Adolescent Immunization Update 2017

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Declaration

- Medical advisor to and on the speaker's bureau for Merck Vaccines
- Faculty member of the Adolescent Immunization Initiative which is sponsored by Sanofi Pasteur
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OBJECTIVES

- Discuss the current ACIP recommended adolescent immunization schedule
- Review the impact of vaccines and less-common vaccine preventable diseases
- Discuss specific adolescent vaccine-preventable diseases
- Discuss specific vaccine recommendations for adolescents
- Review the importance of strong and clear vaccination recommendations and discuss how to increase adolescent vaccine rates

“Nothing on the planet saves children’s lives more effectively and inexpensively than vaccines.”

Bill Gates

Director, Bill and Melinda Gates Foundation

Recommended Childhood Immunization Schedule
United States, January - December 1982

Vaccines are listed under routinely recommended ages. [Bars] indicate range of recommended ages for immunization. Any dose not given at the recommended age should be given as a "catch-up" immunization at any subsequent visit when indicated and feasible. (Ovals) indicate vaccines to be given if previously recommended doses were missed or given earlier than the recommended minimum age.

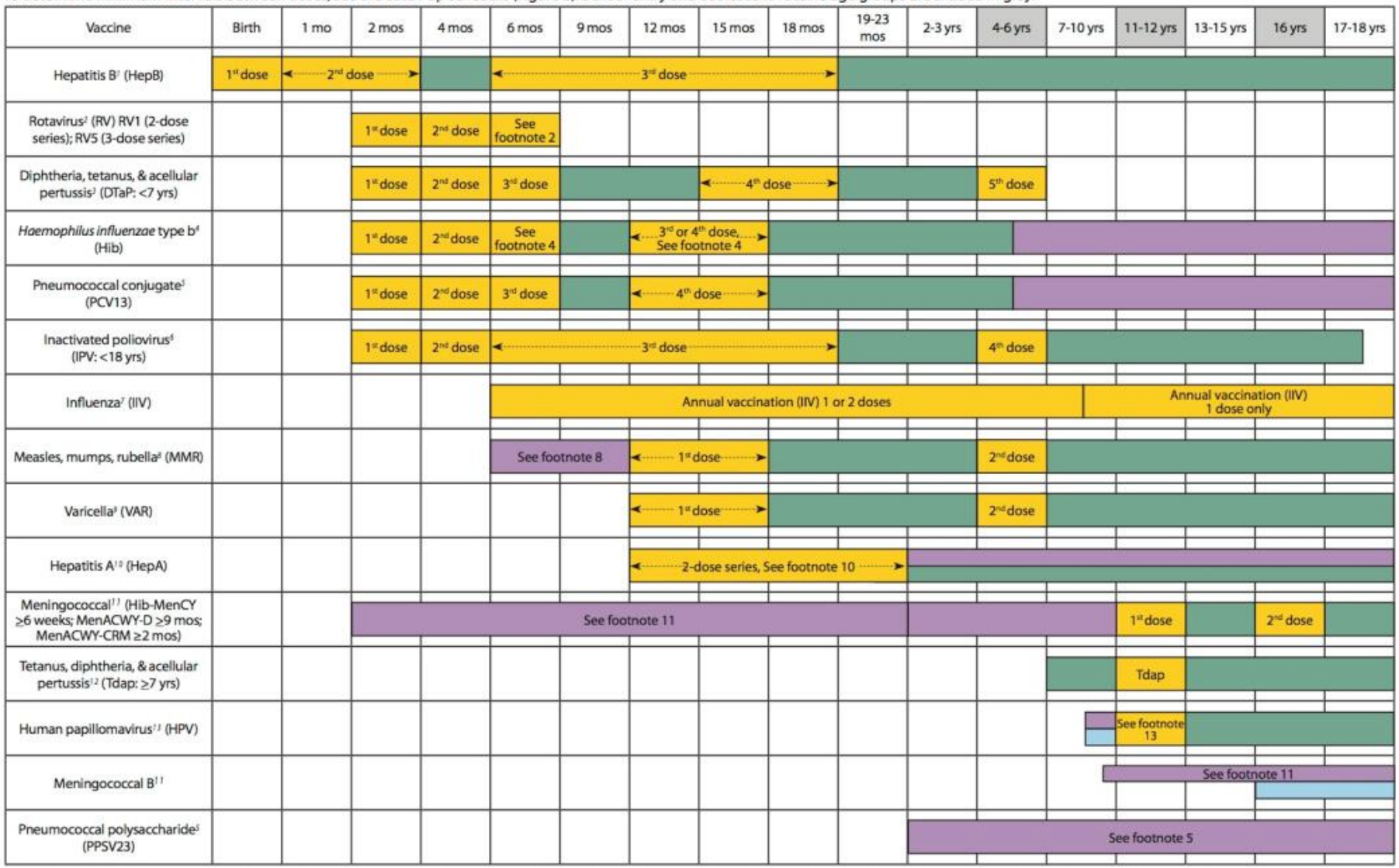
Age ▷ Vaccine ▽	Birth	1 mo	2 mos	4 mos	6 mos	12 mos	15 mos	18 mos	24 mos	4-6 yrs	11-12 yrs	14-18 yrs
Diphtheria, Tetanus, Pertussis			DTP	DTP	DTP			DTP		DTP		Td
Polio			OPV	OPV	(OPV)			OPV		OPV		
Measles, Mumps, Rubella							MMR					

Approved by the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP).

Figure 1. Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger—United States, 2017.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded in gray.



NOTE: The above recommendations must be read along with the footnotes of this schedule.

The figure below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. Always use this table in conjunction with Figure 1 and the footnotes that follow.

Vaccine	Minimum Age for Dose 1	Minimum Interval Between Doses			
		Dose 1 to dose 2	Dose 2 to dose 3	Dose 3 to dose 4	Dose 4 to dose 5
Persons aged 4 months through 6 years					
Hepatitis B[1]	Birth	4 weeks	8 weeks and at least 16 weeks after first dose; minimum age for the final dose is 24 weeks		
Rotavirus[2]	6 weeks	4 weeks	4 weeks		
Diphtheria, tetanus, & acellular pertussis[3]	6 weeks	4 weeks	4 weeks	6 months	6 months[3]
Haemophilus influenzae type b[5]	6 weeks	4 weeks if first dose administered at younger than age 12 months 8 weeks (as final dose) if first dose administered at age 12 through 14 months No further doses needed if first dose administered at age 15 months or older	4 weeks[5] if current age is younger than 12 months and first dose administered at < 7 months old 8 weeks and age 12 months through 59 months (as final dose)[5] if current age is younger than 12 months and first dose administered between 7 through 11 months (regardless of Hib vaccine [PRP-T or PRP-OMP] used for first dose); OR if current age is 12 through 59 months and first dose administered at younger than age 12 months; OR first 2 doses were PRP-OMP and administered at younger than 12 months. No further doses needed if previous dose administered at age 15 months or older	8 weeks (as final dose) This dose only necessary for children aged 12 through 59 months who received 3 (PRP-T) doses before age 12 months and started the primary series before age 7 months	
Pneumococcal[6]	6 weeks	4 weeks if first dose administered at younger than age 12 months 8 weeks (as final dose for healthy children) if first dose administered at age 12 months or older No further doses needed for healthy children if first dose administered at age 24 months or older	4 weeks if current age is younger than 12 months 8 weeks (as final dose for healthy children) if current age is 12 months or older No further doses needed for healthy children if previous dose administered at age 24 months or older	8 weeks (as final dose) This dose only necessary for children aged 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age	
Inactivated poliovirus[7]	6 weeks	4 weeks[7]	4 weeks[7]	6 months[7] minimum age 4 years for final dose	
Meningococcal[13]	6 weeks	8 weeks[13]	See footnote 13	See footnote 13	
Measles, mumps, rubella[9]	12 months	4 weeks			
Varicella[10]	12 months	3 months			
Hepatitis A[11]	12 months	6 months			
Persons aged 7 through 18 years					
Tetanus, diphtheria; tetanus, diphtheria, & acellular pertussis[4]	7 years[4]	4 weeks	4 weeks if first dose of DTaP/DT administered at younger than age 12 months 6 months if first dose of DTaP/DT administered at age 12 months or older and then no further doses needed for catch-up	6 months if first dose of DTaP/DT administered at younger than age 12 months	
Human papillomavirus[12]	9 years	Routine dosing intervals are recommended[12]			
Hepatitis A[11]	12 months	6 months			
Hepatitis B[1]	Birth	4 weeks	8 weeks (and at least 16 weeks after first dose)		
Inactivated poliovirus[7]	6 weeks	4 weeks	4 weeks[7]	6 months[7]	
Meningococcal[13]	6 weeks	8 weeks[13]			
Measles, mumps, rubella[9]	12 months	4 weeks			
Varicella[10]	12 months	3 months if person is younger than age 13 years 4 weeks if person is aged 13 years or older			

NOTE: The above recommendations must be read along with the footnotes of this schedule.

Comparison of 20th Century Annual Morbidity and Current Morbidity: Vaccine-Preventable Diseases

Disease	20th Century Annual Morbidity†	2008 Reported Cases ††	Percent Decrease
Smallpox	29,005	0	100%
Diphtheria	21,053	0	100%
Measles	530,217	132	> 99%
Mumps	162,344	386	> 99%
Pertussis	200,752	10,007	95%
Polio (paralytic)	16,316	0	100%
Rubella	47,745	17	> 99%
Congenital Rubella Syndrome	152	0	100%
Tetanus	580	15	97%
Haemophilus influenzae	20,000	219*	99%

†Source: JAMA. 2007;298(18):2155-2163

††Source: CDC. MMWR January 9, 2009/57(53);1420-1430. (Provisional, week 53 data)

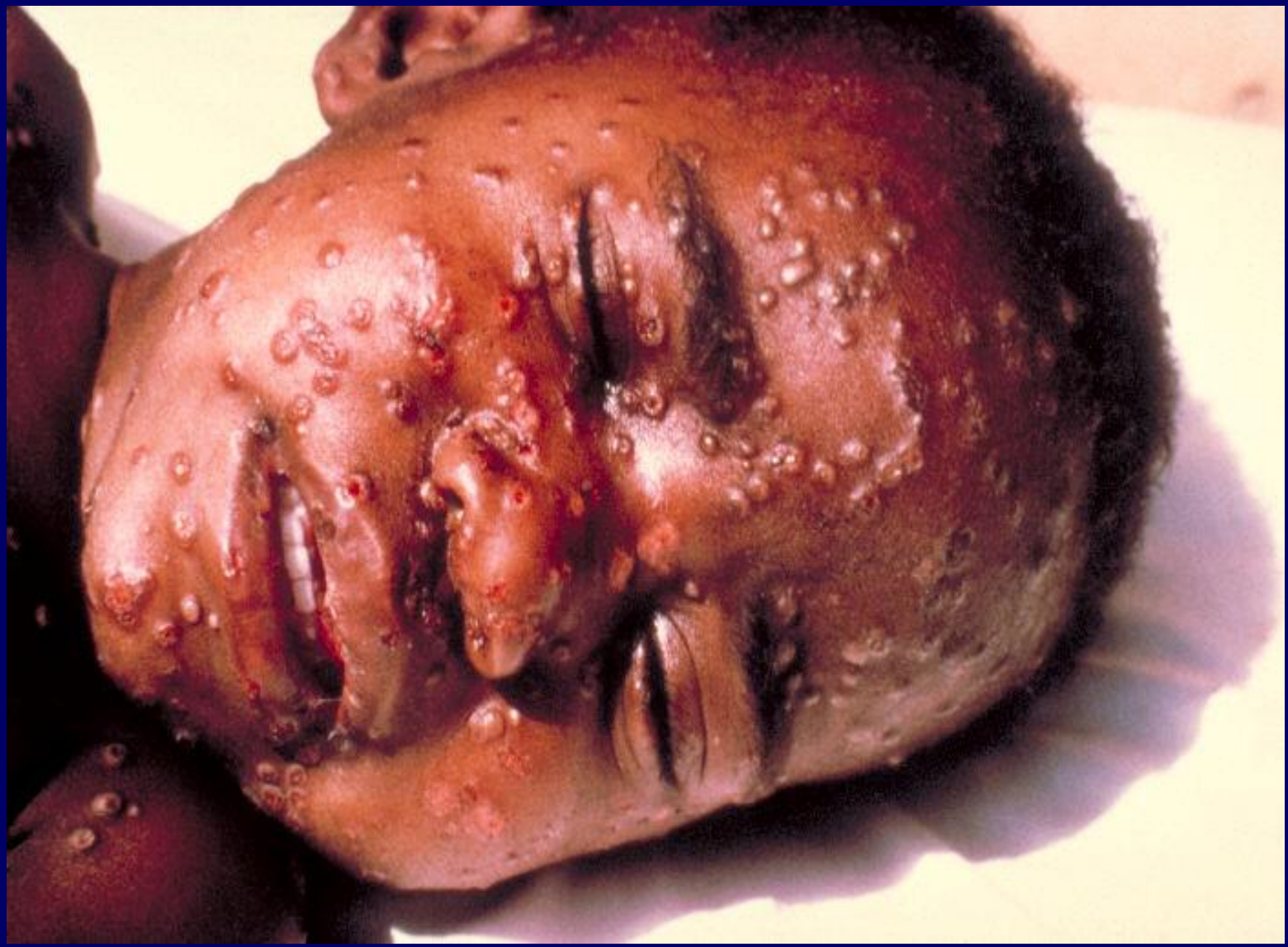
* 27 type b and 192 unknown (< 5 years of age)

Lance Rodewald, MD
Director, Immunization Services Division
National Center for Immunization and Respiratory Diseases

CDC Immunization

United States: 2014

- Number of cases reported to the CDC:
  - Measles: 644
    - ✓ Highest number since the early 1990's
    - ✓ Most recent outbreak in California associated with mostly unvaccinated children who went to Disneyland
  - Mumps: 1,151
    - ✓ 15-20 different players and multiple teams affected in the National Hockey League
  - Varicella: 9,058
    - ✓ Epidemic numbers in many states including Florida
  - Pertussis: 28,660



