



# Pertussis in California – The New Normal

*Prevention, Diagnosis and  
Reporting Recommendations  
for Health Care Providers*

July 23, 2015





# Overview of Today's Webinar

- Background and epidemiology of pertussis
- Pertussis: clinical disease, diagnosis, treatment and prevention
- Common pertussis issues encountered by providers
- Conclusions
- Question and Answer



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## Commercial Support

**There is no commercial support for today's activity**



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His presentation today uses the best available evidence and contains no commercial bias. There will be no mention of any specific brand-name agents.

None of the other speakers or planners for today's webinar have disclosed any financial interests related to the content of this talk.



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# Epidemiology of pertussis in CA

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California Department of Public Health

# Pertussis (whooping cough)

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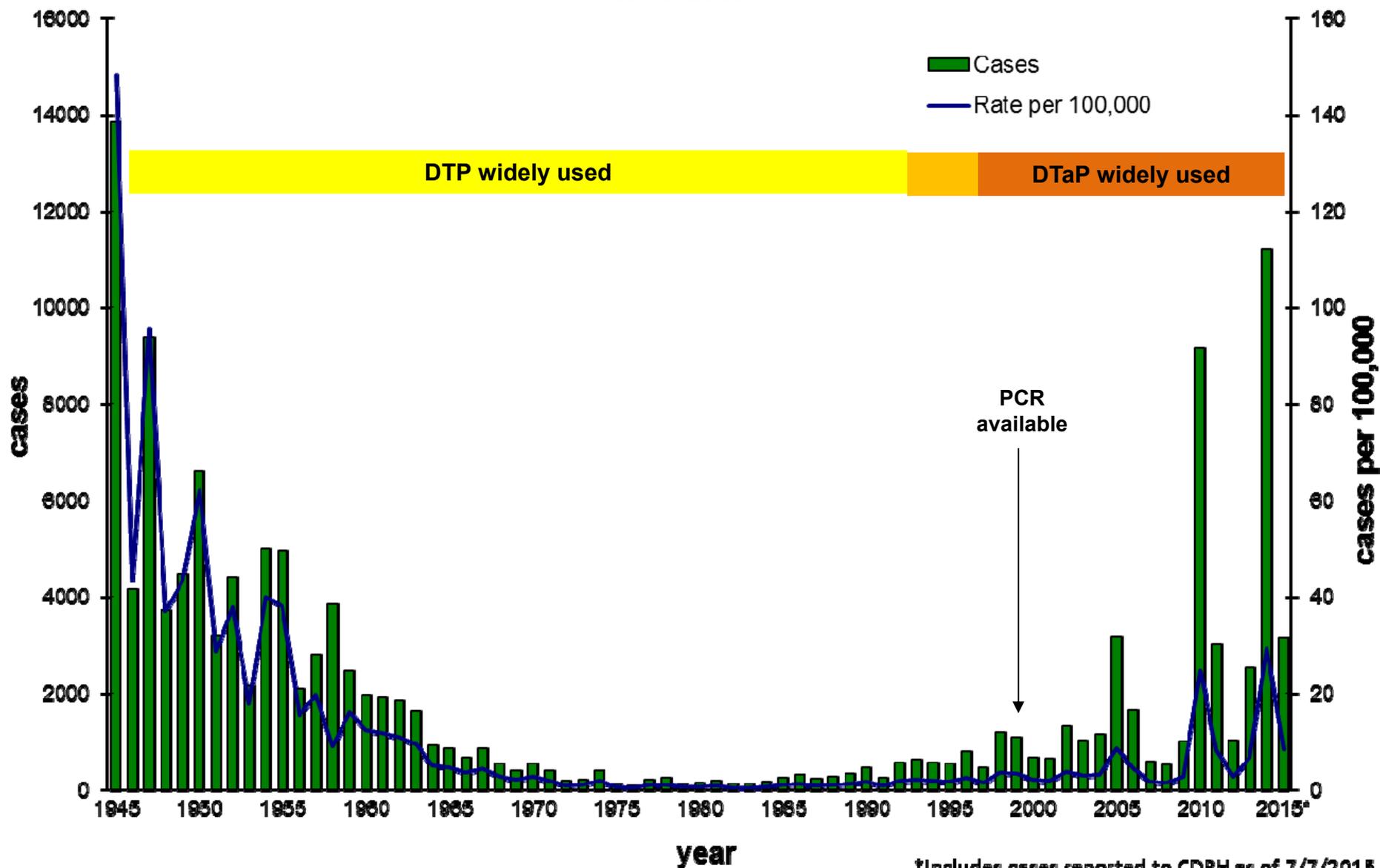
- Caused by *Bordetella pertussis*
- “The 100 day cough”: three stage illness (catarrhal, paroxysmal, and convalescent) that lasts typically 4-12 weeks
- Classic presentation: no fever, coryza, paroxysmal cough, posttussive vomiting, posttussive whoop
- *B. pertussis* infections and illness in adolescents and adults are very common but often not diagnosed (both in the pre-vaccine and present eras)
- Most severe disease and death occurs in infants <4 mos of age
- Highly infectious;  $R_0$  estimated to be 15-17
- Disease patterns are cyclical and peak every 3-5 years
- Cyclic peaks have been increasing since the 1990s causing major epidemics in recent years

# Pertussis vaccines

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- Whole-cell pertussis vaccine (DTP)
  - Widely wide used from 1940-1990s in children <7 years
  - Associated with adverse reactions (real and perceived)
- Acellular (subunit) pertussis vaccines (DTaP & Tdap)
  - Less reactogenic, but less effective and faster waning of immunity than whole cell vaccines
  - DTaP recommended in 1992 for the 4<sup>th</sup>/5<sup>th</sup> doses of childhood series and for entire series in 1997
  - Tdap licensed in 2005 for adolescents and adults
  - Recommended schedule:
    - Pediatric: 2m, 4m, 6m, 18m, 4-6y, 11-12y
    - Pregnant women: 27-36 weeks gestation during each pregnancy
    - Adults: once during adulthood

