Adolescent Immunization: An Update

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 Neither I nor any member of my immediate family have any disclosures relevant to this talk.

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Learning Objectives: At the end of talk you will

- 1) Understand the importance of vaccine preventable diseases in adolescents.
- 2) Identify which vaccines are particularly relevant for adolescents.
- 3) Be able to explain the importance of Meningococcal B vaccine and understand who should receive this vaccine
- 4) Understand some of the controversies surrounding the vaccines commonly used in adolescents



- This 15-year-old is in the office for an ankle injury that occurred during a soccer game
- You last saw him at age 6 when he moved to Washington state
- Mother says he was cared for by someone who "didn't believe in vaccines"
- He has asthma
- What Vaccines is he likely to need?

This 15-year-old is in the office for an ankle injury that occurred during a soccer game. You last saw him at age 6 when he moved to Washington state. Mother says he was cared for by someone who "didn't believe in vaccines". He has asthma. What vaccines does he need?

A. MCV4, HPV, TDAP, and Hep A

• B. TDAP, HPV, Flu, PCN 13, MCV4

• C. MCV4, Men B, Flu, Hep A

• D. MCV4, HPV, Flu, TDAP

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D. MCV4, HPV, Flu, TDAP



ACIP "Highly" Recommended and/or Required vaccines include:

- Tdap
- MCV
- •Influenza
- HPV

Clinical Preventive Services Recommended for Adolescents¹

- Immunizations
 - MCV4
 - Tdap
 - HPV
 - Influenza
 - Pneumococcal^a
 - Hepatitis A^a
 - Men Ba
 - Hepatitis B^b
 - Inactivated poliovirus^b
 - MMRb
 - Varicella^b
 - ^a For certain high-risk groups; ^b If not previously completed.

- Health Guidance
 - Development
 - Nutrition
 - Sexual health
 - Physical activity
 - Injury prevention
 - Dental health
 - Skin protection
 - Self-performed exams(Testicular/breast)

Reference: 1. Broder KR, et al. Pediatrics. 2008;121(suppl 1):S25-S34.

Vaccine-Preventable Diseases are Still a Problem for Adolescents...

Pertussis epidemic in 2014-2015 was driven by substantially increased rates in adolescents

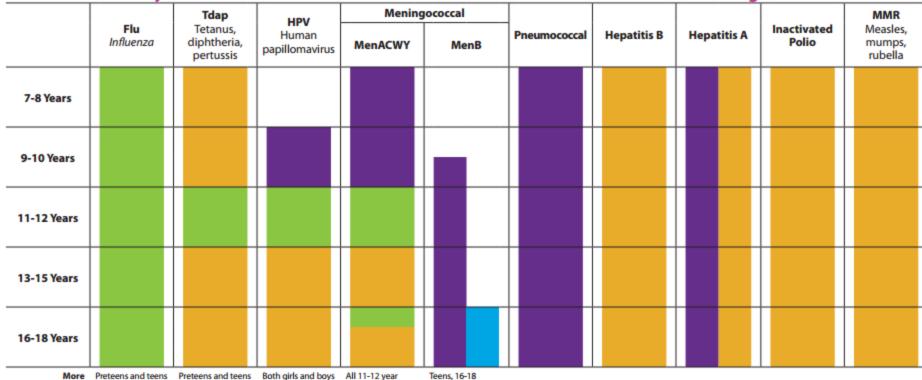
Measles Outbreak in California in 2014-2015 was focused on unvaccinated adolescents and young adults

Seven separate Meningococcal B outbreaks have occurred on college campuses in the past 7 years (2009-2016)

...And More Diseases are now "Vaccine-Preventable"; in the past 10 years ...

- New pertussis vaccine (Tdap) for adolescents
- New conjugate meningococcal vaccine (MenB)
- New human papillomavirus (HPV) vaccine
- New conjugate pneumococcal vaccine

Talk to your child's doctor or nurse about the vaccines recommended for their age.



information:

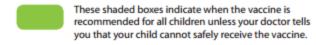
Preteens and teens Preteens and teens should get a flu should get one vaccine every year. shot of Tdap at age 11 or 12 years.

Both girls and boys should receive 3 doses of HPV vaccine to protect against HPVrelated disease. HPV vaccination

age 9 years.

olds should be vaccinated with a single dose of a quadrivalent meningococcal conjugate vaccine can start as early as (MenACWY). A booster shot is recommended at age 16.