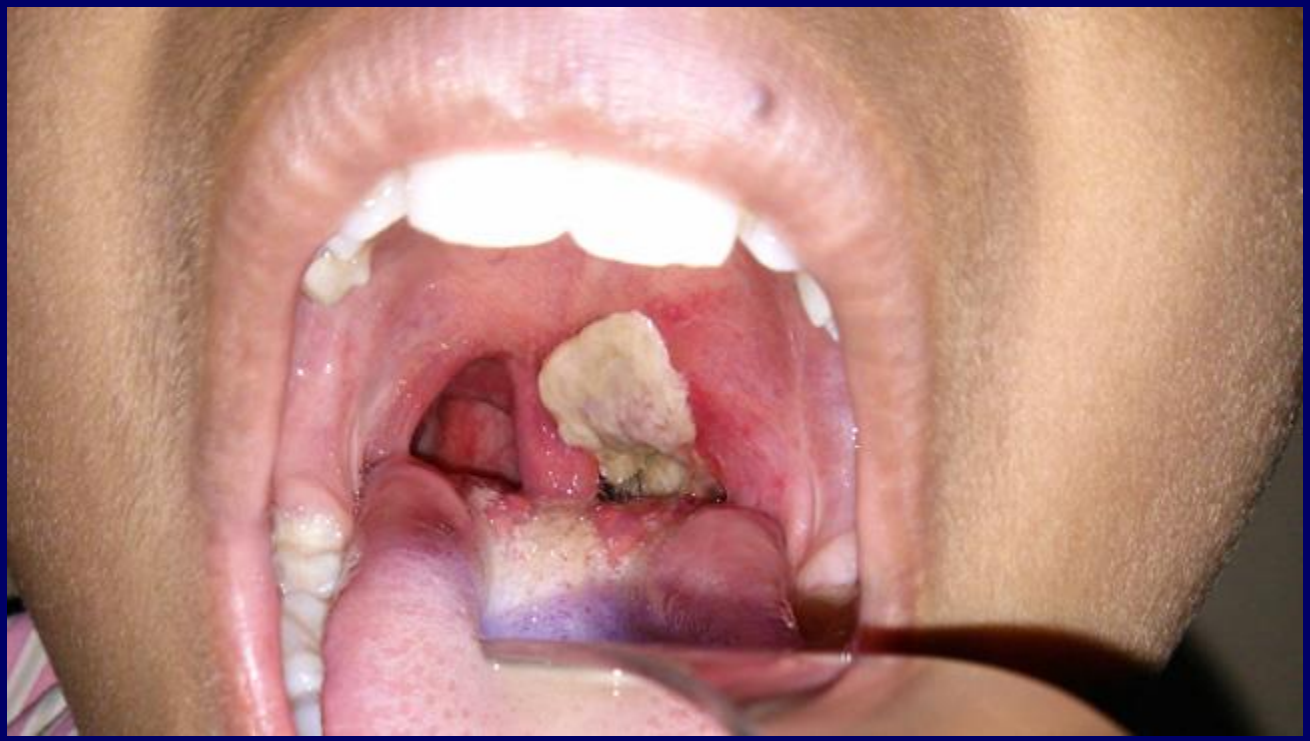
Smallpox (Variola)

- Clinical manifestations:
  - Wide regional variation in death rates
    - Brazil: variola minor (alastrim) 1-2 % fatal
    - Africa/Indonesia: Intermediate severity
    - India: severe form 30% fatal
    - Hemorrhagic smallpox: ~ 100% fatal
  - Complications:
    - Hemorrhagic events
    - Secondary bacterial infection
    - Pneumonia
    - Nephritis/Arthritis
    - Scarring/Blindness

Polio

- Pathogenesis
  - Enters through mouth
  - Replicates NP/GI/lymphatics
  - Hematological spread to CNS
  - Spreads along nerves
  - Destroys motor neurons of anterior horn and brain stem

- Epidemiology/Communicability
  - Persons infected with poliovirus are most infectious from 7-10 days before and after onset of illness
  - Virus can be present in the stool 3-6 weeks
  - Sero-conversion rates among susceptible household members ~ 100%

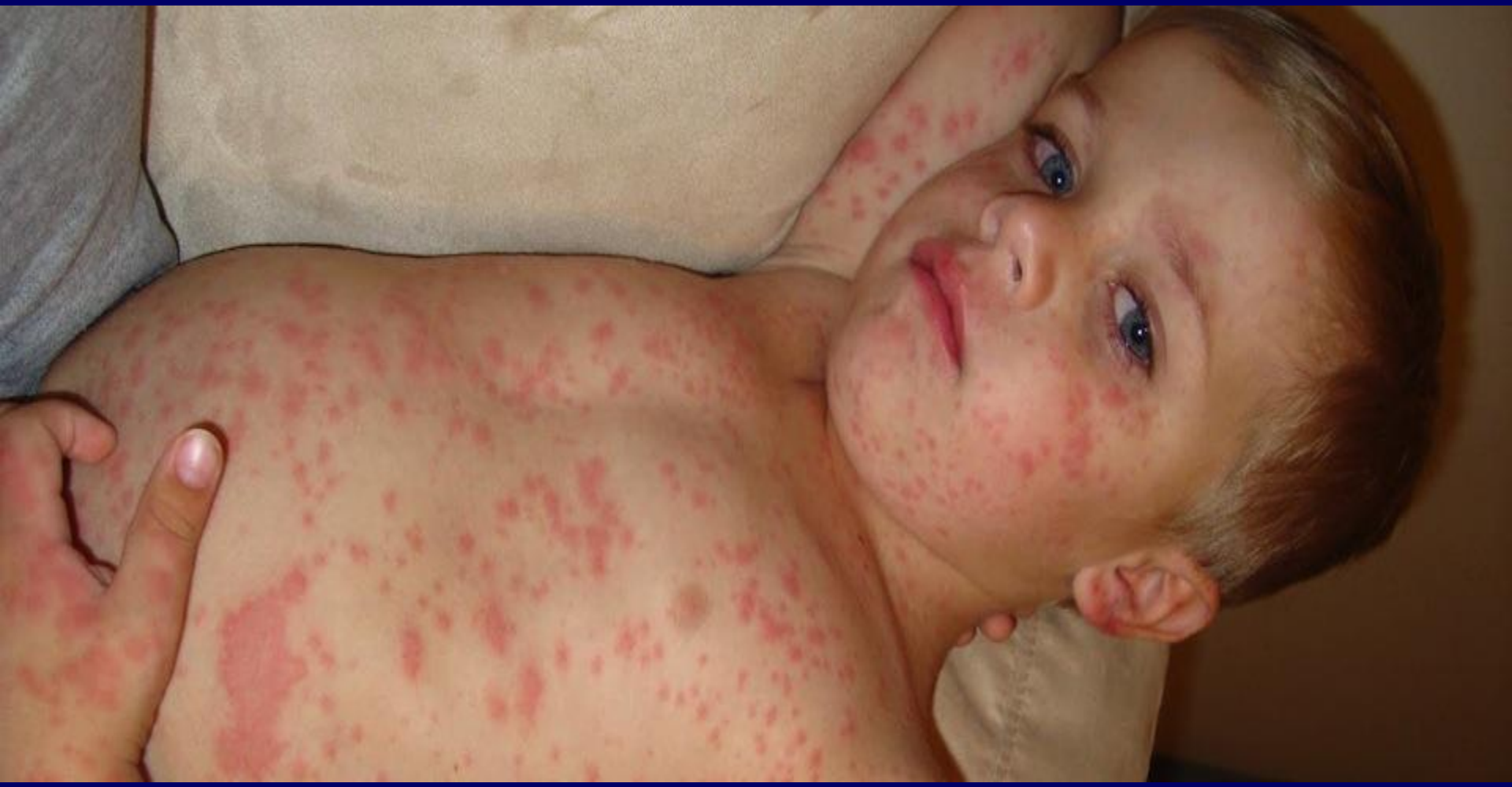


Diphtheria

- Pathophysiology
  - Both toxigenic and non toxigenic C. Diptheriae cause infection
  - Major virulence factor is an exotoxin
  - Toxin inhibits cellular protein synthesis
  - Pseudomembrane forms in the throat, creating a dense membrane of necrotic tissue in the OP that is difficult to remove and may cause airway compromise
  - Cardiomyopathy and neuropathy develop later (often 2-10 weeks) and may be immune-mediated phenomenon
- Epidemiology
  - Respiratory droplet or contact with skin lesions
  - Human Reservoir

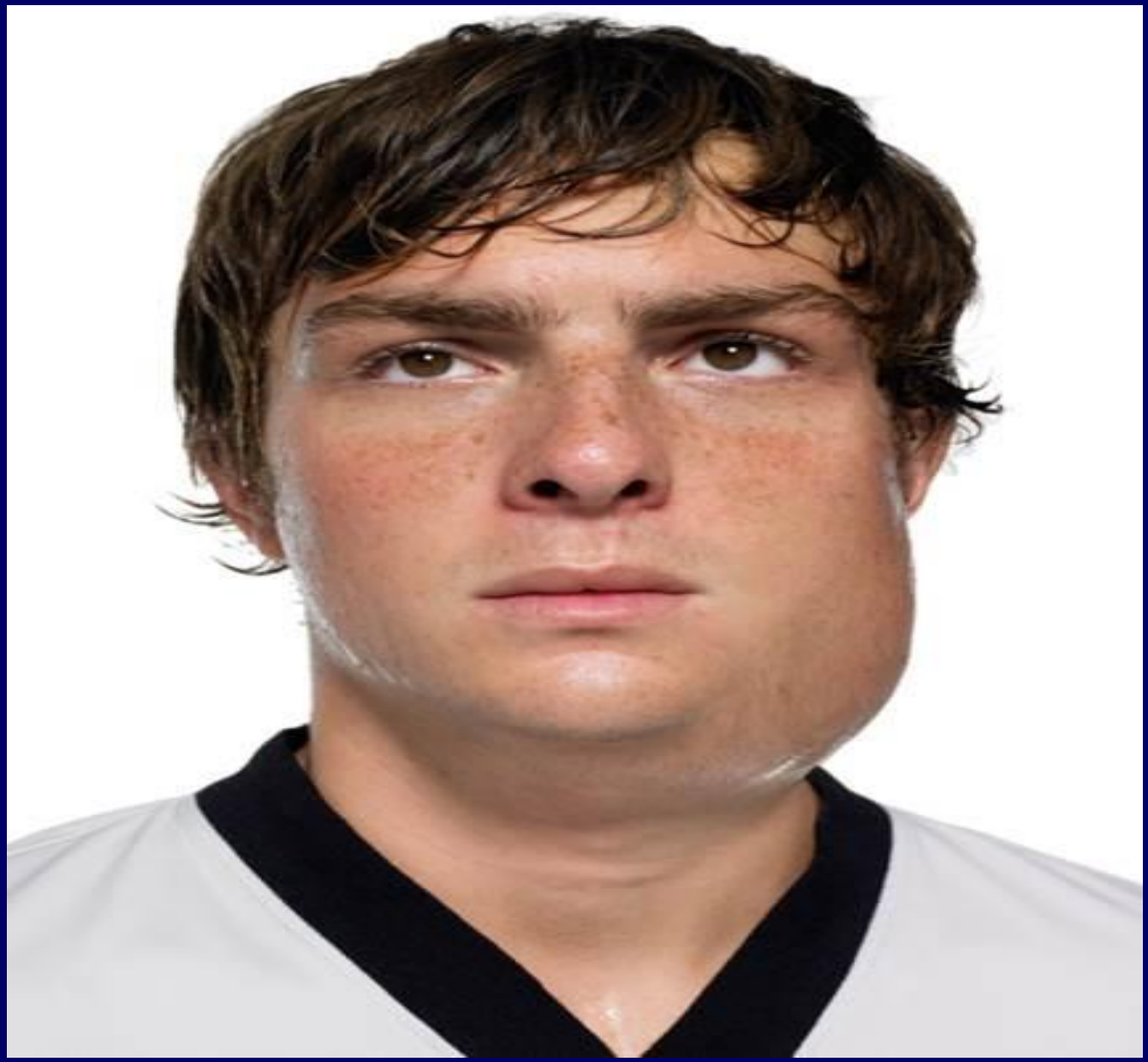
Tetanus

- Pathophysiology
  - A toxin mediated disease
  - Tetanospasmin-2nd most lethal toxin known (2.5 nanograms/kg=lethal dose)
  - Tetanospasmin is thought to penetrate the CNS via transport through peripheral nerves
- Epidemiology/Communicability: A commonly encountered soil organism. Highest rates in summertime/warm climates. Tetanus disease commonly contracted through wounds, or in neonatal causes through umbilical stump



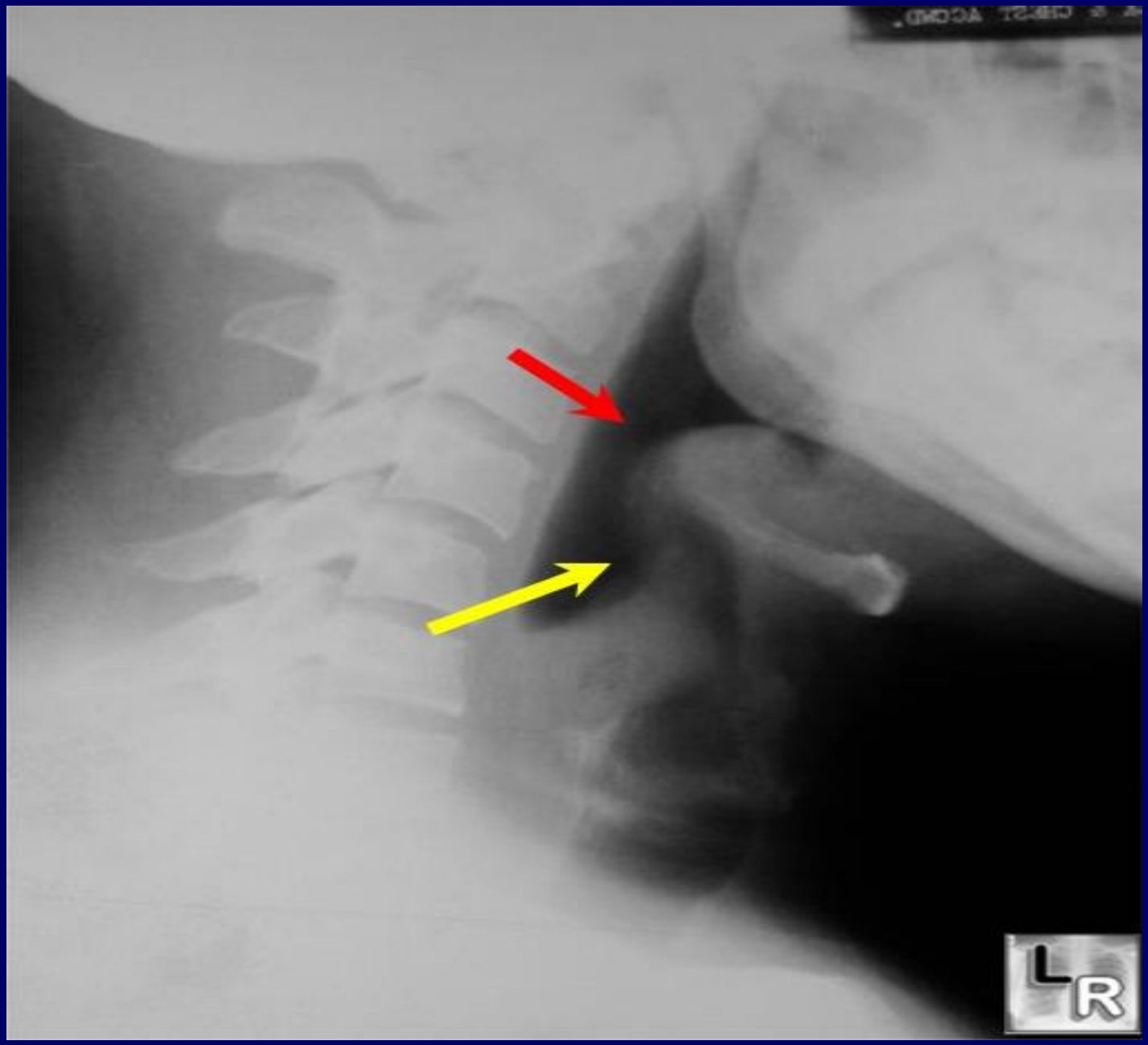
Measles (Rubeola)

- Epidemiology
  - Measles is endemic worldwide
  - Before advent of vaccine in the early 1960's, virtually all children contracted measles at some point during their childhood (5-9 years of age was peak)
  - Epidemics in 2-3 years cycles, usually late winter-early spring
  - Still common worldwide. Accounts for >100,000 deaths/year in developing world
  - Probably the single most contagious pathogen
  - Highest number of cases in the US in decades



