VACCINE PREVENTABLE DISEASE UPDATE-PERTUSSIS

Zack Moore, MD, MPH
Kristin M. Sullivan, MPH
Susan M. Sullivan, MS, RN-BC

Communicable Disease Branch
North Carolina Division of Public Health

April 30, 2015

Vaccine Preventable Disease Update- PERTUSSIS

Zack Moore
Kristin Sullivan
Susan Sullivan

- Wake AHEC requires all speakers to disclose any relevant financial conflicts of interest.

- Zack Moore, Kristin Sullivan and Susan Sullivan have no relevant financial conflicts of interest to disclose.

Objectives

- Describe the clinical features of pertussis
- Describe the current epidemiology of pertussis
- Identify primary goal in pertussis outbreak control
- List 5 strategies used in all VPD investigations

Case Vignette

Case Vignette

- 3 week-old infant
- Born 8 weeks early, home from NICU for 1 week
- c/o sneezing, coughing, congestion for two days
- Grandmother has cold symptoms
- Mom received routine prenatal care, but was never offered Tdap

At the Pediatrician's Office

- Temp 97.7, O_2 sat 99% on room air
- Clear nasal discharge, lungs CTA
- CBC and CRP ordered
- Discharged with presumed viral infection

In the Emergency Department

- Taken to ED two days later
  - Worsening cough, choking episodes
  - Purple-red color around mouth
- Hypoxic during episode in ED
- Labs from office visit:
  - WBC 12.8 (56% lymphs)
  - CRP <5 mg/L
- CXR → no focal infiltrate

In the Hospital

- Apnea, increasing oxygen requirement
- Intubated, conventional → oscillator
- WBC from 8.7 to >37,000 in one day
- Echocardiogram: Severe pulm HTN

Image: www.shotbyshot.com

Outcome

- Attempted transfer for ECMO
- Unable to arrange air transport due to weather
- Coded 15 minutes into ground transport
- Returned to hospital; died 72 hours after initial admission

Clinical Features

Pertussis Transmission

- Highly contagious respiratory infection
- Droplet and airborne transmission
- >80% household contacts infected*

*Mertsola et al, J Pediatr. 1983 Sep;103(3):359-63

Pertussis Pathogenesis

- Attach to the cilia in upper respiratory tract and nasopharynx
- Release toxins
  - Damage to cilia
  - Inflammation
  - Leukocytosis

Stages of Pertussis

Stage	Length	Clinical Features
Catarrhal	1 – 2 weeks	Runny nose, mild cough
Paroxysmal	1–6 weeks; up to 10	Paroxysmal cough
Convalescent	2 – 3 weeks; may be months	Less persistent cough; secondary infxn

Clinical Case Definition

- Cough illness lasting at least 2 weeks with one of the following:
  - Paroxysms of coughing
  - Inspiratory “whoop”
  - Post-tussive vomiting

Clinical Case Definition: Infants*

- Acute cough illness of any duration
- At least one of the following signs or symptoms:
  - Paroxysms of coughing; or
  - Inspiratory "whoop"; or
  - Post-tussive vomiting; or
  - Apnea (with or without cyanosis)

*effective January 1, 2014

http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/PS/13-ID-15.pdf

Pertussis in Adults

- Prolonged cough illness
- Wide spectrum of presentation
- Often undiagnosed
- Most common source of infant infections

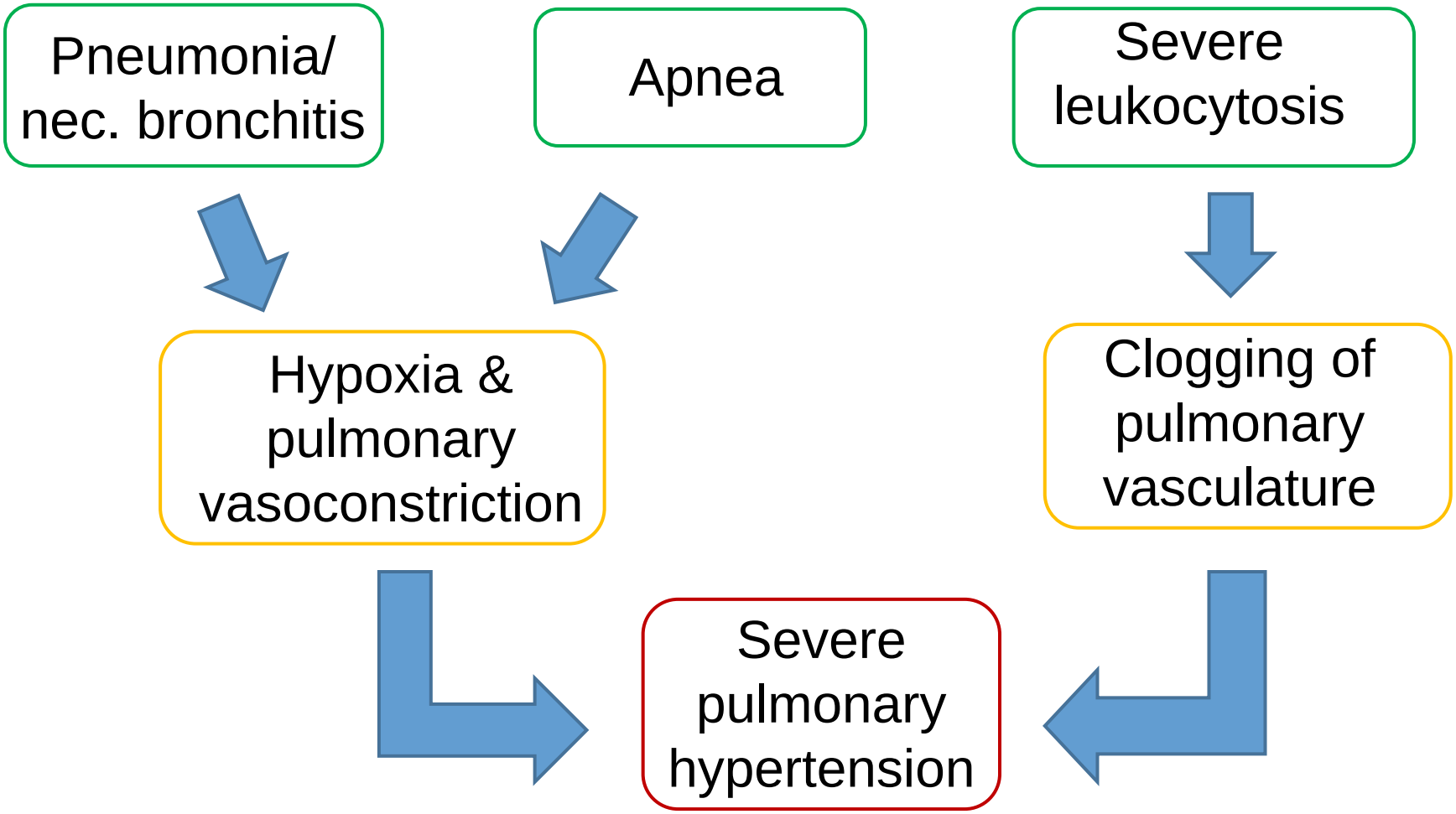
Infant Pertussis

- Highest risk for complications
- Atypical symptoms
  - Catarrhal stage and cough minimal or absent
  - Whoop infrequent
  - Apnea (sometimes with seizures)
  - Sneezing
  - Gagging, choking, vomiting
- >50% require hospitalization
- 1% of hospitalized infants die

Source: ShotofPrevention.com. Brady passed away at 2 months from pertussis.