# Number and Incidence of reported pertussis cases by year of onset -- California, 1945-2015\*



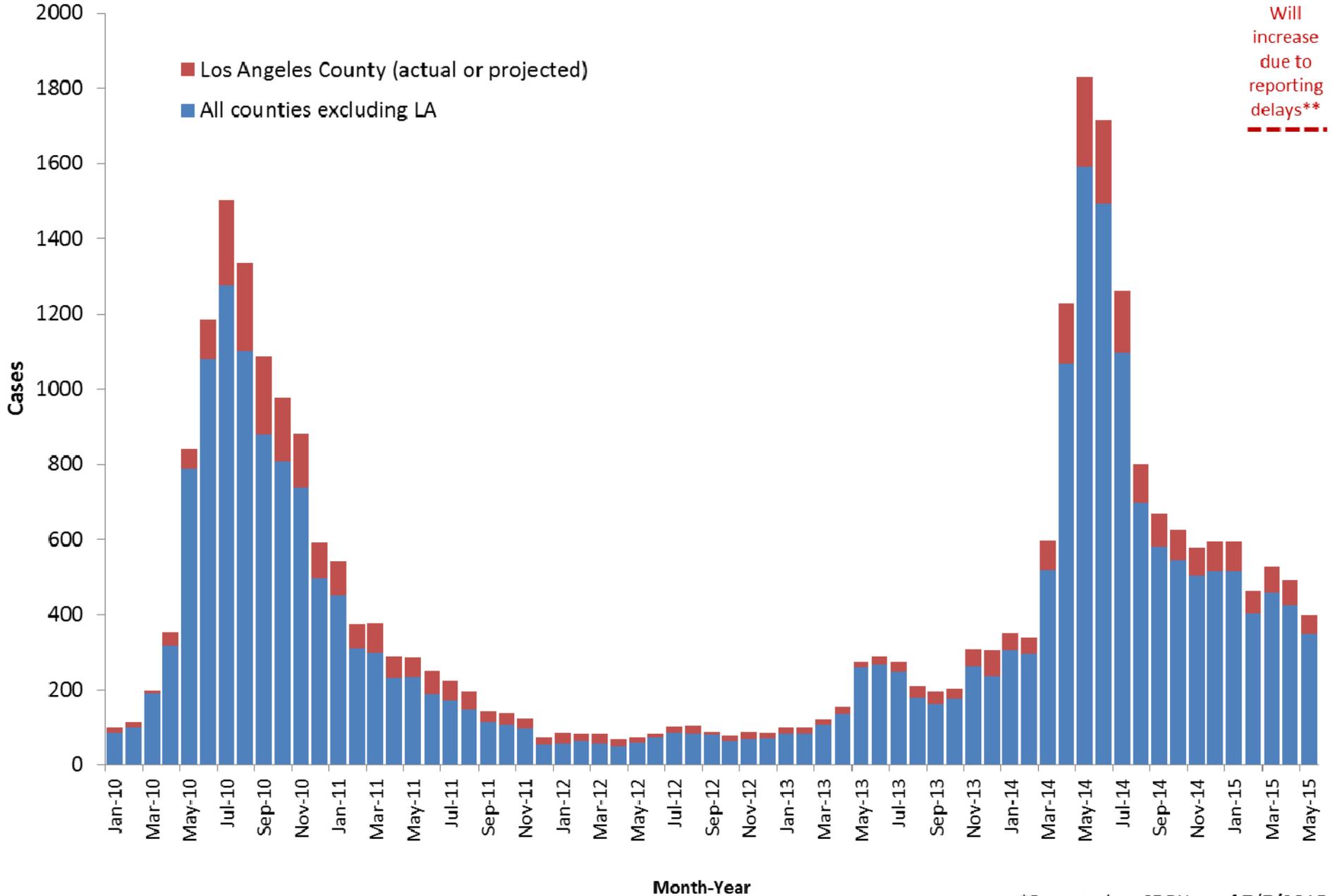
\*Includes cases reported to CDPH as of 7/7/2015

# Current situation in CA - as of 7/7/2015

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- 11,203 reported cases with onset in 2014; state rate 29.3 cases/100,000
  - 456 hospitalized; 119 (26%) required intensive care
    - Most (61%) hospitalized were <4 months of age
  - 3 deaths in infants <2 months of age
- 3,150 reported cases with onset in 2015
  - Including 115 hospitalized and one infant death

# Pertussis cases by month of onset -- California, 2009-2015\*



\*Reported to CDPH as of 7/7/2015

# Why is the incidence of pertussis increasing?

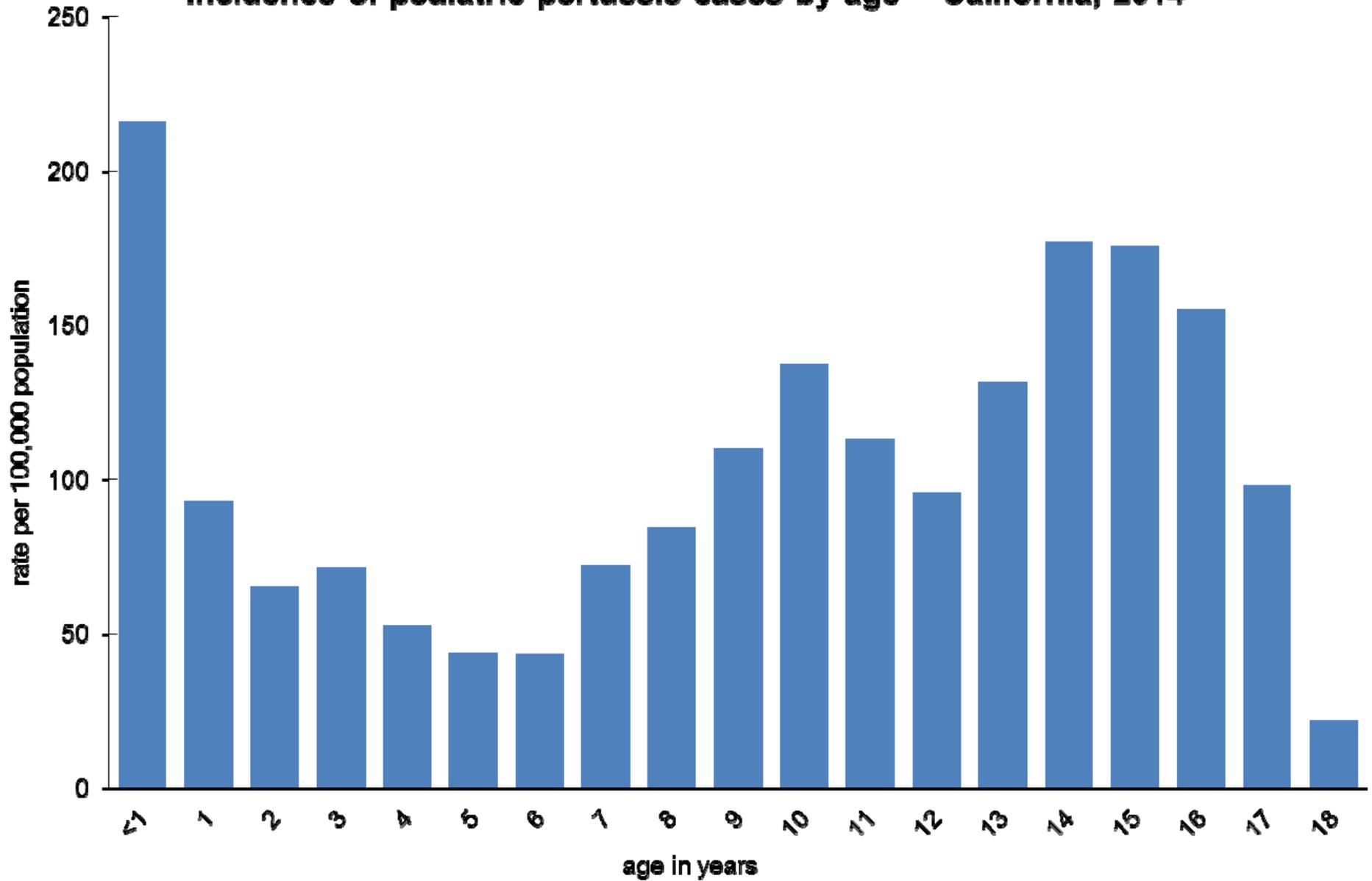
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- Increased public health awareness and reporting
- Use of acellular vaccines (DTaP and Tdap), which replaced whole-cell vaccine (DTP) in the 1990s
  - Faster waning immunity than was expected
- PCR more sensitive and widely available
- Possibly due to genetic changes in *B. pertussis*
  - Recent increase in identification of strains in the USA and other countries which no longer express pertactin antigen<sup>1,2</sup>