Mumps

- Clinical Manifestations
  - 33% of patients with mumps infection have sub-clinical or mildly symptomatic disease
  - Most common manifestation is parotitis, often starting unilaterally and becoming bilateral in 70% of the cases
  - Prodrome of non-specific symptoms (fever, myalgia, abdominal pain) may also precede
  - Earache and pain with eating sour or acidic foods may also occur
- Complications
  - CNS disease-neurotropic virus with >50% pleocytosis in CSF, through 1-10% have meningitis or encephalitis
  - Orchitis 14-35% of males, Sx usually 4-8 days after the parotitis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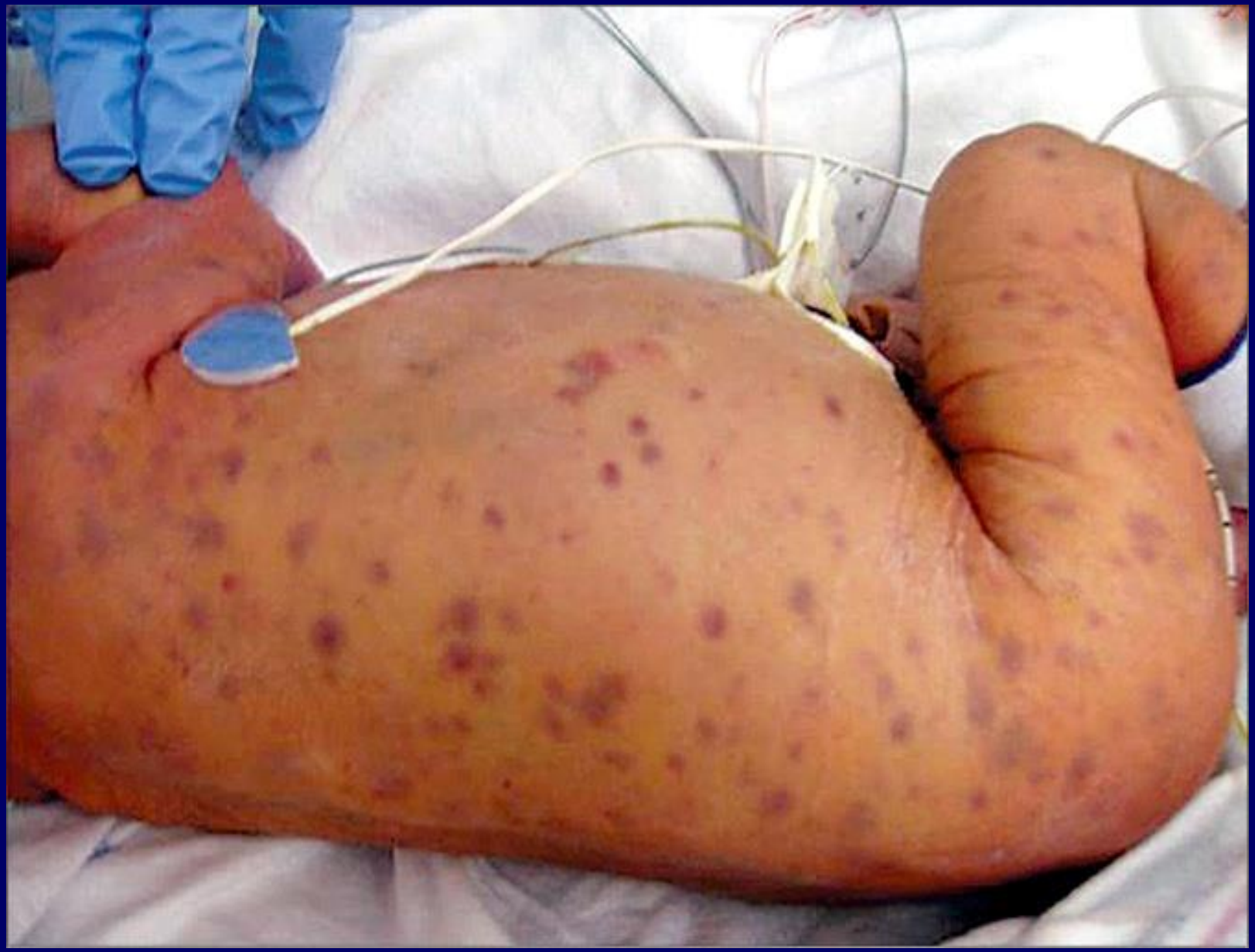
Haemophilus influenzae

- Clinical manifestations
  - Meningitis
  - Epiglottitis
  - Pneumonia
  - Osteoarticular infection
  - Bacteremia
  - Other

- Pathogenesis: Acquisition→NP colonization. A colonized individual could either go on to:
  - Clear the organism
  - Have contiguous spread (respiratory disease)
  - Have translocation to blood stream
    - Systemic disease
    - CNS disease



Rubella

- Pathogenesis-Congenital Rubella
  - Persistent progressive infection
    - Maternal infection in 1st trimester results in fetal infection 90-100%
    - Maternal infection in 2nd trimester results in 10-20% fetal infection
    - After 30 weeks gestation infection rate rises to 60%
  - Pathogenesis of fetal anomalies due to a generalized necrotizing vasculitis produced by the virus which causes hypoplasia of multiple organs
    - Earlier occurrence=more organ system involvement
  - Attack rates in closed communities (dorms, barracks, etc) 75-90%; households~100%

PERTUSSIS (WHOOPING COUGH)

- Acute respiratory tract infection by *Bordetella pertussis*
  - highly communicable
  - 80% secondary attack rates among susceptible persons
- Significant morbidity and mortality in infants
- Milder nonspecific upper respiratory tract infection in adolescents and adults
- Difficult to diagnose
  - Multiple studies have shown that 20-25% of all cough illnesses lasting > 14 days without improvement are pertussis
- Referred to by the Chinese as “the cough of 100 days”

PEDIATRICS

Pediatrics 2005;115;1422-1427

The Epidemiology of Pertussis

James D. Cherry, MD, MSc

ABSTRACT. In the prevaccine era pertussis epidemics followed a cyclic pattern, with peaks every 2 to 5 years. With the marked reduction of pertussis by vaccination, the same cyclic pattern still occurs. Studies relating to reported pertussis and *Bordetella pertussis* infection have been reviewed and analyzed. The increase in reported pertussis over the last 2 decades is mainly due to a greater awareness of pertussis and perhaps to the use of several less efficacious vaccines.

Studies of prolonged cough illnesses in adolescents and adults reveal that 13% to 20% are a result of *B pertussis* infection. Serologic studies suggest that the rate of *B pertussis* infection in adolescents and adults is ~2.0% per year. The rate of cough illnesses (pertussis) caused by *B pertussis* infection in adolescents and adults

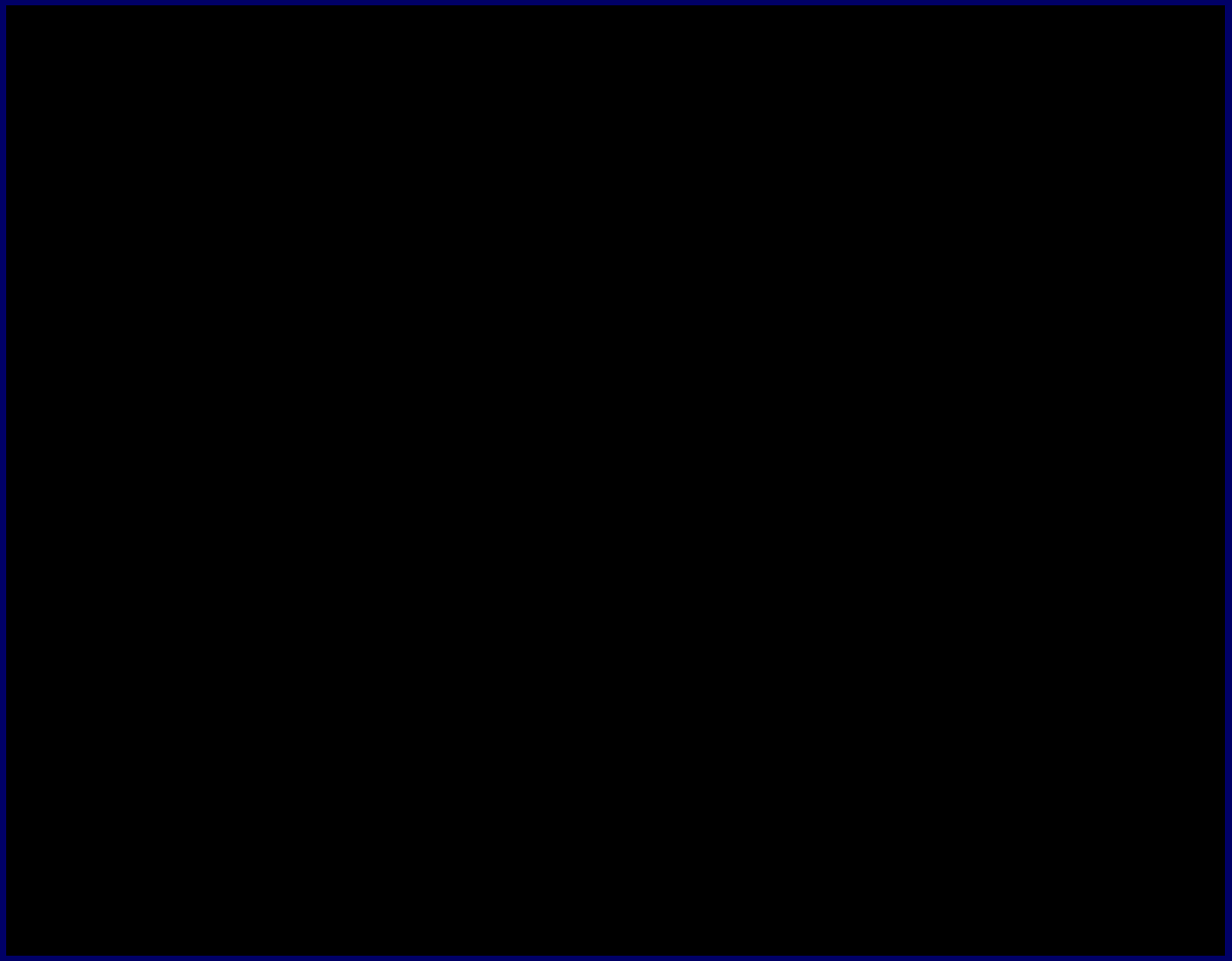
is between 370 and 1500 per 100 000 population. These data suggest that there are between ~800 000 and 3.3 million cases per year in the United States.

The coming availability of adolescent- and adult-formulated diphtheria and tetanus toxoids and acellular pertussis vaccines for adolescents and adults and their widespread use should reduce the reservoir of *B pertussis* disease. It is suggested that a universal program of adolescent and adult boosters would decrease the circulation of *B pertussis* in these age groups and possibly could lead to the elimination of the organism from the population. *Pediatrics* 2005;115:1422–1427; *pertussis, Bordetella pertussis, adult pertussis, adolescent pertussis, pertussis, epidemiology.*

…there are between ~800,000 and 3.3 million cases per year in the United States.

Pertussis: Clinical Presentation in Children

Pertussis: Clinical Presentation in Adults



Complications of Pertussis Among 12,174 Children ≤12 Months of Age (2000-2004)

Complication	Number	Percent of cases*
Hospitalization	6114	62.8
Apnea	5454	55.8
Pneumonia	1063	12.7
Seizures	146	1.5
Deaths	92	0.8

*Percentages are based on total number of cases for which information was available.

Reference:

1. CDC. *MMWR.* 2006;55(RR-17):5.

Advisory Committee on Immunization Practices (ACIP) and the AAP and the AAFP Recommendations for Use of Tdap in Adolescents

- All adolescents 11-18 years of age should receive a single booster dose of Tdap instead of Td
- Preferred age for Tdap vaccination is 11-12 years of age
- Adolescents 11-18 who already received Td should receive Tdap regardless of their Td interval
- There is no longer any minimal interval required relative to previous Td dose
- Administer Tdap simultaneously with the Meningococcal Conjugate Vaccine and the Human Papilloma Virus Vaccine
- Wound management: Tdap preferred over Td

ACIP Recommendations for Use of Tdap in Adults

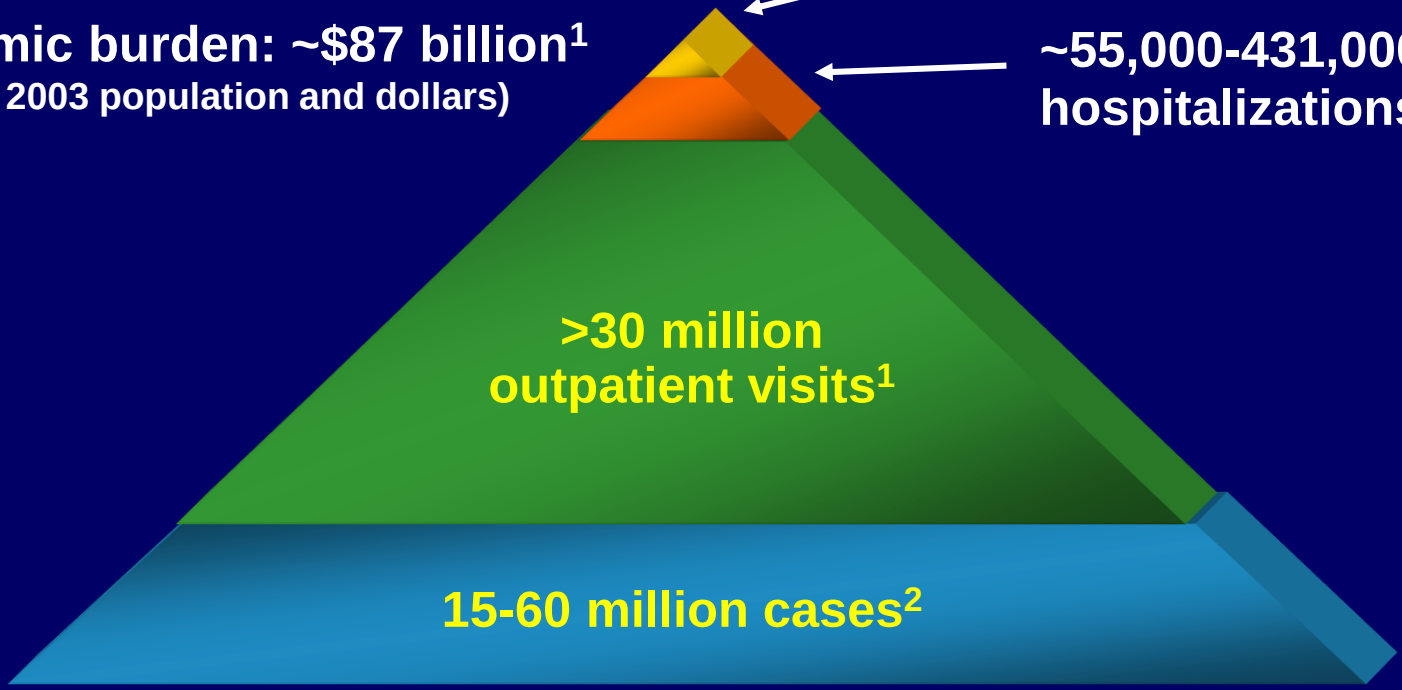
- Routine recommendation for adults 19-64 years of age as well as recommended for adults who are 65 and older:
  - Remember no minimum interval exists relative to previous Td dosing
- Prevention of pertussis among infants <12 months of age:
  - Adults who anticipate having close contact with infants (eg, parents, child-care and health-care givers) should receive Tdap at least 2 weeks before beginning contact
- Other recommendations:
  - Adults who require tetanus vaccination as part of wound management should receive Tdap over Td
  - Regardless of age HCP's should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap

