

# Pertussis and Pertussis Vaccines Updates

Karen Lewis, M.D.  
Medical Director

Arizona Immunization Program Office  
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*Health and Wellness for all Arizonans*

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# Lecture Objectives

- Review the transition from whole cell to acellular pertussis vaccines.
- Describe the changes in pertussis epidemiology over the last seventy years.
- Explain immunologic responses to acellular vaccines that may be contributing to increases in pertussis

# Impact of Vaccines in the 20<sup>th</sup> & 21<sup>st</sup> Centuries

## Comparison of 20<sup>th</sup> Century Annual Morbidity & Current Morbidity

Disease	20 <sup>th</sup> Century Annual Morbidity*	2010 Reported Cases <sup>†</sup>	% Decrease
Smallpox	29,005	0	100%
Diphtheria	21,053	0	100%
Pertussis	200,752	21,291	89%
Tetanus	580	8	99%
Polio (paralytic)	16,316	0	100%
Measles	530,217	61	>99%
Mumps	162,344	2,528	98%
Rubella	47,745	6	>99%
CRS	152	0	100%
<i>Haemophilus influenzae</i> (<5 years of age)	20,000 (est.)	270 (16 serotype b and 254 unknown serotype)	99%

### Sources:

\* JAMA. 2007;298(18):2155-2163

† CDC. MMWR January 7, 2011;59(52);1704-1716. (Provisional MMWR week 52 data)

# Whole Cell Pertussis Vaccines

- *Bordetella pertussis* first isolated in 1906
- Formalin inactivated *B. pertussis* vaccines
  - Developed 1930's
  - Clinical use 1940's
- 70-90% effective
- Duration: 5-10 years
- Local reactions



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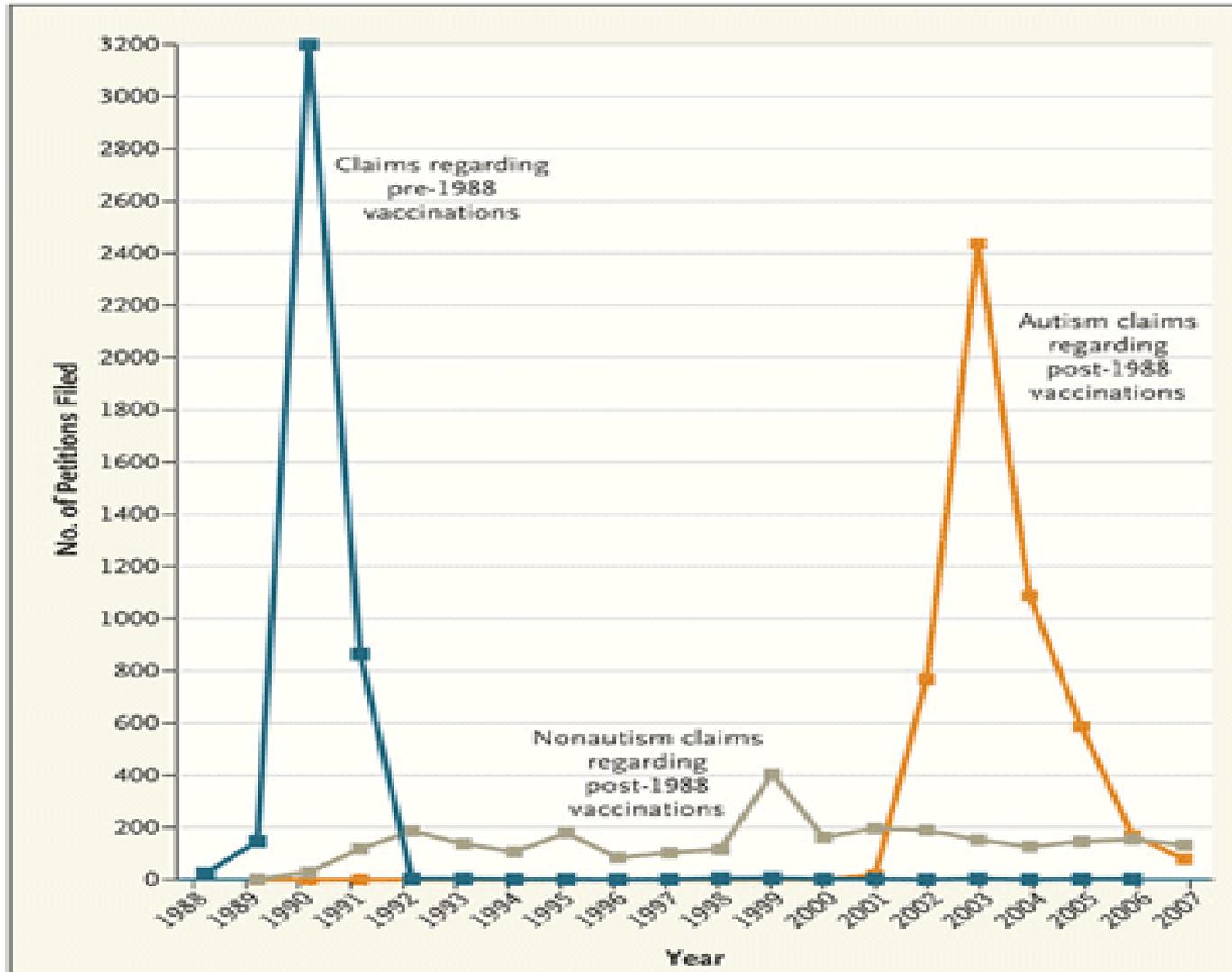
# WHOLE CELL PERTUSSIS VACCINE WEARS OFF WITH TIME

Years since vaccine	Total # Exposed	Attacks	
		# infected	Percent
0-3 years	85	18	21%
4-7 years	61	29	47%
8-11 years	43	28	65%
<b>≥ 12 years</b>	21	20	<b>95%</b>
Total	210	95	45%

# UCLA Study of Side Effects Following 15,752 DTwP

- Fever  $\geq 38^{\circ}\text{C}$ . (37.4%)
- Persistent crying (3.1%)
- Febrile seizures (9)
- Hypotonic hyporesponsive episodes (9)
  