Teens, 16-18 years old, may be vaccinated with a MenB vaccine.





These shaded boxes indicate the vaccine should be given if a child is catching-up on missed vaccines.



MCV4, Tdap, and HPV Vaccination— How Are We Doing?

- Healthy People 2020: any new universally recommended vaccine for adolescents should be at a 90% coverage level within 5 years of the recommendation
 - Recommendations published in 2005 for MCV4, 2006 for Tdap, and 2007 for HPV

Immunization	2006 (%) ¹	2009 (%) ²	2012 (%) ³	2014 (%)4
1 dose MCV4	11.7	53.6	74.0	79.3
1 dose Tdap	10.8	55.6	84.6	87.6
≥1 dose HPV	_	44.3	53.8	60.0
(3doses HPV)		(26.7)	(33.4)	(39.7)

References: 1. CDC. *MMWR*. 2007;56(34):885-888. **2.**. CDC. *MMWR*. 2009;58(36):997-1001 **3.** CDC. *MMWR*. 2012; 62(34);685-693. **4.** CDC. *MMWR*.2015; 64 (29)

What's new in terms of the "adolescent vaccines"?

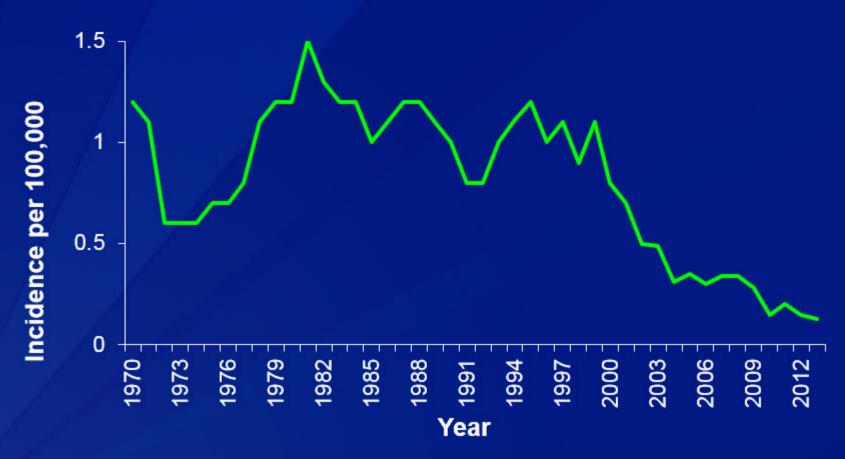
• 1) Meningococcal B vaccine

• 2) A 9-Valent HPV Vaccine

• 3) Waning immunity from TDaP

 4) New recommendation for using Pneumococcal vaccine

Meningococcal Disease Incidence, United States, 1970-2013



SOURCE: CDC. 1970-1996 National Notifiable Diseases Surveillance System, 1997-2013 Active Bacterial Core surveillance estimated to U.S. population

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
В	 A major cause of endemic disease in Europe and the Americas No vaccine commercially available in US
С	 A major cause of endemic disease in Europe, North America Multiple outbreaks in schools/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

Neisseria meningitidis Risk factors for invasive disease

Host factors

- Terminal complement pathway deficiency
- Asplenia
- Genetic risk factors
- Immunosuppression (HIV)

Exposure factors

- Household exposure
- Demographic and socioeconomic factors and crowding
- Concurrent upper respiratory tract infection
- Active and passive smoking
- Living in a dormitory as a first year student!

Estimated Average Annual Cases, Deaths, and Sequelae by Age Group and Serogroup, 2009–2013

	Age Group	Cases ¹	Deaths ²	Sequelae ³
Serogroup B	<5 years	74–94	7-14	7-19
	11-24 years	54–67	5-10	5-13
	All ages	203–260	20-39	20-52
Serogroups C & Y	<5 years	34–43	3-6	3-9
	11-24 years	62–77	6-12	6-15
	All ages	307–393	31-59	31-79

The majority (~80%) of serogroup B cases that occur in 11–24 year
 olds occur in older adolescents and young adults aged 16–24 years

¹Range in estimated cases: Low=NNDSS data supplemented with additional serogroup data from ABCs and state

The Challenge of Creating a Serogroup B vaccine

- Serogroup B bacterial capsule does not induce an immune response because it too closely resembles other human cell proteins.
- Finally isolated isolated protein fragments of the capsule of serogroup B bacteria capable of inducing immunity
- Present on a large enough percentage of B strains to make the vaccine effective for widespread use.
- Caveat: These vaccines appear to be effective against many, but not necessarily ALL strains of Men B.