1. Pawloski et al. Prevalence and molecular characterization of pertactin-deficient *Bordetella pertussis* in the United States. Clin Vaccine Immunol. 2014.

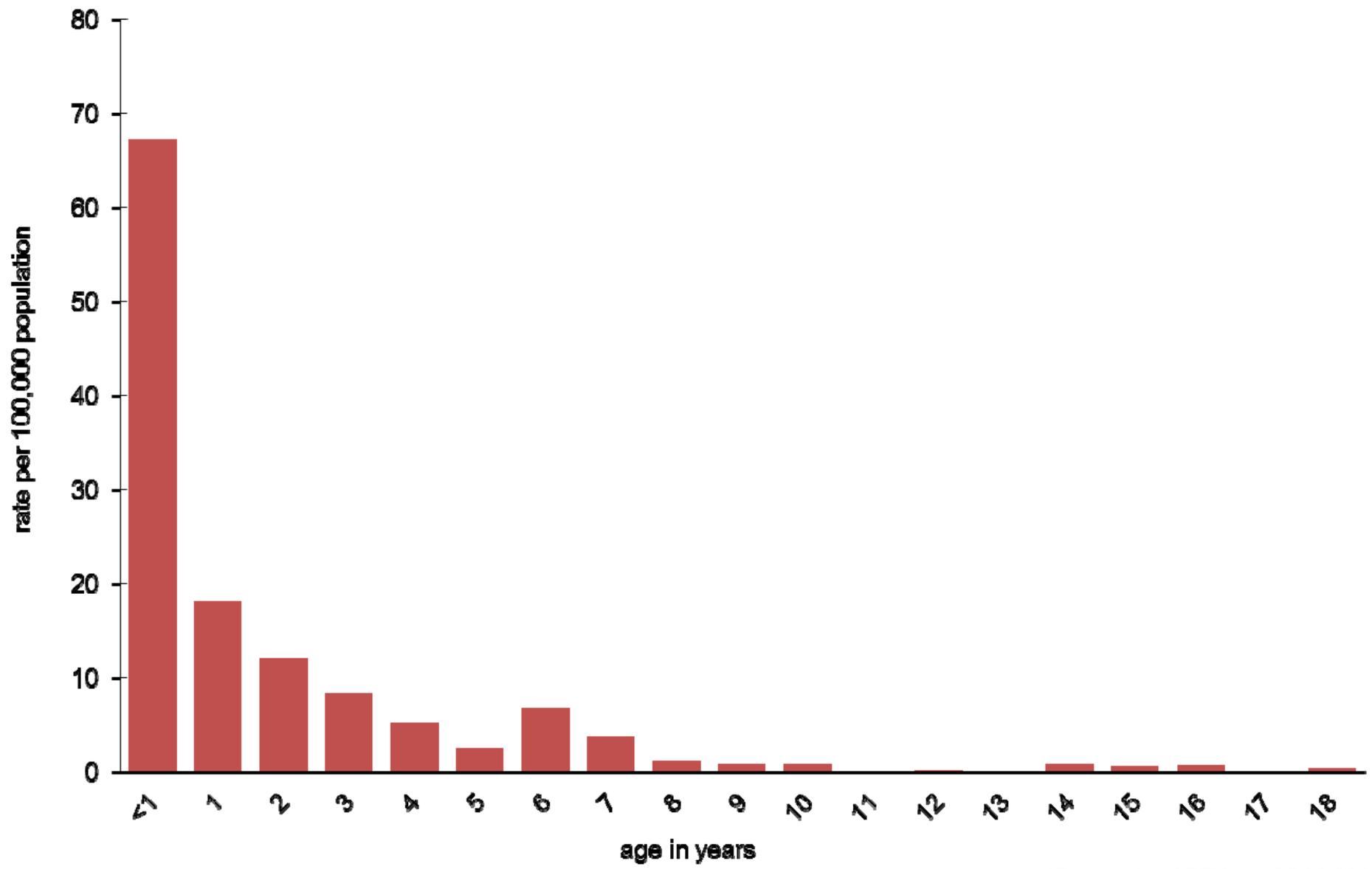
2. Lam et al. Rapid increase in pertactin-deficient *Bordetella pertussis* isolates, Australia. Emerg Infect Dis. 2014.