- Reports of development delay and chronic seizures after DTwP

# Claims Filed VICP 1989-2007



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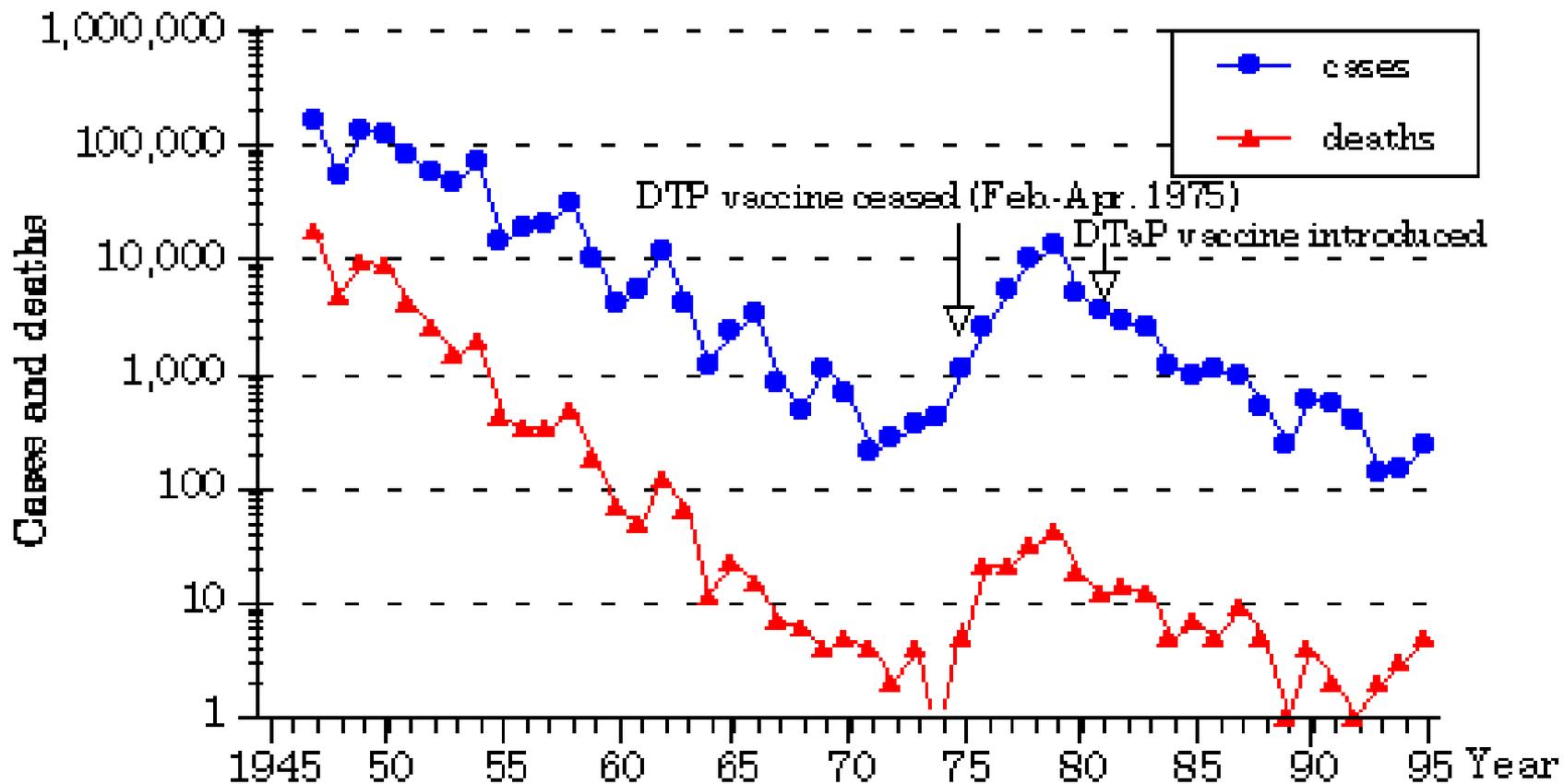


# Dravet Syndrome

- Severe myoclonic epilepsy and developmental delay appearing in infancy
- 1:20,000
- Genetic mutations in *SCN1A* (neuronal sodium channel  $\alpha$ 1 subunit)
  
- *Pediatrics*, Sept 2011
  - 5/5 “pertussis vaccine encephalopathy” → Dravet

# Pertussis in Japan, 1945-1995

Figure 1. Reported cases of and deaths from pertussis in Japan, 1947-1995



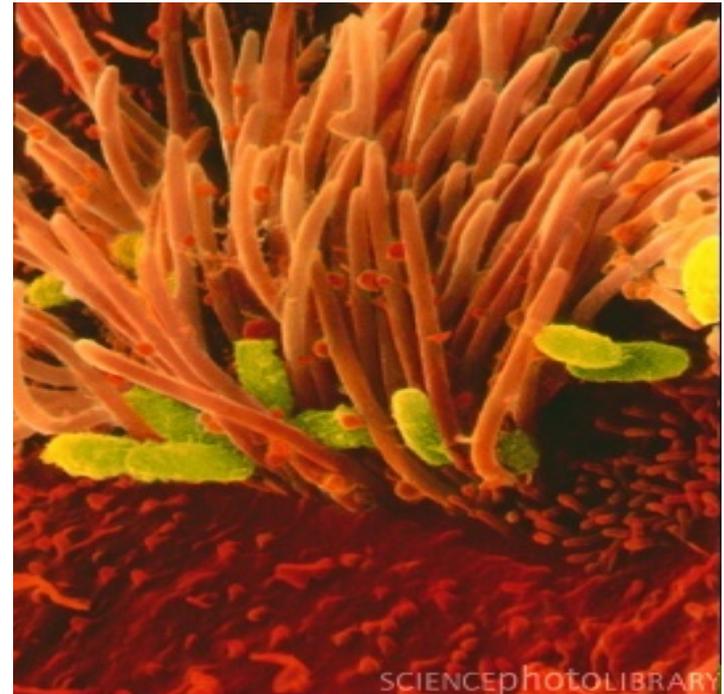
Cases : Statistics on Communicable Diseases in Japan

Deaths: Vital Statistics of Japan

( Ministry of Health and Welfare )

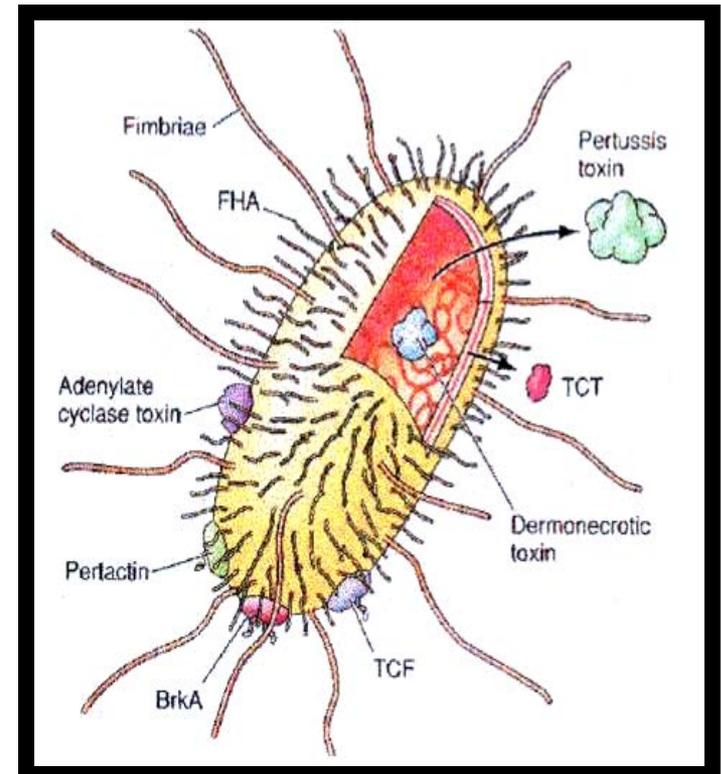
# Whooping Cough or Pertussis (*Bordetella pertussis*)