Two MenB Vaccines For Persons Aged 10–25 Years in the United States

Trumenba ® (Pfizer), 3-dose series (0, 2, 6 months)

- Components: fHbp subfamily A/v2,3; subfamily B/v1
- Licensed in the U.S. on October 29, 2014

Bexsero® (Novartis/GSK), 2-dose series (0, 1–6 months)

- Components: fHbp subfamily B/v1, NhbA, NadA, Por A1.4
- Licensed in the U.S. on January 23, 2015
- Licensed in >30 countries for persons ≥2 months of age

Recent University Based Serogroup B Clusters/Outbreaks†

University	Outbreak Period	Number of c
University 1	Feb – Mar 2009	4
University 2	Nov 2011	2
University 3	Jan 2008 – Nov 2010	13
University 4	Mar 2013 – Mar 2014	9
University 5	Nov 2013	4*
University 6	Jan – Feb 2015	2
University 7	Jan – May 2015	7

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Potential Cases and Deaths Prevented per 4M Cohort

	Cases Prevented	Deaths Prevented	NNV* to prevent case	NNV to prevent death	Cost (\$) per QALY
Series at 11 years	15	2	203,000	1,512,000	\$8.700.000
Series at 16 years	28	5	107,000	788,000	\$4,100,000
Series at 18 years	29	5	102,000	638,000	\$3,700,000
College students	9	1	368,000	2,297,000	\$9,400,000

Considerations for "All Adolescents" Rather Than "College Students Only"

- Approximately 30-60% of serogroup B cases in 18– 23 year olds occur in persons <u>not</u> attending college
- Would be challenging to get students vaccinated with 2-3 doses before arriving on college campuses
- Vaccinating college students would prevent the fewest cases and deaths of options considered
- The Work Group acknowledges the impact that cases and outbreaks have on college campuses
 - Cost for vaccination campaigns
 - Public concern

Challenges when Considering Routine Use of MenB Vaccines in Adolescents

- Proportion of serogroup B cases that could be prevented with MenB vaccines is unknown
 - Breadth of strain coverage estimated; actual breadth of strain coverage unclear
 - Available antibody persistence data suggests limited duration of protection
- Effectiveness data are not available
 - Licensure is based on bactericidal activity
 - Universal programs not implemented in any country to date
- Impact on carriage unknown
- Potential impact of vaccine pressure on circulating strains unknown

Considerations for Timing of Administration of the MenB Series

- Need to administer series in late adolescence in order for protection to last into the highest risk period
 - Concern is that protection may not be long lasting
- Young adults may still be under the care of a pediatrician at 16 years of age, but less likely at 18 years
 - Receive booster at age 16 years for MenACWY
- Majority of work group members prefer administration between 16–18 years
 - For college-bound population, more likely to receive 2–3 doses before entering college and highest age-related risk period

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Guidance for Use

- MenB should be administered as either a 2-dose series of MenB-4C or a 3-dose series of MenB-FHbp
- The same vaccine product should be used for all doses
- Based on available data and expert opinion, MenB-4C and MenB-FHbp may be administered concomitantly with other vaccines indicated for this age, but at a different anatomic site, if feasible

Standard Meningococcal Conjugate Vaccines

- Two licensed meningococcal conjugate vaccines
 - MCV4-D (Menactra®)
 - Licensed for persons 2-55 years
 - Serogroups A, C, Y, W-135
 - Diphtheria toxoid conjugate
 - MenACWY-CRM₁₉₇ (Menveo®)
 - Licensed for persons 2-55 years
 - Serogroups A, C, Y, W-135
 - Diphtheria CRM₁₉₇ conjugate

ACIP Recommendations for Use of Meningococcal Conjugate Vaccine in Adolescents

- Adolescents at their 11- to 12-year health-care visit, with a booster dose at 16 years of age¹
 - If primary dose not given until 13-15 years of age, then booster dose at 16-18 years of age¹
- Adolescents 11-18 years of age who were not vaccinated previously²
- Previously unvaccinated college freshmen living in dormitories³
- Adolescents 11-18 years of age with human immuno-deficiency virus (HIV) infection¹
 - Two-dose primary series, 2 months apart
 - Booster doses: same as for other adolescents