Adapted from http://www.cdc.gov/vaccines/ed/ciinc/Pertussis.htm

Infant Deaths: Pathogenesis



Adapted from Paddock et al, Clin Infect Dis 2008; 47:328–38

Diagnosis and Treatment

When to Suspect Pertussis

- Duration of cough ≥ 2 weeks
- Paroxysmal cough
- Afebrile, with increasing cough duration and severity

Cherry et al. Clin Infect Dis 2012;54:1756-64

Other Clues

- Paroxysms more disturbing to the patient at night
- Cough not truly productive
- Coryza does not become purulent
- Sweating episodes between paroxysms

Cherry et al. Clin Infect Dis 2012;54:1756-64

When to Suspect Pertussis – Infants

- May present with choking, gagging, or apnea with or without cyanosis
  - Cough may be subtle or absent
  - Fever minimal or absent
- Other clues:
  - Severe or prolonged cough in contacts
  - WBC ≥ 20,000 with >50% lymphocytes

http://www.cdph.ca.gov/HealthInfo/discond/Documents/Cherry_Pertussis%20in%20Young%20Infants2_June%202011.pdf

Pertussis Tests

TEST	**PROS**	**CONS**
PCR	•Sensitive •Fast	•False positives
Culture	•Specific •Gold standard	•Slow •Low sensitivity
Serology	•Detect late after onset	•Not standardized
DFA	•None (in 2012)	•Low sensitivity

Pertussis PCR Pitfalls

- False positives
  - Contamination
  - Laboratory error
  - Cross-reactivity
- False negatives
  - Testing too late in illness
  - Improper specimen collection

Proper Technique for NP Swab

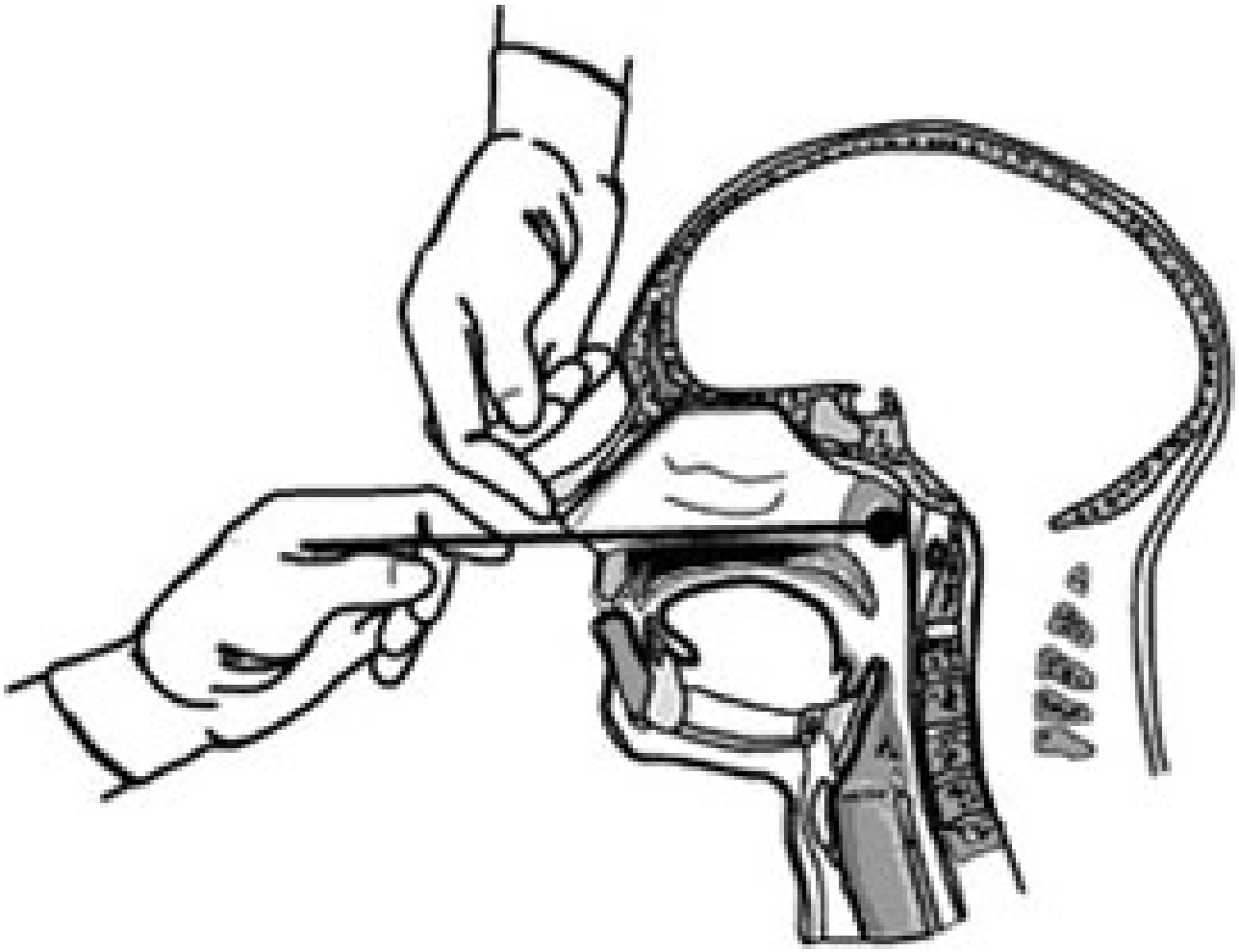
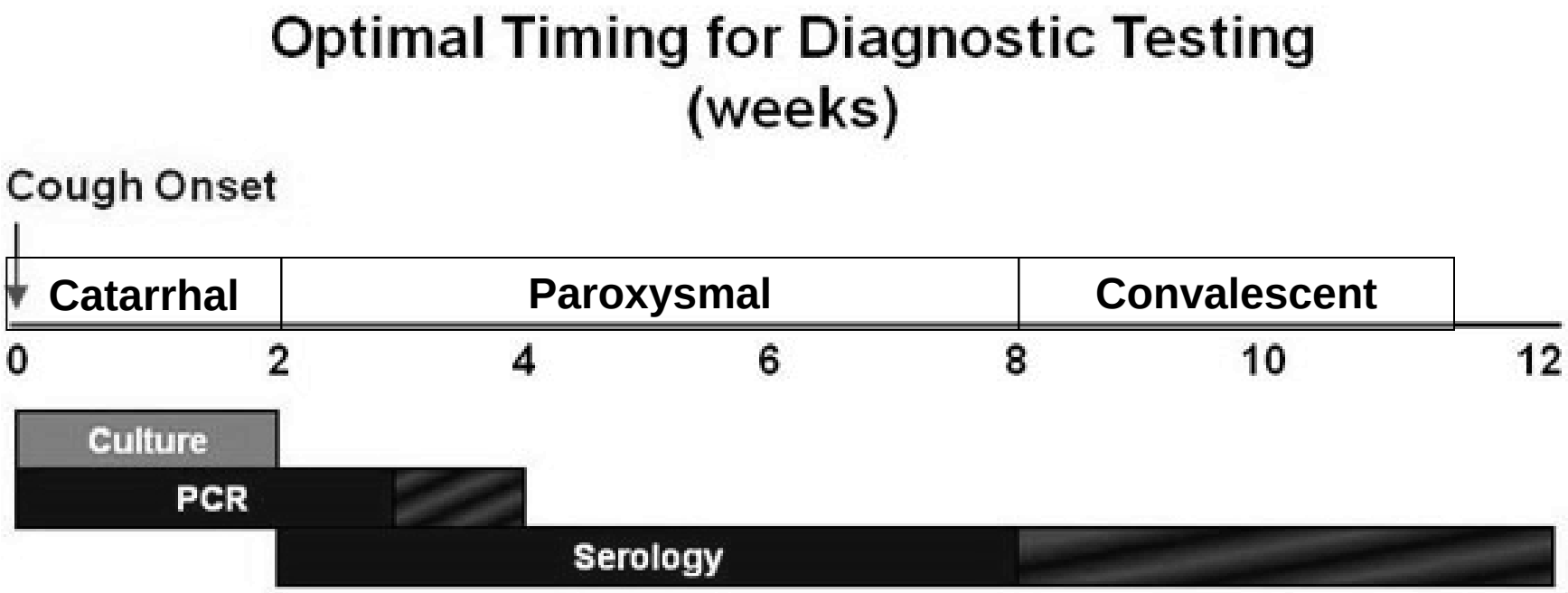


Image: Manual for the Surveillance of Vaccine-Preventable Diseases, 4th ed, 2008

Pertussis Culture

- 100% specificity
- Low sensitivity after first two weeks of cough
- Long time to results
- Important for
  - Avoiding pseudo-outbreaks (false-positive PCRs)
  - Antimicrobial resistance testing



http://www.cdc.gov/pertussis/clinical/diagnostic-testing/diagnosis-confirmation.html

Pertussis Serologies

- Not standardized
- Not recommended for routine clinical diagnosis
- Validated ELISA for anti-PT IgG available through state public health lab with approval

Menzies et al. Clin and Vaccine Immunol 2009; 16(12):1781–1788

Management of Suspected Cases

- Physicians often underestimate impending severity in infants
  - Illness onset not alarming
  - Cough unrecognized
  - Lungs clear to auscultation
- No clinical findings predict severe illness
  - Degree of lymphocytosis correlates with poor outcome

http://www.cdph.ca.gov/HealthInfo/discond/Documents/Cherry_Pertussis%20in%20Young%20Infants2_June%202011.pdf

Management of Suspected Cases

- All infants ≤ 3 months old with possible pertussis should be hospitalized
  - Severity unpredictable
  - Clinical decline often rapid
- Monitor WBC count closely
  - Consider exchange transfusion for infants with WBC >30,000 plus pneumonia and/or tachycardia

http://www.cdph.ca.gov/HealthInfo/discond/Documents/Cherry_Pertussis%20in%20Young%20Infants2_June%202011.pdf

