

## Pertussis Vaccination: Why Bother.

*“Microbe hunting has always been a queer humpty-dumpty business.*

*A janitor with no proper education was the first man to see microbes; a chemist put them on map and made people properly afraid of them; a country doctor turned the hunting of them into something that came near to being a science; to save the lives of babies from the poison of one of the deadliest of them, a Frenchman and a German had to pile up mountains of butchered guinea-pigs and rabbits.”\**

Paul De Kruif, *Microbe Hunters*, 1926

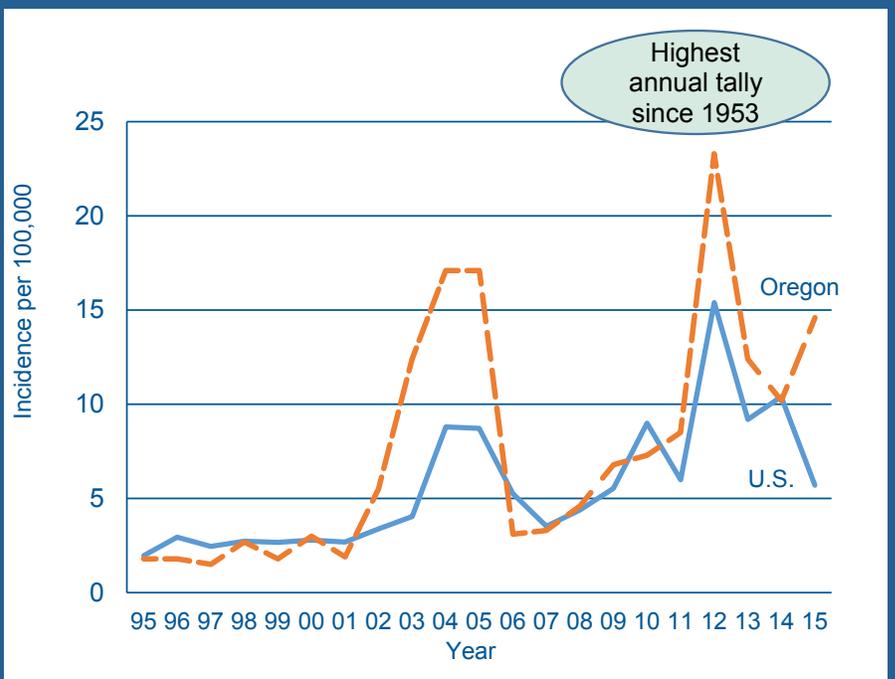
### Ongoing transmission in Oregon

Pertussis is a deplorable, frustrating public health problem — a highly contagious bacterial disease that begets epidemics despite school vaccination requirements. The last epidemic ravaged Oregon in 2012 with the highest number of cases (910) reported here since 1953. In 2015, 593 cases and 27 outbreaks of pertussis were reported in Oregon. This *CD Summary* reviews the latest pertussis trends in Oregon and vaccination strategies, especially for pregnant women.

### Incidence high in infants and older teens

In 2015, the reported pertussis incidence in Oregon was 15/100,000 — well above the national incidence of 6/100,000 (Figure 1). As usual, the incidence among infants remained higher than that in any other age group at 134/100,000. Among infants, those <2 months of age had higher incidence (131/100,000) than did

Figure 1. Reported pertussis incidence rates in the United States and Oregon, 1995–2015



\*Leeuwenhoek, Pasteur, Koch, and Roux & Behring, respectively.

those 6–11 months old (88/100,000). The year 2015 was also noteworthy for a historically high proportion of reported pertussis cases among older teenagers (Figure 2). The increased burden among school-aged children and adolescents is also reflected in the 21 outbreaks reported in school settings last year.

