

# **Prevention and Treatment of Pertussis and Influenza**

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#### Significant Annual Burden of Influenza







### Failure to vaccinate Variable circulating strains impact on vaccine performance Variable populations at risk each season

# The problem with influenza





### "Influenza has been around for a long time, and is remarkable both for the rapidity of its spread, the brevity of the immunity it confers, and the instability of the virus that causes the disease."

### William McNeill *Plagues and Peoples* 1977





**Historical perspective** 

Four out of five American casualties in WWI were attributable to influenza.

Influenza was a key factor in the ultimate defeat of the German army.





### **Influenza Key Points**

- Yearly epidemics
- Marked seasonality
- Emerging/re-emerging pathogen
- Pandemics secondary to antigenic shift (genetic reassortment)
- Characteristic (and uncharacteristic) age distributions



### **Antigenic Drift**







### **Antigenic Shift**







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### Occurrence of Influenza Pandemics and Epidemics



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#### Influenza Impact Varies by Season, Highest with H3N2











#### Influenza-Like Illness Is Earlier With Rapid Increase in Visits











### How Does Influenza Spread?





Droplet (e.g. coughing, sneezing, speaking)

Contact (touching a contaminated surface)



### **To Prevent Spreading of Flu**





Droplet (e.g. coughing, sneezing, speaking)



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#### <u>ALWAYS: Good Personal Hygiene-</u> <u>habits</u> via

- a) covering of mouth when coughing or sneezing
- b) Washing or cleaning hands with soap or alcohol based gel

### CLINCIAL SETTING:

#### Appropriate Screening and Isolation Personal Protective Equipments/PPE

- a) Masks for those who are well
- b) Gowns for those who are well
- c) Protective goggles or faceshields
- d) Gloves



#### **Influenza Vaccination**

- Influenza vaccination is recommended for all persons aged 6 months and older each year
- The 2017-18 influenza vaccine contains a similar H3N2 virus as last season, only the H1N1 virus was updated

#### 2017-18 Influenza vaccine composition:

- A/Michigan/45/2015 (H1N1)pdm09-like virus (updated);
  - A/Hong Kong/4801/2014 (H3N2)-like virus (same)
    - B/Brisbane/60/2008-like virus (same)
- B/Phuket/3073/2013-like virus (same, only in quadravalent)





#### Current influenza vaccines reduce the burden of illnesses in the US

#### In 2016-17, vaccination provided substantial prevention:



Modeled using estimates of disease burden, vaccine coverage and effectiveness, based on Reed et al https://www.cdc.gov/flu/about/disease/2015-16.htm



### National Early-Season Flu Vaccination Coverage, United States, November 2017



Figure 1.





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### National Early-Season Flu Vaccination Coverage, United States, November 2017



- ~ 2 of of every 5 children and adults in the United States had received an influenza (flu) vaccination by early November 2017:
  - 38.6% of all persons 6 months and older
  - 38.8% of children 6 months through 17 years
  - 38.5% of adults 18 years and older
- Early 2017–18 flu season vaccination coverage was similar to coverage at the same time last flu season for children, adults, and all persons 6 months and older
- Among children, flu vaccination coverage was similar across all racial/ethnic groups with one exception—non-Hispanic children of other or multiple races had higher flu vaccination coverage than non-Hispanic black children.
- Among adults, flu vaccination coverage among adults 18-49 years decreased by 3.7 percentage points compared with the same time last season.
- Flu vaccination coverage among Hispanic adults decreased by 7.7 percentage points compared with the same time last season.
- Among adults, non-Hispanic persons of other or multiple races had higher flu vaccination coverage this early season than non-Hispanic whites, non-Hispanic blacks, and Hispanics.
- Among both adults and children, the most common places reported for receiving flu vaccination were medical locations (children: 86.5%, adults: 49.2%). Retail settings (28.2%) and workplaces (17.0%) were other important venues for adults.







\*Only medications active against circulating influenza viruses. Not effective against other viruses.