Antibiotic Treatment

- Goals:
  - Decrease contagion
  - May shorten duration and severity of cough if started during catarrhal phase
- When to treat:
  - Within 3 weeks of cough onset
  - Within 6 weeks of cough onset for infants, pregnant women, HCW, contacts of infants

Tiwari et al, CDC. *MMWR* 2005;54:1-16
Bettiol et al. *Cochrane Database Syst Rev* 2010; 20;(1):CD003257

Antibiotic Treatment

- **Treatment should be initiated at the time of testing: Do NOT wait for lab results**

Some Perspective

"More than 50 years ago when I was a pediatric intern…we had an entire ward devoted to babies with pertussis…The little ones would cough repetitively, whoop… and then stop breathing. We had to race around, intubate them and get them going again- rather hair-raising…"

-Dr. Ron Levine
Personal communication 8/28/2013

Epidemiology

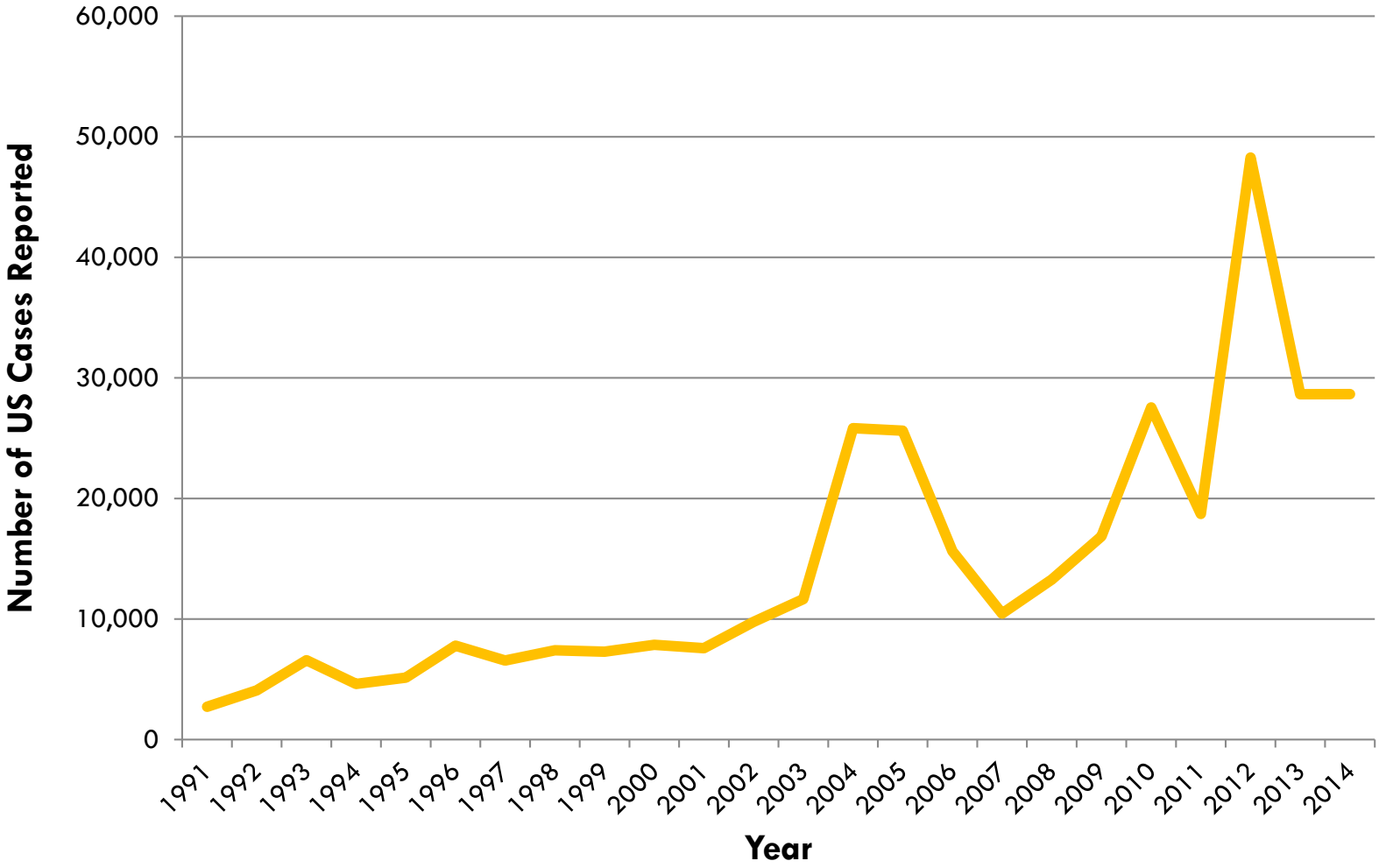
- **All 2014 data are provisional*

Reported NNDSS pertussis cases: 1922-2014*

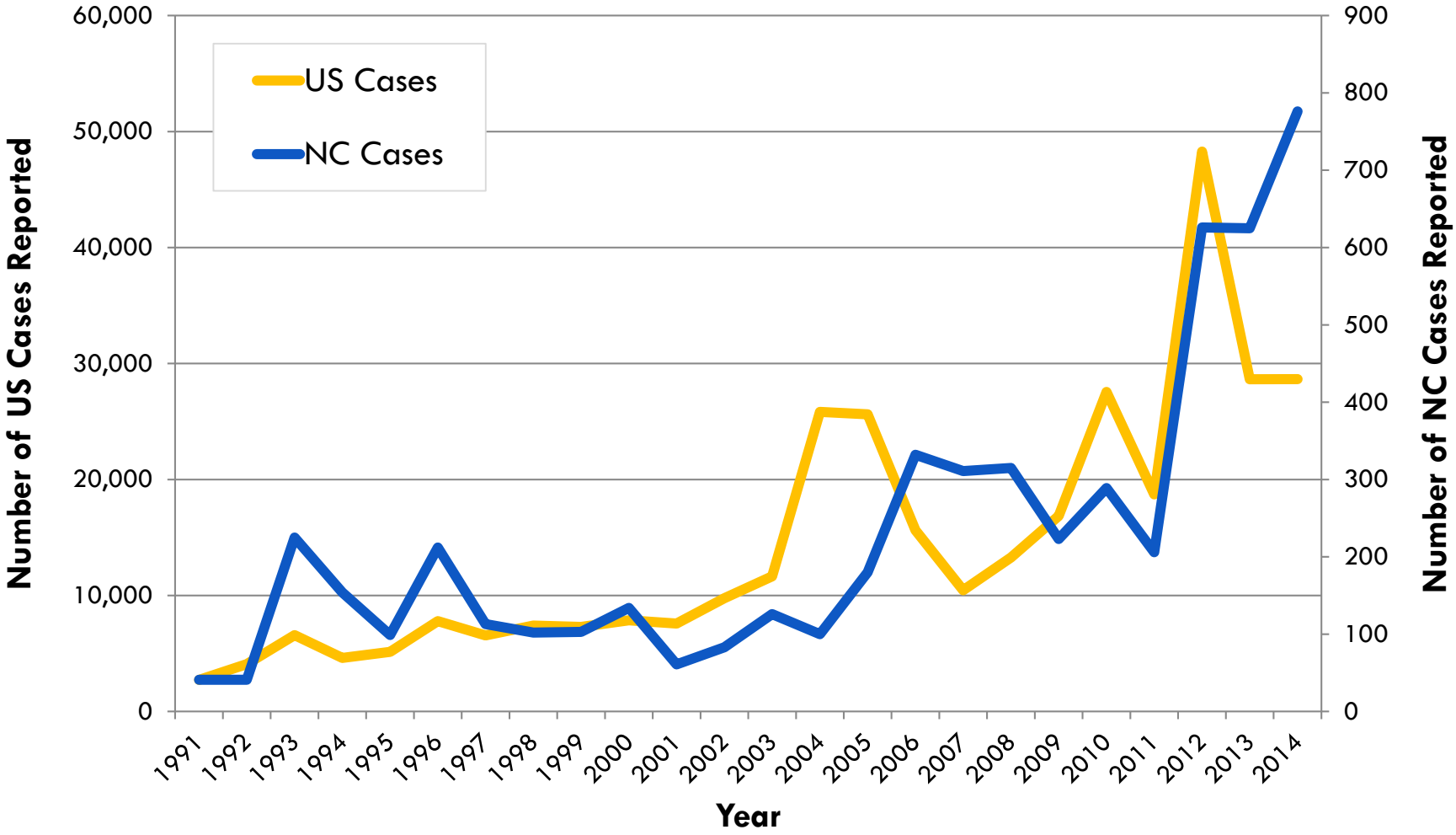
*2014 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service

