



Roadmaps for Clinical Practice

Improving Adolescent Immunizations

A Primer for Physicians

AMA
AMERICAN
MEDICAL
ASSOCIATION



The American Medical Association (AMA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The AMA designates this educational activity for a maximum of 1 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

The expiration date for this activity is January 2, 2010.

If you would like to obtain AMA PRA Category 1 Credit™ after the stated expiration date, please visit www.ama-assn.org/go/cme to determine if this is a currently approved activity of the AMA.

For additional copies please contact:

Sarah F. Duggan Goldstein, MPH

American Medical Association

515 N. State St.

Chicago, IL 60610

Phone: 312-464-2434

E-mail: sarah.goldstein@ama-assn.org

You may fax your request to the AMA at 312-464-4111.

Visit the AMA Medicine and Public Health Website at www.ama-assn.org/go/roadmaps for more information.

This project was funded by the AMA and supported by an unrestricted educational grant from sanofi pasteur.

Date of original release: January 2, 2008.

Improving Adolescent Immunizations is not intended to function as a clinical guide, standard of medical care, or definitive resource for improving adolescent immunizations. The instruments included in this publication are clinical tools, not research tools. Consequently, they have not been evaluated to establish reliability and validity. The American Medical Association neither endorses nor encourages use of the programs listed in this document. They are meant to be a starting point and are not intended to be an exhaustive list of educational resources for physicians or patients seeking medical information.

Medical care is determined on the basis of all the facts and circumstances involved in an individual case and is subject to change as scientific knowledge and technology advance and patterns of practice evolve. This publication reflects the view of experts and reports in the scientific literature as of 2007.

Principal Faculty

Author

Richard Rupp, MD

Planning Committee

Sarah Duggan Goldstein, MPH
Policy Analyst, Medicine and Public Health
American Medical Association

Arthur Elster, MD
Director, Medicine and Public Health
American Medical Association

Litjen (L.J.) Tan, MS, PhD
Director, Immunology, Infectious Disease and
Molecular Medicine
American Medical Association

Barry Dickenson, PhD
Director, Science Policy
American Medical Association

Content Reviewers

James P. Alexander, Jr., MD, MA, MEd
Medical Epidemiologist
National Center for Immunization and
Respiratory Diseases
Centers for Disease Control and Prevention

Carolyn Bridges, MD
National Immunization Program
Centers for Disease Control and Prevention

Amanda Cohn, MD
Medical Epidemiologist
Meningitis and Vaccine Preventable Diseases Branch
National Center For Immunization And
Respiratory Diseases
Centers for Disease Control and Prevention

Pekka Nuorti, MD, DSc
Epidemiologist
Centers for Disease Control and Prevention

Preeta Krishnan Kutty, MBBS, MD, MPH
Medical Epidemiologist
Measles, Mumps and Rubella Team, Division of
Viral Diseases
National Center For Immunization And
Respiratory Diseases
Centers for Disease Control and Prevention

Lauri Markowitz, MD
Epidemiologist
Centers for Disease Control and Prevention

Trudy Murphy, MD
Associate Director for Science (Acting)
Division of Bacterial Diseases, National Center for
Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Meredith A. Reynolds, PhD
Epidemiologist
Centers for Disease Control and Prevention

Abigail Shefer, MD, FACP
CAPT, USPHS
Associate Director for Science
Immunization Services Division
Centers for Disease Control and Prevention

Shannon Stokley, MPH
Health Services Research and Evaluation Branch
Immunization Services Division
National Center for Immunization and
Respiratory Diseases
Centers for Disease Control and Prevention

Susan Wang, MD, MPH
National Center for HIV/AIDS, Viral Hepatitis,
STD, and TB Prevention
Centers for Disease Control and Prevention

Notice to Participants

The following are educational objectives. At the end of this program, participants will be able to:

- Recognize the vaccinations that should be administered to adolescent populations and when they should be delivered.
- Identify specific immunization issues for special adolescent populations.
- Identify sources of vaccine funding for underinsured or uninsured adolescent populations and describe programs targeted at these groups.

It is anticipated that this activity will take approximately one hour to complete. Completion of an evaluation and post-test is required to earn credit for this activity.

The expiration date for this activity is January 2, 2010. If you would like to obtain *AMA PRA Category 1 Credit™* after the stated expiration date, please visit www.ama-assn.org/go/cme to determine if this is a currently approved activity of the AMA.

In order to assure the highest quality of CME programming, and to comply with the ACCME Standards for Commercial Support, the AMA requires that all faculty and planning committee members disclose relevant financial relationships with any commercial or proprietary entity producing health care goods or services relevant to the content being planned or presented. The following disclosures are provided:

Name	Disclosure
Sarah Duggan Goldstein, MPH	Nothing to disclose
Arthur Elster, MD	Nothing to disclose
Barry Dickenson, PhD	Nothing to disclose
Litjen Tan, PhD, MS	Nothing to disclose
Richard Rupp, MD	Research grant recipient from sanofi pasteur and Glaxo Smith Kline Speaker's Bureau for sanofi pasteur and Merck
James Alexander, Jr., MD, MA, MEd	Nothing to disclose
Preeta Krishnan Kutty, MBBS, MD, MPH	Nothing to disclose
Amanda Cohn, MD	Nothing to disclose
Trudy Murphy, MD	Nothing to disclose
Lauri Markowitz, MD	Nothing to disclose
Carolyn Bridges, MD	Nothing to disclose
Meredith A. Reynolds, PhD	Nothing to disclose
Abigail Shefer, MD, FACP, CAPT, USPHS	Nothing to disclose
Shannon Stokley, MPH	Nothing to disclose
Susan Wang, MD, MPH	Nothing to disclose
Pekka Nuorti, MD, DSc	Nothing to disclose

Table of Contents

Introduction	2
Current Recommendations for Adolescents	3
Recent Additions to The Set of Recommended Vaccines	5
Vaccines for Which There Are New Recommendations	10
Catch-up Vaccination	13
Special Populations	15
Vaccination Concerns and Issues	19
Keys to Vaccinating Adolescents	21
Case Presentation	23
Selected References	25

Introduction

Vaccines have played a significant role in the major decrease in childhood morbidity and mortality that has occurred over the last century. Cases of many vaccine-preventable diseases, such as polio and measles, are almost unheard of in the United States. As a result, most people enter adolescence healthy and in good physical condition. Vaccinating adolescents helps maintain that well-being and provides protection that extends into adulthood.