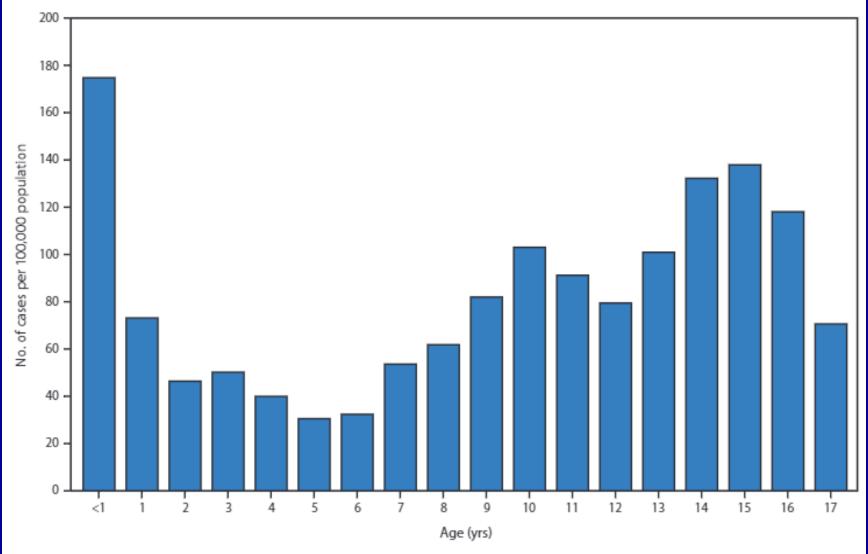
Things to Remember: Meningococcal Vaccine for Adolescents

- 1) MCV4 and MenB can be administered at the same time
- 2) MCV4 and Men B can BOTH be administered with other vaccines; Shortest recommended intervals for boosters are 8 weeks for MCV4 and 4 weeks for Men B
- 3) Men B is also recommended for patients 10-25 years of age with asplenia, complement deficiencies
- 4) Adolescents who receive their first dose of MCV4 after age 16 do not need a booster dose
- 5) While the two MCV4 vaccines are "interchangeable" for adolescents, the Men B vaccines ARE NOT

Pertussis

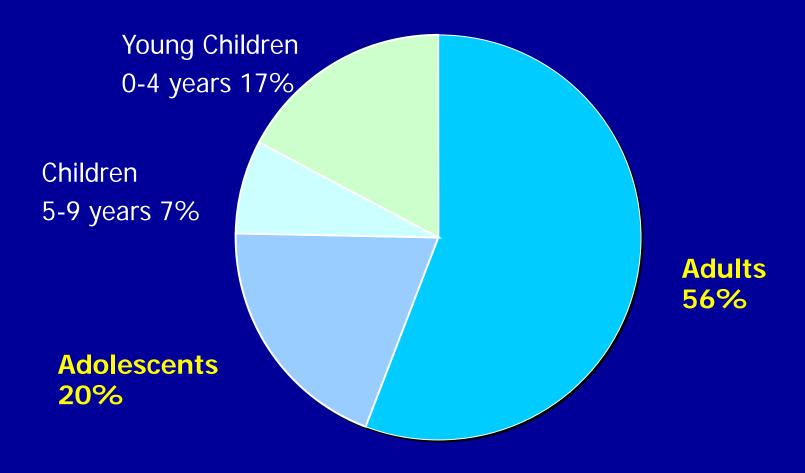
- Overall incidence increased dramatically between 2000 and 2005, decreased, and is now increasing again
- Major outbreak in 2014 in California and in Washington, DC (!)
- Has become common in adolescents and adults, causing significant morbidity and complications
- Adolescent and adult infections may be indistinguishable from other respiratory infections³
- Adolescents serve as a reservoir for infection of unimmunized patients
- Most cases in persons >10 years of age are due to waning immunity⁴

FIGURE. Incidence of pediatric pertussis, by age — California, 2014*



^{*} Reported to the California Department of Public Health as of November 26, 2014.