- Spread by respiratory droplets
- Incubation period of 5-21 days
- Immunity not life-long



# Antigenic and Biologically Active Components of *B. pertussis*

- ❑ pertussis toxin (PT)
- ❑ filamentous hemagglutinin (FHA)
- ❑ pertactin
- ❑ fimbriae
- ❑ agglutinogens
- ❑ adenylate cyclase
- ❑ tracheal cytotoxin
- ❑ dermonecrotic toxin



# PERTUSSIS VACCINE ANTIGENS

Pertussis toxin (PT)

“Lymphocytosis promoting factor”

Filamentous Hemagglutinin (FHA)

Mediates adherence

Pertactin (PRN)

Promotes cell binding

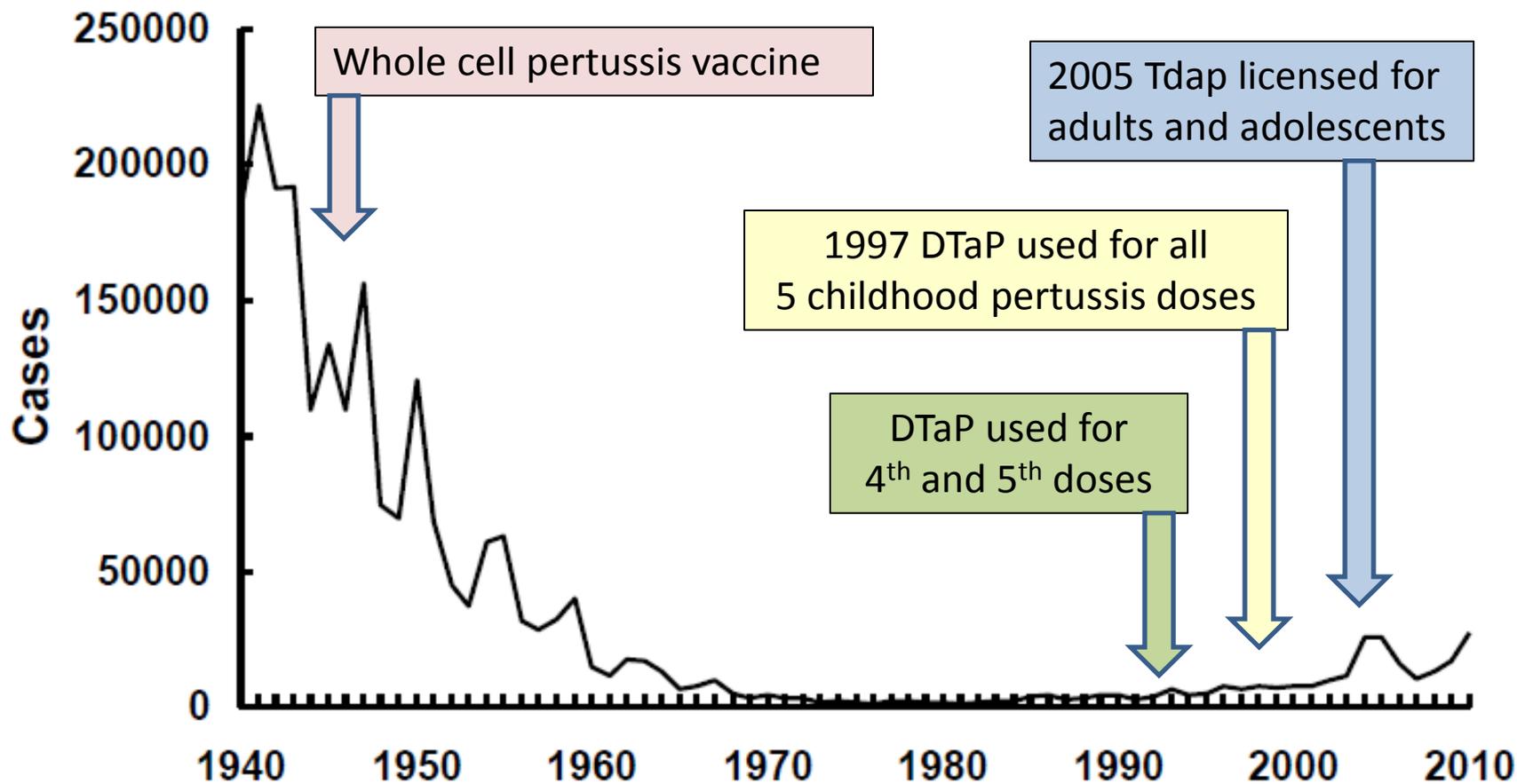
Fimbriae (FIM)

Attachment

# Components of Acellular Pertussis Vaccines

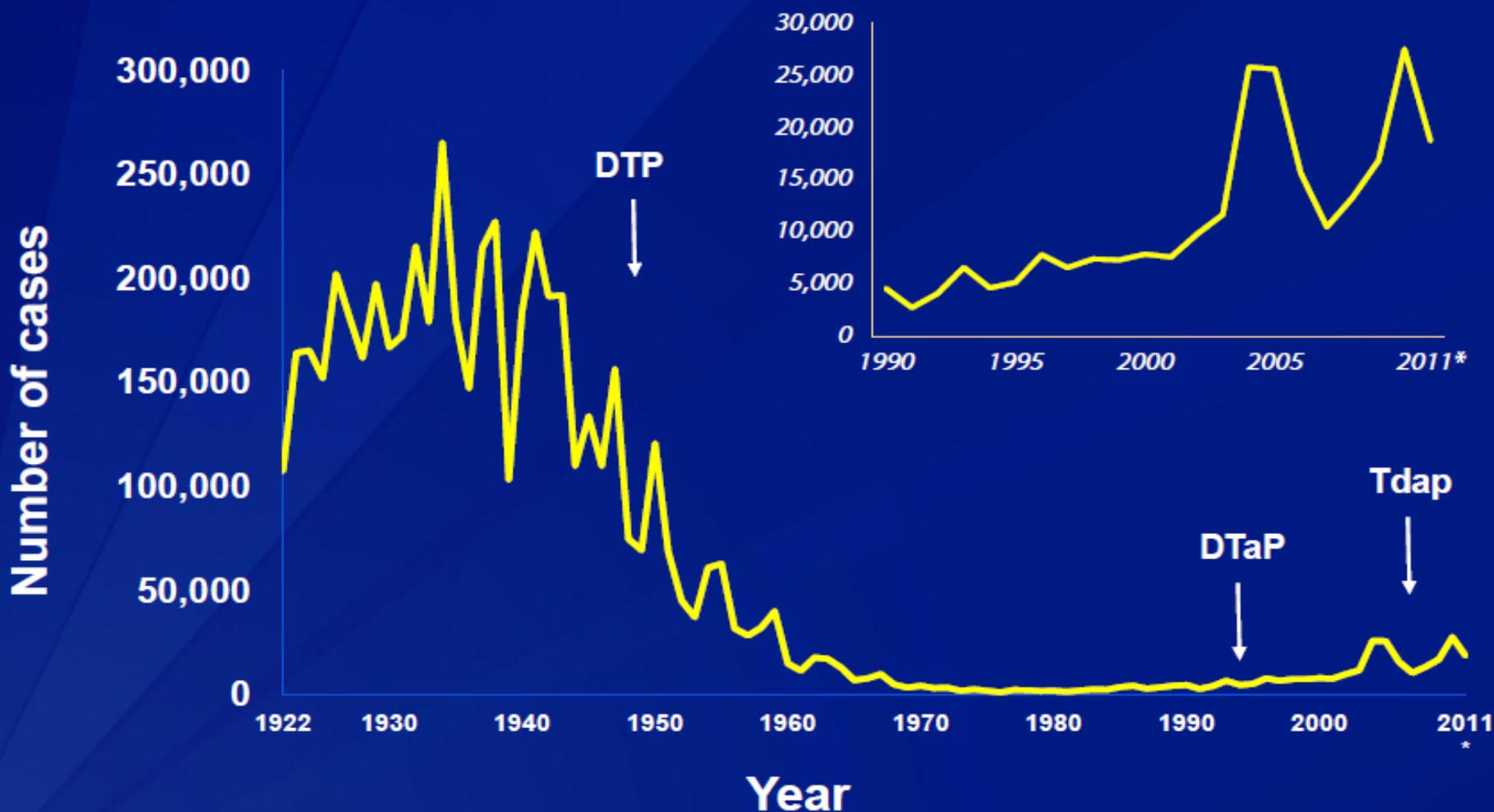
Product	Type	PT μg	FHA μg	PERT μg	FIM μg	DIPH Lf	TET Lf
Daptacel	DTaP	10	5	3	5	15	5
Tripedia	DTaP	23	23	--	--	6.7	5
Infanrix	DTaP	25	25	8	--	25	10
Pediarix	DTaP+	25	25	8	--	25	10
Pentacel	DTaP+	20	20	3	5	15	5
Adacel	Tdap	2.5	5	3	5	2	5
Boostrix	Tdap	8	8	2.5	--	2.5	5