The adolescent population presents many challenges with regard to vaccinations. Teens may have infrequent contact with medical services because of the belief that, from a disease standpoint, adolescence is the healthiest period of one's life. Indeed, major risks to health during adolescence are primarily behavioral. Even when ill, many adolescents will fail to access care due to limited financial resources or inadequate transportation. As a result, many adolescents do not receive the routine preventive care that provides the opportunity for vaccination in younger age groups.

For many years, the adolescent immunization schedule remained relatively simple, consisting of only the routine administration of the tetanus-diphtheria booster. Most vaccines, including varicella, measles, mumps, and rubella and hepatitis B, are now targeted at infants or preschool children, with only those adolescents who fall behind in the series requiring a “catch-up” vaccination. However, in recent years new vaccines have been added to the adolescent immunization schedule and recommendations for others have been expanded. Physicians must stay abreast of these changing recommendations and incorporate them into their practices. New vaccines create new issues for the practice of medicine, such as the need to explain terms such as “meningococemia” and “meningitis” to an adolescent or to counsel parents about vaccinating their daughter against a sexually transmitted disease.

This booklet is designed to assist health care providers with the issues surrounding vaccinating adolescents. It examines the new recommendations

for adolescent immunizations and the rationale behind them. Key concepts involved in “catching-up” adolescents with delinquent/deficient vaccinations are addressed, as well as vaccinating special adolescent populations, such as those with chronic illness or who are pregnant. Important information is provided on how government programs, like the National Vaccine Injury Compensation Program and the Vaccine Adverse Event Reporting System, help protect the physician as well as the patient. Lastly, at the practice level, this booklet reviews the topics of reimbursement, maximizing rates of vaccination, and ways to enhance relationships with adolescents and their family members.

Current Recommendations for Adolescents

In regard to childhood vaccinations, the public often confuses the words “required” and “recommended.” The recommendations in this booklet come from the Advisory Committee on Immunization Practices (ACIP), which provides advice and guidance to the Centers for Disease Control and Prevention (CDC). ACIP develops written recommendations for the routine administration of vaccines, including the appropriate periodicity and dosage, and identifies contraindications for each vaccine. Individual states consider these recommendations when determining which vaccines to require for school or day care attendance.

In January 2007, the childhood immunization schedule was divided into two separate tables (for those aged 0-6 years and those aged 7-18 years). A table providing recommendations for ages 7-17 years is less complex and focuses on the special issues of this age group. The table places common vaccines into three different categories: (1) routinely recommended; (2) catch-up of missed vaccines; and (3) recommended for certain high-risk groups. The most current recommended immunization schedule is available online on the CDC’s National Center for Immunization and Respiratory Diseases (CIRD) Website (<http://www.cdc.gov/vaccines>). This information is presented in Table 1.

Table 1. Recommended immunization schedule for persons aged 7-18 years - United States 2007 (adapted from: CDC 2007 Childhood & Adolescent Immunization Schedules (<http://www.cdc.gov/nip/recs/child-schedule.htm#printable>)).

Vaccine	Age®				
	7-10 years	11-12 years	13-14 years	15 years	16-18 years
Tetanus, Diphtheria, Pertussis ¹	see footnote 1	Tdap	Tdap		
Human Papillomavirus ²	see footnote 2	HPV (3 doses)	HPV series		
Meningococcal ³	MCV4	MCV4	MCV4		
Pneumococcal ⁴	PPV				
Influenza ⁵	Influenza (yearly)				
Hepatitis A ⁶	HepA series				
Hepatitis B ⁷	HepB series				
Inactivated Poliovirus ⁸	IPV series				
Measles, Mumps, and Rubella ⁹	MMR series				
Varicella ¹⁰	Varicella series				

Range of recommended ages
 Certain high-risk groups
 Catch-up immunizations

1. Tetanus and diphtheria toxoids and acellular pertussis vaccine (Tdap)
 - Administer at age 11-12 years for those who have completed the recommended childhood DTP/DTaP vaccination series and have not received a tetanus and diphtheria toxoids (Td) booster dose. If there is no record of a primary series of DTaP, DTP, or DT, adolescents should receive a primary series of a tetanus-toxoid containing vaccine. One of these doses can be Tdap.
 - Adolescents aged 13-18 years who missed the 11-12 year Td/Tdap booster dose should receive a single dose of Tdap if they have completed the recommended childhood DTP/DTaP vaccination. There should be an interval of 5 years since the last tetanus- or diphtheria toxoids-containing vaccines.
2. Human papillomavirus virus (HPV) vaccine
 - Administer the first dose of the HPV vaccine series to females aged 11-12 years.
 - Administer the second dose 2 months after the first dose and the third dose 6 months after the first dose.
 - Administer the HPV vaccine series to females aged 13-18 years if not previously vaccinated.
3. Meningococcal vaccine
 - Administer MCV4 at ages 11-12 years.
 - Administer MCV4 as a catch-up dose to unvaccinated adolescents aged 13 through 18 years. Anyone aged 2 through 55 years should preferably receive MCV4; MPSV is an acceptable alternative.
 - Vaccination against invasive meningococcal disease is recommended for children and adolescents aged ≥ 2 years with terminal complement deficiencies or anatomic or functional asplenia and for certain other high-risk groups. Anyone aged 2 through 55 years should preferentially receive MCV4; MPSV is an acceptable alternative.
4. Pneumococcal polysaccharide vaccine (PPV) is administered to certain high-risk groups
5. Influenza vaccine
 - Influenza vaccine is recommended annually for persons with certain risk factors, health care workers, and other individuals (including household members) in close contact with persons in groups at high risk.
 - For healthy adolescents, live attenuated influenza vaccine (LAIV) can be used as an alternative to the trivalent inactivated influenza vaccine (TIV).
6. Hepatitis A vaccine (HepA)
 - The 2 doses in the series should be administered at least 6 months apart.
 - HepA is recommended for certain other groups of children, including in areas where vaccination programs target older children. See MMWR. 2006;55(No. RR-7):1-23.
7. Hepatitis B vaccine (HepB)
 - Administer a 3-dose series to those who were not previously vaccinated.
 - A 2-dose series of Recombivax HB[®] is licensed for children aged 11-15 years.
8. Inactivated poliovirus vaccine (IPV)
 - Administer a 3-dose series to those who are unvaccinated or incompletely vaccinated with either IPV or OPV (4 doses with the fourth dose after age ≥ 4 years)
 - The first two doses of IPV should be administered at intervals of 4 to 8 weeks and the third dose should be administered 6 to 12 months after the second.
9. Measles, mumps, and rubella (MMR)
 - If not previously vaccinated, administer 2 doses of MMR, with ≥ 4 weeks (i.e., a minimum of 28 days) between doses.
 - If previously vaccinated with 1 dose, administer a second dose of MMR at least 1 month (i.e., a minimum of 28 days) after the first dose.
10. Varicella vaccine
 - Administer 2 doses of varicella vaccine to persons without evidence of immunity.
 - Administer 2 doses of varicella vaccine to persons aged <13 years at least 3 months apart. Do not repeat the second dose if administered ≥ 28 days after the first dose.
 - Administer 2 doses of varicella vaccine to persons aged ≥ 13 years at least 4 weeks apart.