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



ACIP Recommendations for Use of Tdap Among Adolescents

- Adolescents 11-18 years of age should receive a single dose of Tdap instead of Td as a booster if they have completed the childhood DTP/DTaP series and have not received Td or Tdap¹
 - Preferable age of administration: 11-12 years¹
- Adolescents 11-18 years of age who received Td, but not Tdap, may receive a single dose of Tdap if they have completed the childhood DTP/DTaP series¹
 - Tdap can be administered regardless of the interval since the last tetanus and diphtheria toxoid—containing vaccine²

Things to Remember: Tetanus/Diphtheria/Acellular Pertussis vaccine for Adolescents

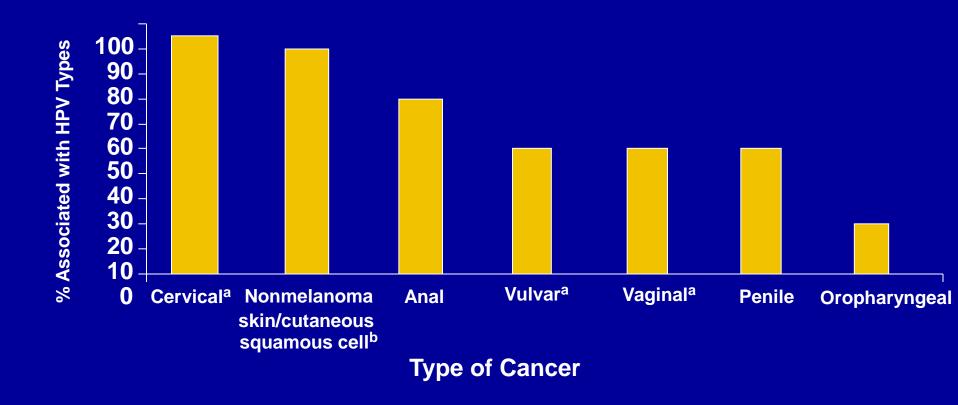
- 1) Tdap can be given regardless of the interval since the last Td was given. There is NO need to wait 2–5 years to administer Tdap following a dose of Td.
- Adolescents should receive a single dose of Tdap (instead of Td) at the 11–12-year-old visit.
- 3) Adolescents and adults who have not received a dose of Tdap, or for whom vaccine status is unknown, should receive a single dose of Tdap as soon as feasible.
- 4) All healthcare workers, regardless of age, should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap and regardless of the time since the last dose of Td.
- 5) Pregnant teens and women should receive Tdap during each pregnancy, preferably between 27 and 36 weeks' gestation. Women who have never received Tdap and who do not receive it during pregnancy should receive it immediately postpartum.
- 6) Vaccine efficacy is likely as low as 50% in adoelscents

The Impact of HPV in the US

- The lifetime risk of HPV infection is 50% for sexually active men and women¹
 - By 50 years of age, at least 80% of sexually active women will have acquired genital HPV infection¹
- Estimated incidence: 6.2 million per year¹
- Estimated prevalence: 20 million¹
- Up to 75% of new HPV infections occur among persons
 15-24 years of age¹
- In studies of women ≤25 years of age, prevalence rates range from 27%-45%²

References: 1. CDC. Human papillomavirus. In: Atkinson W, et al, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases.* (The Pink Book) 11th ed. Washington, DC: Public Health Foundation; 2009:123-134. **2.** CDC. *MMWR.* 2007;56(RR-2):1-24.

Cancers Associated With HPV¹



Reference: 1. González Intxaurraga MA, et al. Acta Dermatoven APA. 2002;11(3):95-99.

^a Includes cancer and intraepithelial neoplasia; ^b Immunocompromised patients.

HPV vaccines licensed in the US

	Bivalent 2vHPV (Cervarix)	Quadrivalent 4vHPV (Gardasil)	9-valent 9vHPV (Gardasil 9)
L1 VLP types	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58
Manufacturer	GlaxoSmithKline	Merck & Co.	Merck & Co.
Adjuvant	AS04: 500 μg aluminum hydroxide 50 μg 3- <i>O</i> -desacyl-4'- monophosphoryl lipid A	AAHS: 225 μg amorphous aluminum hydroxyphosphate sulfate	AAHS: 500 μg amorphous aluminum hydroxyphosphate sulfate
Schedule	3-dose series	3-dose series	3-dose series

Licensed age groups for available HPV vaccines

	Bivalent	Quadrivalent	9-valent
	(Cervarix)	(Gardasil)	(Gardasil 9)
Licensure	Females 9-25 years	Females 9-26 years Males 9-26 years	Females 9-26 years Males 9-15 years