ACIP Recommendations for Use of Tdap During or After Pregnancy

- Routine postpartum administration of Tdap
  - To women who have not previously received it prior to being discharged from the hospital or birthing center
  - There is no longer a minimum interval from last Td
- Pregnant women
  - ACIP states Tdap should be given to pregnant women during each pregnancy preferably at 27 – 36 weeks gestation. No evidence of teratogenicity and the safety profile is similar to Td
  - Plan is to provide a “cocooning” effect for the newborn

Influenza in the US : Annual Impact

- Annual direct medical costs: $10.4 billion[1]
- Lost earnings: $16.4 billion[1]
- Total economic burden: ~$87 billion[1]
  (estimated using 2003 population and dollars)



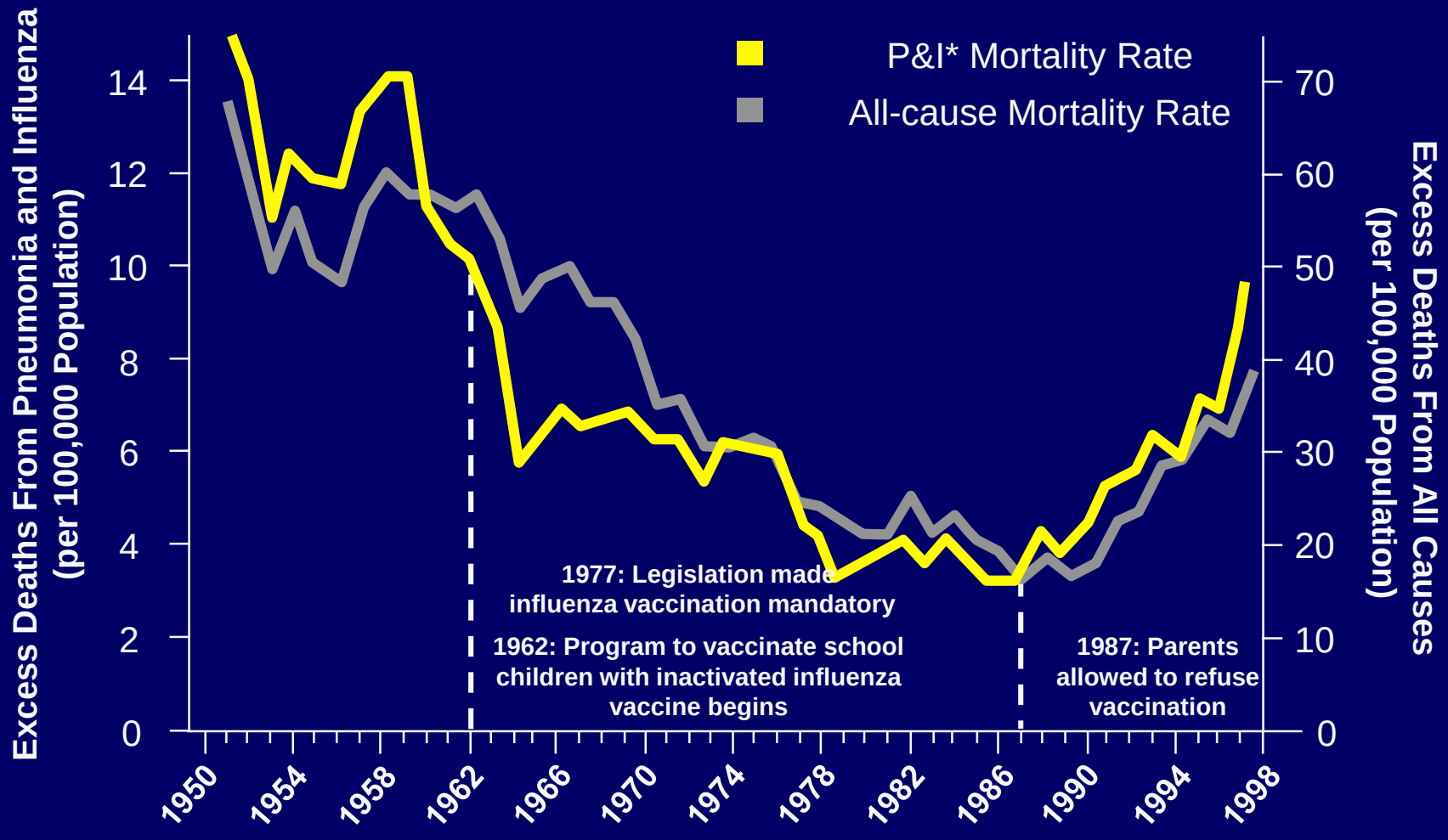
References: 1. Molinari NM, et al. *Vaccine*. 2007;25(27):5086-5096. **2.** CDC. Seasonal influenza: questions & answers. http://www.cdc.gov/flu/about/qa/disease.htm. Accessed August 26, 2013. **3.** CDC. *MMWR*. 2010;59(33):1057-1062. **4.** CDC. *MMWR*. 2010;59(RR-8):1-62. **5.** Thompson WW, et al. *JAMA*. 2004;292(11):1333-1340.

Children Play a Significant Role in Spreading Influenza

- Influenza attack rates are highest in children
- Children adhere less to cough-and-sneeze etiquette
- Children shed influenza longer than adults
  - Children may be infectious for more than 10 days
  - Young children may shed virus (type A virus) for up to 8 days prior to appearance of symptoms

1. Glezen WP, et al. *Pediatr Infect Dis J.* 1997;16:1065-1068.
2. CDC. *MMWR*. 2008;57(RR-7):1-60.
3. Frank AL, et al. *J Infect Dis.* 1981;144:433-441.

Influenza Vaccination Program for School Children in Japan Using the Flu Shot



*P&I=pneumonia and influenza.

Reichert TA, et al. *N Engl J Med.* 2001;344:889-896.

The 4 Clinically Important Influenza Viruses

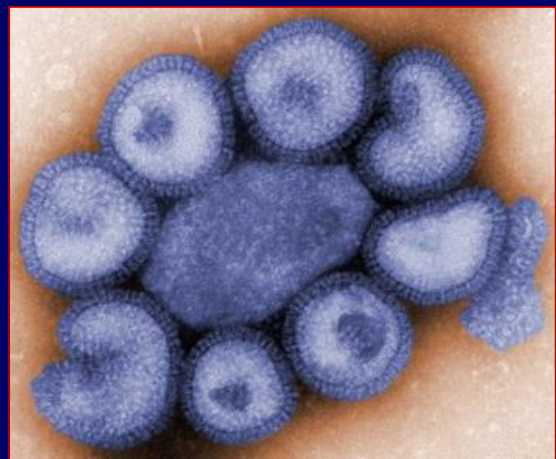
2 influenza A strains

- Categorized into subtypes on the basis of 2 surface antigens, hemagglutinin (HA) and neuraminidase (NA)
- Large reservoir in domestic animals, resulting in frequent antigenic change
- A(H1N1) and A(H3N2) circulate globally and are the most important subtypes when it comes to human infections

2 influenza B strains

- 2 distinct genetic lineages : Yamagata and Victoria
- Largely limited to humans
- Both B Yamagata and B Victoria have co-circulated globally for more than a decade

CDC/Dr. F.A. Murphy.

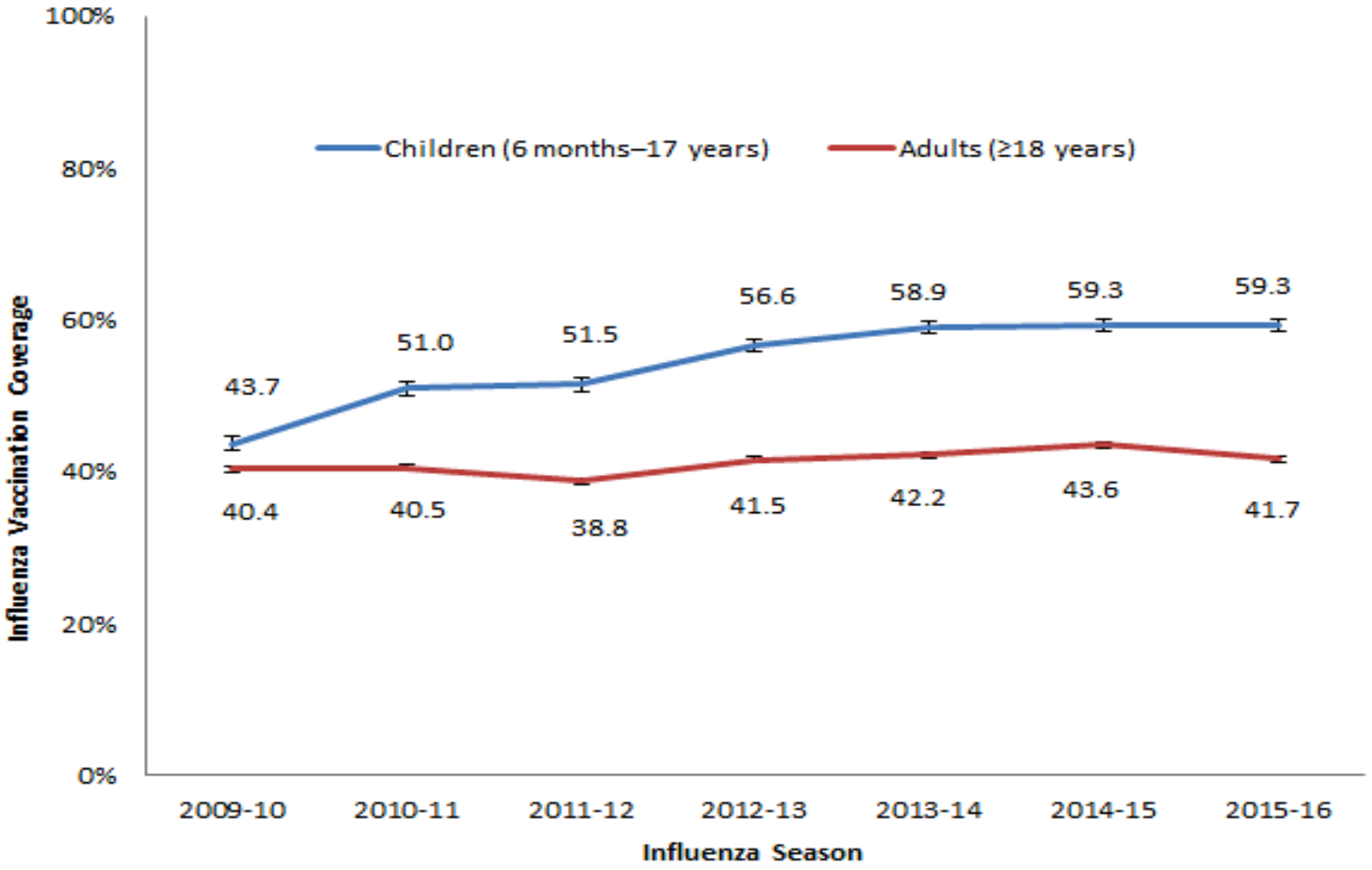


References: **1.** CDC. *MMWR.* 2010;59(RR-8):1-62. **2.** Belshe RB. *Vaccine.* 2010;28(Suppl 4):D45-D53. **3.** Li W-C, et al. *J Clin Virol.* 2008;42(1):45-51.

Influenza Vaccine Recommendations

- Annual Influenza vaccination is routinely recommended by the ACIP for all people 6 months of age and older
- If under 9 years of age and vaccine naïve then should receive 2 doses 4-8 weeks apart
- Multiple influenza vaccines exist with different age recommendations and precautions (IIV and LAIV)
  - A cell-culture based and egg free alternative was approved in May, 2016 for ages 4 and older but people with egg allergies are allowed to receive any licensed, recommended, age-appropriate influenza vaccine
  - LAIV was not recommended for use the past 2 seasons
- Most are quadrivalent but some are still trivalent

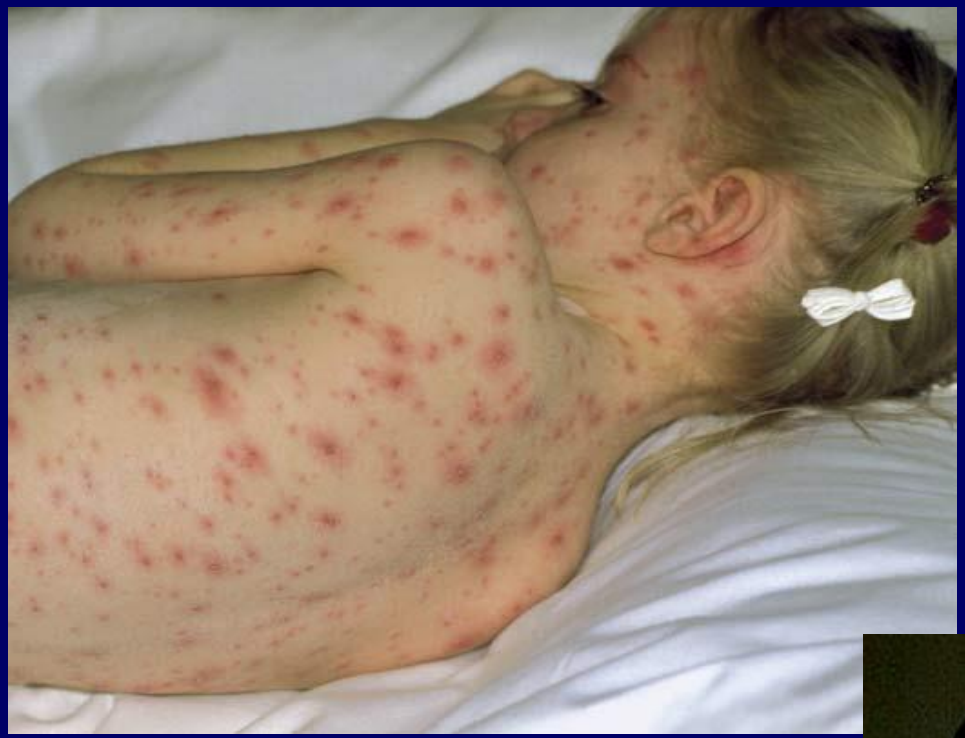
Figure 1. Seasonal Flu Vaccination Coverage by Age Group and Season, United States, 2009–2016

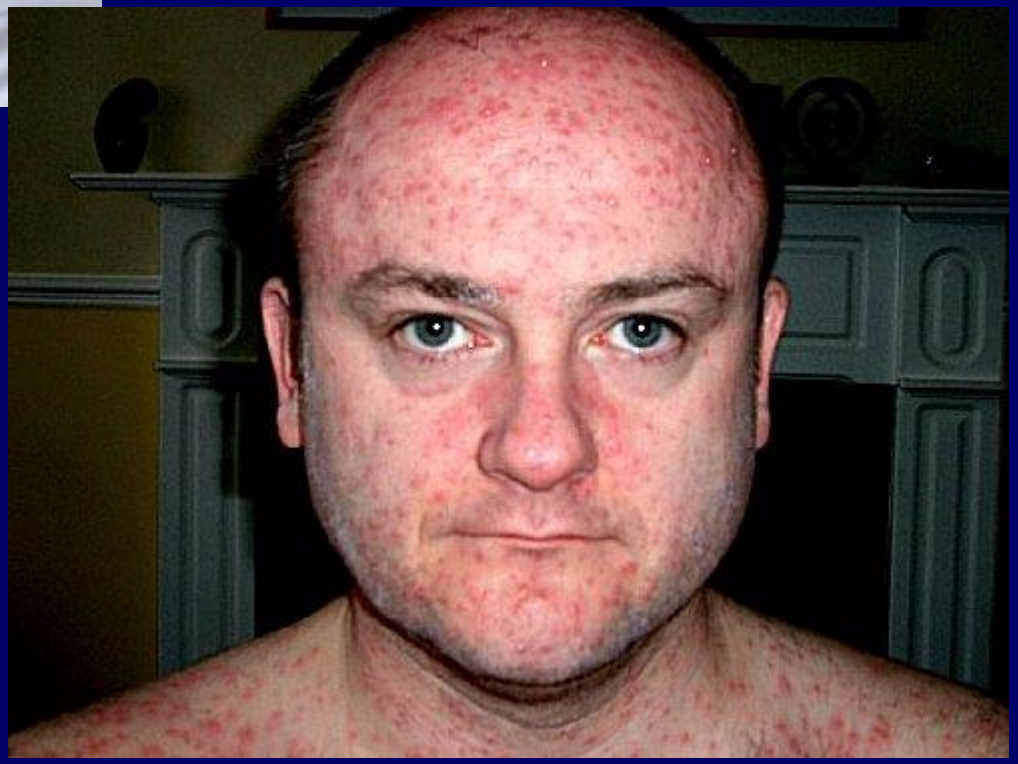


Error bars represent 95% confidence intervals around the estimates.
The 2009-10 estimates do not include the influenza A (H1N1) pdm09 monovalent vaccine.
Starting with the 2011-12 season, adult estimates reflect changes in BRFSS survey methods: the addition of cellular telephone samples and a new weighting method.

