

PERTUSSIS PROPHYLAXIS — PASSÉ?

CURRENTLY WE and most other state health authorities in the US recommend that all close contacts of a pertussis case receive macrolide prophylaxis to prevent further spread. Last year this turned out to be a lot of people: 626 cases were reported—the highest total since 1959—and each case had about 8 close contacts. We recently revised our Investigative Guideline for pertussis to help suppress paroxysms of prescriptions for prophylactic antibiotics and to focus our efforts on protecting those most vulnerable to serious morbidity and mortality from pertussis. (This Guideline is intended for public health nurses, but you may want to be familiar with our approach; you'll find a link to the guideline at <http://www.oregon.gov/DHS/ph/acd/diseases/pertussis/pertussis.shtml>). Oregon epidemiology and rationales for the old and new strategies follow.

THE PERTUSSIS BOOM

In 2002, reported pertussis cases in Oregon began a steep rise to reach a 45-year high in 2004. Two other features are notable: 70% of the pertussis victims were ≥ 10 years of age; and disease activity was concentrated in certain cities and counties, e.g., last year Benton, Douglas, and Lane counties, home to 14% of Oregonians, reported 60% of all cases. Hospitalization and death (3 in the past 3 years) have been limited to those under 1 year of age—an age group that, fortunately, has contributed little to the recent surge of cases.

Why has pertussis exploded in Oregon? Several factors are probably responsible, including a true increase in disease, improved clinician awareness, productive case finding by local health departments, and more sensitive detection of *Bordetella pertussis* by polymerase chain reaction (PCR) testing than by culture.

CAN ANTIBIOTICS PREVENT TRANSMISSION?

In the quest to control pertussis, antibiotics are used in two ways: treatment of contagious cases and prophylaxis of close contacts. Although these practices might seem sensible, scientific support for them is scanty. The good news is that some antibiotics (macrolides and trimethoprim-sulfamethoxazole) eliminate *B. pertussis* from the nasopharynx; sadly however, they have little effect on clinical symptoms, such as duration of cough, and few patients ever volunteer for the second NP swab needed to savor the laboratory triumph.

Does the traditional two-week course of erythromycin treatment (recommended since the mid-1970s) protect others from illness? Two retrospective studies often cited as showing its preventive value were confounded by concurrent antibiotic prophylaxis among contacts, rendering this conclusion dubious at best.^{1,2} Modest decreases in household attack rates were found in two prospective studies appended to pertussis vaccine trials in Europe, but the results reached statistical significance in only one subgroup of one study (absolute risk reduction 13–16%, number needed to treat to prevent one additional case = 6–7).^{3,4}

CLOSE CONTACT PROPHYLAXIS: ROSE-COLORED GLASSES REQUIRED

For the past 30 years, erythromycin prophylaxis of close contacts of pertussis cases has been recommended in the US. The studies supporting this recommendation have been mostly retrospective, small and uncontrolled. The best was a large, retrospective cohort from Canada; cases occurred in 17% of household contacts receiving prophylaxis versus 25% of those that didn't—a statistically significant but modest

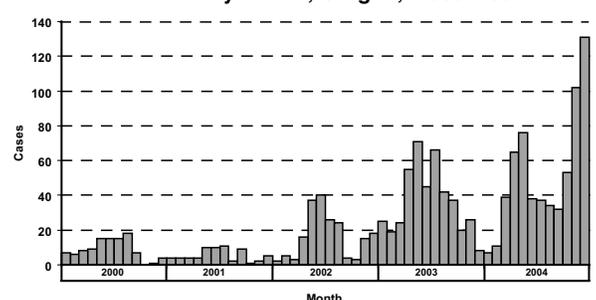
effect⁵; 13 households needed to receive prophylaxis in order to prevent cases in one.