# Pertussis—United States, 1940-2010



Graph from CDC Pink Book, 12<sup>th</sup> edition

# Reported NNDSS pertussis cases: 1922-2011\*



\*2011 data have not been finalized and are subject to change. 2011 data were accessed on July 5, 2012.

# Pertussis-Related Deaths, U.S. 1980-2009

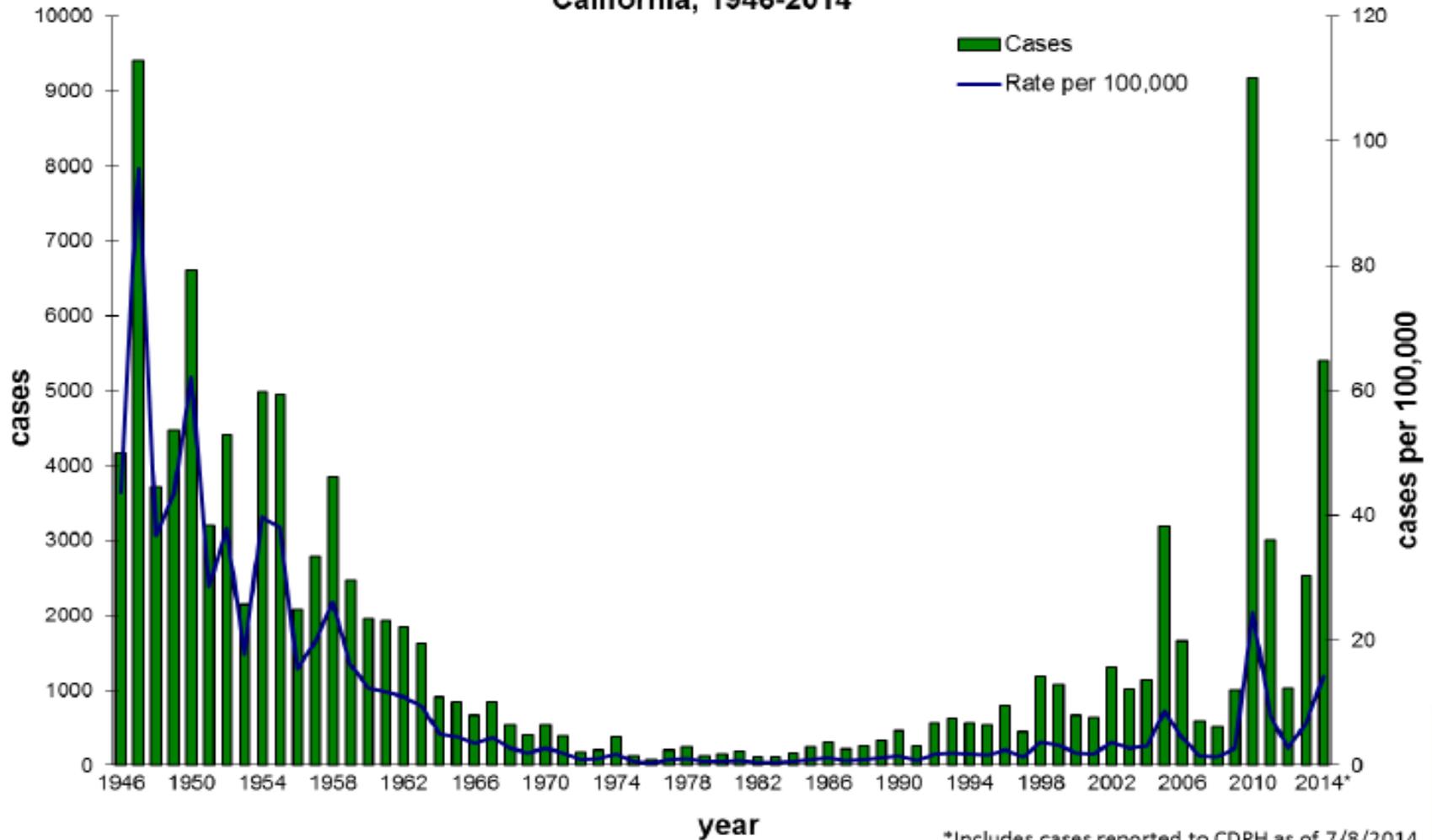
Age Group	1980-1989	1990-1999	2000-2009
0-1 month	38	68	152
2-3 months	11	16	24
4-5 months	5	5	2
6-11 months	7	4	1
1-4 years	13	2	2
5-10 years	1	6	3
11-18 years	0	0	3
> 18 years	1	2	8
Total	77*	103	194