ACIP VARICELLA VACCINE RECOMMENDATIONS

- Recommended for all ages 12 months and older
- First dose recommended at 12 months
- Second dose recommended at age 4-6 years
- Administer 2 doses of Varicella vaccine to persons younger than 13 years of age at least 3 months apart who have no Varicella vaccine history and no medical documentation of Varicella disease
- Administer 2 doses of Varicella vaccine to persons 13 years or older at least 4 weeks apart who have no Varicella vaccine history and no medical documentation of Varicella disease





Meningococcal Disease

- Historically, 800-2800 cases per year in the United States
  - Fewer in recent years: ~800-1200 per year during 2006-2010 (~100-200 cases per year are serogroup B)
  - More than 95% of cases are sporadic; fewer than 5% are related to outbreaks
- Case-fatality rate of 9%-12%
  - Up to 40% for meningococcemia
- Significant sequelae in 11%-19% of survivors
  - Amputation, hearing loss, neurologic or cognitive deficits

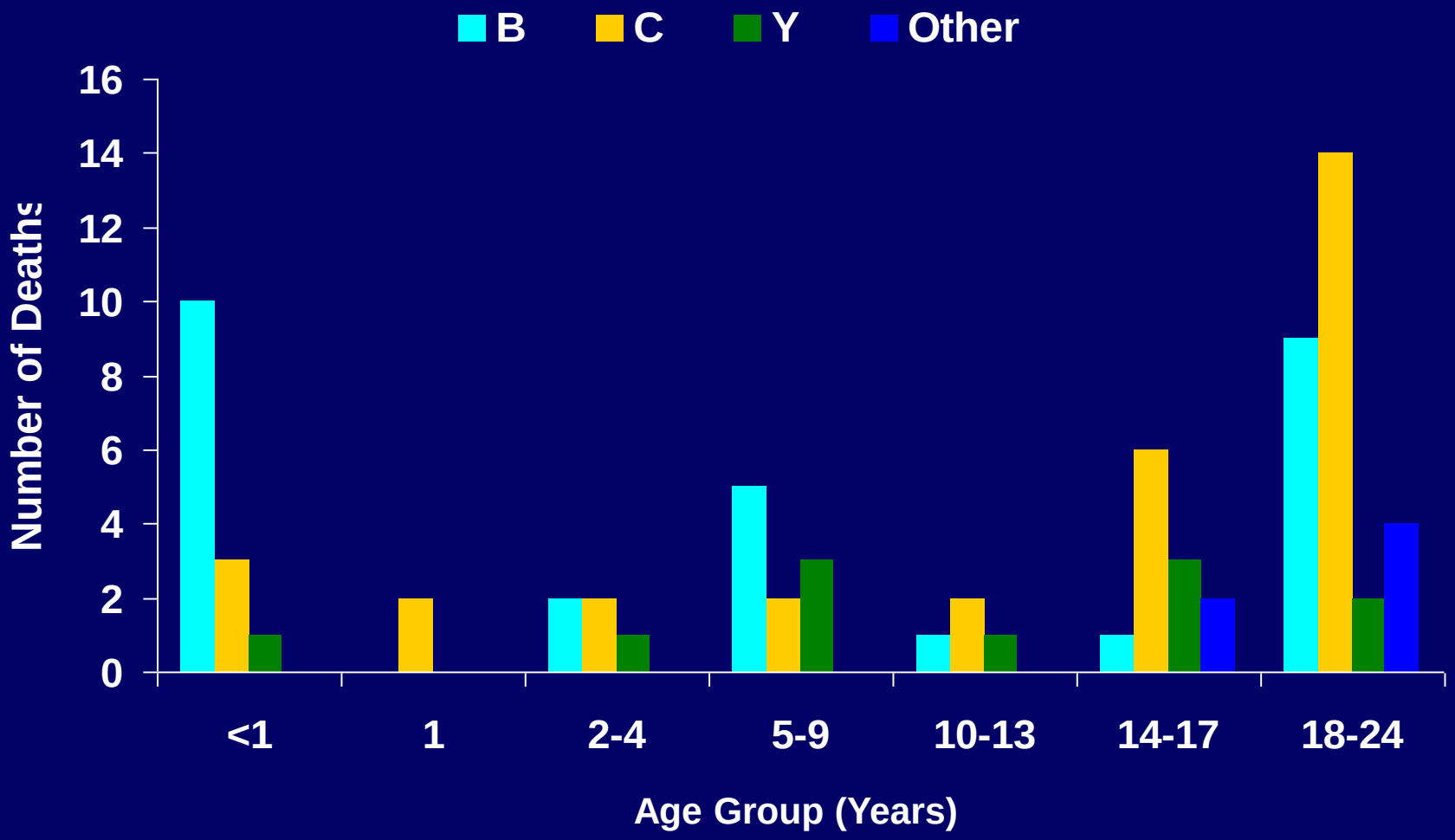
References: **1.** CDC. Meningococcal disease. In: *Epidemiology and Prevention of Vaccine-preventable Diseases. (The Pink Book).* Atkinson W, Wolfe S, Hamborsky J, eds. 12th ed. Washington, DC: Public Health Foundation, 2011:193-204. **2.** CDC. *MMWR.* 2011;60(32):1088-1101. **3.** Rosenstein N, et al. *N Engl J Med*. 2001;344(18):1378-1388.

Clinically Significant *N meningitidis* Serogroups

Serogroup	Characteristics
A	• Leading cause of epidemic meningitis worldwide • Most prevalent serogroup in Africa and China • Rare in Europe and the Americas
B	• A major cause of endemic disease in Europe and the Americas • Two vaccines recently licensed in the US
C	• A major cause of endemic disease in Europe, North America • Multiple outbreaks in schools and/or community
Y	• Associated with pneumonia • Increasing problem in the United States, affecting all age groups
W-135	• Small percentage of infections worldwide • Recent outbreaks associated with hajj pilgrims

Reference: Granoff DM, et al. Meningococcal vaccines. In: Plotkin SA, et al, eds. *Vaccines*. 5th ed. Philadelphia, PA: Saunders Elsevier, 2008:399-434.

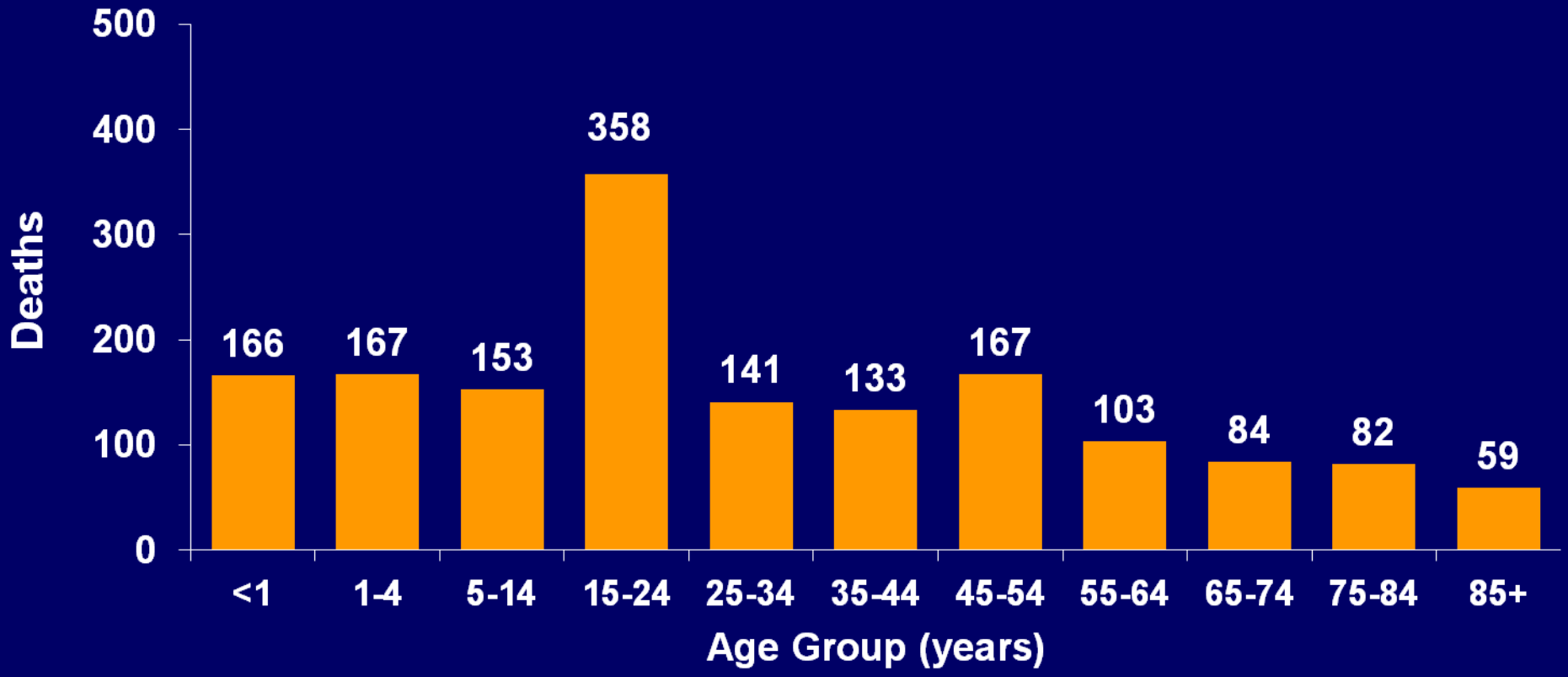
Annual US Deaths from Meningococcal Disease, 0-24 Years of Age, All Serogroups, 1998-2007



Reference: 1. Cohn AC, et al, CDC. *Clin Infect Dis.* 2010;50(2):184-191.

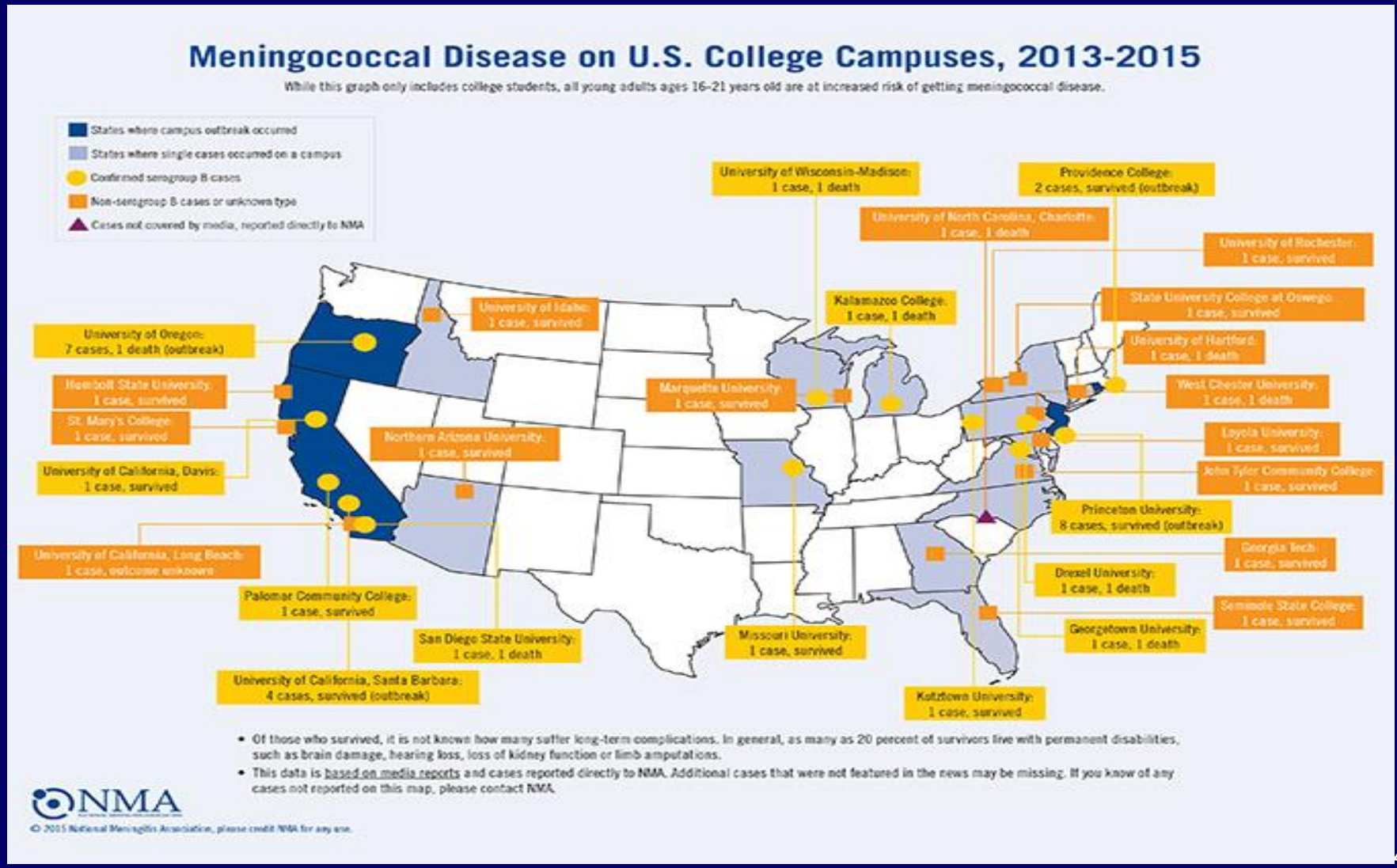
Age-specific Fatalities From Meningococcal Disease

United States, 1999-2009



References: **1.** Hoyert DL, et al. *Natl Vital Stat Rep*. 2001;49(8):1-116. **2.** Miniño AM, et al. *Natl Vital Stat Rep*. 2002;50(15):1-120. **3.** Arias E, et al. *Natl Vital Stat Rep.* 2003;52(3):1-116. **4.** Kochanek KD, et al. *Natl Vital Stat Rep*. 2004;53(5):1-116. **5.** Hoyert DL, et al. *Natl Vital Stat Rep*. 2006;54(13):1-120. **6.** Miniño AM, et al. *Nat Vital Stat Rep*. 2007;55(19):1-120. **7.** Kung H-C, et al. *Natl Vital Stat Rep.* 2008;56(10):1-124. **8.** Heron M, et al. *Natl Vital Stat Rep*. 2009;57(14):1-136. **9.** Xu J, et al. *Natl Vital Stat Rep*. 2010;58(19):1-136. **10.** Miniño AM, et al. *Nat Vital Stat Rep*. 2011;59(10):1-126. **11.** Kochanek KD, et al. *Nat Vital Stat Rep*. 2011;60(3):1-166.