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#### Persons at High Risk for Influenza Complications

- Children <2 years</p>
- Adults <u>>65</u> years
- Pregnant and postpartum women
- Persons with immunosuppression



- Persons with underlying medical conditions: chronic pulmonary, cardiovascular, renal, hepatic, hematologic, and metabolic disorders (i.e., diabetes), or neurologic/neurodevelopment conditions, morbid obesity
  American Indians and Alaska Natives
- Persons <19 years who are receiving long-term aspirin therapy</p>

https://www.cdc.gov/flu/about/disease/high\_risk.htm





Failure to vaccinate Adverse events following vaccination Acellular vaccine performance Prevention of neonatal pertussis

### The problem with pertussis



### **Resurgence of Epidemic Pertussis**



- Pertussis outbreaks will continue to occur because neither infection nor immunization produce lifelong immunity
- Pertussis increases gradually began in 1982 and have continued since then
- Initially, increases were likely to increased physician awareness and diagnosis
- More recently, it is clear that DTaP vaccines are less potent that the DTP vaccines
- There is also evidence of waning vaccine-induced immunity



### Pertussis Background



- Pertussis is the most poorly controlled vaccine-preventable disease
  - Incidence increasing since the 1990s
  - Cyclical: peaks every 2-5 years as numbers of susceptible people increase enough to allow sustained transmission; last prior peak year 2005 with 25,616 U.S. cases, a 45 year high
- Adults are vulnerable to pertussis
  - 27% of reported cases in 2004 were among adults
  - Pertussis immunity is not lifelong and wanes 4-12 years after the DTaP series and 4-20 years after natural infection\*
  - ~20% of cough illness lasting >2 weeks is pertussis
- First pertussis vaccines (Tdap)<sup>+</sup> for adolescents and adults licensed in 2005, but uptake suboptimal – in 2008, ~40% of adolescents and ~6% of adults were estimated to have ever received Tdap

\*Wendleboe et al. Infect Dis J 2005;24 (Suppl 5):S58-61.





### Pertussis Background, continued



- Bordetella pertussis bacteria are inhaled and attach to cilia of respiratory epithelium where they attach to the cilia\*
- In a study of fatal cases, *B. pertussis* was frequently isolated from alveoli and less commonly from the trachea or bronchi\*
- Pertussis toxin exerts its biological effects on systemic sites via the bloodstream
- HIGHLY contagious: basic reproduction number (*Ro*) estimate is 12-17 (similar to measles and in contrast with influenza, which has an *Ro* of 1-2); approximately 90% of susceptible household contacts become infected
- MINIMUM PROPORTION of population that must be immune to eliminate transmission estimated to be 92-95%; achieving this level of population immunity will difficult without a vaccine that confers lifelong immunity

#### \* Weiss and Hewlett. Ann Rev Microbiol. 1986;40:661-86



### Reported Pertussis-related Deaths by Age Groups, US, 1980-2010\*



Age-Group	<b>1980-1989</b> <sup>1</sup>	1990-1999 <sup>1</sup>	2000-2010 <sup>2</sup>
0-1 month	38	68	170
2-3 month	11	16	28
4-5 month	5	5	2
6-11 month	7	4	1
1-4 years	13	2	3
5-10 years	1	6	3
11-18 years	0	0	3
>18 years	1	2	11
Total	77±	103	221

 $^{\pm}$  Includes one case with unknown age



th Lucile Packard Children's Hospital <sup>1</sup>Vitek CR, et al. *Pediatr Infect Dis J* 2003; 22(7):628-34. Children's Hospital <sup>2</sup>National Notifiable Diseases Surveillance System, CDC, \*Provisional 2010 data Stanford

# Source of Pertussis Transmission to Infants



- Household members responsible for 75%–83%
- Parents and siblings were common sources
  - Parents (55%)
  - Siblings (16%-20%)
  - Aunts/uncles (10%)
  - Friends/cousins/others (10%-24%)
  - Grandparents (6%)
  - Caretakers (2%)

Wendelboe AM., et al. Transmission of Bordetella pertussis to Young Infants. Pediatr Infect Dis J 2007;26: 293–299

Bisgard KM, Pascual FB, Ehresmann KR, Miller CA, Cianfrini C, Jennings CE et al. Infant pertussis: who was the source? *Pediatr Infect Dis J* 2004; 23(11):985-989.