### Morbidity gravest in infants

While the disease is less severe among adolescents and other age groups, infants suffer complications, are often hospitalized and sometimes die from pertussis. During 2012–2015, 259 infants were reported with pertussis, 68 (26%) of whom required hospitalization for a total of 643 (median, 4; range, 1–90) days. Of the 52 infants <2 months of age with reported pertussis, 34 (65%) were hospitalized.

Among these cases was an Oregon newborn who was hospitalized with pertussis for 90 days, required extracorporeal oxygenation for 43 days, respiratory support for 72 days, hemodialysis for 31 days, and suffered complications including stroke. The baby required extensive, specialized follow-up after discharge. The infant's mother had declined Tdap offered during pregnancy.<sup>1</sup>

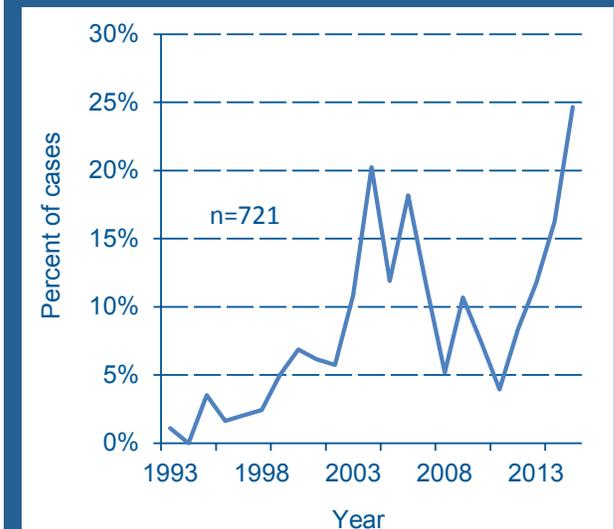
From 2012 through 2015, 2,136 cases of pertussis beyond infancy were reported in Oregon; of these, only 21 (1%) were hospitalized.

### Microbe hunters and death fighters

Pertussis claimed 5,000–10,000 deaths each year in the United States until the whole cell vaccine was widely distributed in 1940s.<sup>2</sup> In the early 1930s, Pearl Kendrick and Grace Eldering, while working in the Michigan Department of Health, developed improved methods for growing and inactivating *Bordetella pertussis*, created a safe vaccine and conducted the first large-scale, well-controlled clinical trial for pertussis vaccine. As Paul De Kruif, author of the best-selling classic *Microbe Hunters*, said, “one of the greatest field tests in microbe-hunting history”.<sup>3</sup>

The whole-cell vaccine was a killed suspension of the entire *B. pertussis* bacterium. After half-century decades of successful whole-cell vaccine use, however, concerns of adverse events associated with it led to their replacement by acellular vaccines for the entire childhood series in 1997.<sup>4</sup> These acellular vaccines contain several pertussis antigens in different concentrations and are combined with tetanus and diphtheria toxoids in the standard “DTaP” vaccines. Their effectiveness in preventing pertussis is about 98% following the fifth DTaP shot. It wanes down to 70% after 5 years, but the remaining 30% of recipients retain protection against serious disease.<sup>5</sup>

Figure 2. Proportion of pertussis case load among persons 15–19 years of age, Oregon, 1993–2015



Today, immunization with acellular vaccine remains the best prevention tool available. DTaP vaccination is recommended as a series starting at 2 months of age and finishing during pre-school. Then, a single dose of Tdap vaccine, which also contains several pertussis antigens and is combined with tetanus toxoid, but with less diphtheria toxoid than is contained in DTaP, is recommended for adolescents and adults. A Tdap shot is additionally recommended for pregnant women during each pregnancy (*vide infra*).