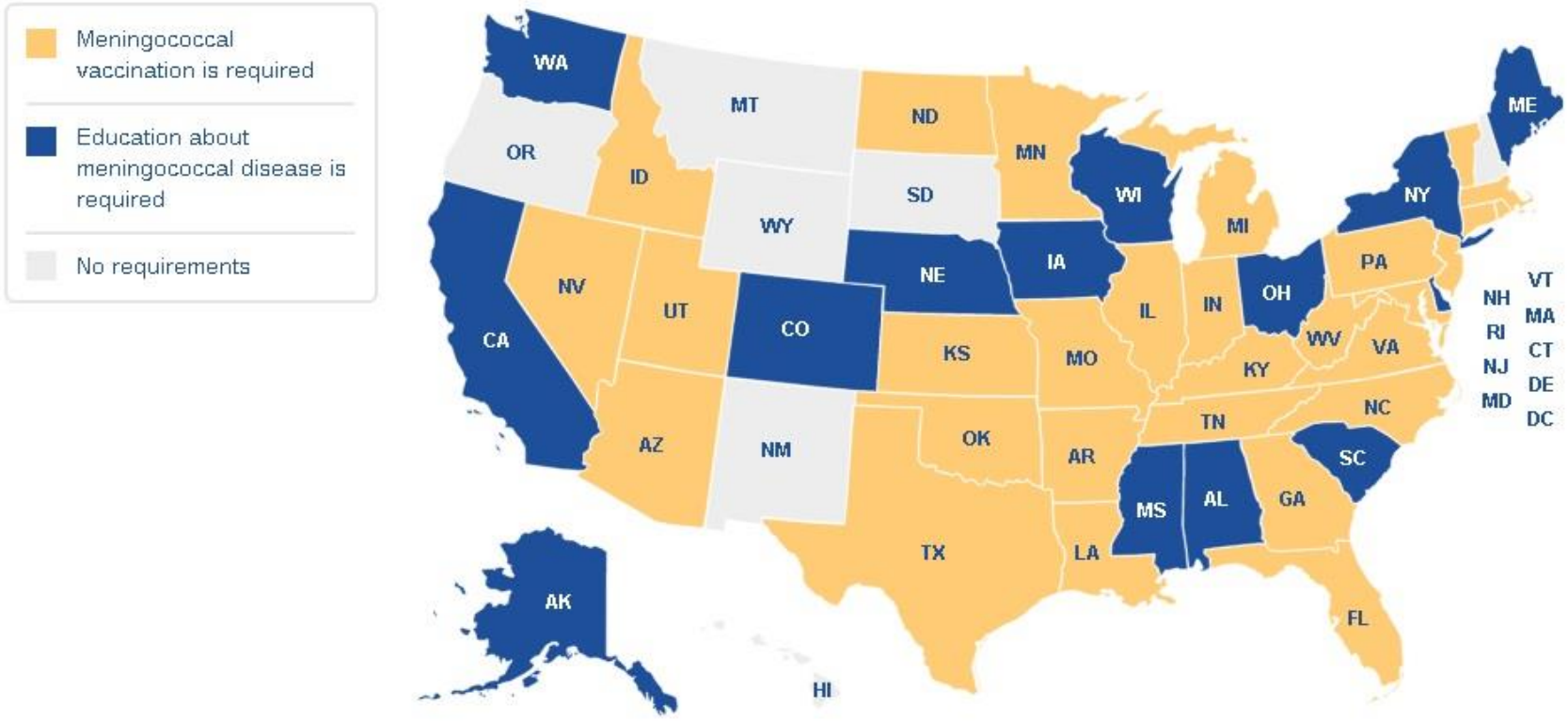
Meningococcal Disease on U.S. College Campuses



Meningococcal Vaccine Requirements by State for College Students

Meningococcal Vaccination Requirements State by State

Note: Most requirements were implemented before serogroup B meningococcal vaccines were available in the U.S. and may only apply to the vaccine that protects against serogroups A,C, W and Y. No matter where you live parents and teens should ask about vaccination against all serogroups (A, C, W, Y and B) of meningococcal disease.



Meningococcal Vaccines Currently Licensed in the United States

- Menomune (Meningococcus Groups A, C, Y, and W-135 Polysaccharide Vaccine)
  - Licensed: 1981, Indicated for Individuals 2 years of age and older
  - Discontinued and no longer available as of mid-2017
- Menactra (Meningococcus Groups A, C, Y, and W-135 Conjugate Vaccine)
  - Licensed: 2005
  - Indicated for Individuals 9 months-55 years of age
- Menveo (Meningococcus Groups A, C, Y and W-135 Conjugate Vaccine)
  - Licensed: 2010
  - Indicated for Individuals 2 months-55 years of age
- MenHibrix (Meningococcal Groups C and Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine)
  - Licensed: 2012, Indicated for Individuals 6 weeks-18 months of age
  - Discontinued and no longer available as of mid-2017
- Trumenba (Meningococcal Serogroup B vaccine) Licensed in 2014
  - Indicated for individuals 10–25 years of age
  - 3-dose series given at 0, 2, and 6 months, 2-dose series given at 0, 6 months
- Bexsero (Meningococcal Serogroup B vaccine) licensed in 2015
  - Indicated for individuals 10-25 years of age
  - 2 dose series with doses given 1-2 months apart

ACIP Recommendations for Use of the Quadrivalent Meningococcal Conjugate Vaccine in Adolescents

- Routine vaccination with quadrivalent meningococcal conjugate vaccine is recommended at 11 or 12 years of age
- A booster dose is also routinely recommended at 16 years of age
  - For adolescents who received the first dose of meningococcal conjugate vaccine at 13-15 years of age, a single booster dose should be administered preferably at 16-18 years of age
  - Persons who receive their first dose of meningococcal conjugate vaccine at or after 16 years of age do not need a booster dose
- Unvaccinated persons 11-18 years of age should be vaccinated at “the earliest possible health-care visit”
- Routine vaccination of healthy persons not at increased risk for exposure to *N meningitidis* is not recommended after 21 years of age

References: CDC. *MMWR*. 2015

ACIP Recommendations: 2-Dose Primary Series for Certain Persons at High Risk

Two doses of the quadrivalent meningococcal conjugate vaccine, 2 months apart, are recommended as a primary series for:

- Persons 2-55 years of age with persistent complement component deficiencies or functional or anatomic asplenia
  - Booster vaccination then needed every 5 years
- Persons infected with human immunodeficiency virus (HIV)
  - For HIV-infected persons 11-18 years of age:
    - Give booster at 16 years of age if primary dose is given at 11-12 years of age
    - Give booster at 16-18 years of age if primary dose is given at 13-15 years of age
    - No booster needed if primary dose is given at ≥16 years of age

Reference: CDC. *MMWR*. 2015

ACIP Recommendations: Vaccination of Persons at "Prolonged Increased Risk"

- Persons 2-55 years of age who are at prolonged increased risk for exposure to *N meningitidis* include:
  - Travelers to or residents of countries where meningococcal disease is hyperendemic or epidemic
  - Microbiologists who routinely work with *N meningitidis*
- These individuals should receive
  - 1 primary dose of meningococcal conjugate vaccine
  - Booster dose if the person remains at increased risk:
    - If 2-6 years of age at primary dose, give booster dose 3 years later
    - If ≥7 years of age at primary dose, give booster dose 5 years later

Reference: CDC. *MMWR. 2015*

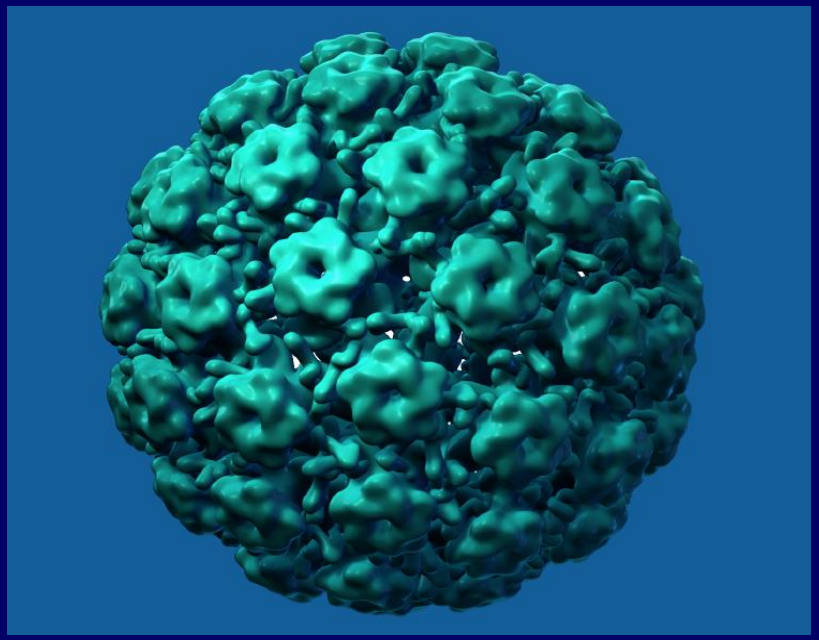
ACIP Recommendations for the Serogroup B Meningococcal Vaccine

- There are 2 serogroup B meningococcal vaccines licensed for use in the United States for adolescents and young adults 10 – 25 years of age
- Although the ACIP states the vaccine may be administered to adolescents and young adults 16-23 years of age the preferred age of use is 16–18 years of age (category B recommendation)
- The routine recommendation (category A) is for certain groups of persons at increased risk, including during outbreaks of serogroup B meningococcal disease
  - This includes college campuses that have experienced outbreaks of serogroup B disease

Reference: CDC.*MMWR*. 2015

Human Papillomavirus (HPV)

Nonenveloped double-stranded DNA virus



- >100 types identified
- 30–40 anogenital
  - 15–20 oncogenic types including 16, 18, 31, 33, 35, 39, 45, 51, 52, 58
    - ✓ HPV 16 and HPV 18 account for the majority of worldwide cervical cancers
  - Nononcogenic types include: 6, 11, 40, 42, 43, 44, 54
    - ✓ HPV 6 and 11 are most often associated with external anogenital warts

1. Howley PM. In: Fields BN, Knipe DM, Howley PM, eds. *Fields Virology.* 4th ed. Philadelphia, Pa: Lippincott-Raven; 2001:2197–2229. Reprinted with the permission of Lippincott-Raven. 2. Schiffman M, Castle PE. *Arch Pathol Lab Med*. 2003;127:930–934. 3. Wiley DJ, Douglas J, Beutner K, et al. *Clin Infect Dis*. 2002;35(suppl 2):S210–S224. 4. Muñoz N, Bosch FX, de Sanjosé S, et al. *N Engl J Med*. 2003;348:518–527. 5. Clifford GM, Smith JS, Aguado T, Franceschi S. *Br J Cancer*. 2003:89;101–105.

HPV Is Widespread

- Approximately 79 million people in the US are currently infected with HPV.
  - ~39,000 new HPV infections occur every day
  - ~14 million new HPV infections occur each year in the United States .
- Most HPV infections clear on their own; however, persistence of certain HPV types can lead to clinically significant diseases.
- For HPV-associated cervical disease, it cannot be reliably predicted which patients with infection or abnormal cytology will progress to clinically significant disease versus spontaneously regress.

1. Centers for Disease Control and Prevention (CDC). Genital HPV infection - CDC fact sheet. cdc.gov/std/hpv/hpv-factsheet-march-2014.pdf. Accessed March 10, 2015. **2.** CDC. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 12th ed. Chapter 10: Human Papillomavirus. cdc.gov/vaccines/pubs/pinkbook/hpv.html. Accessed February 4, 2015. **3.** Woodman CB et al. *Nat Rev Cancer*. 2007;7:11–22. **4.** Satterwhite CL et al. *Sex Transm Dis*. 2013;40(3):187–193.

HPV Transmission

Sexual Routes

- Skin-to-skin contact of genital areas[1]
  - Genital-genital, manual-genital, oral-genital contact[2–4]
  - Nonpenetrating sexual contact; rare[2]
- Through sexual intercourse[5]

Nonsexual Routes

- Self-inoculation from an infected site to a previously uninfected site[6]
- Mother to newborn: vertical transmission; rare[7]
- Fomites (eg, undergarments, surgical gloves, biopsy forceps)[8,9]
  - Hypothesized, but not well documented

HPV=human papillomavirus.

1. Burchell AN et al. *Vaccine*. 2006;24(suppl 3):52–61. **2.** Winer RL et al. *Am J Epidemiol*. 2003;157:218–226. **3.** Fairley CK et al. *Epidemiol Infect*. 1995;115:169–176. **4.** Herrero R et al. *J Natl Cancer Inst*. 2003;95:1772–1783. **5.** Kjaer SK et al. *Cancer Epidemiol Biomarkers Prev*. 2001;10:101–106. **6.** Hernandez BY et al. *Emerg Infect Dis*. 2008;14:888–894. **7.** Smith EM et al. *Sex Transm Dis*. 2004;31:57–62. **8.** Ferenczy A et al. *Obstet Gynecol*. 1989;74:950–954. **9.** Roden RB et al. *J Infect Dis*. 1997;176:1076–1079.

HPV and Cancer: A Broader Picture

Cancer	% Associated With Certain HPV Types
Cervical*	>95%
Vaginal*	~75%
Vulva*	~70%
Penile	~70%
Anal	>90%
Oropharyngeal	>70%
Nonmelanoma skin/cutaneous squamous cell	90%†

*Includes cancer and intraepithelial neoplasia

†Immunocompromised patients

Annual US HPV-related Cancer and Disease Cases Caused by certain HPV Types

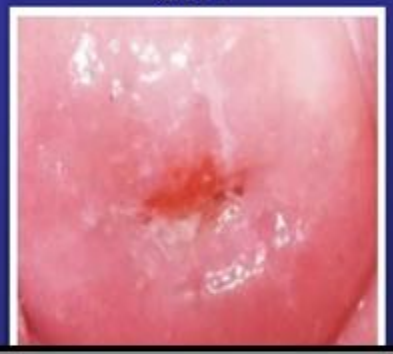
According to estimates for males and females:

- Cervical cancer[1,2] 11,124 cases
- Low-grade cervical lesions[3,4,5] 468,750 cases
- Anal cancer[2,6] 5,386 cases
- High-grade cervical precancers[3,4,5] 216,000 cases
- Vulvar and vaginal cancers[2,7,8] 3,263 cases
- Genital warts[9,10] 324,000 cases

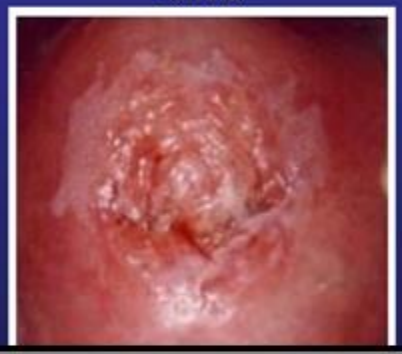
1. de Sanjose S et al. *Lancet Oncol*. 2010;11(11):1048–1056. **2.** American Cancer Society (ACS). *Cancer Facts & Figures 2014*. Atlanta, GA: American Cancer Society; 2014. **3.** Joura EA et al. *Cancer Epidemiol Biomarkers Prev*. 2014;23(10):1997–2008. **4.** Guan P et al. *Int J Cancer*. 2012;131(10):2349–2359. **5.** Centers for Disease Control and Prevention (CDC). Chapter 5: Human Papillomavirus. In: Roush SW, McIntyre L, Baldy LM, eds. *Manual for the Surveillance of Vaccine-Preventable Diseases.* 5th ed. Atlanta, GA: Centers for Disease Control and Prevention; 2012:5-1–5-11. **6.** Alemany L et al. *Int J Cancer*. 2015;136(1):98–107. **7.** de Sanjose S et al. *Eur J Cancer*. 2013;49(16):3450–3461. **8.** Alemany L et al. *Eur J Cancer*. 2014;50(16):2846–2854. **9.** Garland SM et al. *J Infect Dis*. 2009;199(6):805–814. **10.** CDC. Genital HPV infection - CDC fact sheet. cdc.gov/std/hpv/hpv-factsheet-march-2014.pdf. Accessed October 31, 2014.