### **CDC DTaP and Tdap Recommendations**



- DTaP for those younger than 7 years of age, and Tdap or Td for those 7 years or older across the lifespan
- Infants and children should receive 5 doses of DTaP, usually administered at 2, 4, and 6 months, 15 through 18 months, and 4 through 6 years of age. DT can be used for infants and children who should not receive acellular pertussiscontaining vaccines.
- Adolescents should receive a single dose of Tdap, preferably at 11 to 12 years of age.
- Pregnant women should receive a single dose of Tdap during every pregnancy, preferably at 27 through 36 weeks gestation. Tdap is recommended only in the immediate postpartum period before discharge from the hospital or birthing center for new mothers who have never received Tdap before or whose vaccination status is unknown.
- Adults should receive a single dose of Td every 10 years. For adults who did not receive Tdap as an adolescent, a dose of Tdap can replace one of the 10-year Td booster doses.



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### Tetanus, Diphtheria, and Pertussis (Tdap) Vaccines



- There are two Tdap vaccines used in the United States: Adacel<sup>®</sup> and Boostrix<sup>®</sup>.
- Each 0.5-mL dose of Adacel<sup>®</sup> (Sanofi Pasteur) contains 5 Lf tetanus toxoid, 2 Lf diphtheria toxoid, and acellular pertussis antigens (2.5 μg detoxified PT, 5 μg FHA, 3 μg pertactin, 5 μg FIM). Other ingredients per 0.5-mL dose include 1.5 mg aluminum phosphate (0.33 mg aluminum) as the adjuvant, ≤5 μg residual formaldehyde, <50 ng residual glutaraldehyde, and 3.3 mg (0.6% v/v) 2-phenoxyethanol (not as a preservative).</li>
- Each 0.5-mL dose of Boostrix<sup>®</sup> (GlaxoSmithKline) is formulated to contain 5 Lf of tetanus toxoid, 2.5 Lf of diphtheria toxoid, 8 μg of inactivated PT, 8 μg of FHA, and 2.5 μg of pertactin (69 kiloDalton outer membrane protein). Each 0.5-mL dose contains aluminum hydroxide as adjuvant (not more than 0.39 mg aluminum by assay), 4.5 mg of sodium chloride, ≤100 μg of residual formaldehyde, and ≤100 μg of polysorbate 80 (Tween 80).





- Pertussis is nationally-notifiable and clinicians should notify the appropriate health department of all patients with suspected pertussis.
- Diagnostic laboratories should notify health departments of all positive pertussis laboratory results and state health departments then report confirmed and probable pertussis cases to CDC through the National Notifiable Diseases Surveillance System (NNDSS).
- Although many pertussis cases are not diagnosed and therefore not reported, the surveillance system is useful for monitoring epidemiologic trends.



















#### Figure 2. Number and incidence of reported pertussis cases by year of onset --California, 1945-2016\*

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### Pertussis immunization landmarks



- 1948 DTP becomes commercially available
- 1980's DTP required for school entry
- 1993 DTP reformulated as DTaP (attenuated pertussis) to reduce adverse events
  - Reformulation is less immunogenic and immunity wanes more readily
- 2005 Tdap recommended for adolescents and adults
- 2015 Tdap recommended for pregnant women in third trimester to prevent deaths in infancy



### Whole-cell pertussis vaccine Adverse events



Reaction	DTP Group		DT Group		P Value
	No.	(%)	No.	%	
Local reactions					
Redness	5,891	37.4	60	7.6	<.0001
Swelling	6,411	40.7	60	7.6	<.0001
Pain	8,018	50.9	78	9.9	<.0001
Systemic reactions	2.5				
Fever (≥38 C)*	3,605	46.5	27	9.3	<.0001
Drowsiness	4,962	31.5	117	14.9	<.0001
Fretfulness	8,412	53.4	177	22.6	<.0001
Vomiting	977	6.2	20	2.6	<.0001
Anorexia	3,292	20.9	55	7.0	<.0001
Persistent crying	488	3.1	5	0.7	.0003
High-pitched, unusual cry	17	0.1	0	0.0	.3574

TABLE 1.	Less Serious Reactions	Following 15,752 DTP	and 784 DT Immunizations
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• Fever was evaluated following 7,753 DTP and 292 DT immunizations. Children whose temperature was recorded at three and six hours after immunization are reported.