**It still works!**

With the skyrocketing numbers of pertussis cases being reported in Oregon during the 2012 epidemic year, we evaluated the effectiveness of pertussis vaccines currently in use. Using data from Oregon’s statewide ALERT Immunization Information System (ALERT IIS), we calculated the risk of reported pertussis among persons up to date on their pertussis vaccinations and compared it to the risk in the unvaccinated. For young children, the number of vaccines required to be “up to date” varies by age; but our data demonstrated that at any age, an unvaccinated child was more likely to contract pertussis than was an up-to-date vaccinated or partially vaccinated one. Measured vaccine effectiveness ranged from 47% among adolescents 13–16 years of age to 95% among children 15–47 months old (Table). Of the pertussis cases 2 months – 6 years of age, 89 (31%) were completely unvaccinated, and 71 (24%) were only partially vaccinated. Of the unvaccinated cases, 70%

**Pertussis among children and adolescents  
2 months–19 years of age, by vaccination status, Oregon, 2012**

Age	Case counts by vaccination status			Cases per 100,000 by vaccination status§			Vaccine effectiveness % (95%CI)*
	UTD†	Partial	None	UTD†	Partial	None	
2–3 mo	14	NA	14	225	NA	833	73 (43–87)
4–5 mo	8	4	4	140	286	494	72 (6–91)
6–14 mo	22	9	13	81	146	573	86 (72–93)
15–47 mo	41	28	40	40	119	823	95 (92–97)
4–6 yr	44	30	18	48	64	431	89 (81–94)
7–10 yr	121	15	17	69	144	415	83 (72–90)
11–12 yr**	25	NA	89	58	NA	166	65 (46–78)
13–16 yr**	94	NA	30	56	NA	105	47 (19–65)
17–19 yr**	14	NA	15	13	NA	37	66 (30–84)

†“Up to date” (UTD) was defined according to ACIP recommendations: one pertussis-containing vaccine for 2–3-month-olds, two pertussis-containing vaccines for 4–5-month-olds, three for 6–14-month-olds, four for 15–47-month-olds, five for 4–10-year-olds and a single dose of Tdap for those ≥11 years of age.

§ Cohort-specific incidence rates were calculated as the total number of persons with a given vaccination status who developed pertussis, divided by the estimated population of persons with the same vaccination status. Population immunization coverage estimates were obtained from ALERT IIS for persons 2 months – 19 years of age.

\*Vaccine effectiveness (VE) was calculated from attack rate (AR) as shown by the formula

$$VE = (1 - [AR_{\text{vaccinated}} / AR_{\text{unvaccinated}}])$$

\*\*Persons ≥11 years of age were considered up to date if they had received a single dose of Tdap; therefore, “partially vaccinated” was not applicable.

Adapted from Liko J, et al. Clin Infect Dis 2014; 59:261–3.

were unvaccinated because parents had declined to consent to vaccination. Our data argue strongly that the problem in Oregon has been one of failure to vaccinate, rather than of vaccine failure.<sup>6</sup>

Alas, the 2015 case data continue to confirm that failure to vaccinate remains a major issue in Oregon. Among the 269 cases 2 months – 10 years of age, 102 (38%) had not received a dose of pertussis-containing vaccine; only 124 (46%) were up-to-date for age. Of 314 pertussis cases  $\geq 11$  years of age, 118 (38%) had not received the recommended Tdap vaccination.

### Vaccinated = milder disease

A published analysis of pertussis cases reported in the Portland metropolitan area data from August 2010 through July 2012 showed that only 45% of cases were up to date with vaccination. Those who developed pertussis despite a history of having received any pertussis vaccine were significantly less likely than other cases to be hospitalized or to develop severe illness. Unvaccinated cases coughed significantly longer than vaccinated ones.<sup>7</sup>

### Risk factors

A higher rate of pertussis was reported among Hispanic than among non-Hispanic infants during 2012. Data collected as part of an enhanced pertussis surveillance effort in the Portland metro area during 2010–2012 showed that Hispanic infants had 2.3 times the risk for pertussis compared to non-Hispanic infants. Much of this ethnic disparity might be explained by the finding that infants living in household of  $>4$  people had 2.4 times the risk for pertussis compared to those living in households of  $\leq 4$  people — presumably a consequence of increased opportunity for exposure. Hispanic infants were more likely than non-Hispanic ones to live in these larger households (55% vs. 33%), but household size of  $>4$  people was accompanied by a similarly elevated relative risk for non-Hispanic infants.<sup>8</sup>