The only randomized, placebo-controlled trial of prophylaxis for pertussis concluded that household erythromycin prophylaxis, although 67% efficacious in preventing culture-confirmed secondary cases, did not prevent clinically defined spread (the definition used in the studies supporting prophylaxis) within households; 70% of household contacts in *both* groups developed pertussis-like symptoms!⁶ In a *post-hoc* analysis, the authors eliminated household contacts who were already coughing at the time prophylaxis started; the protective effect became negligible (absolute risk reductions 3% to 0%; number needed to treat to prevent one additional case 35– ∞). Not surprisingly, adverse events, mostly gastrointestinal, were more common in those receiving erythromycin, and only 54% of erythromycin recipients completed the prescribed 10-day course. The final conclusion: household erythromycin prophylaxis was not an effective public-health tool. Whether rapid, more sensitive PCR testing and more tolerable drugs like azithromycin or clarithromycin can improve the efficacy of prophylaxis is unknown.

A SEASON TO REFLECT

Each winter, pertussis reports briefly recede; during this year's respite, we and our local health departments took a deep collective breath and pondered the

Pertussis by month, Oregon, 2000–2004





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explosion of the last 2 years: over 1,000 pertussis cases reported, estimated pertussis underreporting by 10–100 fold,⁷ the large case load in adolescents, questionable effect of all the prophylaxis (one unfortunate Benton County student was prophylaxed 4 times!), diversion of public-health resources, our concurrent efforts to promote judicious use of antibiotics, and—most importantly—the shaky scientific support for our current practice.

Others are also questioning the conventional wisdom. After a decade battling their own pertussis bloom (also with an adolescent focus), in 2002 our Canadian colleagues held a national consensus conference (<http://www.phac-aspc.gc.ca/publicat/ccdrmtc/03pdf/29s3e.pdf>) that led to recommendations that now sharply limit prophylaxis to “vulnerable” close contacts (infants, pregnant women, and households and child-care centers including same), similar to practice in the United Kingdom and other western European countries. The global trend to limit prophylaxis is also reflected in the 2004 edition of the American Public Health Association’s *Control of Communicable Diseases Manual*, which now counsels prophylaxis à la the Canadian model. CDC is sponsoring a US pertussis consensus conference this month and plans to update national guidelines last revised in 2000. Stay tuned.

NEW PERTUSSIS RECOMMENDATIONS FOR OREGON

The goal of our new guideline is to prevent serious morbidity and mortality from pertussis while minimizing excessive use of antibiotics. To do this we will recommend prophylaxis for close contacts *only* if they are “high-risk,” viz., for

- Infants under age 1; and
- Pregnant women in their third trimester.

In addition, the entire household of a case or the entire childcare setting of a case should receive prophylaxis *if* an infant or a pregnant woman is among the exposed in those settings. Other “low-risk” close contacts will be educated; any symptomatic close contacts will be encouraged to seek care promptly and to inform their providers about the pertussis exposure. Asymptomatic close contacts will be educated to do the same if they become ill.

Controlling Spread of Pertussis

1. Treat cases as soon as possible
2. Update immunization of child contacts
3. Antibiotic prophylaxis to protect vulnerable contacts only
4. Get symptomatic exposed persons evaluated and treated

CLINICIAN RESPONSIBILITY

Our review of case reports from 2004 leads us to expect a 90% drop in prophylaxis prescriptions; practitioners in high-incidence counties should notice fewer requests. “Low-risk” close contacts of cases, however, may present for evaluation in greater numbers; if respiratory symptoms develop 1–3 weeks after an exposure to a contagious case, we recommend pertussis testing of nasopharyngeal specimens if feasible and macrolide treatment unless there is a compelling alternative explanation for the new symptoms. See the Investigative Guideline for low-cost testing options at the public health lab and a shorter, more tolerable erythromycin treatment course.

VACCINE FOR ADOLESCENTS AND ADULTS

Our new guideline will not control pertussis better than the old one; long-term community control of pertussis requires an effective vaccine that can be used beyond age 7. On May 3 as we went to press with this issue, the FDA approved the first pertussis-containing vaccine for use beyond childhood. Approval of a second similar diphtheria, tetanus and pertussis vaccine is anticipated prior to the June 2005 meeting of the ACIP, after which national guidelines on the use of these products are eagerly anticipated. An effective method of pertussis control throughout the lifespan may finally be here.

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