CIN and Cervical Adenocarcinoma

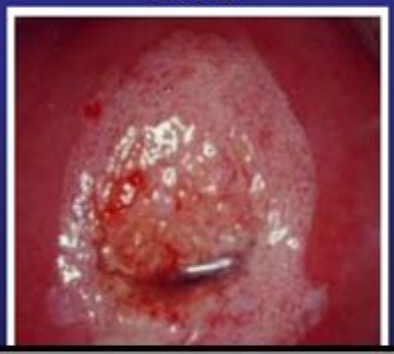
CIN 1



CIN 2

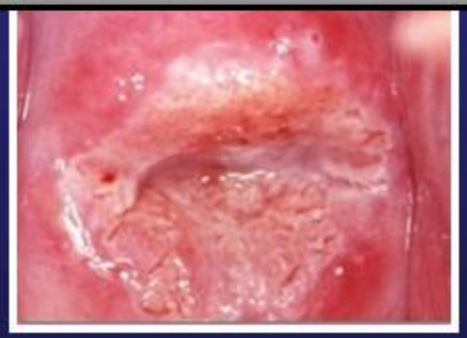


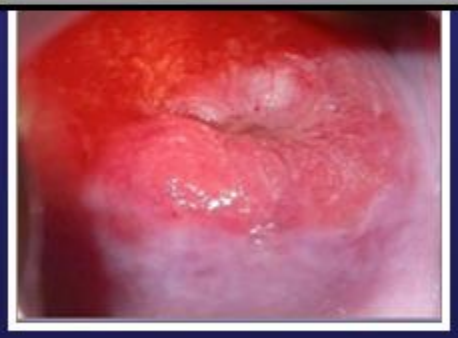
CIN 3



Estimated ~12,200 new cases of cervical cancer in the US in 2012[1]
~75% of cases of cervical cancer are caused by HPV types 16 and 18[2]

Cervical Adenocarcinoma In Situ



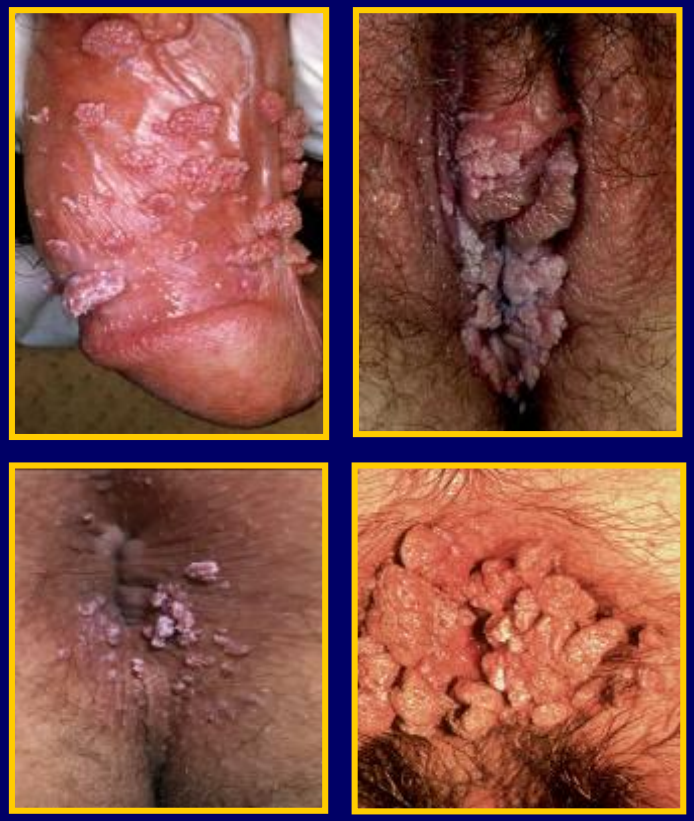


Images reprinted with permission from Sellors J.W. and Sankaranarayanan R. *Colposcopy and Treatment of Cervical Intraepithelial Neoplasia. A Beginner's manual*. Lyon, France, IARC Press, 2003, http://screening.iarc.fr/doc/Colposcopymanual.pdf

CIN = cervical intraepithelial neoplasia; HPV = human papillomavirus.

1. American Cancer Society (ACS) Cancer Facts & Figures 2012. cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-031941.pdf. Accessed January 7, 2013. **2**. Castellsagué X et al, eds. *Vaccine*. 2007;25(Suppl3):C211.

HPV and Anogenital Warts



Images top left and top right: Reprinted with permission from NZ DermNet (www.dermnetnz.org).

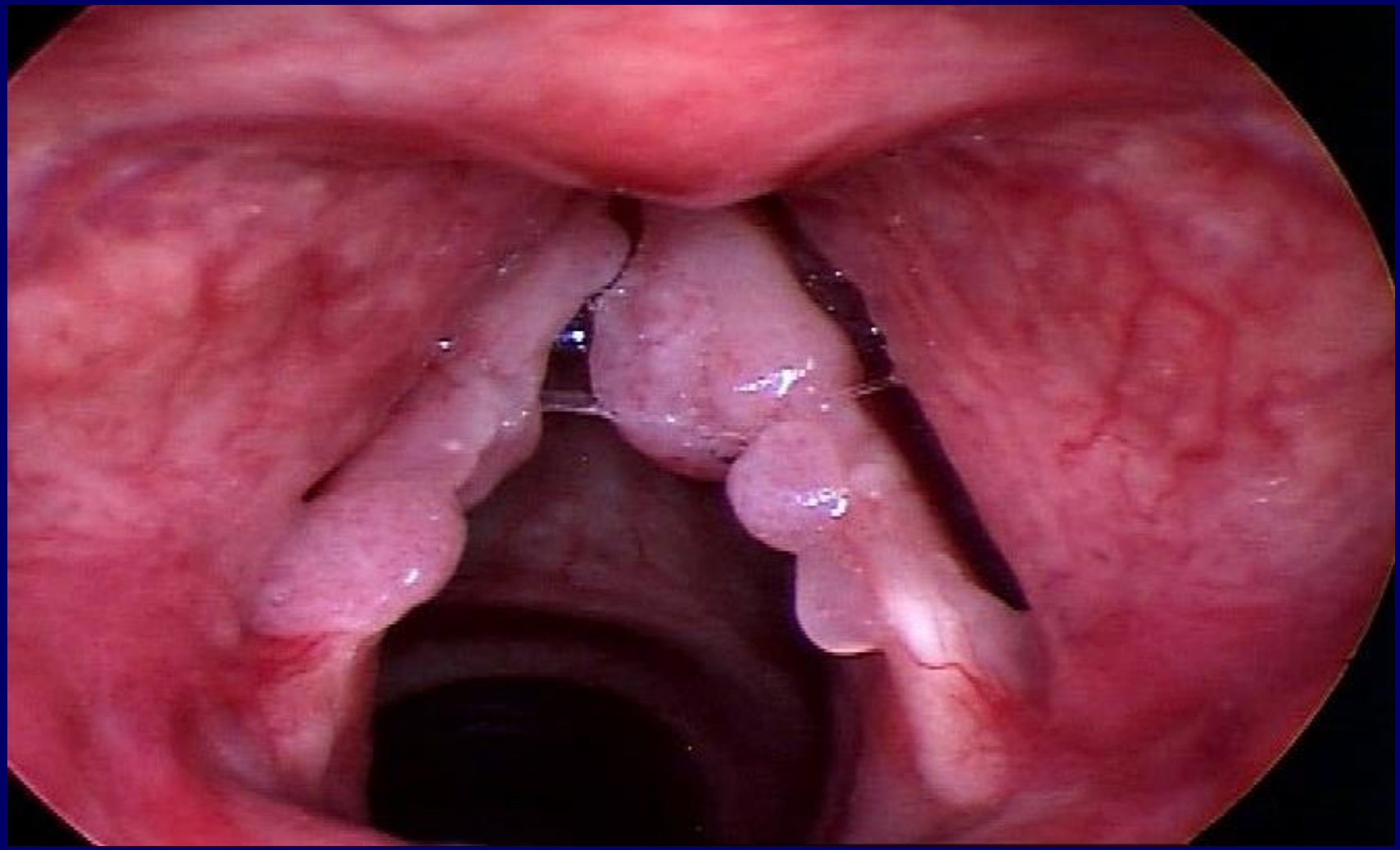
- HPV 6 and 11 responsible for >90% of anogenital warts
- Infectivity >75%
- Up to 30% spontaneously regress within 4 months in women
- Treatment can be painful and embarrassing
- Topical and surgical therapies are available for genital warts
- Recurrence rates vary greatly
  - As low as 5% with podofilox or laser treatment
  - As high as 65% with other treatments

1. Jansen KU, Shaw AR. *Annu Rev Med*. 2004;55:319–331. **2**. Soper DE. In: Berek JS, ed. *Novak's* Gynecology. 13th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2002:453–470. **3**. Lacey CJN. *J Clin Virol*. 2005;32(suppl):S82–S90. **4**. Maw RD, Reitano M, Roy M. *Int J STD AIDS.* 1998;9:571–578. **5**. Kodner CM, Nasraty S. *Am Fam Physician.* 2004;70:2335–2342.

Recurrent Respiratory Papillomatosis

- Caused by HPV types 6 and 11
- ~20,000 active cases in the US with fewer than 2,000 children developing RRP each year
- RRP in children results from vertical transmission of HPV from mother to child during vaginal delivery particularly in mothers with active condyloma
- Characterized by growth of tumors (papillomas) in the larynx, trachea, and bronchi
- Surgery is the primary method of removing the tumors but they have a tendency to return unpredictably

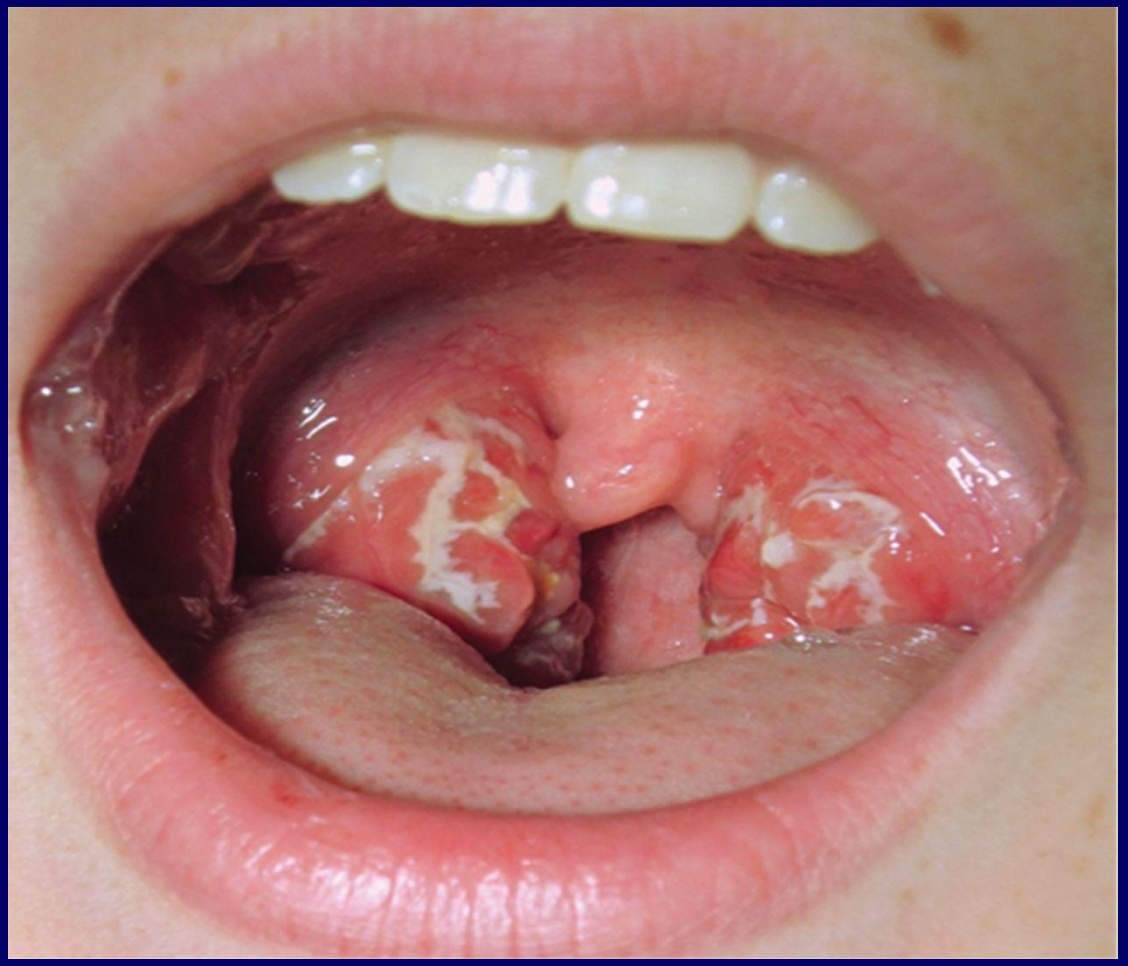
Recurrent Respiratory Papillomatosis



HPV-Related Oropharyngeal Cancers

- >12,000 cases in the US each year of which ~9,000 are attributable to HPV
- HPV type 16 is responsible for the majority of HPV-related oropharyngeal cancers
- Males account for 80% of the cases
- Primarily occurs in the posterior regions of the pharynx such as the base of the tongue, back of the throat, the tonsils, the tonsillar crypts, and the tonsillar pillars
- Treatment may include surgery, radiotherapy, and chemotherapy

HPV-Related Oropharyngeal Cancers



HPV Vaccines

- Quadrivalent HPV vaccine (licensed 2006)
  - Protects against HPV serotypes 6, 11, 16, 18
  - Indicated for females and males 9-26 years of age
- Bivalent HPV vaccine (licensed 2009)
  - Protects against serotypes 16 and 18
  - Only indicated for females 9-25 years of age
  - Not commercially available in the United States as of October 2016
- Nonavalent HPV vaccine (licensed 2014)
  - Protects against serotypes 6, 11, 16, 18, 31, 33, 45, 52, and 58
  - Indicated for females and males 9-26 years of age

9-Valent Human Papillomavirus Vaccine

- Approved by the FDA in December 2014
- Covers HPV types 6, 11, 16, 18, 31, 33, 45, 52, 58
- Currently approved for females 9 – 26 years of age for the prevention of cervical, vaginal, vulvar, and anal cancers as well as cervical, vaginal, vulvar, and anal pre-cancerous or dysplastic lesions and genital warts caused by the 9 HPV types
- Currently approved for males 9 – 26 years of age for the prevention of anal cancer and anal precancerous or dysplastic lesions and genital warts caused by the 9 HPV types

9–Valent HPV Vaccine (Continued)

- By adding the 5 additional HPV types coverage against specific HPV diseases increases to:
  - Approximately 90% of cervical cancer cases
  - Approximately 80% of high-grade cervical lesions
  - Approximately 50% of low-grade cervical lesions
  - 85-90% of HPV-related vulvar cancers
  - 80-85% of HPV-related vaginal cancers
  - 90-95% of HPV-related anal cancers
- HPV types 6 and 11 cause approximately 90% of genital wart cases

New HPV Vaccine Schedule Recommendations

- In October 2016 the Advisory Committee on Immunization Practices voted to recommend a 2-dose HPV vaccine schedule for pre-teens and teens who start the vaccination series before their 15th birthday
  - The 2 doses should be separated by 6-12 months
  - The minimum interval between doses is 5 months
- A 3-dose schedule (0, 2, 6 months) continues to be recommended for people who start the series on or after their 15th birthday
- The 3-dose schedule (0, 2, 6 months) also continues to be recommended for people with certain immunocompromising conditions including HIV Infection

Advisory Committee on Immunization Practices (ACIP) October, 2016

Question

- The CDC's ACIP recommends routine vaccination with HPV vaccine for which age groups?