### Incidence of pediatric pertussis cases by age -- California, 2014\*



\*Reported to CDPH as of 5/20/2015

### Incidence of hospitalized pertussis cases by age -- California, 2014\*



\*Reported to CDPH as of 5/20/2015

# Pertussis among infants in California

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- Since 2009, more than 2,400 pertussis cases in infants <4 months of age have been reported in California
  - 1,378 (56%) were hospitalized
    - 38% of those with detailed hospitalization information were admitted to the ICU; 28% of these required intubation
  - 20 (1%) died

# California Pertussis Deaths

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- All California pertussis deaths since 1998 have been in infants  $\leq 3$  months of age
- 83% Hispanic
- Of those with known status, all had pneumonia and pulmonary hypertension
- The median WBC count of fatal cases in 1998-2014 was 77,000 (range 15,000-148,000)
- Only 1 had received any doses of DTaP vaccine; this child was premature with bronchopulmonary dysplasia

# Risk factors for death among infants

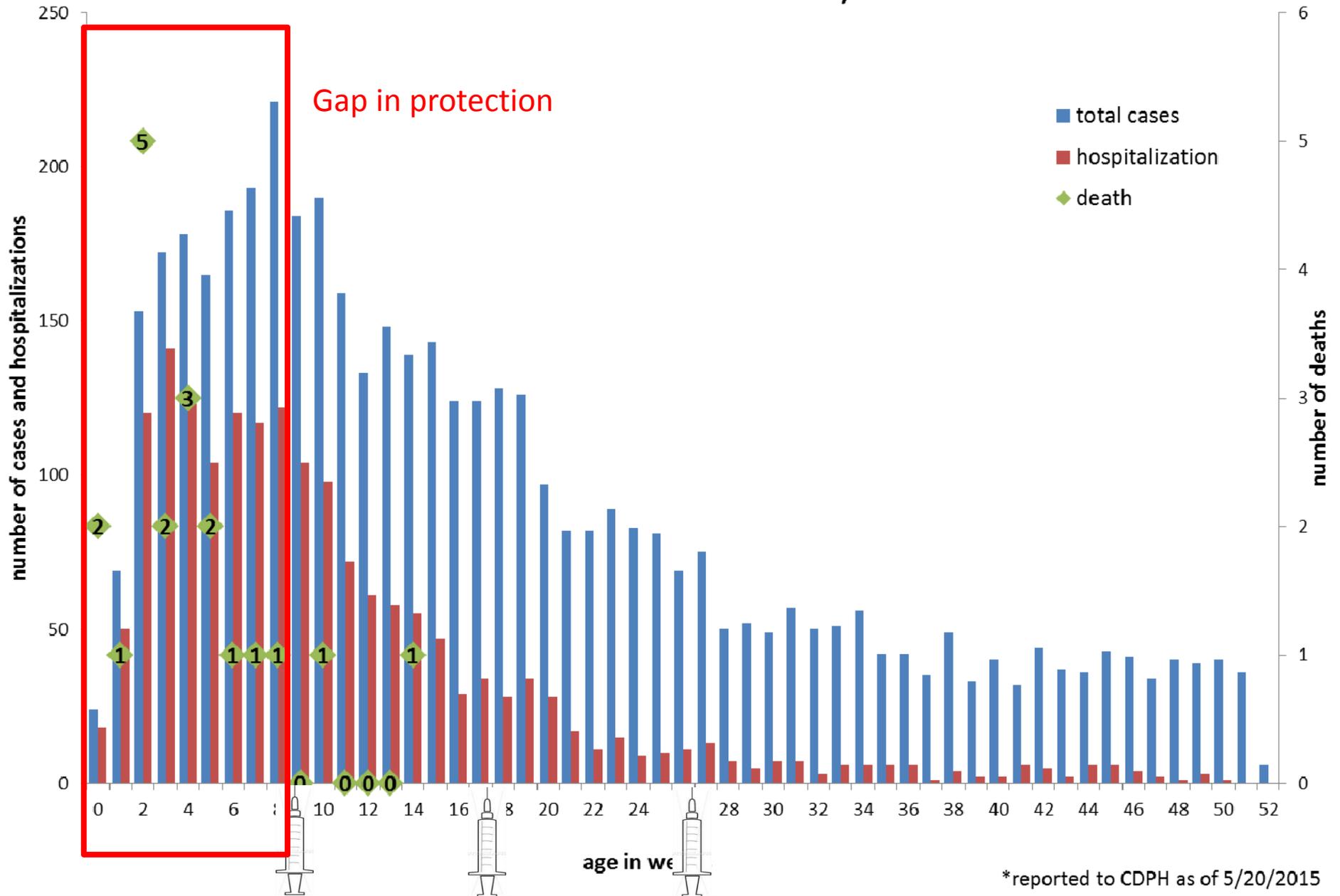
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- In small study of infants admitted to an ICU, more severe cases had higher WBC counts, higher heart rates and respiratory rates and more likely to develop pneumonia<sup>1</sup>
- In a larger case-control study comparing fatal and non-fatal hospitalized cases<sup>2</sup>
  - Younger infants and those with a low birth weight have higher odds of death; LBW <2800g a predictor of death
  - Elevated WBC, particularly >46K was important predictor of death
  - All fatal cases required intubation
  - DTaP protective against high WBC counts and death

1. Murray et al. J. of the Pediatric Infectious Diseases Society. 2013.

2. Winter et al. CID. 2015

# Pertussis cases, hospitalizations and deaths in infants, by age in weeks at time of disease onset -- California, 2009-2015\*



# Maternal Tdap in pregnancy

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- ACIP, AAFP and ACOG recommend that all pregnant women receive Tdap vaccine during each pregnancy between 27-36 weeks gestation, regardless of her Tdap vaccination history
  - Antibodies to pertussis are actively transported across the placenta to the baby<sup>1,2</sup>
- UK Tdap program for pregnant women estimates 90% reduction in disease in infants <2 months of age<sup>3</sup>
- However, uptake of Tdap among pregnant women in CA is improving but still low and many barriers are reported
  - CDPH convenience survey of L&D hospitals: 44% in 2014; 22% in 2013
  - N. CA Kaiser: >80% in 2015; 15-30% in 2010-2012

1. de Voer RM, et al. Clin Infect Dis. 2009.