Recent Additions to the Set of Recommended Vaccines

Recent changes to the recommendations for adolescents include the addition of tetanus-diphtheria-acellular pertussis vaccine (Tdap), meningococcal conjugate vaccine (MCV4), and human papillomavirus (HPV) vaccine. The newest addition to the recommendations for adolescents is the human papillomavirus (HPV) vaccine.

Tetanus-diphtheria-acellular pertussis vaccine (Tdap)

In 2005, ACIP recommended replacing the routine Td (tetanus-diphtheria vaccine) at 11-12 years of age with the Tdap (tetanus toxoid-reduced diphtheria toxoid-acellular pertussis vaccine). In addition, it was recommended that the Tdap should be offered to those 13-18 year olds who received a Td vaccine 5 or more years earlier. The addition of pertussis coverage came in response to increases in reported pertussis cases, coupled with the availability of a safe and efficacious vaccine formulated for adolescents and adults.

Pertussis, a highly contagious disease spread primarily through respiratory droplets, is caused by *Bordetella pertussis*. After an incubation period of 4 to 21 days, the individual enters the catarrhal stage during which symptoms are indistinguishable from those of a cold (runny nose, sneezing, low-grade fever, and a mild, nonproductive cough). The paroxysmal stage begins after a week or two and is notable for fits of coughing that may end in vomiting and/or a “whoop” sound when the person tries to inhale. Improvement marks the beginning of the convalescent stage, with the cough being milder and less severe.

Pertussis is easily transmissible in the catarrhal stage, well before even the most astute clinician would consider the diagnosis. Disease severity may run the full spectrum, from classic “whooping cough” to a mild cold, particularly in individuals with partial immunity from previous immunization or infection. Further complicating the situation is that testing to confirm the diagnosis of pertussis is not straightforward. Nasopharyngeal specimens are used to isolate *Bordetella pertussis*, the bacterium

that causes pertussis, in culture, and for DNA polymerase chain reaction (PCR) and immunofluorescent tests. Although serological tests are available, only culture and PCR testing are recommended by the CDC to confirm pertussis. Both tests have their highest sensitivity in the first 3 weeks of the illness. PCR tests may remain positive longer and the results are more rapid than for culture. However, no PCR test is Food and Drug Administration (FDA)-approved. Many PCR tests have not been clinically validated and their use has resulted in false-positive tests.

Unless begun during the first week of the paroxysmal stage, antibiotics have little effect on the course of the illness, although they are taken to decrease contagiousness of infant pertussis and during the first 3 weeks of pertussis in adolescents and adults. These disease features make recognition, treatment and prevention difficult. Thus, immunization has remained the mainstay of pertussis control. Unfortunately, immunity from infection and immunization wanes over time and adolescents and adults may be susceptible to disease. Adolescents may serve as a reservoir, transmitting disease to infants too young to be vaccinated who are at greatest risk of complications and death.

Over the past two decades, the reported number of pertussis cases has risen dramatically, with the greatest increase occurring among adolescents and adults. This may be partially due to greater awareness by health care providers and increasing use of PCR tests to confirm the diagnosis. However, evidence from prospective studies demonstrates under-recognition of pertussis, especially in adolescents and adults. Pertussis is believed to account for 13% to 20% of prolonged cough illnesses in adolescents and adults; current estimates place the rate of prevalence at nearly 2% in these age groups.

DTaP: Evolution and use

Until recently, no vaccine was available in the United States for immunizing adolescents against pertussis. Although widespread use of the pertussis vaccine began in the 1940s, it was limited to infants and children. The DTP vaccine was created by combining the diphtheria and tetanus

vaccines. The pertussis portion of the vaccine was derived from preparations of the entire *B. pertussis* bacterium. Although the whole-cell vaccine was extremely effective in controlling pertussis, it was associated with side effects ranging from fever and inflammation to rare but more serious events, such as seizures. Because of the severity of local reactions to the whole-cell vaccine, it was reserved for use in children less than 8 years of age who generally have the most severe cases of pertussis. Concerns over local and systemic side effects lead to the development of acellular vaccines produced from purified bacterial subunits and therefore lacking the components that induced undesired adverse effects. By 1997, diphtheria-tetanus-acellular pertussis vaccine (DTaP) had completely replaced the diphtheria-tetanus-pertussis vaccine (DTP) for infants in the United States. Meanwhile, Canada and some European countries began protecting adolescents by replacing the tetanus-diphtheria vaccine (Td) booster with diphtheria-tetanus-acellular pertussis vaccine (Tdap). Evidence showed effectiveness of the vaccine in these countries, and the vaccines became available in the United States. Products include BOOSTRIX® (GlaxoSmithKline), licensed for individuals 10-18 years of age, and ADACEL® (sanofi aventis), licensed for those 11-64 years of age.

Possible side effects of Tdap

Tdap is safe and well tolerated in adolescents. Physicians in practice before DTaP became readily available remember the side effects following vaccination with the whole-cell preparations that were contraindications to further vaccination. These included:

- hypotonic/hyporesponsive episodes,
- persistent inconsolable crying (3 or more hours)
- fever greater than 40.5 degrees C
- seizure with or without fever

Adolescents and adults who suffered these events as infants or children can receive Tdap vaccine. At this time, the only contraindications specific to Tdap are a history of serious allergic reaction to vaccine components or a history of encephalopathy (e.g., coma, prolonged seizures) not attributable to an identifiable cause within 7 days following administration of a pertussis vaccine.