Table 4 Stockholm study of whole-cell DTP and acellular DTaP vaccines

Type of vaccine	High fever per 1000 doses	HHE per 1000 doses	Seizures per 1000 doses	
Acellular DTaP vaccine	0.24	0.26	0.03	
Whole-cell DTP vaccine	0.61	0.56	0.21	
Relative risk following whole-cell DTP vaccine	2.5	2.2	7.0	
Per cent association with whole-cell DTP vaccine	71	69	88	
Statistical significance of the increase following whole-cell DTP vaccine	<i>p</i> < 0.01	<i>p</i> < 0.01	<i>p</i> < 0.01	

HHE, hypotonic, hyporepsonsive episodes

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Olin P, Rasmussen F, Gustasffson L, et al. Randomized controlled trial of two-component, three-component and five-component acellular pertussis vaccines compared to whole-cell pertussis vaccine. Lancet 1997; 350:1569-77.





# Annual rate of pertussis and pertussis vaccine type received during the first 2 years of life in the entire KPNC population from January 2010 to December 2011, by birth year



Klein NP, BartlettJ, Fireman B, Rowhani-Rahbar A, Baxter R. Comparative effectiveness of acellular versus whole-cell pertussis vaccines in teenagers. Pediatrics 2013; 131:e1716-22.

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#### What you can do to manage a suspected or confirmed Infectious Disease Outbreak

**Goals:** 

□ Identify and eliminate the source of infection

For example, separate waiting room area for coughing children

Prevent additional cases

- Screening questions regarding symptoms at the front desk
- Ongoing surveillance and communication essential to confirm cessation of outbreak
  - Track disease trends and advice through AAP, CDC, local county public health officials, local disease experts





#### Managing a suspected or confirmed Infectious Disease Outbreak

#### **General Principles:**

- Establish a plan for evaluating suspected or confirmed infectious disease outbreaks in your office setting
- Prompt and consistent ongoing evaluation so that transmission to healthcare workers, patients and visitors is prevented or minimized
- □ The source(s) and route(s) of exposure must be determined
  - To understand why an outbreak occurred
  - How to prevent similar outbreaks in the future
  - Treat exposed individuals
  - Prevent others from being exposed to the source(s) of infection.





#### What the Public Health System Will Do:

- 1) Establish case definition(s)
- 2) Confirm that cases represent true infections
- 3) Establish the background rate of disease
- 4) Find cases, decide if there is an outbreak, define scope of the outbreak
- 5) Examine the descriptive epidemiologic features of the cases
- 6) Generate and test hypotheses
- 7) Collect and test environmental samples if appropriate
- 8) <u>Assist providers and others in implementation of infection control</u> <u>measures in accordance with CDC, State or local public health</u> <u>recommendations</u>
- 9) Communicate with other organizations or individuals as necessary
- 10) Report when outbreak has been contained





#### What the Public Health System Will Do:

Determine whether the control measures are effective.

- 1. No new cases have occurred after the control measures were implemented.
  - The time period for new cases will vary depending on the nature of the infection but will likely be days to weeks
- 2. Continue to conduct ongoing prospective surveillance to ensure the outbreak has been terminated.
- 3. Notify providers and public health agencies at various levels that the outbreak has terminated



### **References/Resources**



- NNII (<u>www.immunizationinfo.org</u>)
- VEC (<u>www.vaccine.chop.edu</u>)
- IAC (<u>www.immunize.org</u>)
- CDC/NIP (<u>www.cdc.gov/nip</u>)
- AAP (<u>www.aap.org</u>)
- AAFP (<u>www.aafp.org/</u>)
- IVS (<u>www.vaccinesafety.edu</u>)
- Vaccine Page (<u>www.vaccines.org</u>)
- Every Child by Two (<u>www.ecbt.org</u>)
- PKIDS (<u>www.pkids.org/</u>)

#### http://www.cdc.gov/vaccines/acip/meetings/slides-2014-06.html http://www.cdc.gov/measles/travelers.html



# Thank you

# Questions?



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### WE DID IT! SB277 is law.

#sb277 #vaccineswork

vaccinatecalifornia.org