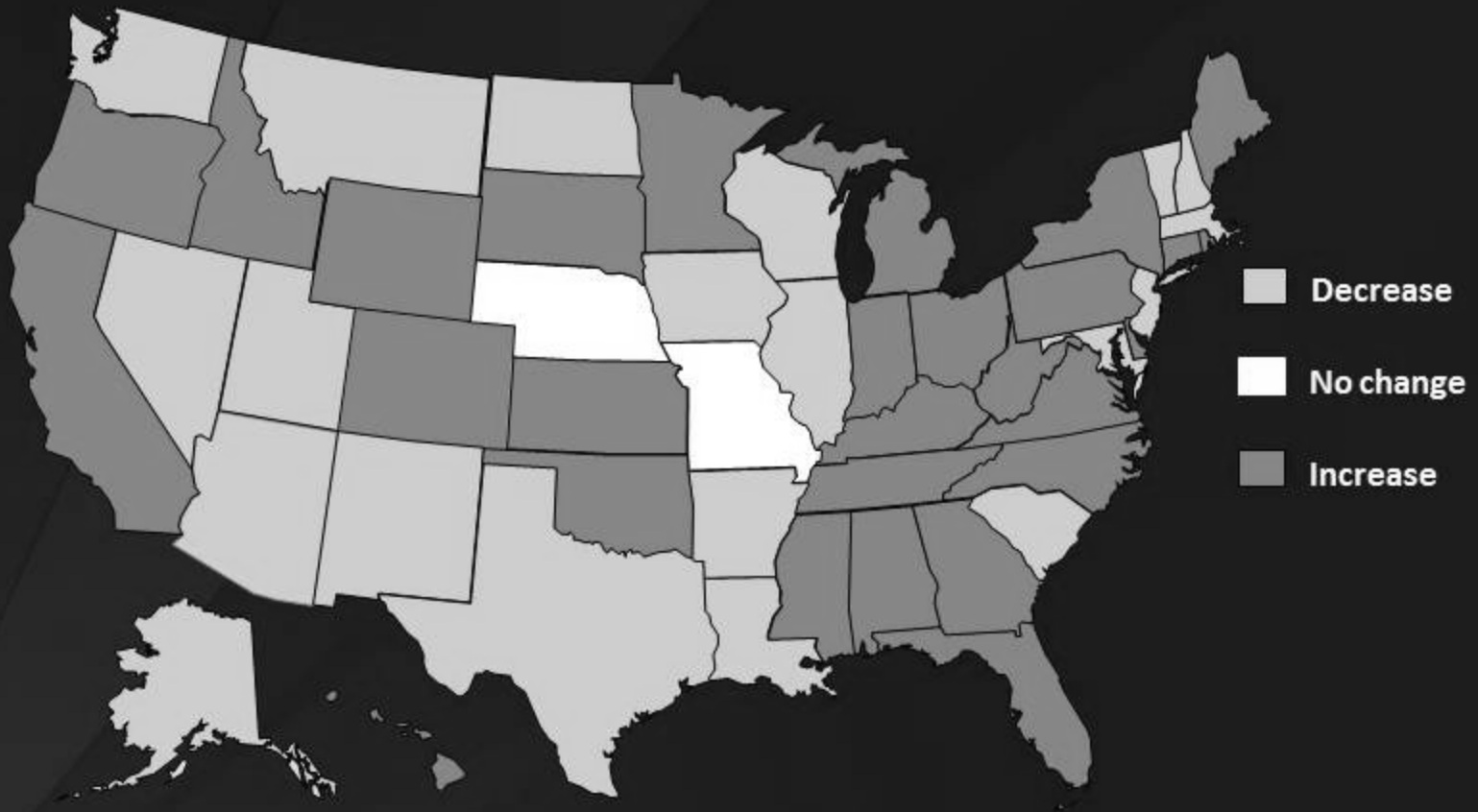
Reported Pertussis Cases US: 1991-2014



Reported Pertussis Cases US & NC: 1991-2014



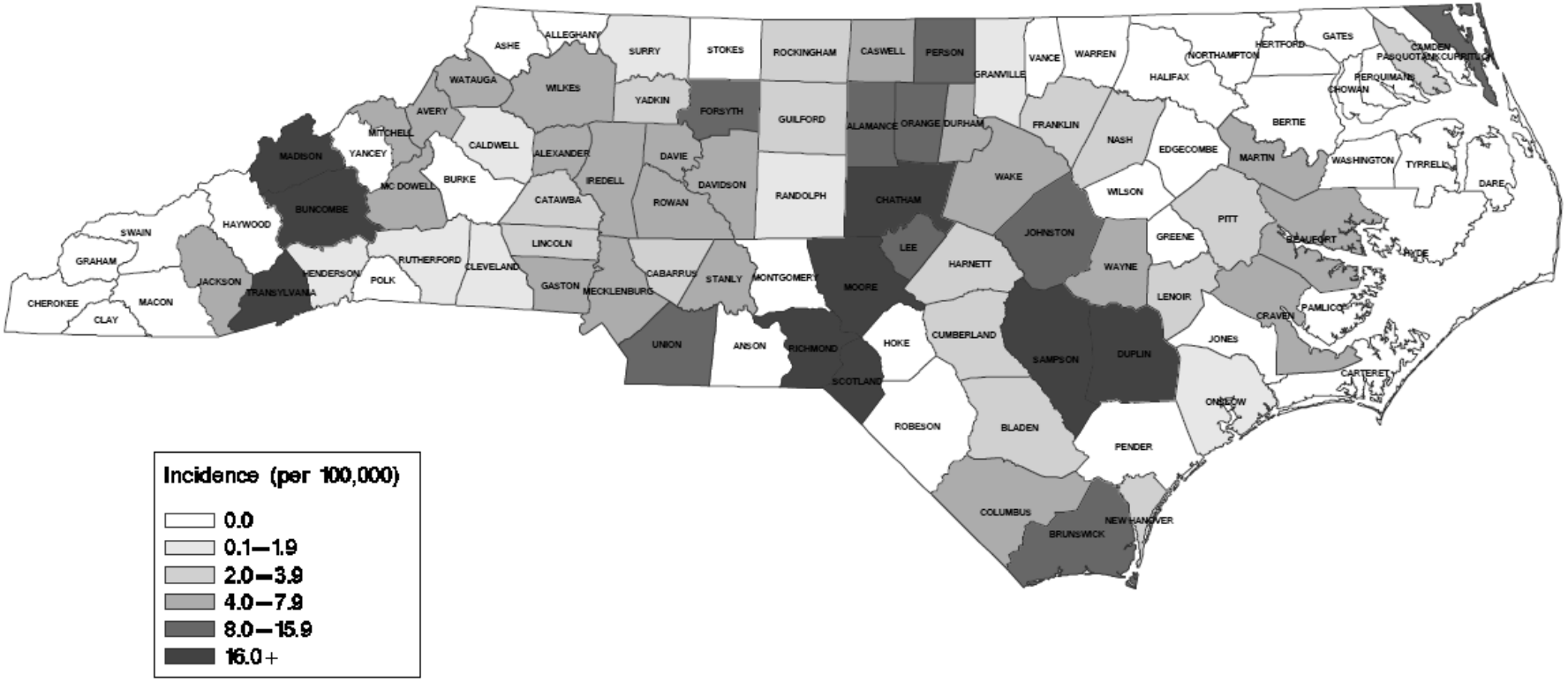
Changes in Pertussis Reporting by State from 2013 to 2014* †