\*One with age unknown

# Pertussis in California

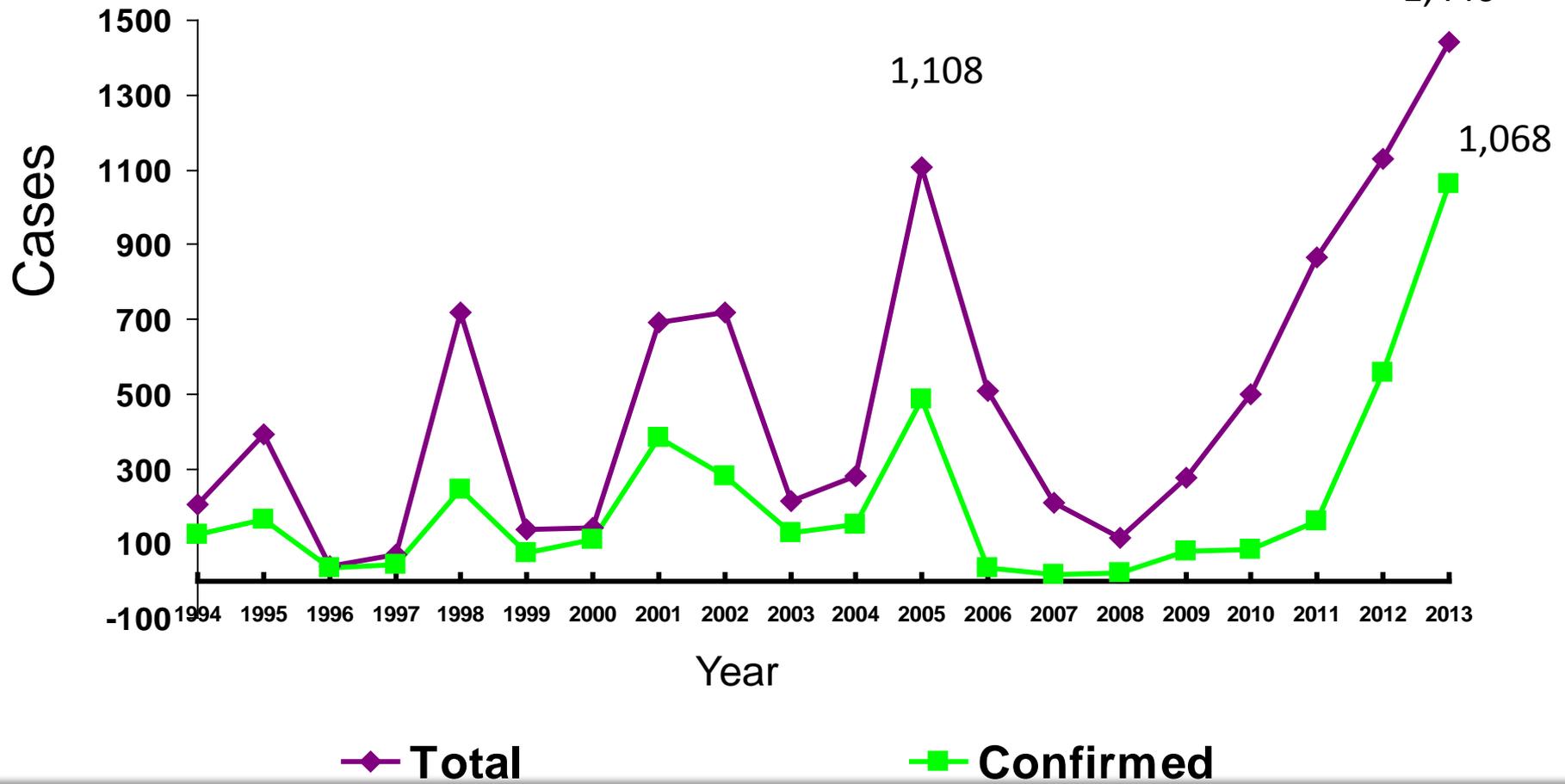
## as of 7/8/2014

Figure 2. Number and incidence of reported pertussis cases by year of onset -- California, 1946-2014\*