Meningococcal conjugate vaccine (MCV4)

Licensure of a conjugate meningococcal vaccine along with recognition of the increased risks of meningococcal disease in teens led to the recommendation for universal vaccination of all adolescents. Currently, ACIP recommends routine administration of MCV4 to adolescents aged 11-18, preferably at the 11-12 year old visit. The ultimate goal is to vaccinate all adolescents at age 11 years by 2008. ACIP also recommends immunization of college freshman living in dormitories and other high-risk groups. Pre-vaccination counseling may be challenging because this serious disease is relatively rare, has varied clinical presentations, and the vaccine has been associated with Guillain-Barré syndrome (GBS). While it may be relatively rare, 1 in 4 people who get the disease will die or have lifelong disability. The most common presentation of meningococcal disease is meningitis, and the terms “meningococcal disease” and “meningitis” in this age group are often considered virtually synonymous. Meningococcemia, a severe bloodstream infection, is less well known but can be more serious. While rare cases of GBS have been reported in recipients of MCV4, ACIP continues to recommend MCV4 due to the serious and ongoing risk of meningococcal disease. There are 1400 to 2800 cases of meningococcal disease in the United States each year.

Meningococcal disease consists of a constellation of conditions caused by *Neisseria meningitidis*. The bacterium is spread via respiratory droplets or intimate contact. It is carried asymptotically in the nasopharynx of 5% to 10% of healthy individuals. On rare occasions, especially with recent colonization, the bacterium may become invasive, causing illness. Although it can occur in epidemics, more than 95% of cases are sporadic (endemic). *N. meningitidis* is classified into serogroups determined by their capsular polysaccharides. Serogroups A, B, C, Y, and W-135 cause the vast majority (95%) of human disease worldwide, while B, C and Y account for most occurrence of the disease in the United States.

At onset, the disease is frequently mistaken for a mild viral infection but often progresses rapidly to a life-threatening illness. The two most common forms are meningitis and meningococcemia. Signs of meningitis include headache, photophobia, altered

mental status and nuchal rigidity. Meningococemia is marked by shock, disseminated intravascular coagulation and multi-organ failure. Although some clinicians may believe that disseminated meningococcal disease is easily recognized by a petechial or purpuric rash, in reality the rash only occurs in 30% to 60% of cases and may not develop until the third day of illness. Even with early treatment, 11% to 19% of survivors of invasive disease suffer permanent complications such as seizures, mental retardation, deafness, paralysis, renal failure, skin scars and limb loss from gangrene. For all age groups combined, mortality rates are 10% to 14% in the United States. Risk of death increases with increasing age.

Among all age groups, infants have the highest incidence of meningococcal disease, followed by adolescents 15 to 19 years old. Associated risk factors for this age group include being a freshman living in a college dormitory.

Meningococcal polysaccharides vaccines (MPSV4) have been used successfully to protect against serogroups A, C, Y and W-135. Unfortunately, while serogroup B accounts for about a third of meningococcal disease, its capsular polysaccharide is non-immunogenic in humans. Similar to polysaccharide vaccines for other pathogens (e.g., pneumococcus), MPSV4 stimulates only mature B-lymphocytes, resulting in protection that wanes after only a few years. Therefore, MPSV4 use has been limited to outbreaks and high-risk populations such as military recruits and college freshmen living in dormitories.

Newer vaccine strategies employ covalently linking (or conjugating) capsular polysaccharides to bacterial proteins. The meningococcal polysaccharide (i.e., A, C, Y, or W-135) is bound to diphtheria toxoid. Conjugate vaccines stimulate both B-lymphocytes and T-lymphocytes, which results in a strong antibody response with the induction of immunologic memory, thereby lengthening the duration of protection. Immunologic memory allows for the use of booster shots as with tetanus-diphtheria vaccines. Because the meningococcal conjugate vaccines have not previously been used in the adolescent and adult age groups, it is unclear whether booster injections will

be needed in the future. The efficacy of a conjugate monovalent serogroup C vaccine was demonstrated in the United Kingdom after institution of a program in which children from infancy through adolescence received the vaccine. Overall coverage among school-aged children and adolescents was 86.7%. In the year following completion of the program, confirmed cases of serogroup C disease fell by 85%.

In 2005, the FDA licensed the meningococcal conjugate vaccine (MCV4; MenactraTM; sanofi pasteur) for people aged 11-55 years. MCV4 is the recommended vaccine for individuals ≥ 2 years of age, although in times of vaccine shortage, MPSV4 is considered adequate for vaccinating those at high risk (e.g., individuals exposed to meningococcal disease or students in dormitories).

Guillain-Barré syndrome

In October 2005, an alleged association between Guillain-Barré syndrome (GBS) and receipt of MCV4 was reported. ACIP states that parents and adolescents should be informed about GBS prior to administration of MCV4.

GBS is a rare but serious disorder in which the body's immune system attacks peripheral nerves. The trigger is poorly understood but is often associated with bacterial or viral infections. The first symptoms of GBS include varying degrees of weakness or tingling sensations in the legs that spread to the upper body and arms. In some cases, paralysis may result and the individual may require a respirator to assist breathing. Even in severe cases, the majority of individuals fully recover although some may be left with residual weakness.

As of July 2007, 22 confirmed cases of GBS within 6 weeks of immunization with MCV4 had occurred in 11- to 19-year olds. Over 8 million doses have been distributed to this age group since January of 2005. In 1- to 19-year olds, the ratio of observed cases following MCV4 vaccination to the expected number of cases of GBS in that population is 1.3 (95% confidence interval [CI] = .8-1.9). In 15-19 year olds, the ratio of observed cases following vaccination is 1.7 (95% confidence interval [CI] = 1.0-2.5). A simulation model was performed on a birth cohort of greater than 4 million 11-year-old patients for an

8 year period. The model incorporated the reported risk of GBS and compared the health outcomes of vaccination with MCV4 versus no vaccination. Thus, it assumed a vaccine efficacy of 93% and an incidence of GBS in unvaccinated children of 1.4/100,000 and an incidence of 1.8/100,000 based on VAERS reports. Based upon this model, despite the slight excess risk of GBS incidence, vaccination is still recommended due to the difference of Quality Adjusted Life Years lost between vaccinated and unvaccinated children. Children in this cohort who received full vaccination would only lose 455 Quality Adjusted Life Years where as unvaccinated children were estimated to lose approximately 2,709 years.

ACIP continues to recommend routine vaccination with MCV4 because of the risk of meningococcal disease and its associated morbidity and mortality. ACIP considers a history of GBS a precaution, but not a contraindication, to vaccination with MCV4. A precaution is a condition that may increase the chance of an adverse reaction following immunization or that may compromise the ability of the vaccine to produce immunity. In general, vaccines are deferred when a precaution is present. However, there may be circumstances when the benefits of giving the vaccine outweigh the potential harm, or when reduced vaccine immunogenicity still results in significant benefit to a susceptible, immunocompromised host.