- At the time of the first application to FDA, 9vHPV immunogenicity trials in males 16-26 years had not been completed
- Immunogenicity data for males 16-26 years were presented to ACIP and submitted to FDA
- In February 2015, ACIP recommended use of 9vHPV in the currently recommended age groups – through 21 years for males*
 - Use in males 16-26 years is off label at this time

^{*}through age 26 for MSM and immunocompromised males and those with HIV infection

ACIP Recommendations for Use of HPV Vaccine Among Adolescents

- A 3-dose series of the HPV vaccine is recommended for females 11-12 years of age:1,2
 - 1st dose: at elected date
 - 2nd dose: 2 months after the first dose
 - 3rd dose: 6 months after the first dose
- Vaccination is recommended for females 13-26 years of age who have not been vaccinated previously or have not completed the full series^{1,2}
- Females may receive either the nonavalent, quadrivalent or bivalent vaccine to protect against HPV-related cervical cancers and precancers²
 - Nonavalent vaccine also protects against vulvar and vaginal cancers and precancers and genital warts²
- Nonavalent vaccine is approved as a 3-dose series for males 9-21(26) years of age to reduce the likelihood of genital warts^{3,4}



- This 14-year-old has come in for a sports physical for camp. She is up- to-date on all of her vaccinations, except her mother has decided to "wait until there is more data" on the HPV vaccine.
- What data can you provide to reassure the mother that vaccination now is preferable?

HPV Vaccine Parental Concerns

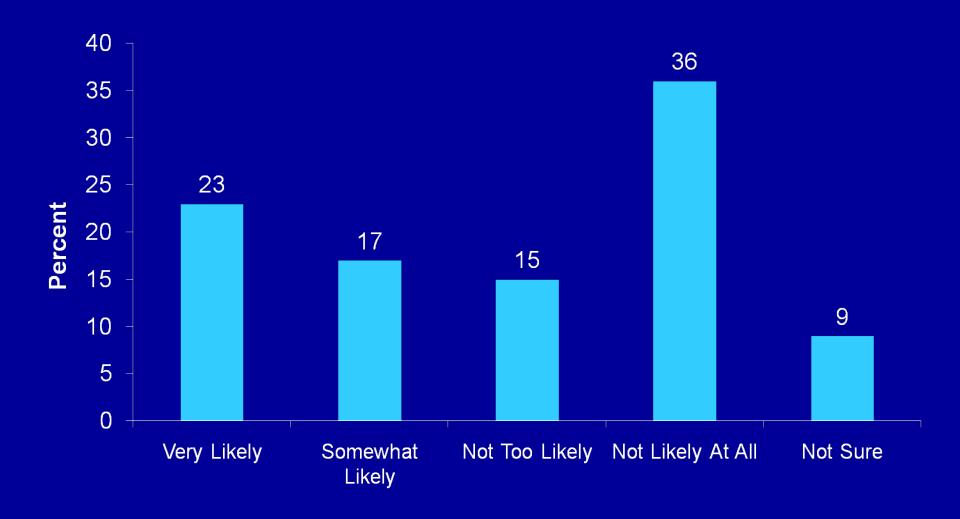
- Parents discomfort with child sexuality
 - Great opportunity to start talking about sexuality issues
 - Communicate the importance of completing the 6-month immunization series <u>before</u> the adolescent becomes sexually active
 - Improved immunogenicity at younger ages
- Emphasize cancer prevention
- Communicate the universality of the vaccine recommendation
- No evidence that vaccination supports sexual activity
 - Not supported by other interventions such as free condom distribution, availability of emergency contraception
- Provider recommendation is perhaps the most important factor in parent decision-making!

HPV Postlicensure Safety Data

Vaccine Adverse Event Reporting System (VAERS)

- HPV4
 - **>** 6/1/06–8/31/10
 - > 33 million doses in females
 - > 16,442 VAERS reports; 8% serious
 - Ongoing monitoring
 - No new adverse event concerns or clinical patterns identified
- HPV2
 - Licensed 10/16/09
 - Insufficient usage to date in US to assess AEs
 - > Total US reports through 8/31/10: 9
- Vaccine Safety Datalink Rapid Cycle Analysis
 - HPV4
 - No significant increased risk for pre-specified AEs after vaccination
 - ➤ GBS, seizures, syncope, appendicitis, stroke, VTE, allergic rxns

Intent to Vaccinate with HPV among Parents of Females Who Have Not Received Any HPV Vaccine; NIS-Teen 2009



ACIP. http://www.cdc.gov/vaccines/recs/acip/downloads/mtg-slides-oct10/08-3-hpv-Female.pdf. Accessed Nov 2010.