2. Gall SA, et al. Am J Obstet Gynecol 2011.

3. Amirthalingam et al. Lancet. 2014.

# Accelerating first dose of DTaP from 8 weeks to 6 weeks

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- AAP recommends that when pertussis is present in a community, DTaP can be started as early as 6 weeks<sup>1</sup>
- Among infants in the U.S. aged  $\geq 42$  days, one dose of DTaP protected against death, hospitalization and pneumonia (aORs 0.28, 0.69 and 0.80, respectively)<sup>2</sup>
- Acceleration of DTaP to 6 weeks estimated to reduce average notifications, hospitalizations, and hospital bed-days by 8%, 9%, and 2%, respectively in Australia<sup>3</sup>
- Similarly in the U.S., acceleration from 2 months to 6 weeks was predicted to prevent 1236 cases of pertussis, 898 hospitalizations, and 7 deaths per year<sup>4</sup>

1. AAP. In: Pickering LK et al, eds. Red Book: Report of the Committee of Infectious Diseases. 2015.

2. Tiwari et al. Pediatrics. 2015.

3. Foxwell et al. PIDJ. 2011.

4. Shinall et al. Pediatrics. 2008.

# Pertussis in older children and adolescents

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- In 2014, the largest burden of disease occurred in adolescents/teenagers 10-16 years of age; many middle and high school outbreaks reported statewide
  - Nearly all cases had been previously immunized with pertussis vaccines
  - Most cases did not have severe disease and very few required hospitalization
- A recent study in San Diego of pertussis cases 13-17 years of age found that students (Varan et al. 2015, manuscript in preparation)
  - Missed an average of 5.4 days of school and 15.4 days of sports activities during their illness.
  - Nearly all (96%) had received their Tdap booster; median time from vaccination to illness was 3.3 years

# Vaccine effectiveness and waning immunity for DTaP and Tdap

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- Recent studies indicate that immunity from DTaP vaccine is high immediately following receipt but quickly wanes within a few years<sup>1-3</sup>
- Tdap effectiveness similarly shows moderate short-term protection (53-75%) and rapid waning of immunity 2-4 years after receipt<sup>4-6</sup>
- Three studies also suggest that immunity wanes faster in children and adolescents born in 1998 and later who have only received acellular pertussis vaccines (DTaP and Tdap)<sup>7-9</sup> (i.e., no doses of whole-cell vaccine)

1. Klein et al. N Engl J Med. 2012.

2. Misegades et al. JAMA. 2012.

3. Tartof et al. Pediatrics. 2013.

4. Liang. June 2013 ACIP meeting.

5. Koepke et al. J Infect Dis. 2014

6. Baxter et al. BMJ. 2013.

7. Klein et al. Pediatrics. 2013.

8. Sheridan et al. JAMA. 2012

9. Witt et al. CID. 2013.

# What about additional doses of Tdap?

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- Safe and provide short-term immunity
- Only currently recommended for pregnant women
  - Not considered cost-effective on a population level due to short duration of immunity
  - Limited/no data on effectiveness of Tdap for “cocooning” – may be beneficial on an individual basis, but no longer seen as a public health priority
- Highest burden of disease is in adolescents and teens; very few have known complications
  - <1% hospitalized among 10-17 age group
- Repeated doses of Tdap doses can be given and would likely provide short-term protection
  - May not be covered by insurance



# Pertussis: Clinical Disease, Diagnosis, Treatment and Prevention

James D. Cherry, MD, MSc

# Pertussis Fact #1

The rate of reported pertussis today is ~20 fold less than in the pre-vaccine era. This fact is often overlooked today when experts and the media discuss the resurgence of pertussis

# Pertussis Fact #2

Illness in DTaP vaccine failures is less severe than illness in similar aged unvaccinated children

# Pertussis in Adolescents and Adults

- Many believe that adolescent and adult pertussis is a relatively new phenomenon
  - This is incorrect
- Pertussis was common in adolescents and adults in the pre-vaccine era
- Vaccine use may have changed the clinical expression rate

# Clinical Illness

# Major Manifestations of Typical Pertussis

- Three-stage illness (catarrhal, paroxysmal and convalescent) that lasts 4-12 weeks
- Specific manifestations:
  - paroxysmal cough
  - lack of fever
  - no systemic illness
  - coryza; no pharyngitis
  - posttussive vomiting
  - posttussive whoop
  - absolute lymphocytosis

# Pertussis in Young Infants

# Clinical Presentation in Infants

- Initially infant looks deceptively well; coryza, sneezing, clearing throat, no fever, mild cough
- Paroxysmal stage: gagging, gasping, eye bulging, bradycardia?, cyanosis, vomiting
  - Leukocytosis with lymphocytosis
  - Apneic episodes
  - Seizures
  - Pneumonia
  - Pulmonary hypertension
  - Adenovirus or RSV coinfection can confuse the picture

# 2010 Pertussis Death

- Pertussis Case : April 2010
  - Previously healthy, Hispanic female
  - Lived with mom, dad, sister – no daycare
  - Father had cough illness for several weeks
  - Cough onset at age 5 weeks, one week prior to admission
  - Seen in ER 4 days prior to admission with cough, post-tussive vomiting and cyanosis; pertussis not considered - discharged home
  - Seen in ER 4 days later and admitted
  - Hospitalized in children's hospital for one week before transfer to PICU and intubation
  - WBC 80,000; pulmonary HTN - single volume exchange transfusion done
  - Transferred to second children's hospital PICU for ECMO, but not done due to multi-organ failure

# Pertussis in Adolescents and Adults

# Clinical Pertussis in Adolescents and Adults

- It is an afebrile illness unless there is a concomitant or secondary infection
- The severity of illness is variable but virtually all will have a paroxysmal cough
- The cough is non-productive
- The onset is insidious; medical care is usually not sought until the 3<sup>rd</sup> or 4<sup>th</sup> week
- The duration is 2 weeks to 4 months; there is memory for the cough - it may reoccur with a URI

# Symptoms of Pertussis in 664 Adolescents and Adults\*

<u>Characteristic</u>	<u>Percent</u>
Paroxysms	99
Posttussive apnea	87
Posttussive vomiting	65
Whoop	69
Sweating episode	32

\* De Serres et al. JID 2000; 187: 174-9

# Complications of pertussis in 664 Adolescents and Adults\*

<u>Characteristic</u>	<u>Percent</u>
Sinusitis	13
Otitis media	4
Urinary incontinence	4
Pneumonia	4
Weight loss	3
Rib Fracture	2
Fainting	2

\*De Serres et al. JID 2000; 187: 174-9

# Clinical Diagnoses Assigned by the Primary Care Providers and Antibiotic Therapy in Students with Cough $\geq$ 6 Days (Mink et al. CID.1992;14:464-471)

Diagnosis	Subjects with <i>B. pertussis</i> infection (n = 31)	Subjects without <i>B. pertussis</i> infection (n = 84)	p value*
URI	39%	33%	0.68
Bronchitis	48%	64%	0.14
Otitis/Sinusitis/Pharyngitis	0%	10%	0.11
Pertussis	0%	1%	0.99
Other	16%	8%	0.30
Antibiotics taken for illness prior to clinic visit	23%	14%	0.26
Antibiotics prescribed at the time of clinic visit	39%	64%	0.02
Erythromycin prescribed at the time of clinic visit	35%	52%	0.14