Populations at high risk for meningococcal disease

- Students living in dormitories
- Microbiologists who are routinely exposed to isolates of *N. meningitidis*.
- Military recruits
- Persons who travel to or reside in countries in which *N. meningitidis* is hyperendemic or epidemic
- Persons who have terminal complement component deficiencies
- Persons who have anatomic or functional asplenia

Questions about administration of Tdap and MCV4

Should Tdap (or Td) be administered with MCV4 since they both contain diphtheria toxoid?

Yes, studies indicate it is safe and effective to administer both in the same office visit. If only

one vaccine is available, that vaccine should be administered.

If not given at the same visit, does the immune response to the diphtheria toxoid from the vaccine given first increase adverse reactions to the vaccine given at a later time?

It does not appear that this is a concern.

Human papillomavirus (HPV) vaccine

The newest addition to the recommendations for adolescents is the human papillomavirus (HPV) vaccine. Girls 11-12 years of age are the primary target of the ACIP recommendations, while unvaccinated females 13-26 years of age should receive “catch-up” vaccination. Many of the concepts surrounding the HPV vaccine are new. It is the first vaccine directed at a cancer and its precursors that are caused by a disease that is almost exclusively transmitted sexually. The public will have many questions for physicians about this vaccine.

More than 100 types of HPV have been identified; 30 to 40 preferentially infect the anogenital region. Anogenital types are broken into low- and high-risk groups depending on their oncogenic potential. Low-risk HPV types (such as HPV 6 or 11) have a negligible risk of progressing to malignancy, while high-risk types are often associated with high grades of dysplasia and cancer. HPV is implicated as a causative agent in more than 99% of cervical cancer cases and is involved in other anogenital and oropharyngeal cancers as well. Regardless of risk group, the majority of HPV infections spontaneously clear within 24 months. Persistence of infection places an individual at risk for progression to malignancy over a period of many years to decades. Of the 15 to 20 oncogenic types, HPV 16 and HPV 18 account for almost 70% of cervical cancers.

Anogenital HPV is the most common sexually transmitted infection in the United States and is spread via genital-genital, oral-genital and hand-genital contact. It is important to understand that anogenital HPV is ubiquitous, with a lifetime risk among sexually active men and women of at least 50%. The vast majority of infections go unrecognized. Some have worried that the vaccine will not gain widespread acceptance due to the

stigma related to the sexual transmission of HPV or because of parental concerns that the vaccine will increase sexual activity among teens. However, study results suggest that for all vaccines, parents make decisions based on the severity of disease and the safety and efficacy of the vaccine. The mode of transmission is much less important. Once educated about HPV, the majority of parents are interested in these vaccines for their adolescent children.

Epidemiologic studies have shown that HPV infection produces type-specific immunity. Recombinant technologies have enabled the production of large amounts of the capsid structural protein L1. This protein self-assembles into virus-like particles (VLPs) without any of the infective genetic components being present. When injected, these VLPs induce type-specific antibodies that have been shown to protect women from persistent infection and cervical, vulvar and vaginal dysplasia. Efficacy in preventing moderate to high grade cervical dysplasia caused by covered HPV types is in the order of 95% to 100%. Although cancer was not an endpoint of these studies, the vaccines are assumed to prevent HPV-associated cancers because they block the development of the moderate and high grade dysplasia that are the immediate precursors of cancer.

The results of clinical trials demonstrated that the HPV vaccines are prophylactic and not therapeutic. They do not appear to affect the natural course of already established infections or dysplasia, which underscores the importance of vaccinating females before exposure. Data from studies of youth in the United States indicate a rapid rise in anogenital HPV infections beginning around age 15 years. This coincides with 2005 data from the Youth Risk Behavior Surveillance System (YRBSS) in which 29.3% of female 9th graders reported having had sexual intercourse, compared to only 3.7% before age 13 years. ACIP recommends the vaccine at 11-12 years of age, well before most females are exposed to anogenital HPV. Some have argued that this age group is too young because the duration of protection is unknown and because vaccinating at this age could leave the girls unprotected in young adulthood when the incidence of anogenital HPV is highest. However, there is much reassuring

information on this issue. The first is that studies demonstrate that girls aged 9-15 years have a higher antibody response to the vaccine than the older (aged 16-26 years) group. Another is that women who participated in the original clinical trials have now been followed for more than 5 years and they remain protected. In addition, a few of these women have been given a repeat vaccine dose and have shown a booster response. If indeed the vaccine does not provide lifetime protection, booster doses may be recommended in the future.

In 2006, the FDA licensed a quadrivalent vaccine (Gardasil™; Merck). GlaxoSmithKline Biologicals is expected to seek FDA approval of its bivalent vaccine, Cervarix™, soon. Both vaccines protect against HPV types 16 and 18, which are found in more than two thirds of cervical cancer cases worldwide. Gardasil™ also contains VLPs for HPV types 6 and 11, which are the two most common causes of genital warts. Gardasil™ is licensed for females aged 9-26 years. The vaccine is not licensed for use in males in the United States.

The FDA has asked manufacturers for data demonstrating vaccine efficacy in males, and studies are ongoing at this time. The vaccine is administered as a series of intramuscular injections at 0, 2 and 6 months. Current contraindications are limited to a history of severe allergic reactions to the vaccine or any of the vaccine components, and pregnancy. The vaccine is priced around \$120 per dose (\$360 for the series). This cost, coupled with administration fees, places it out of reach for many families. In addition, some physicians find the cost prohibitive, taking into account investment in inventory, potential for inadvertent vaccine wastage and poor reimbursement by various insurers. It will be essential that policymakers work to ensure that the vaccine is accessible to all female adolescents so as not to place an undue burden on families or physicians.

Please see the Case Presentation on page 23 for further information on this vaccine.

Vaccines for Which There Are New ACIP Recommendations

Recommendations have changed for varicella and influenza. Please see below for details.

Varicella

In 2006, ACIP expanded its recommendations for use of the live attenuated varicella vaccine. Previously, children received only one dose, while unvaccinated, nonimmune individuals ≥ 13 years of age routinely received two doses. Under the new recommendations, all individuals are to receive two doses. The first dose is to be administered at age 12-15 months and the second between ages 4-6 years. Individuals requiring catch-up vaccination with a second dose should be vaccinated after the proper interval has elapsed (3 months for those under 13 years of age and at least 4 weeks for those ≥ 13 years of age). Furthermore, ACIP revised the criteria for evidence of immunity to varicella.