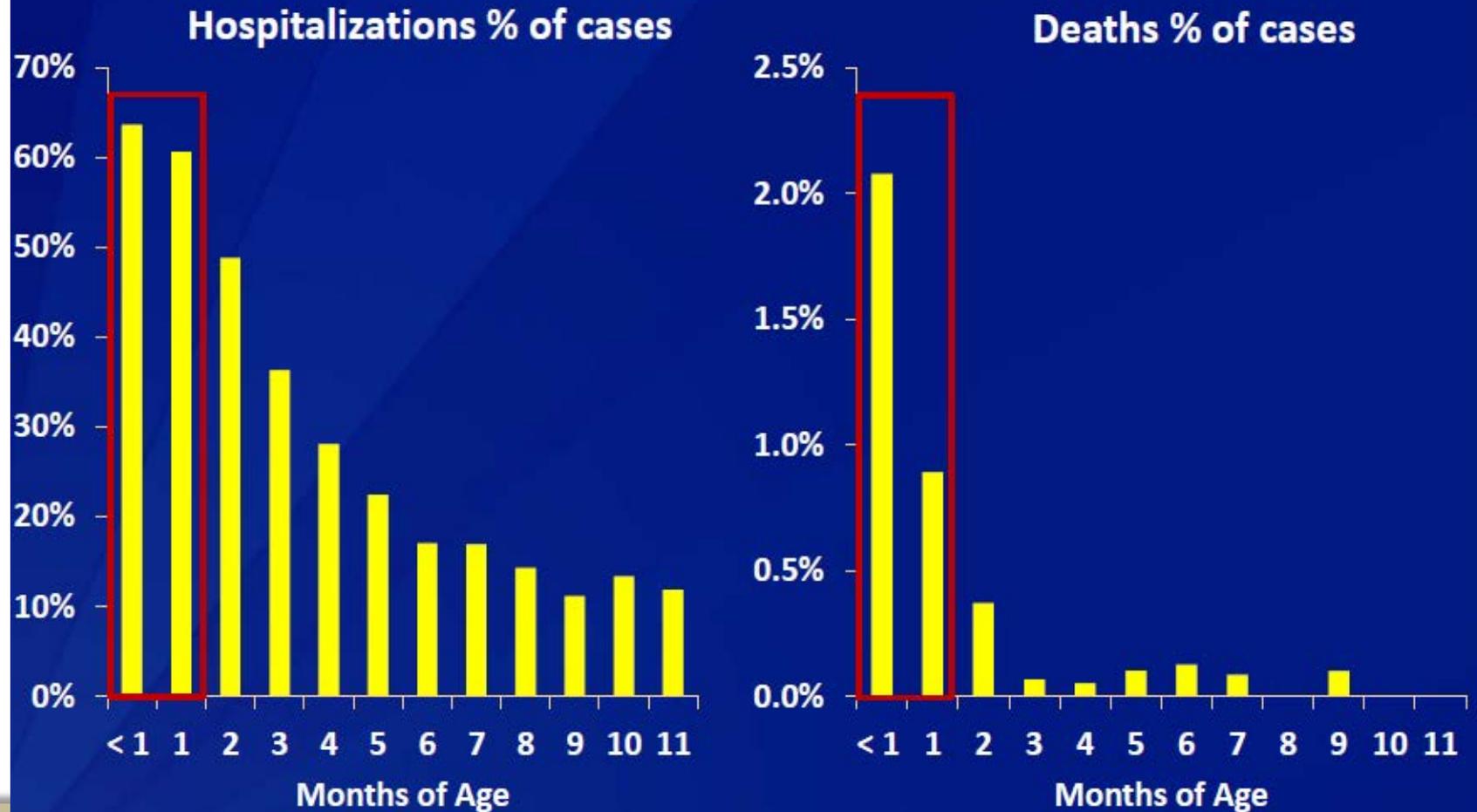


\*Includes cases reported to CDPH as of 7/8/2014

# Pertussis Cases, Arizona, 1994–2013

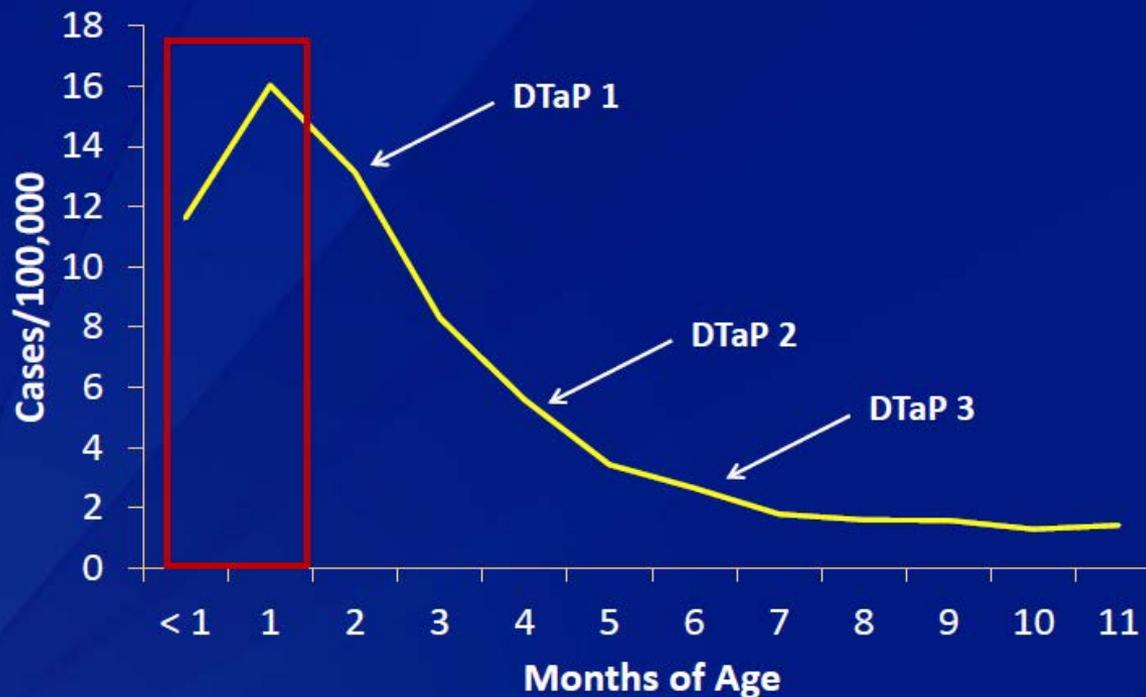


# Hospitalizations and Deaths % Total Infant Cases, 2001-2011

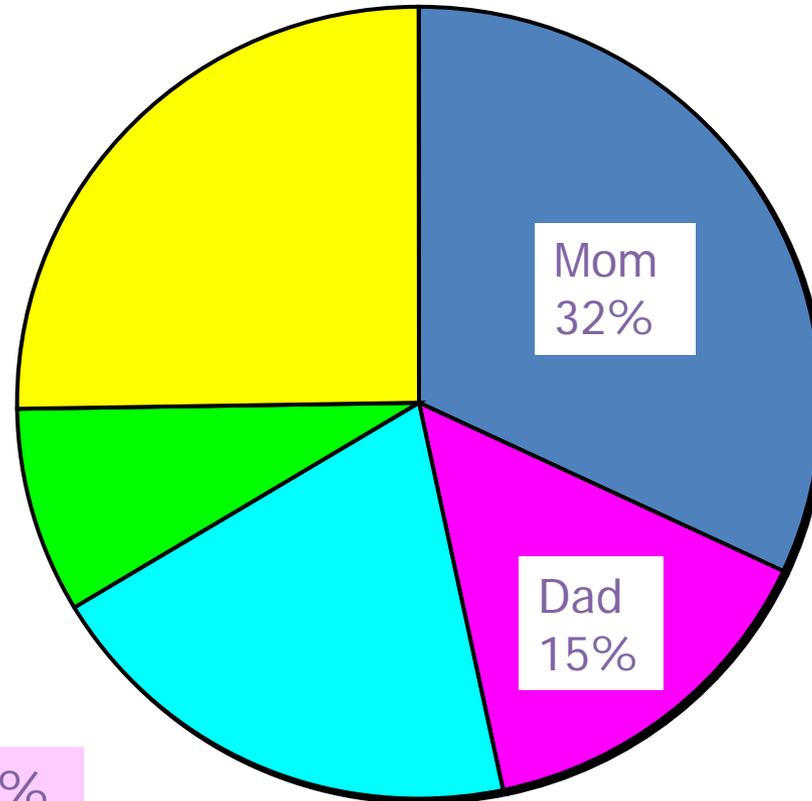


# Acellular Pertussis Vaccines Protects Infants

## Pertussis incidence among infants, 2001-2011



# 75% of suspected sources for infant pertussis cases were family members



Other 25%

Grandparent 8%

Sibling 20%

Mom  
32%

Dad  
15%

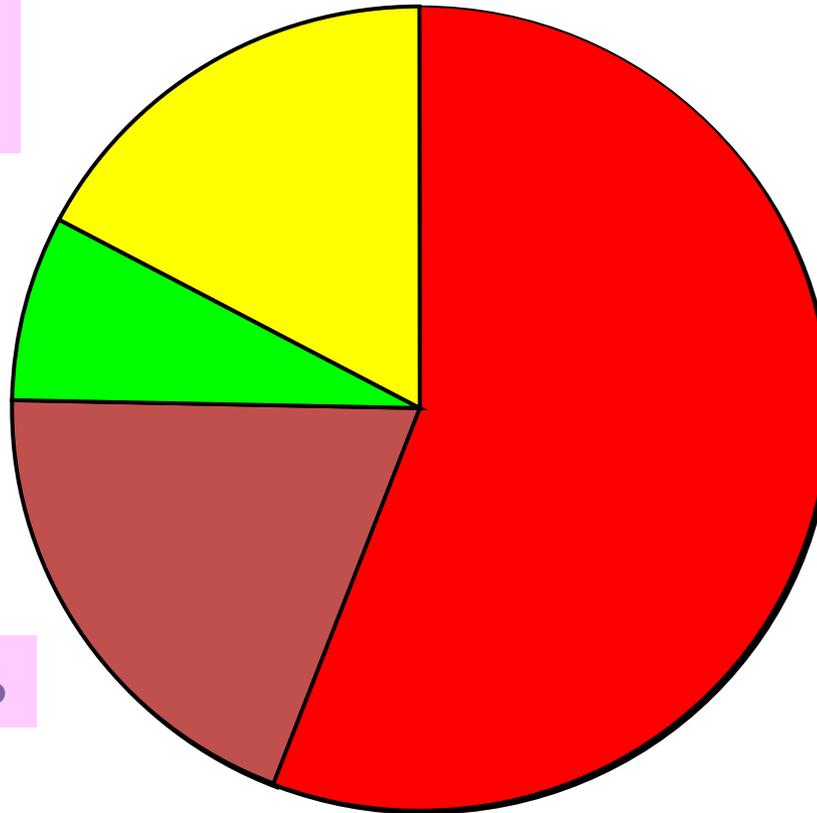