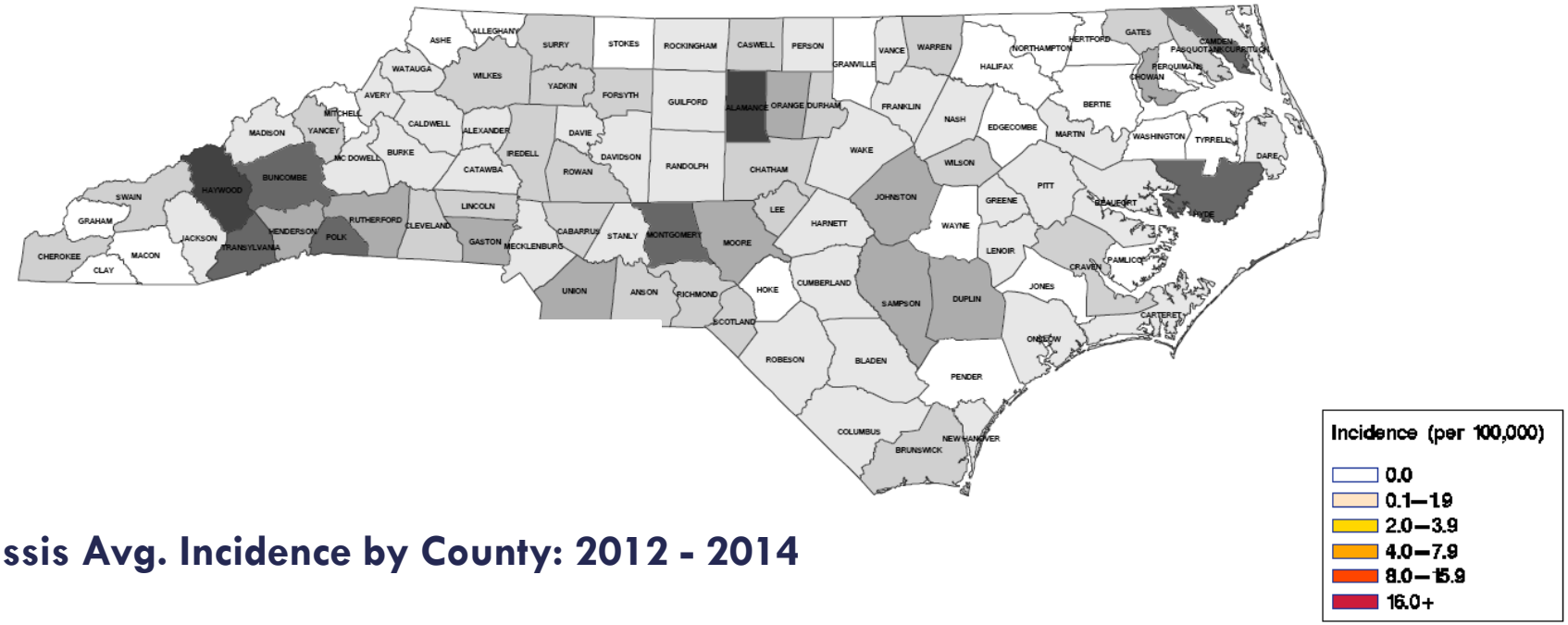
*Data for 2014 are provisional and subject to change. †Cases reported through Week 33 in 2013 were compared with cases reported through Week 23 in 2014.

CDC

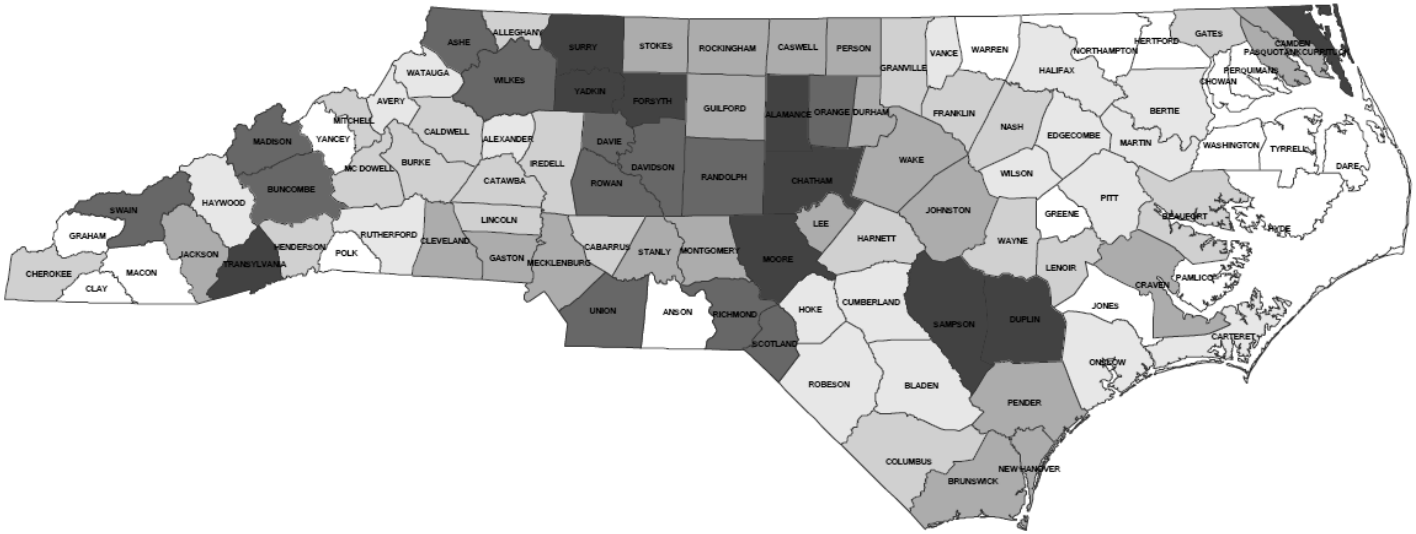
Pertussis Incidence by County: 2014



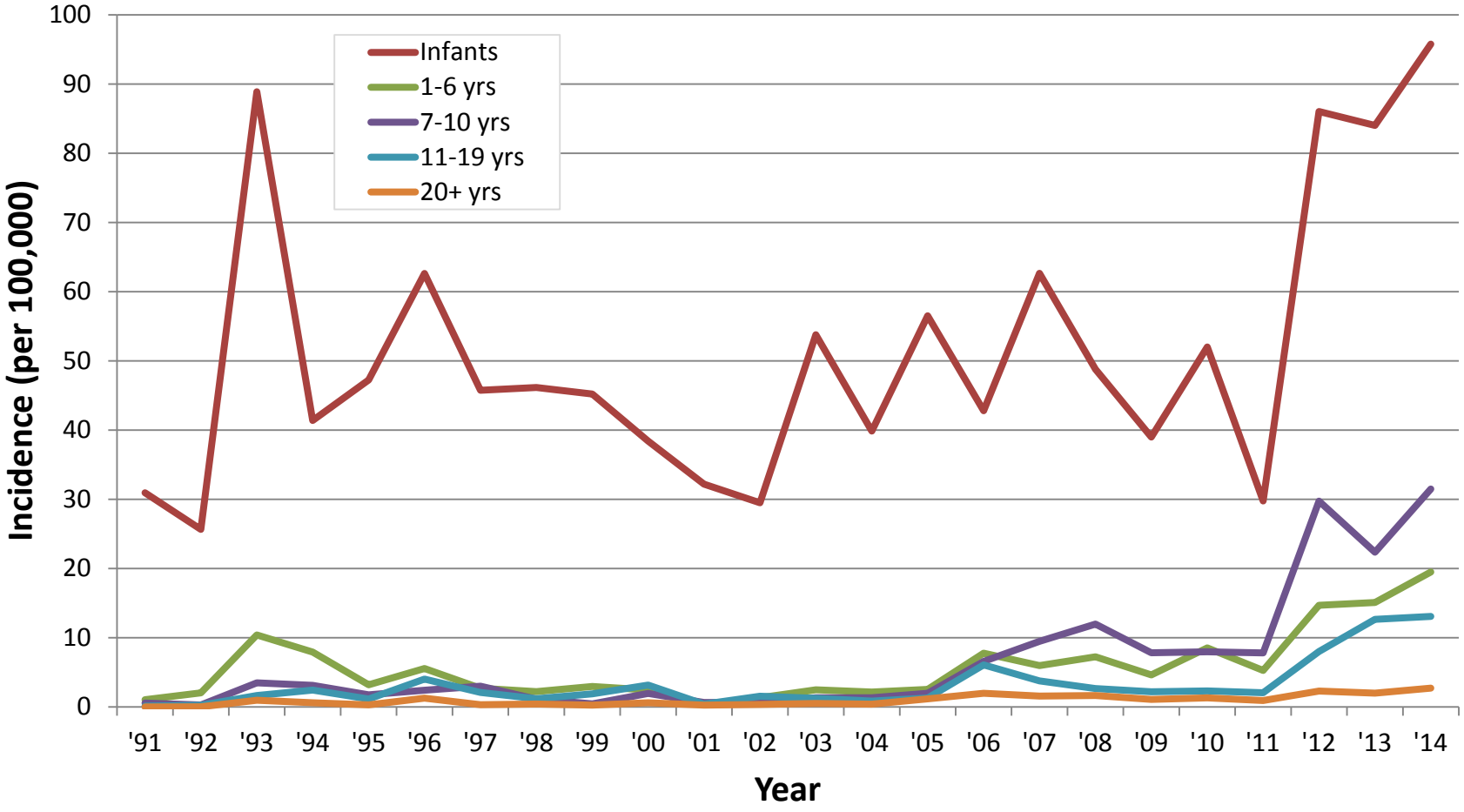
Pertussis Avg. Incidence by County: 2009 - 2011