Before the United States began vaccinating for varicella, approximately 4 million cases occurred annually, accounting for countless days of missed school and work. Although varicella is perceived by many as a minor illness, it is estimated to be responsible for more than 11,000 hospitalizations and 100 deaths each year. The majority of these deaths and complications occur in previously healthy individuals. Complications from varicella include disseminated disease, neurological disorders (ataxia, meningoencephalitis), Reyes syndrome, and secondary bacterial infection. Secondary bacterial infections, which may be severe, include bacterial pneumonia, necrotizing fasciitis, osteomyelitis, septicemia, toxic shock syndrome, and septic arthritis. Varicella vaccination is especially important for nonimmune adolescents and adults because they are more likely to develop serious complications than children.

The changes in recommendations came in response to concerns about breakthrough disease, which is defined as cases of chickenpox that occur more than 42 days after vaccination. These infections are usually of short duration and very mild, with little or no fever and fewer than 50 skin lesions.

Only 30% of vaccinated individuals who have varicella suffer ≥ 250 skin lesions as compared to 65% of unvaccinated individuals. Complications and hospitalizations are exceedingly rare among breakthrough cases. Breakthrough disease is infectious and can be spread to susceptible individuals.

The number of varicella cases decreased with initiation of the vaccine as did disease-related hospitalizations and deaths. However, in spite of high vaccination rates, a plateau has been reached, and in some areas the bulk of disease occurs in vaccinated individuals. Before routine varicella vaccination, the average age of those developing chickenpox was 3-6 years. In 2004, the average age was 9-11 years, thus suggesting that the burden of disease is shifting to adolescents. Several outbreaks have occurred in highly vaccinated school populations. Attack rates in some classrooms have reached 41%, indicating that the single-dose regimen does not induce adequate community immunity. All of this gives rise to the specter of large varicella epidemics occurring among older age groups due to the accumulation of both vaccinated and unvaccinated susceptible individuals in the population.

One dose of attenuated live vaccine administered to children has proven to be less effective over time than previously hoped. Study results demonstrate that a second dose improves cell-mediated and humoral immunity. In a study of children over a 10-year period, the two-dose regimen was superior at preventing breakthrough disease.

In an attempt to decrease the number of susceptible individuals ACIP tightened the criteria for evidence of immunity. Parents' recollections of whether their children have had chickenpox are often unreliable. Physicians should not take a past history of chickenpox at face value but should elicit information about the illness, such as duration, fever, and a description of lesions.

The revised criteria for evidence of immunity in adolescents include any of the following: (1) documentation of two doses of varicella vaccine; (2) laboratory evidence of immunity or laboratory confirmation of disease; (3) health care provider diagnosis of varicella or health care provider

verification of varicella disease; and (4) history of herpes zoster based on health care provider diagnosis. An epidemiologic link to a typical case of varicella should be sought when cases are mild or atypical. If no link is identified, laboratory confirmation should be obtained. If such information or testing is lacking, people should not be considered to have a valid history of disease, because other diseases may resemble mild or atypical varicella.

Influenza vaccine

The recommendations for the influenza vaccine have been considerably broadened over the last few years. ACIP currently recommends the routine vaccination of children aged 6-59 months and their household contacts and out-of-home caregivers along with other high-risk groups. ACIP recommends that providers routinely offer influenza vaccine to all patients, including adolescents, throughout the influenza season. Unfortunately, much confusion and many myths surround influenza and the “flu” vaccine, which leads to low rates of vaccination even in high-risk groups. Rates of serious illness and death are highest among those less than 5 years old, people 65 years and older, and those of any age with medical conditions that place them at increased risk (e.g., pulmonary or cardiovascular disease).

Vaccination remains the primary method of prevention and is associated with decreases in influenza-related respiratory illness, school and work absenteeism, health care visits, hospitalization and death. Two vaccines are available, the TIV and the LAIV. Both contain strains of influenza viruses that are antigenically equivalent to the annually recommended strains: one influenza A (H3N2) virus, one A (H1N1) virus, and one B virus. Recommended strains may change annually depending on patterns observed in global surveillance. Both vaccines are made from viruses grown in eggs. They are administered annually to optimize protection.

The TIV contains killed viruses and is administered by intramuscular injection. All of the groups for which annual influenza vaccination is indicated may receive the inactivated vaccine. The LAIV licensed for use in the United States is FluMist™

(MedImmune, Inc.). The attenuated viruses produce either no or very mild symptoms. The vaccine is administered intranasally. The temperature-sensitive nature of influenza viruses limits their reproduction to the upper airways as they are unable to replicate efficiently in the warm lower airways. Healthy non-pregnant persons aged 2-49 years who are not contacts of severely immunosuppressed persons and are not pregnant may receive LAIV. LAIV should not be given to anyone with asthma or to children less than 5 years old who have a history of wheezing in the past year.

Who should be vaccinated for influenza?

1. High-risk adolescents including those:
 - Who will be pregnant during influenza season
 - With cardiac or pulmonary disease (including asthma)
 - Are at increased risk for aspiration (e.g., cognitive dysfunction, neuromuscular dysfunction)
 - With chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies or immunodeficiency (e.g., medications, human immunodeficiency virus)
 - On long-term aspirin therapy (to prevent Reye syndrome)
2. All adolescents who live in the same household with or who are close contacts of adolescents in high-risk groups and other high-risk individuals.
3. Adolescents who wish to reduce the likelihood of becoming ill with influenza.

Common myths associated with the influenza vaccine that should be explored with patients:

Myth #1: The influenza vaccine can give you influenza.

Fact #1: The influenza vaccine **cannot** give you influenza. The influenza vaccine contains dead or attenuated influenza viruses that cannot multiply or cause infection.

Myth #2: The influenza vaccine makes people sick.

Fact #2: Influenza vaccine is extremely safe.

Most people experience no symptoms after their influenza shot other than some redness or soreness

at the injection site that lasts for one or two days. Mild influenza-like symptoms may occur in some individuals, especially those being vaccinated against influenza for the first

Myth #3: The vaccine doesn't work because you still get influenza.

Fact #3: While it is true that the vaccine does not cover all influenza strains circulating each year, chances are that most people are protected. In addition, a flu-like illness does not mean that a person actually has influenza; many different types of viruses other than the influenza virus can cause similar symptoms to influenza. However, influenza vaccine only prevents illness caused by influenza viruses.

Myth #4: The influenza vaccine is only for people who are at high risk.

