used as an alternative agent in patients ≥2 months of age who are allergic to or cannot tolerate macrolides or who are infected with a rare macrolide-resistant strain of *B. pertussis*. The recommended dose in children ≥2 months of age is trimethoprim 8 mg/kg/day, sulfamethoxazole 40 mg/kg/day in 2 divided doses for 14 days. For adults, the recommended dose is trimethoprim 320 mg/day, sulfamethoxazole 1600 mg/day in 2 divided doses for 14 days. Because of the risk of kernicterus, TMP-SMZ should not be given to pregnant women in the 3rd trimester, nursing mothers, premature neonates, or infants <2 months of age.

<sup>2</sup>. Azithromycin is not licensed for use in infants <6 months of age. Although safety data are limited, the data suggest that azithromycin results in fewer adverse effects in this age group and with no increased risk of IHPS. As a result, the CDC recommends azithromycin for infants <6 months of age, and it is the preferred drug for infants <1 month of age. Azithromycin is classified as a Food and Drug Administration (FDA) pregnancy Category B drug. (Animal reproductive studies have failed to demonstrate a risk to the fetus, and there have not been any adequate and well-controlled studies on pregnant women.)

<sup>3</sup>. Clarithromycin is not licensed for use in infants <6 months of age. Although safety data are limited, the data suggest that clarithromycin results in fewer adverse effects in this age group and with no increased risk of IHPS. As a result, the CDC recommends clarithromycin for use in infants <6 months of age, but not in infants <1 month of age. Clarithromycin is classified as an FDA pregnancy Category C drug.

Adapted from: [Recommended Antimicrobial Agents for Treatment and Postexposure Prophylaxis of Pertussis](#). CDC. *MMWR*. 2005; 54(RR-14). This document can be found on the CDC website at [www.cdc.gov/mmwr/PDF/rr/rr5414.pdf](http://www.cdc.gov/mmwr/PDF/rr/rr5414.pdf).

## Prophylaxis of Close Contacts

Administer a course of antibiotics to close contacts within 3 weeks of exposure, especially in high-risk settings. The agents, doses and duration of treatment of close contacts are the same as for treatment of pertussis. Close contacts include household contacts; those who have had direct contact with respiratory, oral, or nasal secretions from an infectious case; and those who have had close face-to-face contact, regardless of duration, with a case that is symptomatic and infectious (e.g., in the catarrhal or paroxysmal period of illness). This does not include casual contact, like sharing the same classroom, waiting room, office space, or other casual types of interactions. **Antibiotic prophylaxis of a broadly-defined group of contacts is no longer routinely recommended.** In general, during a school or community outbreak, antibiotics are now only indicated for a limited number of individuals who are close contacts.

## Disease Reporting

Confirmed cases of pertussis are reportable to your local board of health. A comprehensive list of reportable diseases is available at the [MDPH web site](#). For questions about pertussis and diagnostic testing, please call an epidemiologist at the Massachusetts Department of Public Health at 617-983-6800.

## Resources

- More information about pertussis is available on the MDPH website at [mass.gov/dph/imm](http://mass.gov/dph/imm)
- MDPH fact sheets about pertussis in the following languages:
  - [Pertussis](#) (English)
  - [Chinese \(Simplified\) - 百日咳](#)
  - [Haitian Creole - Kolich](#)
  - [Portuguese - Coqueluche](#)
  - [Spanish - Tos ferina/convulsa](#)
  - [Vietnamese - Ho gà \(Ho rit\)](#)
- [U.S. Centers for Disease Control](#) (CDC) website:
  - Homepage: <http://www.cdc.gov/pertussis/>
  - Information for clinicians: <http://www.cdc.gov/pertussis/clinical/index.html>
  - Diagnostic testing: <http://www.cdc.gov/pertussis/clinical/diagnostic-testing/index.html>
  - Pertussis vaccination: <http://www.cdc.gov/pertussis/vaccines.html>
  - Surveillance and reporting: <http://www.cdc.gov/pertussis/surv-reporting.html>
  - Posters and other free resources: <http://www.cdc.gov/pertussis/pubs-tools/index.html>
- [Immunization Action Coalition](#) website:
  - Vaccine information statements: <http://www.immunize.org/vis/>
  - Handouts for patients and staff: <http://www.immunize.org/handouts/>
  - “Ask the Experts”: <http://www.immunize.org/askexperts/>