\*Fisher's Exact Test

# Clinical Characteristics of Cough in Students with Cough for $\geq 6$ Days

(Mink et al. CID. 1992; 14: 464-471)

Characteristic of Cough	34 Students with <i>B. pertussis</i> Infection	96 Student without <i>B.</i> <i>pertussis</i> Infection
Median duration prior to study	21 days	14 days*
Frequency $\geq 1$ episode/hour	94%	89%
Quality Staccato or paroxysmal	90%	82%
Productive with each episode	3%	21% <sup>†</sup>
Severity severe ‡	40%	35%

\* p = 0.92

† p = 0.02

‡ Definition: required interruption of all activities during episode

# Diagnosis

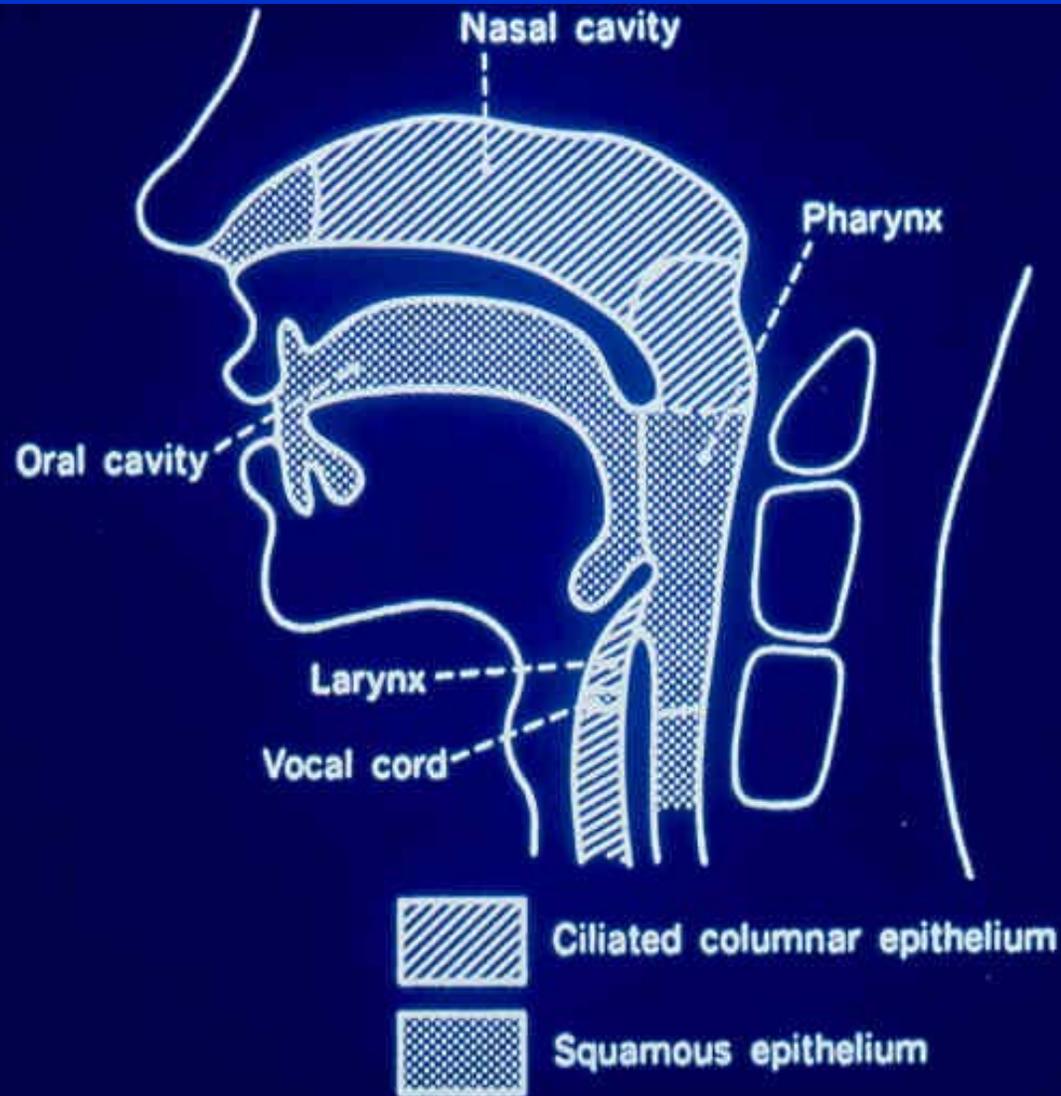
# Clues in the Clinical Dx of Pertussis in Young Infants

- They have a cough illness without fever
- They don't have wheezing unless there is a concomitant viral infection
- They have a rapidly rising WBC count with a lymphocytosis. Therefore do a WBC count on all infants with a new afebrile cough illness
- Most often there is an adult family member with an afebrile cough illness

# Clues in the Clinical Dx of Pertussis in Older Children, Adolescents and Adults

- Lack of fever
- Lack of a truly productive cough
- WBC,ESR and CRP normal
- Feeling of a choking sensation
- Cough worse at night; need to sleep sitting up
- Sweating episodes
- Normal between coughing episodes

# Laboratory Diagnosis



# Collection of Specimens

- NP wire with dacron swab
- NP aspirate with plastic catheter and specimen trap.

# Culture of NP Secretions

The main reasons for failure to isolate *B. pertussis* from correctly collected and transported specimens are:

- 1) Bacterial and fungal contamination
- 2) Lack of fresh media
- 3) Specimen collected too late in illness