Fact #4: The vaccine reduces a person's chances of becoming ill and missing work or school, and importantly, of spreading the flu to people who are at high risk. Everyone who wishes to reduce their chances of the above should be vaccinated.

Myth #5: The influenza vaccine causes Guillain-Barré syndrome (GBS).

Fact #5: Investigations to date have not documented GBS to be associated with current influenza vaccines; the only exception was the swine influenza vaccine in 1976. If influenza vaccine does pose a risk, it is probably slightly more than 1 additional case per each million people vaccinated. If a person has a history of GBS, it is important to discuss this with a physician before being vaccinated.

Catch-up Vaccination

More adolescents than is generally realized miss routine vaccines as young children. Reasons include a lack of medical visits, vaccine shortages at the time of visits or simple oversight. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Many studies demonstrate adequate efficacy even when vaccine doses are administered over an extended time period (see Table 2).

Hepatitis B

Many adolescents have not completed vaccination for hepatitis B despite the 1999 ACIP recommendation that all children <19 years be vaccinated. According to the most recent data from the 2006 Teen National Immunization Survey,

approximately 80% of adolescents aged 13-15 years have medical records indicating they received the full series.

ACIP emphasizes the importance of reviewing adolescent immunization records, as many teens are at increased risk of acquiring the virus through sexual activity, illicit drug use and from tattooing and piercing.

The ACIP has recently updated its recommendations for hepatitis B immunization of adolescents and adults. In addition to the catch-up recommendations for immunization of adolescents under 19 years of age, the ACIP mentions as another possible strategy encourages providers to immunize all older adolescents and adults as part of an age-based approach targeting those with highest incidence

Table 2. Catch-up immunization schedule for persons aged 7-18 years (adapted from: CDC 2007 Childhood & Adolescent Immunization Schedules. Accessed at <http://www.cdc.gov/nip/recs/child-schedule.htm#printable>).

Vaccine	Minimum Interval Between Doses		
	Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4
Tetanus, Diphtheria or Tetanus, Diphtheria, Pertussis ¹	4 weeks	8 weeks if first dose administered <12 months of age 6 months if first dose administered ≥ 12 months of age	6 months if first dose administered <12 months of age
Human Papillomavirus ²	4 weeks	12 weeks	
Hepatitis A	6 months		
Hepatitis B	4 weeks	8 weeks (and 16 weeks after the first dose)	
Inactivated Poliovirus ³	4 weeks	4 weeks	4 weeks
Measles, Mumps, and Rubella ⁴	4 weeks		
Varicella ⁵	4 weeks if first dose is administered at age ≥ 13 years 3 months if first dose is administered at age <13 years		

of infection (e.g., 19-26 year olds). This approach might simplify vaccination-related decision-making by practitioners. This intervention is supported by numerous medical associations including the American College for Preventive Medicine, the Society for Adolescent Medicine, and the National Viral Hepatitis Roundtable, and is intended to reach those children that may have been missed by the implementation of the universal pediatric recommendation in 1994.

Hepatitis A

Although universal vaccination of children 12-23 months of age has been instituted, the hepatitis A vaccine (HepA) is currently recommended only for certain high-risk adolescents. The recommendations for adolescents are based on availability of resources, the likelihood of contracting disease, and the risk of complications. ACIP recommends considering vaccination of children through age 18 years if their community has a program for vaccinating this age group, if there is an outbreak in the community, or if the child falls into certain high-risk groups.

Those who should receive hepatitis A vaccine due to increased risk of infection or complications include adolescents who:

- Are traveling to or living in countries with high or intermediate endemicity of infection
 - Have sex with men
 - Use injection and non-injection illicit drugs
 - Have clotting factor disorders
 - Have chronic liver disease
1. Tetanus and diphtheria toxoids vaccine (Td) and tetanus, diphtheria toxoids and Tdap
 - Tdap should be substituted for a single dose of Td in the primary catch-up series or as a booster if age appropriate; use Td for other doses.
 2. Human papillomavirus (HPV) vaccine
 - Administer the HPV vaccine series to females aged 13-18 years if not previously vaccinated.
 3. Inactivated poliovirus vaccine (IPV)
 - Administer a 3-dose series to those who are unvaccinated or incompletely vaccinated with either IPV or OPV (4 doses with the fourth dose after age ≥ 4 years)
 - The first 2 doses of IPV should be administered at intervals of 4 to 8 weeks and the third dose should be administered 6 to 12 months after the second.
 4. Measles, mumps, and rubella (MMR)
 - If not previously vaccinated, administer 2 doses of MMR, with ≥ 4 weeks (i.e., a minimum of 28 days) between doses.
 - If previously vaccinated with 1 dose, administer a second dose of MMR at least 1 month (i.e., a minimum of 28 days) after the first dose.
 5. Varicella vaccine
 - Do not repeat the second dose in persons aged <13 years if administered ≥ 28 days after the first dose.
 - Although the recommended minimal interval is >3 months after the first dose, if given ≥ 28 days, it can still be considered a valid dose.

Special Populations

Pregnant adolescents

Each year in the United States, there are approximately 750,000 pregnancies among adolescents aged 19 years and younger. Ideally, each adolescent would be fully vaccinated prior to pregnancy but this is often not the case. The benefits of vaccination are twofold: the adolescent is protected from illness and the risk of transmission of infection to the infant is decreased. As with other recommendations related to vaccination, decisions on whether to vaccinate during pregnancy are based on the risk-benefit ratio. ACIP places vaccines during pregnancy into three broad categories: those that are contraindicated, those recommended under special conditions and those recommended or considered if otherwise indicated (see Table 3).

The contraindicated category consists of vaccines with live-virus components. Among routine vaccines this includes measles, mumps, and rubella, varicella and live attenuated influenza. The theoretical risk of transplacental transmission of vaccine virus to the fetus is thought to outweigh the benefits of vaccination, although years of observation have not demonstrated increased risk to the fetus. If a live virus component is inadvertently given during pregnancy or if a woman becomes pregnant within 4 weeks of vaccination, she should be counseled about the potential risks to the fetus. Vaccination is not ordinarily an indication to terminate the pregnancy. Unvaccinated, susceptible women should be vaccinated as soon as the pregnancy ends.