Mom or Dad  
47%

# 76% of suspected sources\* for infant pertussis cases were adolescents or adults

Young Children  
0-4 years 17%

Children  
5-9 years 7%

Adolescents 20%



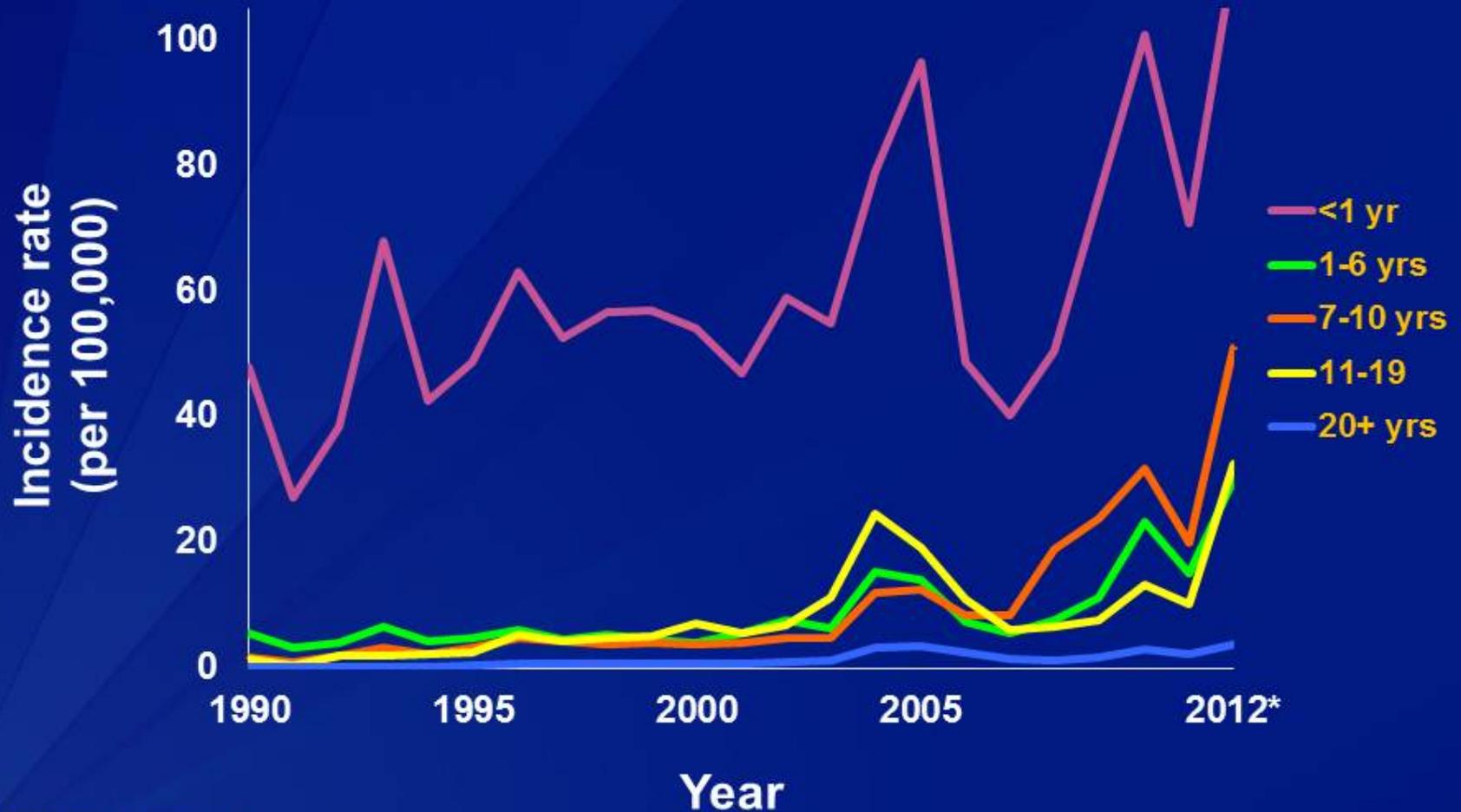
Adults  
56%

# CDC Emphasis on Tdap to All Contacts of Infants

- Family members are source in most of newborn cases
- **Cocooning**
- Everyone around infant needs Tdap
- 2012: Give Tdap to pregnant women if not already received



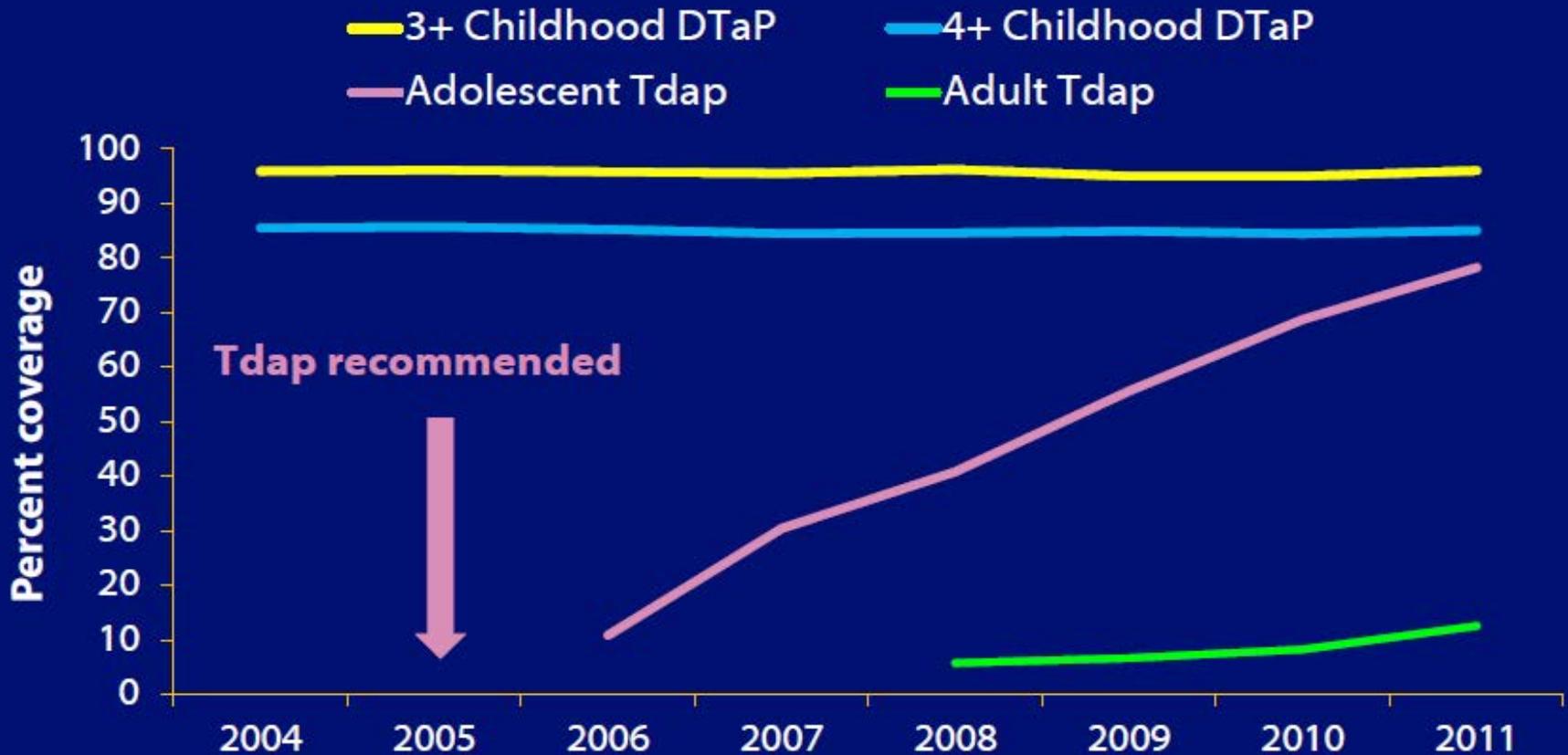
# Reported pertussis incidence by age group: 1990-2012\*