Pertussis Avg. Incidence by County: 2012 - 2014

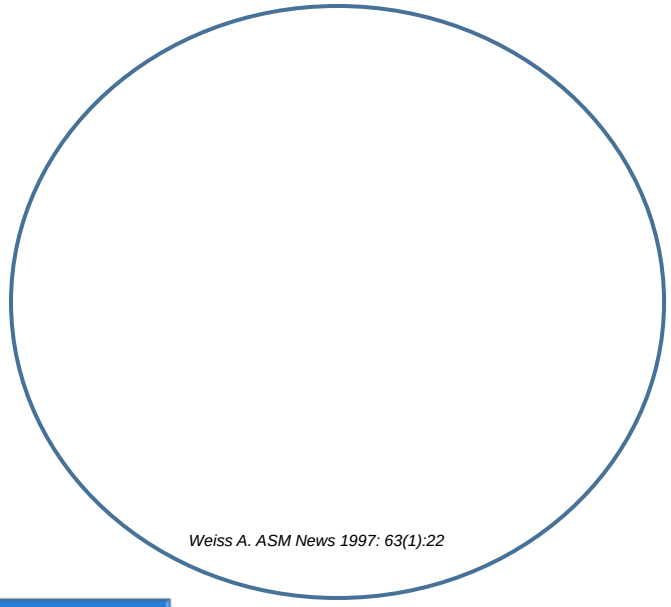


Reported Pertussis Incidence by Age Group, NC: 1991 - 2014



Whole Cell vs. Acellular Vaccine

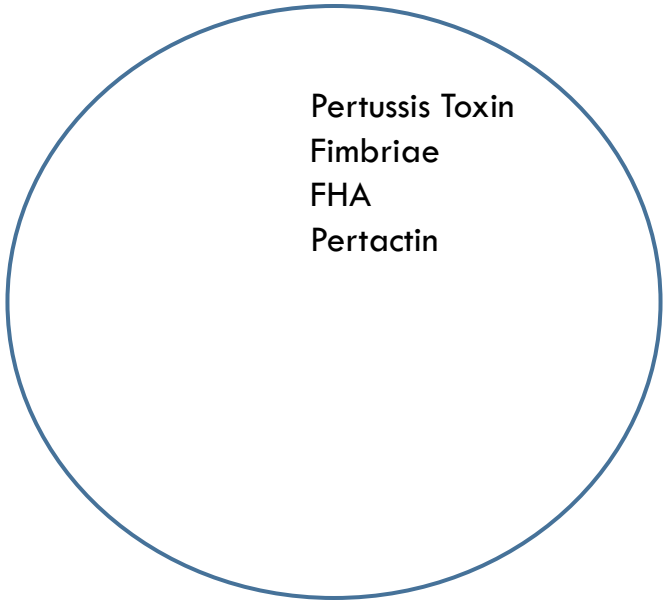
- Whole Cell Vaccine



Weiss A. ASM News 1997: 63(1):22

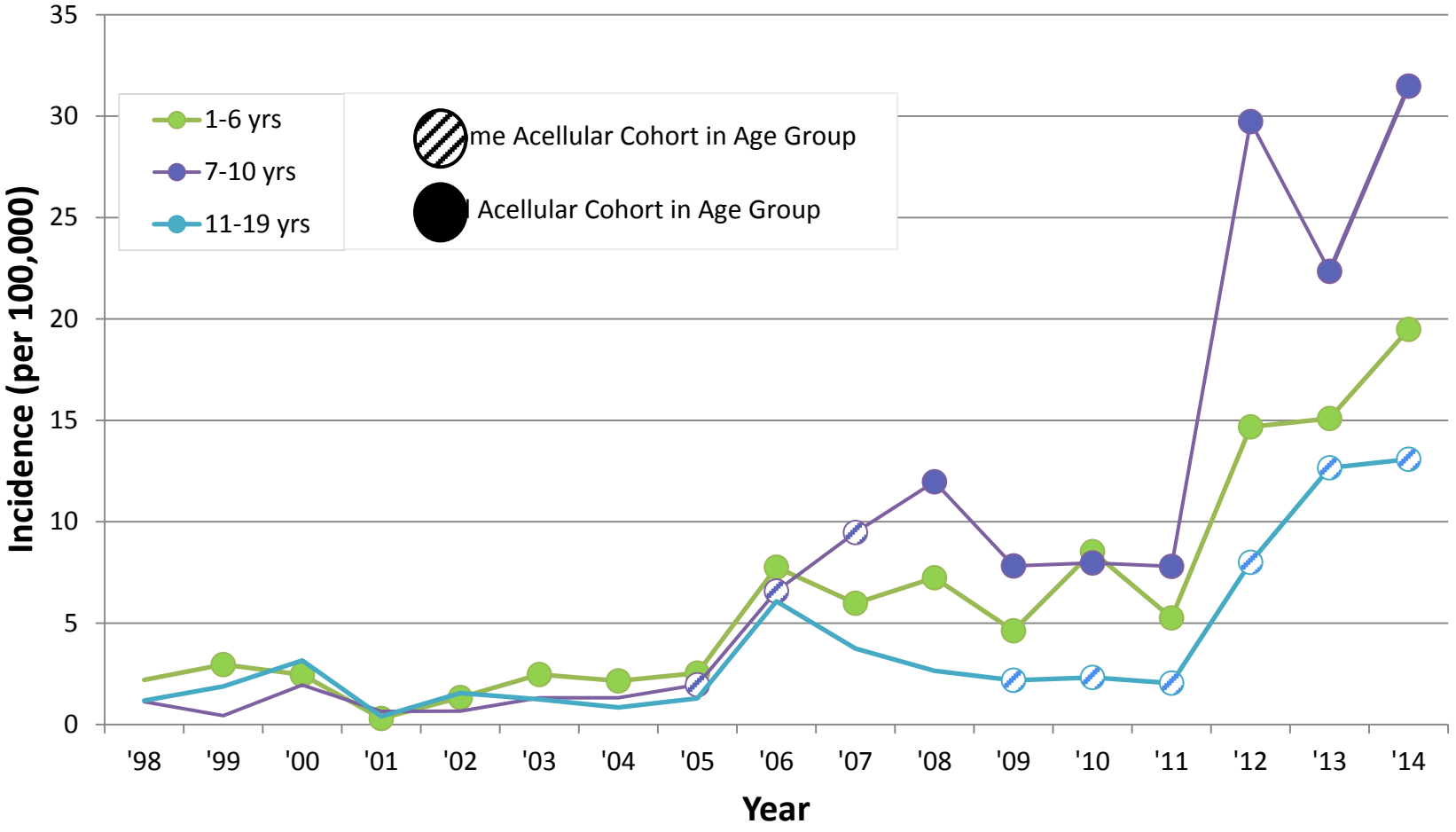
~3,000 antigens

- Acellular Vaccine



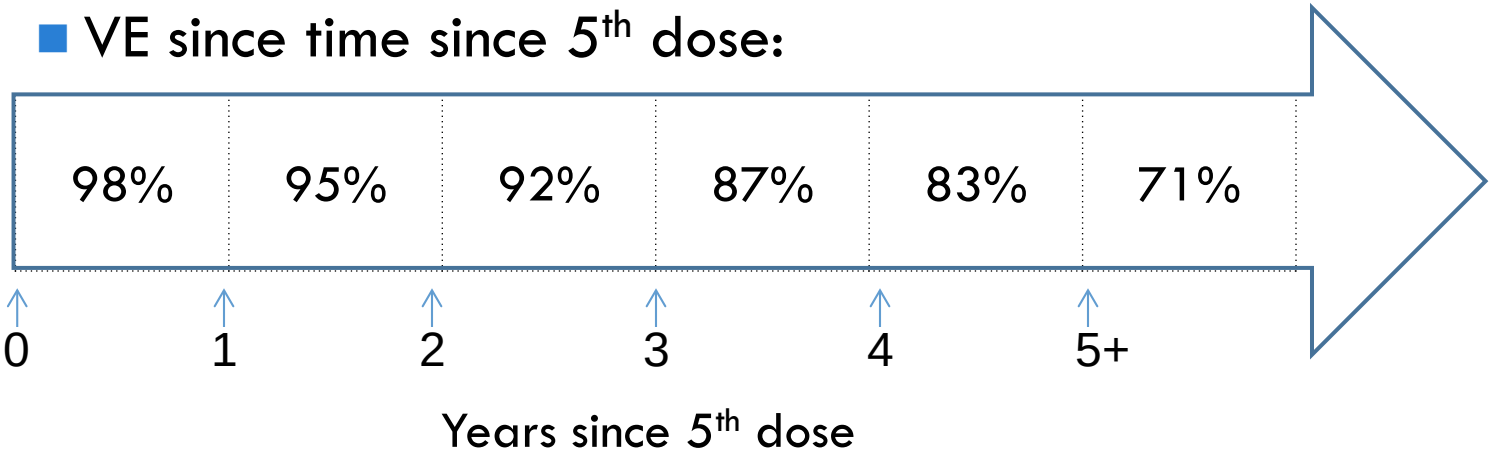
2-5 antigens

Reported Pertussis Incidence by Select Age Groups, NC: 1998 - 2014



DTaP Effectiveness & Duration

- Case-control study
  - Children 4 – 10 years old
  - California
  - 2010
- Results:
  - Overall VE: 89%
  - VE since time since 5th dose:



JAMA. 2012 Nov 28;308(20):2126-32. doi: 10.1001/jama.2012.14939.