A. 11 - 12 year old girls and boys
B. 9 - 26 year old males and females
C. 9 - 15 year old males and females

CDC=Centers for Disease Control and Prevention; ACIP=Advisory Committee on Immunization Practices.

1. CDC. *MMWR Recomm Rep*. 2015;64(11):300–304.

ACIP Recommendation: Routine HPV Vaccination

Males: HPV Vaccination with HPV4 or HPV9

Routine: 11- or 12-year-olds

Females: HPV Vaccination with HPV2, HPV4, or HPV9

Routine: 11- or 12-year-olds

- Males and females: Vaccination series can be started at age 9 years

ACIP=Advisory Committee on Immunization Practices; HPV=human papillomavirus; HPV2=bivalent HPV vaccine; HPV4=quadrivalent vaccine; HPV9=9-valent HPV vaccine.

[a]For complete ACIP recommendations on HPV vaccination, please see the *MMWR.*

1. Centers for Disease Control and Prevention (CDC). *MMWR Recomm Rep*. 2015;64(11):300–304.

Further Support For The ACIP HPV Vaccine Recommendations

Recommendations[a]	ACOG[1]	AAFP[2,3]	ACP[2,3]	AAP[2,3]	SAHM[4]
Age 9–10 years can be vaccinated	✓	✓	✓	✓	✓
Routine vaccination for age 11 or 12 years	✓	✓	✓	✓	✓
Catch-up vaccination for age 13–26 years	✓	✓	✓	✓	✓

[a]It is recommended that patients receive 3 doses of the HPV vaccine.

AAFP = American Academy of Family Physicians; AAP = American Academy of Pediatrics; ACIP = Advisory Committee on Immunization Practices; ACOG = American College of Obstetricians and Gynecologists; ACP = American College of Physicians; HPV = human papillomavirus; SAHM = Society for Adolescent Health and Medicine.

1. American College of Obstetricians and Gynecologists (ACOG). *Obstet Gynecol.* 2010;116:800–803. **2.** Centers for Disease Control and Prevention (CDC). cdc.gov/vaccines/schedules/downloads/adult/adult-schedule.pdf. Accessed January 8, 2013. **3.** CDC. cdc.gov/vaccines/schedules/downloads/child/7-18yrs-schedule-pr.pdf Accessed January 8, 2013. **4.** Middleman AB et al. *J Adolesc Health.* 2006;38:321–327.

A Rationale For Making HPV Vaccination Routine For 11 – 12 Years and Younger

- The immune response to the HPV vaccine has been well demonstrated to be more robust (significantly higher post-vaccination antibody titers) in 9-14 year olds compared to 15-26 year olds
- Preventive care visits decline significantly after age 14 making series completion of the HPV vaccine far more difficult compared to 11-12 year olds who come in for recommended preventive healthcare visits
- Data suggests minimal exposure to HPV at 11-12 years of age and younger
  - The most effective time to vaccinate is prior to exposure

Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep. 2014;63(RR-5):1-30

Additional recent information on the HPV vaccine

- Review of 20 studies in 9 high income countries
  - In countries with >50% coverage, among 13-19 year old
  - HPV 16/18 prevalence decreased at least 68% Anogenital warts decreased by ~61%
  - Evidence of herd effects
  - Some evidence of cross protection against other types
- Studies suggest that vaccine protection is long-lasting
  - No evidence of waning protection
  - Available evidence indicates protection for at least 10 years
  - Multiple studies are in progress to monitor
- HPV Vaccine is SAFE
  - Benefits far outweigh any potential risks
  - Safety studies findings for HPV vaccination are reassuring and similar to MenACWY and Tdap vaccine safety reviews

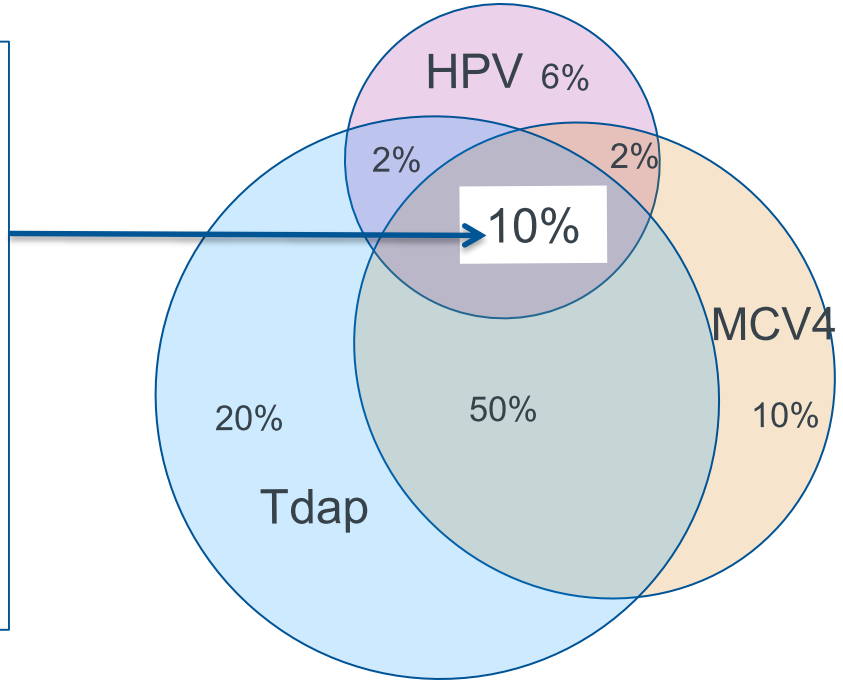
Question

- Are you recommending HPV, Tdap, and MCV4 vaccines to all 11–12 year old males and females at the same visit?

HPV=human papillomavirus; Tdap=Tetanus, Diphtheria and Pertussis vaccine; MCV4=Meningococcal Conjugate Vaccine.

Well-Child Visits are Underutilized for Administration of HPV Vaccine

Although ACIP recommends that eligible preteens ages 11 or 12 years receive recommended adolescent vaccines at a single visit,[1,2] **only 10%** received Tdap, MCV4, and HPV during a single visit, based on Commercial Claims database[3]

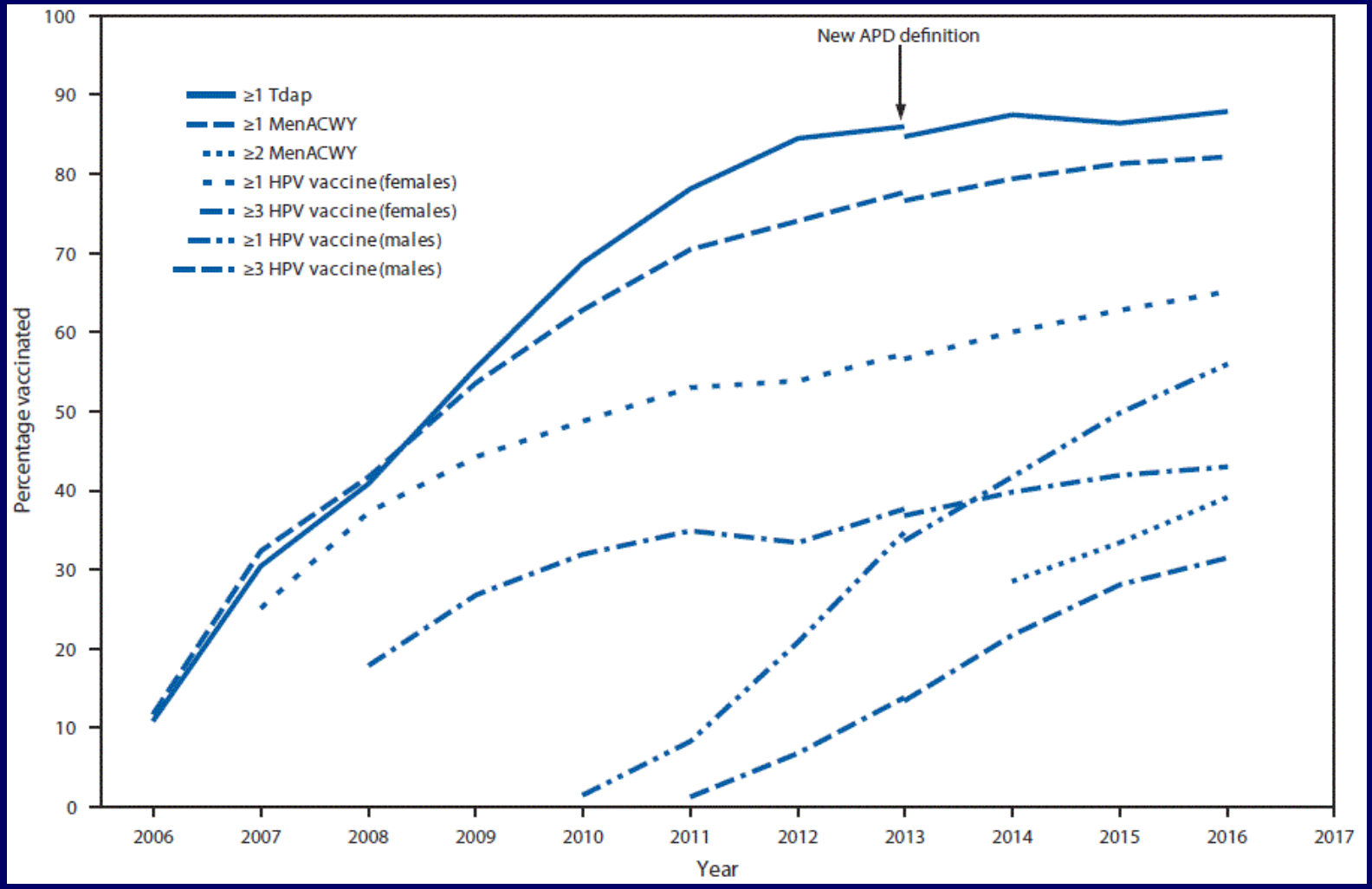


HPV=human papillomavirus; ACIP=Advisory Committee on Immunization Practices; MCV4=Meningococcal Conjugate Vaccine; Tdap=Tetanus, Diphtheria and Pertussis vaccine.

[a]Study of 1,245,336 eligible preteens aged 11–12 years who were continuously enrolled in Truven Health® MarketScan® Commercial Claims and Encounters Database between January 2010 and December 2014 who had at least 1 vaccination visit for any of the 3 recommended vaccines during the study period.[3]

1. Centers for Disease Control and Prevention (CDC). cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf. Accessed February 26, 2015. **2.** CDC. *MMWR Morb Mortal Wkly Rep*. 2014;66(29):620–633. **3.** Borse NN et al. Missed Opportunities to Adhere to the ACIP Vaccine Initiation Schedule Among Privately Insured Preteens in the United States, 2010–2012. Poster presented at: IDWeek 2014; 2014 October 8–12; Philadelphia, PA.

Estimated US Vaccine Coverage Among Adolescents 13-17 Years



Top 5 Reasons Why Primary Care Physicians Do Not Discuss HPV Vaccination

- I know the patient is not yet sexually active
- I don't have enough time to discuss it
- I think the patient is too young
- The patient is already getting other vaccines at that visit
- I expect the parents to refuse

Allison MA, Hurley LP, Markowitz L, et al. Primary Care Physicians' Perspectives About HPV Vaccine. Pediatrics.2016;137(2):e20152488

2013 NIS-Teen: Top 5 Parental Reasons For Not Vaccinating Adolescents With HPV Vaccine

Top 5 reasons for not vaccinating adolescents with HPV vaccine, NIS-Teen 2013

- Not recommended by HCP or clinician
- Not needed or necessary
- Lack of knowledge
- Not sexually active
- Safety concern/side effects

[a]Analysis limited to parents reporting that they were not likely to seek HPV vaccination for their teen in the next 12 months or were unsure of their HPV vaccination plans.
NIS=National Immunization Survey; HPV=human papillomavirus.

1. Centers for Disease Control and Prevention. *MMWR Morb Mortal Wkly Rep.* 2014;63(29):613–641.

Helping to Improve Overall Vaccination Rates

How to get the vaccine out of the refrigerator and into the patient!

CDC Recommended Strategies to Increase Overall Vaccination Coverage in the US

- Using vaccination prompts available through electronic health records
- Checking local and state immunization information systems to assess vaccination needs at every encounter
- Scheduling appointments for second and third doses before patients leave office after receiving first dose
- Automated reminder-recall systems

CDC=Centers for Disease Control and Prevention.

1. CDC. *MMWR Morb Mortal Wkly Rep*. 2013;62(29):581–595.

Role of the Health Care Provider

- 86% of adults cite their health care provider as a source of health information.[1]
- 88% of parents say that they generally do what their doctor recommends regarding vaccines for their children.[2]

1. Pew Internet. pewinternet.org/Reports/2009/8-The-Social-Life-of-Health-Information.aspx. Accessed January 25, 2011. **2.** Freed GL et al. *Pediatrics*. 2010;125:654–659.

Potential Strategies To Help Improve Overall Immunization Rates

- **Provide clear same-day recommendations**
- Follow the ACIP, AAFP and AAP recommendations
- Consider appropriate opportunities to vaccinate
  - Well and acute visits, sports physicals, etc.
  - Use standing vaccination orders in the office
- Make use of reminder systems to help ensure series completion
- Check local and state immunization information systems to assess vaccination needs at every encounter

WEB SITES FOR ACCURATE VACCINE INFORMATION

• www.cdc.gov/vaccines	The CDC's National Immunization Program
• www.immunize.org	The Immunization Action Coalition
• www.aap.org	The American Academy of Pediatrics
• www.vaccine.chop.edu	The Children's Hospital of Philadelphia Vaccine Education Center
• www.aafp.org	The American Academy of Family Physicians
• www.nih.gov	The National Institute of Health

CONCLUSION

- The impact that vaccines have had on health and disease prevention is enormous
- Vaccines have a long history of proven efficacy and safety in keeping once-common diseases uncommon
- Still, public concern about vaccines is pervasive and fear of vaccines can lead to public harm
- Overall immunization rates are still not where they should be especially in adolescents
- To increase immunization rates Health Care Providers should provide clear recommendations that follow the ACIP guidelines

The decision not to immunize is an active decision to remain susceptible to disease

Questions