\*2012 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System

# Pertussis Vaccination Coverage\*† Among the US Population, 2004-2011

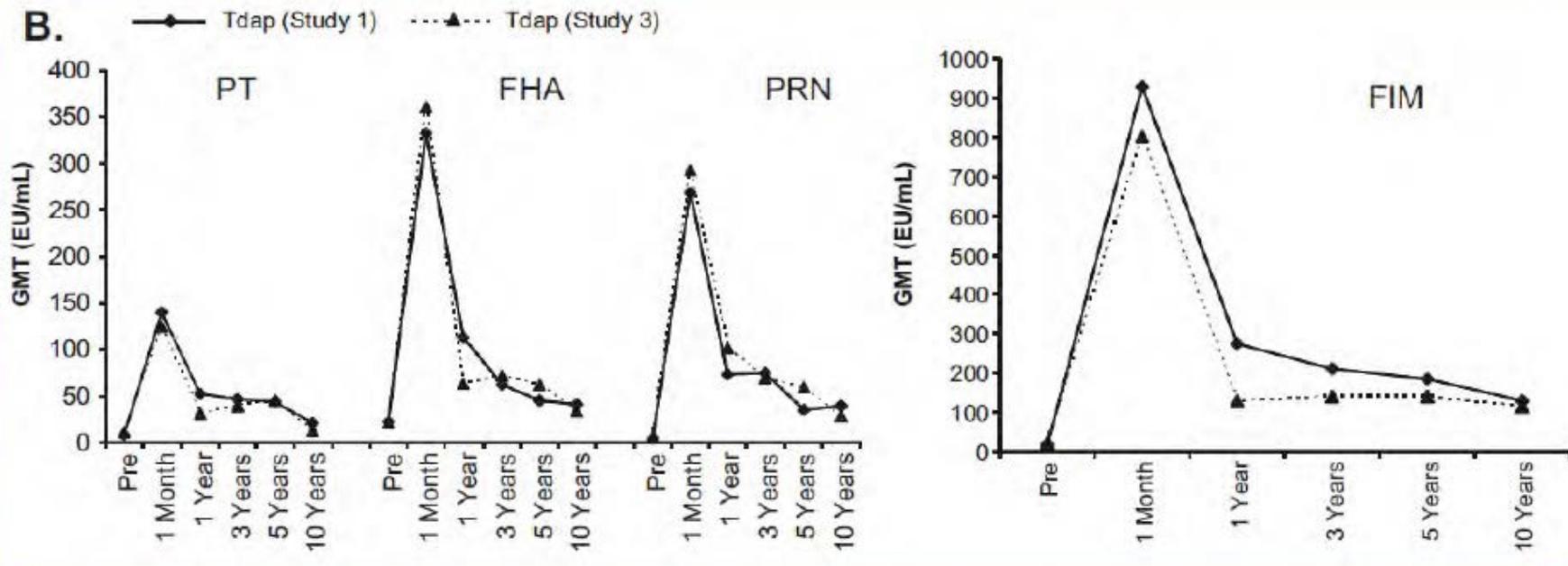


# Possible Reasons for More Pertussis

1. Waning immunity after acellular vaccines
2. Whole cell vaccines gave better immunity than acellular
3. *Bordetella pertussis* strain change
4. Local collections of unvaccinated and susceptible children and adults

# Pertussis Antigens GMC up to 10 Years After Tdap (Adacel)

Adults (n=644)



PT: pertussis toxin; FHA: filamentous hemagglutinin; PRN: pertactin; FIM: fimbriae types 2&3

Tomovici A, et al. Humoral immunity 10 years after booster immunization with an adolescent and adult formulation combined tetanus, diphtheria, and 5-component acellular pertussis vaccine. *Vaccine*. 2012 Mar 30;30(16):2647-53.

# CDC: Tdap for Every Pregnancy

- Waning pertussis antibodies after Tdap
  - Rapid decrease over 1 year
  - Cord blood antibodies within 2 year Tdap not high
- Average 2 children per woman in US
  - Only 5% have  $\geq 4$  children
  - Only 2.5% have intervals between babies of  $\leq 12$  months
- Active transport of IgG starts about 30 weeks
- Safe

# Pertactin Negative *Bordetella pertussis* in the U.S.

	Total isolates	Pertactin negative	%
Historical isolates, 1935-2009	666	1	0.0015%
2010 CA outbreak	33	4	12%
US 2010-2012	385	144	37%
2012 Washington state outbreak	216	157	73%

# Pertactin Negative *B. pertussis* (BP) Does Not Change Disease Severity

- No difference in severity of illness between pertactin positive and negative infants
- Pertactin NEG infants more likely to be diagnosed later ( $p=0.04$ )
  - Pertactin POS: 9.9 days
  - Pertactin NEG: 14.6 days
- Infants who had one or two DTaP vaccines had less severe illness and fewer complications

## BP Nasal Challenge at 7 Months

Baboons		Results
Uninfected		Sick and shed BP for 30 days
Previous BP infection		Not ill, did not shed BP
DTwP at 2, 4, 6 months		Not ill, shed BP for 18 days
DTaP at 2, 4, 6 months		Not ill, lower # of BP but shed BP for 35 days & easily spread BP to unvaccinated baboons

# Current Efforts to Control Pertussis

- Surveillance
- Diagnosis BP early, treat, prophylaxis
- Vaccinate
  - One Tdap for every teenager and adult.
  - Tdap for pregnant women in every pregnancy
  - Cocooning
  - **Develop better pertussis vaccine.**