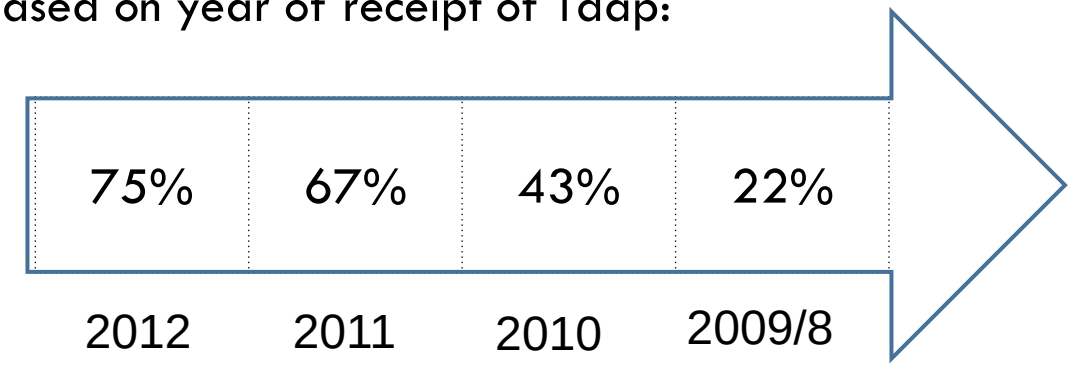
DTaP Effectiveness & Duration

- Case-control study
  - Children 4-12 years old
  - California
  - 2006-2011
- Results: Odds of getting pertussis increased by 42% each year after 5th dose

N Engl J Med. 2012 Sep 13;367(11):1012-9. doi: 10.1056/NEJMoa1200850.

Tdap Effectiveness & Duration

- Cohort study
  - Persons born between 1998-2000 (Adolescents 12-14 years old)
  - Wisconsin
  - 2012
- Results
  - VE based on year of receipt of Tdap:



J Infect Dis. 2014 Sep 15;210(6):942-53. doi: 10.1093/infdis/jiu322. Epub 2014 Jun 5.

Pertactin (PRN)

- Protein that helps pertussis bacteria attach to the lining of the airways
- Vaccine component

Product	PT	FHA	PRN	FIM
Daptacel	10	5	3	5
Infanrix	25	25	8	--
Tripedia	23	23	--	--
Boostrix	8	8	2.5	--
Adacel	2.5	5	3	5

**mcg per dose*

PRN$^-$: Prevalence

- CDC study to evaluate prevalence
- Pertussis isolates in CDC collection bank
  - 1,300 *B. pertussis* isolates
    - 1935 – 2009 historical isolates (n=666)
    - 2010 California outbreak (n=33)
    - 2010 – 2012 routine surveillance (n=385)
    - 2012 Washington outbreak (n=216)

Clin Vaccine Immunol. 2014 Feb;21(2):119-25. doi: 10.1128/CVI.00717-13. Epub 2013 Nov 20.

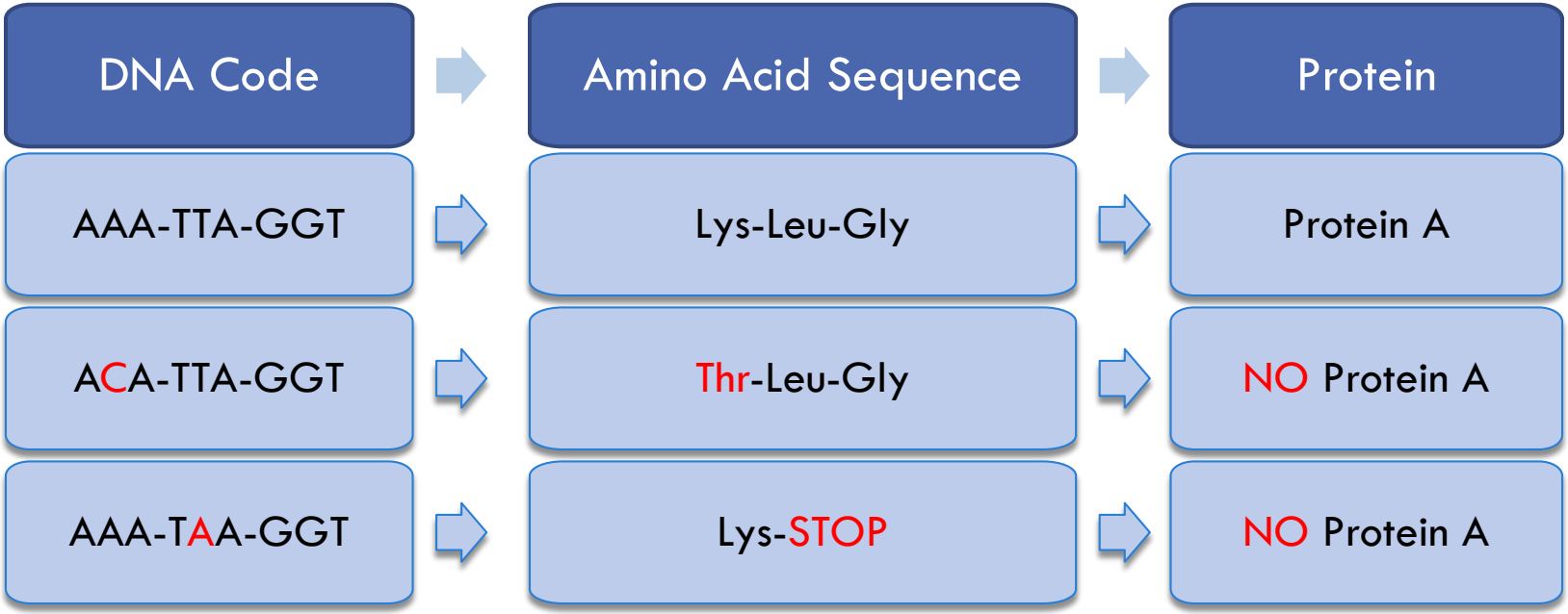
PRN$^-$: Prevalence

- Pertussis isolates in CDC collection bank
  - 1,300 *B. pertussis* isolates
    - 1935 – 2009 historical isolates (n=666)
      - 1/666 PRN- (1994)
    - 2010 California outbreak (n=33)
      - 2 (6%)
    - 2010 – 2012 routine surveillance (n=385)
      - 2010: 14%
      - 2011: 40%
      - 2012: 53%
    - 2012 Washington outbreak (n=216)
      - 137 (63%)
- Identified 10 different mutations leading to loss of PRN

Clin Vaccine Immunol. 2014 Feb;21(2):119-25. doi: 10.1128/CVI.00717-13. Epub 2013 Nov 20.

Mutations

- Changes to the genetic code
- Example:



PRN$^-$: Evidence for Selective Advantage

- Looked at 753 case-patients (8 states) and evaluated:
  - PRN status of isolate
  - Clinical presentation
  - Vaccine history
- May 2011 – February 2013

Clin Infect Dis. 2015 Jan 15;60(2):223-7. doi: 10.1093/cid/ciu788. Epub 2014 Oct 9.

PRN$^-$: Evidence for Selective Advantage

- Results:
  - 640 (85%) PRN-
  - Higher proportion of PRN$^+$ reported apnea

Case Status	Odds Ratio
Unvaccinated	Reference
At least 1 dose of vaccine	2.2
1+ years old and unvaccinated	Reference
1+ year old and up-to-date	3.7

  - Multiple mutations leading to loss of PRN

Clin Infect Dis. 2015 Jan 15;60(2):223-7. doi: 10.1093/cid/ciu788. Epub 2014 Oct 9.