# PCR on NP Secretions

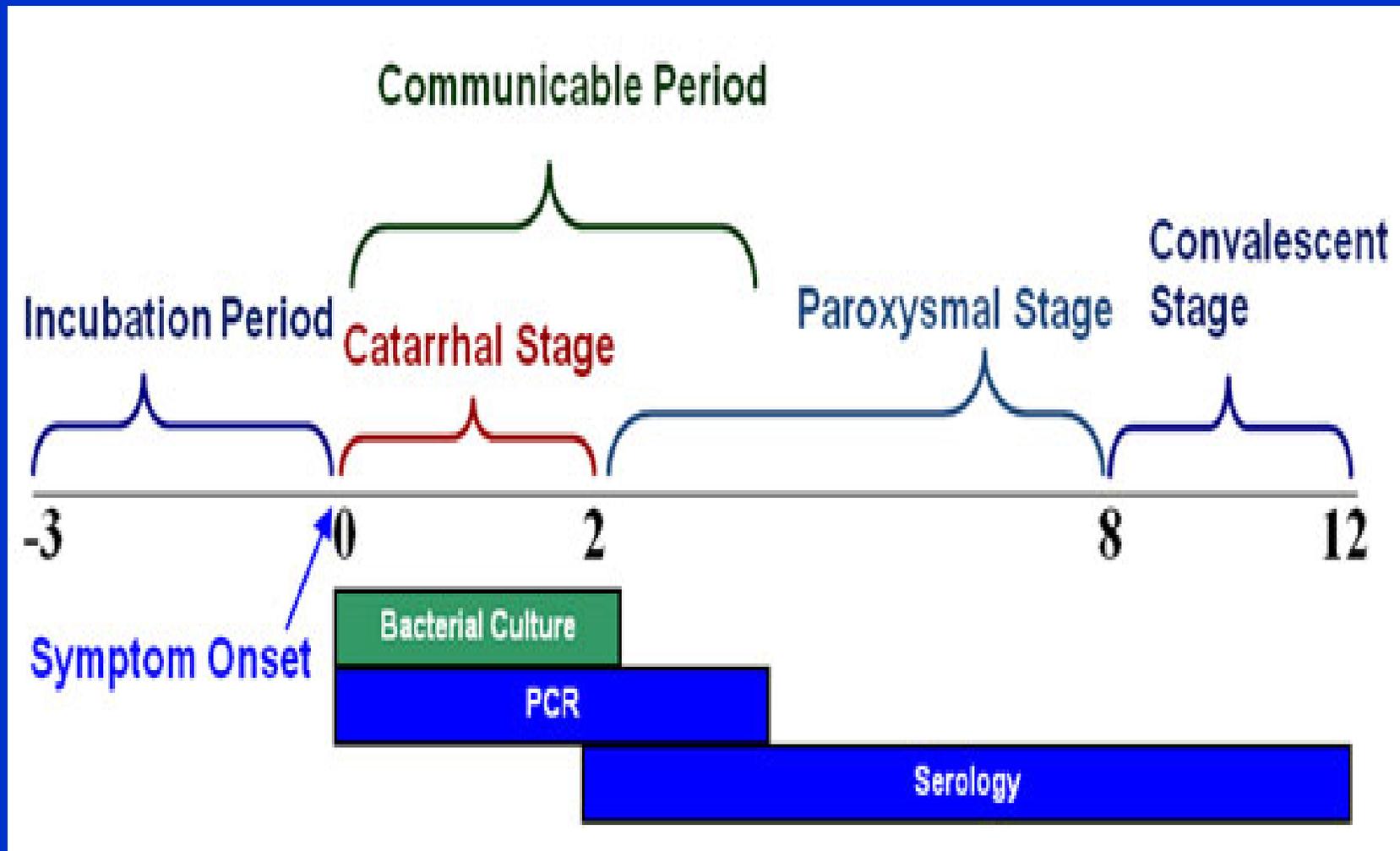
- 1) More sensitive than culture
- 2) With use of multiple primers can identify and separate other *Bordetella* sp
- 3) Delay in specimen collection is main reason for negative PCR

# Serologic Dx of Pertussis

# ELISA

Diagnosis is made on the basis of high single serum IgG and/or IgA titer to PT. It is a practical and reasonably sensitive and specific test

# When Pertussis Tests are Likely to be Positive in Infected People



# Treatment

# Antimicrobial Agents for the Treatment and Prevention\* of Pertussis

## Children

Erythromycin† = 40-50 mg/kg/day for 14 days administered every 6 hours (maximum dose = 2 gms/day)

Azithromycin = 10 mg/kg on day 1 and 5 mg/kg on days 2-5 as a single dose/day (maximum dose = 500 mg on day 1 and 250 mg on days 2-5)

Clarithromycin = 15-20 mg/kg in 2 divided doses for 7 days (maximum dose = 1gm/day)

Trimethoprim-sulfamethoxazole = 8-12 mg of trimethoprim, 40-60 mg of sulfamethoxazole /day in 2 doses for 14 days (maximum dose = 320 mg of trimethoprim)

\* Prophylactic dose is the same as the treatment dose

† Data suggest that a 7 day treatment course is effective

# Treatment in Young Infants

- \*\*\* Neonates should be treated with Azithromycin and not Erythromycin because of the risk of pyloric stenosis
- \*\*\* Treat with Azithromycin immediately; do not wait for PCR/culture

# Treatment in Young Infants

- Nearly all infants < 4 months of age should be admitted to a hospital with a PICU and seen by a PID MD
- Risk factors for death in infants < 4 months of age are: WBC count > 46,000; rapid pulse rate; rapid resp. rate; pneumonia

# Antimicrobial Agents for the Treatment and Prevention\* of Pertussis

## Adults

Azithromycin = 500 mg on day 1 and 250 mg on days 2-5 as a single dose/day

Clarithromycin = 1 gm/day in 2 divided doses for 7 days

Trimethoprim-sulfamethoxazole = 320 mg of trimethoprim, 1.6 gm of sulfamethoxazole/day in 2 doses for 14 days

\* Prophylactic dose is the same as the treatment dose

# Prophylaxis

# Who Should Receive Prophylaxis?

- Restrict to high risk situations (young infants, NICUs)
- Focus on high risk persons (e.g., pregnant women, caregivers of young infants) in low risk settings such as classrooms, schools, and work places
- It is better to do post-exposure surveillance and Rx early onset cases than to provide prophylaxis to large population groups

# Summary

- The hallmark of pertussis is paroxysmal cough and the cause of this unique cough is not known
- Clinical manifestations vary by age
- Pertussis is common and occurs in all age groups (this is not new)
- Infants get pertussis from adolescents and adults
- Deaths in young infants are caused by PT
- Method of laboratory Dx depends upon stage of illness
- Antimicrobial Rx can shorten the illness course and prophylaxis is highly effective



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# Common Pertussis Issues Encountered by Medical Providers

# Diagnosing Pertussis: Does prior vaccination rule out pertussis?

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Without indication of a prior pertussis exposure to the patient, consider pertussis as a differential diagnosis in patients with...