### Rethinking pertussis control

Faced with persistent disease despite vaccination and surprised by the enormous reservoir of pertussis revealed by more sensitive PCR testing, in 2005 we revised pertussis control guidelines in Oregon to focus on protecting those who are at highest risk for serious morbidity and mortality — i.e., infants, especially the youngest of them.<sup>†</sup> Babies  $<2$  months of age — those too young to have received even a first dose of DTaP — have the highest incidence of disease and are most likely to be hospitalized, to require intensive care, and to die from pertussis. To suppress paroxysms of prescriptions for prophylactic antibiotics for contacts of pertussis cases, while maintaining protection for infants, we recommended that antibiotics be reserved for situations in which an infant or pregnant woman might be exposed.

### Pregnancy plea

A better strategy, however, is to arm babies with immunity from birth. Tdap given to mothers during pregnancy can induce anti-pertussis antibodies that are actively transferred across

<sup>†</sup> Pertussis Prophylaxis—Passé? CD Summary 2005; (Vol. 54, No. 9).

the placenta to the baby at 27–36 weeks' gestation. In light of this fact, and recognizing that maternal antibody titers wane substantially over the ensuing months, Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) recommended in October 2012 that pregnant women receive a dose of Tdap during each pregnancy to protect their newborns. After the pregnant woman has received Tdap, it takes about two weeks to generate protective levels of antibody. Tdap might be given any time during pregnancy, but preference is to be given between 27 and 36 weeks' gestation since it enables transplacental transfer at a point when maternal titers are likely to be highest.<sup>9</sup>

So how are we doing with this recommendation? We reviewed adult immunization data for mothers of children born between December 2014 through March 2015, and with residence in a CDC-sponsored special "Sentinel" immunization surveillance region of Oregon, comprising Clackamas, Marion, Multnomah, Polk, Washington, and Yamhill counties.

Tdap vaccine during each pregnancy, with preference between 27 and 36 weeks' gestation

For this study both mothers and infants were required to have a record in the ALERT IIS. Evidence of Tdap immunization during pregnancy was found for only 2,164 (26%) of 8,196 mothers.

A review of reported pertussis in Oregon during January 1, 2013, through June 16, 2016, identified 29 cases among infants <2 months of age, 18 (62%) of whom had been hospitalized; and only 4 (14%) of the 28 mothers had received Tdap during the pregnancy. Unlike the U.S., the United Kingdom has achieved high vaccine coverage during pregnancies, and published evidence there has demonstrated the vaccination of pregnant women late in the 3<sup>rd</sup> trimester to be 90% effective in protecting infants during the first 2 months of life.<sup>10</sup>

We urge providers to recommend and administer the Tdap vaccine to pregnant women during each pregnancy, and to document the vaccination in ALERT IIS. If you do not stock the vaccine, please refer the patient to a location that offers vaccination, and follow up to ensure that it happens.

## Conclusion

Pertussis will be with us indefinitely. Although the vaccine is not sufficiently effective to eradicate the disease, it still provides substantial protection. Vaccination of pregnant women with Tdap is safe and has been shown to be effective in preventing disease in the most vulnerable patients — i.e., infants too young to have received the primary vaccine series. We recommend it highly.

## Epilogue

*"It is sure as the sun following the dawn of to-morrow that there will be other microbe hunters to mold other magic bullets, surer, safer, bullets to wipe out for always the most malignant microbes of which the history has told."*<sup>11</sup>

## For more information

- Oregon Public Health Division pertussis web page: <http://1.usa.gov/vdpertussis>
- CDC pertussis page: [www.cdc.gov/pertussis](http://www.cdc.gov/pertussis)

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