PRN- Strains

- Unknown:
  - Contributing to the increase in cases?
  - Mechanism for selective advantage?
- Currently known/thought:
  - High proportion of isolates PRN-
  - No evidence they are causing more severe disease
  - Vaccinated cases have a 2- to 4-fold greater odds of having PRN- *B. pertussis*
  - Vaccines continue to prevent disease caused by both PRN+ and PRN- pertussis

Summary

1. Infants at highest risk for complications and death
2. Increase in cases is likely due in part to suboptimal duration of immunity with acellular vaccines
3. Vaccine is highly effective, but immunity wanes
4. Emergence of new strains is being monitored and its impact evaluated
5. Vaccines contain multiple antigens and prevent or reduce severity of disease in all strains

Pertussis – Outbreak Investigation Overview

VPD Investigation Strategies

1) Identify the infection
2) Define the at-risk population
3) Manage non-immune persons
    a) Vaccinate
    b) Exclude
4) Obtain appropriate clinical specimens
5) Maintain surveillance

Basic VPD Investigation Questions

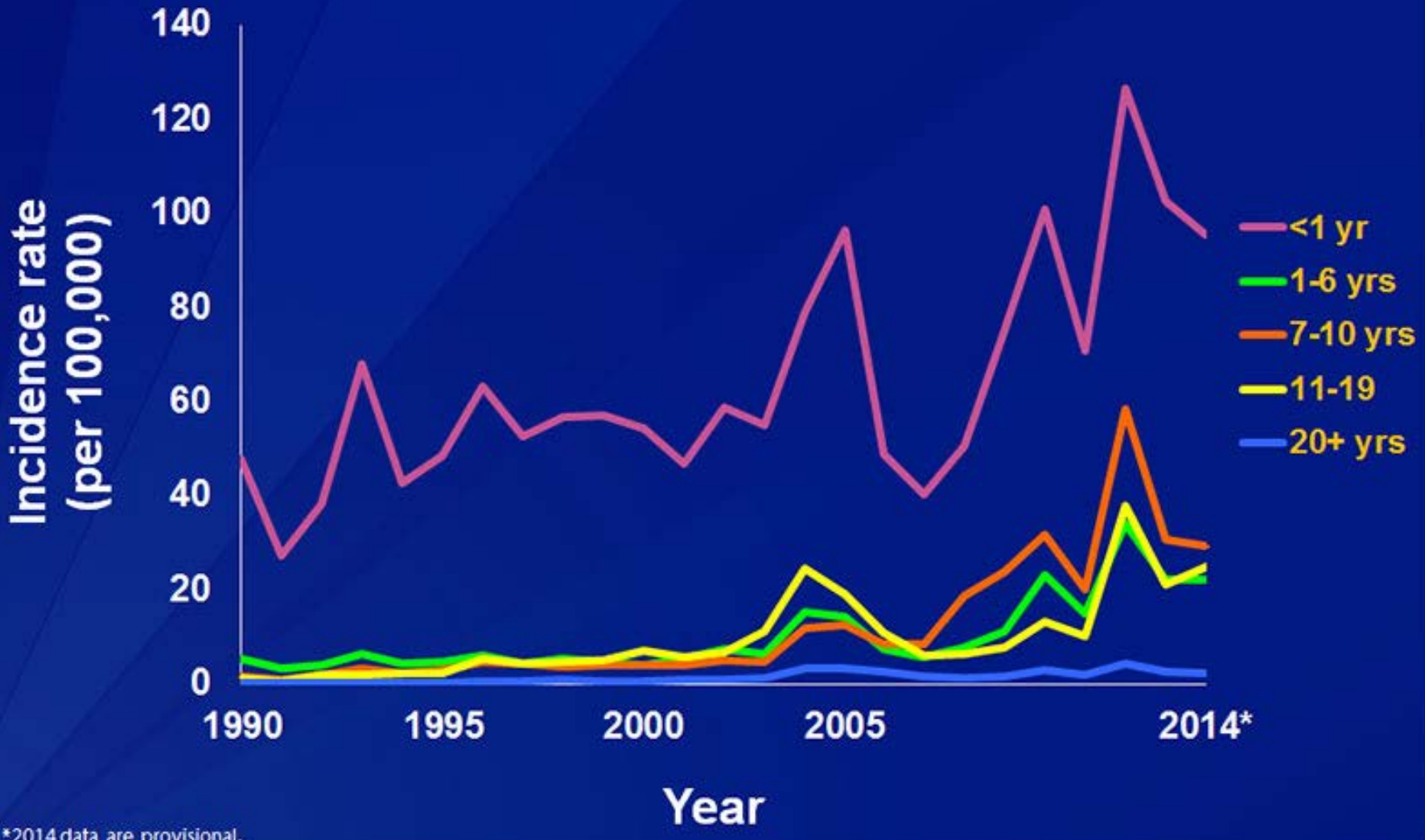
- Immune status?
- Clinical presentation?
- Epidemiological information?

Goals of pertussis outbreak control

- Primary-to decrease morbidity (amount of disease) and mortality (death) among infants

- Secondary-to decrease morbidity among people of all ages

Reported pertussis incidence by age group: 1990-2014*



*2014 data are provisional.

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

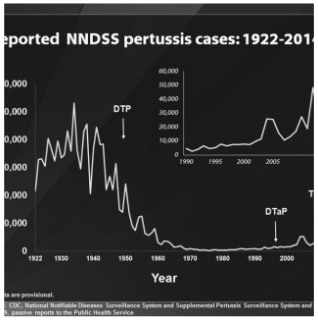
Pertussis Outbreak in Institutions

- Two or more cases clustered
  - in time (within 42 days of each other) and
  - in space (one building) where transmission is suspected to have occurred in that setting
- High risk settings require prompt reporting-24 hrs.

Pertussis Outbreak in Communities

- When the number of reported cases is:
  - higher than what is expected on the basis of previous reports during a non-epidemic period
  - for a given population
  - in a defined time period (historical disease patterns)

Strategies For Increasing Incidence



Surveillance

HCP Alerts

Vaccination

Public Education

Local Work Flow

VPD Resources

Surveillance

- Confirm with culture
- Consider active screening in high risk settings
- Consider active surveillance through providers, labs
- Monitor N.C. Pertussis Monthly Report
  - http://epi.publichealth.nc.gov/cd/diseases/pertussis.html

Healthcare Provider Alerts

- Use blast faxes, press releases, email, social media
- Educate birthing hospitals on NC GS 131E-79.2
- Provide education on
  - Current epi in your area
  - Prompt reporting of suspect, probable
  - Diagnosis and treatment
  - Waning immunity
  - Maternal Tdap recommendation-ACIP, ACOG, ACNM

Public Education

- Inform public about pertussis in your community
- Include basic pertussis information
  - Know signs, symptoms, diagnosis, treatment
  - Protect infants from others with cough
  - See provider for unexplained cough
  - Recognize importance of pertussis vaccination
- Use CDC, IAC materials for lay audience
- Consider school-wide alerts when needed

Vaccination

- Convey importance of vaccination in all alerts
- Message to OB providers (Tdap 27-36 weeks)
- Expanded Tdap criteria for uninsured pregnant and postpartum women
- Offer Tdap to eligible clients at LHD
- Complete NC EDSS Maternal Tdap package

http://www.ncbi.nlm.nih.gov/pubmed/25332078

Workload Considerations

- Identify pre-translated materials and translators
- Obtain templates from CD Branch for
  - Press releases
  - School letters
  - Contact investigation worksheets
- Target strategies to focus on infants, infant settings
- Identify and cross-train staff who can assist

VPD Notifications

- *Who do I call?*
  - CD Branch - control measures, testing guidance
  - Immunization Branch - vaccine logistics, schedule issues
  - Local/regional partners - case finding, reporting, testing

Pertussis Resources

North Carolina Communicable Disease Manual

Pertussis Resources

1. LHD Disease Investigation Steps (PDF)
2. Pertussis Investigation Overview (PDF)
3. Pertussis Case Definition (PDF)
4. Pertussis Case Definition Chart (PDF)
5. Pertussis Sample Letter (Word)
6. Pertussis Sample Letter 2 (Word)
7. Pertussis Contact Investigation Worksheet (Excel)
8. CDC Pertussis Fact Sheet, English (PDF)
9. CDC Pertussis Fact Sheet, Spanish (PDF)
10. Local Health Department Strategies to Address Increasing Incidence of Pertussis (PDF)
11. Pertussis Monthly Report (see blue box on right side of linked page)
12. Recommended Antimicrobial Agents for Treatment and Postexposure Prophylaxis of Pertussis, 2005 CDC Guidelines (PDF)

Acknowledgments

- Some slides adapted from
  - Stacey Martin, MSc. "Coughing up the Facts on Pertussis – Emerging Trends and Vaccine Recommendations", available at http://www.cdc.gov/vaccines/ed/ciinc/Pertussis.htm
  - Vera Luther, MD. "Pertussis in Adults: What's the Whoop All About?", available at http://ahecms.wakehealth.edu/Mediasite/Play/ae3383b27b984c75b8ff195a413ffc921d

Contact Information

- Zack Moore, MD, MPH
  - Medical Epidemiologist
  - Zack.moore@dhhs.nc.gov
- Kristin M. Sullivan, MPH
  - VPD Epidemiologist
  - Kristin.sullivan@dhhs.nc.gov
- Susan Sullivan MS, RN-BC
  - VPD Nurse Consultant
  - Susan.sullivan@dhhs.nc.gov