- ✓ Afebrile paroxysmal cough illness (with or without whoop or post-tussive vomiting)
- ✓ Apnea (for young infants)

***...regardless of vaccination status and duration since most recent dose.***

# Reporting Pertussis: Do providers need to report if the lab is reporting?

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YES! Medical providers are legally required to report patients suspected of having pertussis to the Los Angeles County Department of Public Health within **1 working day** of identification.<sup>1</sup>

*Do not wait for lab confirmation*

*Do not assume that the lab will send the report to the Health Department*

1. California Code of Regulations. Title 17, Sections 2500 and 2505

# Pertussis Treatment: Clearing patients to return to activities

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Prescribe azithromycin, erythromycin, trimethoprim-sulfamethoxazole (TMP-SMX), or clarithromycin for your symptomatic patients and their contacts

*Inform symptomatic patients that they must complete 5 days (of an appropriate antibiotic therapy) before returning to school or work*

# Asymptomatic Pertussis Contacts: what should you do if they present at your clinic?

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1. Do **NOT** perform a test for pertussis in an asymptomatic patient/contact who was exposed to a person with pertussis
2. **Household/day care contacts:** If the asymptomatic patient lives in the household or attends daycare with a person with pertussis, provide antibiotic prophylaxis regardless of vaccination status.

# Asymptomatic Pertussis Contacts: what should you do if they present at your clinic?

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- 3. School contacts:** If the asymptomatic patient was exposed at school to a person with pertussis, only provide antibiotic prophylaxis to high risk contacts (i.e., immunocompromised, pregnant, unvaccinated/under-vaccinated).
- 4. All unvaccinated and under-vaccinated contacts to a person with pertussis should be immunized right away.**

## Summary: Checklist when a patient presents to you with possible pertussis:

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1. **Consider pertussis** in your differential diagnosis if a paroxysmal cough of any duration is mentioned or observed (regardless of the patient's vaccination status)
2. **Test for pertussis:** nasopharyngeal swab for *Bordetella pertussis* PCR, ideally within 3 weeks of cough onset (*preferred*)
3. **Treat for pertussis:** prescribe an appropriate antibiotic

## Summary: Checklist when a patient presents to you with possible pertussis:

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4. **Return to work/school:** the patient can return after completing the 5<sup>th</sup> day of an appropriate antibiotic.
5. **Provide antibiotic prophylaxis:** if possible, provide antibiotic prophylaxis to all household contacts when a pertussis diagnosis is confirmed.
6. **Consult with and/or report the suspect pertussis case** to the Los Angeles County Department of Public Health (report within 1 working day).

# Conclusions

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- Increased incidence is the new normal, especially among acellular vaccine recipients
- In spite of less efficacious vaccines, incidence is still lower than in the pre-vaccine era
- Illness in vaccine failures is less severe
- Public health focus has changed from reducing overall morbidity to targeting those at highest risk of severe disease and death

# Conclusions

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- Key strategies to reducing severe disease are prompt infant immunization with the primary series and prenatal vaccination with Tdap during the 3<sup>rd</sup> trimester.
- Lowering the start age of immunization to 6 weeks and the immunization of all pregnant women (each pregnancy) is likely to prevent virtually all infant deaths due to pertussis.

# Pertussis Resources

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- ✓ Reporting pertussis cases to the Los Angeles County Department of Public Health:

<http://publichealth.lacounty.gov/acd/reports/CMR-H-794.pdf>

- ✓ Pertussis Laboratory Testing Guidelines:

<http://www.cdph.ca.gov/programs/immunize/Documents/PertussisLaboratoryTesting.pdf>

- ✓ Recommended pertussis treatment and post-exposure prophylaxis information:

[http://www.cdph.ca.gov/HealthInfo/discond/Documents/CDPH\\_Pertussis\\_Quicksheet.pdf](http://www.cdph.ca.gov/HealthInfo/discond/Documents/CDPH_Pertussis_Quicksheet.pdf)

# Pertussis Resources

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✓ General Pertussis and Pertussis Vaccination Information

[www.publichealth.lacounty.gov/ip/DiseaseSpecific/Pertussis.htm](http://www.publichealth.lacounty.gov/ip/DiseaseSpecific/Pertussis.htm)

[www.cdc.gov/vaccines/vpd-vac/pertussis/default.htm](http://www.cdc.gov/vaccines/vpd-vac/pertussis/default.htm)

[www.cdph.ca.gov/healthinfo/discond/pages/pertussis.aspx](http://www.cdph.ca.gov/healthinfo/discond/pages/pertussis.aspx)

✓ Downloadable Educational Materials:

[www.eziz.org/resources/](http://www.eziz.org/resources/)

# Questions





## **Thank you for attending the pertussis webinar**

To view a recording of this webinar, download handouts or  
request CME/certificates of attendance visit

**[publichealth.lacounty.gov/ip/PertussisWebinar.htm](http://publichealth.lacounty.gov/ip/PertussisWebinar.htm)**

# Acronym & Abbreviation Guide (A-I)

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**AAFP** American Academy of Family Physicians

**AAP** American Academy of Pediatrics

**ACIP** Advisory Committee on Immunization Practices

**ACOG** American Congress of Obstetricians and Gynecologists

**aOR** Adjusted Odds Ratio

**CI** Confidence Interval

**CRP** C-Reactive Protein

**DTaP** Diphtheria, Tetanus, & acellular Pertussis

**DTP** Diphtheria, Tetanus, Pertussis

**DTwP** Diphtheria, Tetanus, & whole-cell Pertussis

**Dx** Diagnosis

**ECMO** Extracorporeal Membrane Oxygenation

**ELISA** Enzyme-Linked Immunosorbent Assay

**ER** Emergency Room

**ESR** Erythrocyte Sedimentation Rate

**HTN** Hypertension

**ICU** Intensive Care Unit

**IgA** Immunoglobulin A

**IgG** Immunoglobulin G

# Acronym & Abbreviation Guide (L-Z)

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**LBW** Low Birth Weight

**LPS** Lipopolysaccharide

**NIAID** National Institute of Allergy & Infectious Diseases

**NICU** Neonatal Intensive Care Unit

**NIH** National Institutes of Health

**NP** Nasopharyngeal

**OR** Odds Ratio

**PCR** Polymerase Chain Reaction

**PICU** Pediatric Intensive Care Unit

**PID** Pediatric Infectious Diseases

**PT** Pertussis Toxin

**R<sub>0</sub>** Number of persons infected by single disease source

**RSV** Respiratory Syncytial Virus

**Rx** Prescription

**Tdap** Tetanus, diphtheria, & acellular pertussis

**URI** Upper Respiratory Infection

**WBC** White Blood Cell

**WHO** World Health Organization