Things to Remember: HPV Vaccine for Adolescents

- 1) Approved for BOTH males and females, but adolescent recommended time for administration STOPS at age 21 for males
- 2) If the HPV series has been started with 4vHPV, it can be finished with the 9vHPV
- 3) If a patient misses the recommended interval for HPV boosters (0, 1-2, and 6 months), there is no need to restart the series
- 4) The vaccine continues to be safe! 67 Million doses administered with 25,000 reports made to Vaccine Advserse Events Registry with 92% classified as minor
- 5) NO proven deaths from this vaccine
- 6) Your advice matters! Endorse the use of this vaccine if challenged

Pneumococcal Vaccine

- 7 valent conjugate vaccine available since 2000; has significantly reduced invasive disease in children
- New 13 valent vaccine now available and recommended for all children 4-71 months
- Also recommended for "high risk" children 6-18 years (asplenia, immunocompromised, cochlear implant, CSF leak), regardless of prior PV7 or PPSV 23
- "High Risk" adults (including asthmatics!) should receive one dose of PCV 13 and PPSV23 no sooner that 8 weeks later
- Can improve antibody response by giving PPSV23 > 8 weeks

Indications for Pneumococcal Vaccine by Age Group

Ages 7-18 years

- Cerebrospinal fluid (CSF) leaks
- Cochlear implant(s)
- Sickle cell disease and other hemaglobinopathies
- Functional or anatomic asplenia
- Congenital or acquired immunodeficiencies
- HIV infection

Ages > 19 years

- Chronic renal failure
- Nephrotic syndrome
- Leukemia
- Hodgkin disease
- Generalized malignancy
- Long-term immunosuppressive therapy
- Solid organ transplant
- Multiple myeloma
- Asthma

Things to Remember: Pneumococcal Vaccine for Adolescents

- For adolescents "vaccinated for a reason" PCV 13 ALWAYS proceeds PPSV 23 and interval between is at least 8 weeks
- PPSV 23 is recommended for adolescents with asthma, but ONLY for those > 19 years of age (insurance will not pay for younger adolescents)
- 3) If you are administering PPSV 23, you need to give a booster in 5 years
- 4) For patients needing BOTH PCV 13 and MCV4, preferably wait 4 weeks between vaccines and give PCV13 first

"Catch-up" Schedule for Adolescents

Minimum Interval Between Doses

Vaccine	Dose 1 to 2	Dose 2 to 3	Dose 3+
Tdap	4 wks	6 mos	5-10 yrs
IPV necessary)	4 wks	4 wks	4wks (if
Hep B	4 wks	8 wks (and 16 after #1)	
MMR	4 wks		
Varicella	4 wks		

Future Vaccines for Adolescents and Young Adults

- Herpes simplex virus
- HIV
- Cytomegalovirus
- Chlamydia
- Group B streptococcus

Summary

- Vaccine preventable diseases continue to pose clinical and public health challenges
- Adolescents are an important target for an increased immunization initiative
- The availability of new vaccines promises to significantly reduce morbidity and mortality in adolescents and young adults
- Vaccines in development will further improve the health of this and other age groups

The Rationale for Emphasizing Adolescent Immunization

- Adolescent immunization:
 - Protects during a period of increased risk and increased chance to disseminate illness
 - Prevents lifelong complications of disease
 - Increases herd immunity for entire population
 - Example: Morbidity and mortality of the elderly could be reduced >40% with a 15% increase in immunization rates for those <19 years of age¹
 - Promotes adolescent health-care visits
- New vaccines may be available soon!

National Immunization Survey-Teen

- Conducted by CDC since 2006 to estimate vaccination coverage from a national sample of adolescents aged 13-17 years
- Random-digit—dialing sample of telephone numbers of households
 - After parent/guardian respondents grant permission, surveys are mailed to the adolescents' vaccination providers to obtain vaccination histories

Meningococcal Disease

Why?

- This is an often serious, rapidly progressing infection that leaves little time for diagnosis and treatment
- Early meningococcal disease can present with symptoms similar to common viral illnesses, making diagnosis difficult
- Neisseria meningitidis is now the most prevalent etiologic agent of bacterial meningitis among those 2 to 18 years of age in the US
- Adolescents and young adults are 5x more likely to die of meningococcal disease than younger children