Adolescents who will be pregnant during the influenza season are recommended to be vaccinated with the inactivated influenza vaccine. Pregnant women with influenza are at increased risk for complications, hospitalization and death. Concerns also have been raised because thimerosal, a mercury-containing preservative, is used in vaccine production. A study of approximately 2000 pregnant women who received the inactivated vaccine demonstrated no adverse fetal effects. Because the quantity of organic mercury is small and there is a substantial safety margin, ACIP states that the benefits of influenza vaccine with reduced or standard thimerosal content outweigh

the theoretical risk, if any, of thimerosal. However, for patients or providers who are concerned about thimerosal, thimerosal-free vaccine is also available from manufacturers.

Pregnant women younger than 18 years old who have not been previously vaccinated for hepatitis B need to be caught up on hepatitis B vaccination. Pregnancy is not a contraindication to vaccination. Pregnant women 19 years old or older should start the series if they are identified as being at risk for this infection. Risk factors include having more than one sex partner during the previous 6 months, having been treated and/or diagnosed with a sexually transmitted disease, and recent or current injection drug use.

A tetanus toxoid-containing vaccine is indicated for pregnant women who have not received a Td vaccine within the past 10 years or have not completed a series of three Td vaccinations. Maternal tetanus antibodies are important in preventing neonatal tetanus, which results in rigidity, muscle spasm and often death of the neonate. Neonatal tetanus still occurs in developing nations where women are not adequately vaccinated. It is caused by infection of the umbilical cord stump with the bacterium, *Clostridium tetani*.

The Td vaccine has long been administered during pregnancy; however, although there is no evidence of adverse effects on the fetus, it is reasonable to delay the vaccine until the second trimester. Because it was only recently licensed, data on the Tdap and pregnancy are limited. Although ACIP does not consider pregnancy a contraindication for use of Tdap, it continues to recommend Td rather than Tdap for pregnant women. Evidence is lacking to support a role for transplacental maternal antibody in protecting the infant against pertussis. In addition, a theoretical concern is that the maternal antibodies may interfere with the infant's immune response to DtaP and conjugate vaccine that contain diphtheria and/or tetanus toxoids, leaving the infant less protected in the long run. The available data seem to indicate that the detrimental effect of maternal Tdap on the infant's later response to DTaP vaccine occurs with the first dose of DTaP and does not have a long-term effect on the ability of subsequent doses of DTaP to produce an antibody response.

ACIP states that providers can choose to administer Tdap instead of Td in situations of increased incidence of exposure to pertussis, which occurs in some groups (e.g., adolescents, health care and child care providers, or those living in a community with increased pertussis activity). When more than one dose of Td is required (i.e., the woman has not completed a series of three vaccinations), two doses of Td should be administered 4 weeks apart and a dose of Tdap given postpartum, 6 months after the second Td. To prevent transmitting pertussis to the infant, Tdap is recommended

postpartum for adolescents who have not previously received Tdap.

Other routine vaccines should be delayed until after the conclusion of pregnancy unless special conditions arise. These vaccines are prepared from inactivated bacterial or viral components and theoretically should pose little or no risk. However, the benefits of vaccination during pregnancy are small and do not warrant vaccination except in circumstances such as an outbreak of disease in the community or travel to high-risk geographic areas.

Table 3. Routine vaccines and use during pregnancy (Adapted from the ACIP Guidelines for Vaccinating Pregnant Women. Accessed at: http://www.cdc.gov/nip/publications/preg_guide.htm)

Vaccine	Should be considered if otherwise indicated	Contraindicated	Special/Conditional Recommendation
Hepatitis A			High risk of exposure
Hepatitis B	X		
Human Papillomavirus (HPV)			The vaccine has not been linked to adverse fetal or pregnancy outcomes. Currently ACIP does not recommend the HPV vaccine during pregnancy.
Influenza (inactivated)	Recommended		
Influenza (LAIV)		X	
Measles, Mumps, and Rubella		X	
Meningococcal (MCV4)			No data are available on use during pregnancy. Vaccination during pregnancy should be reported to the manufacturer.
Polio (inactivated)			No adverse effects of IPV have been documented. Use during pregnancy may be considered if immediate protection from polio is required.
Tetanus & Diphtheria (Td)	X		Please see discussion in text.
Tetanus, Diphtheria, & Pertussis (Tdap)			Please see discussion in text. Use of BOOSTRIX® during pregnancy should be reported to GlaxoSmithKline Biologicals (888-825-5249) and use of ADACEL® to sanofi pasteur (800-822-2463).
Varicella		X	Vaccination 3 months before or any time during pregnancy should be reported to the pregnancy registry (800-986-8999).

Immunocompromised youth

Adolescents may be immunocompromised due to inherited or congenital immunodeficiencies or secondary to malignancy, chronic illness or infection with human immunodeficiency virus (HIV).

Special attention must be given to ensure that immunocompromised adolescents are vaccinated due to their increased susceptibility to vaccine-preventable diseases. Additionally, the live-virus vaccines themselves may present some risk to certain immunocompromised individuals. Persons with most forms of altered immunocompetence should not receive live vaccines (MMR, varicella vaccine, LAIV, yellow fever vaccine, oral typhoid, BCG, and rotavirus) except in certain circumstances (see below).

Killed or inactivated vaccines are not a danger and should be administered as recommended for healthy persons. Unfortunately, being immunocompromised may lead to inferior immune response to a vaccine, resulting in suboptimal protection.

A dose of the 23-valent pneumococcal polysaccharide vaccine (PPV23) is recommended for many immunocompromised adolescents including those with:

- HIV infection
- Leukemia and other malignancies
- Functional or anatomic asplenia (e.g., sickle cell disease or splenectomy)
- Chronic renal failure
- Nephrotic syndrome
- Receiving immunosuppressive therapy (e.g., organ transplantation, systemic corticosteroids)

Vaccine recipients should be informed that vaccination does not guarantee protection against fulminant pneumococcal disease. Patients with unexplained fever or manifestations of sepsis should receive prompt medical attention. When elective splenectomy is planned, PPV23 should be administered at least 2 weeks prior to surgery. Currently, ACIP states that there are insufficient data for a recommendation for repeat vaccination, although some providers revaccinate extremely high-risk individuals after 3 to 5 years.

Adolescents on systemic corticosteroids are often encountered in routine practice. The immunosuppressive effects of steroid treatment vary, but many consider a dose of prednisone equivalent to either 2 mg/kg of body weight or a total of 20 mg/day as sufficiently immunosuppressive to raise safety concerns over the use of live-virus vaccines. Live-virus vaccines may be given during systemic steroid therapy under any of the following conditions: (1) duration of therapy of less than 2 weeks; (2) low to moderate dosing; (3) long-term, alternate-day treatment with short-acting preparations; (4) replacement therapy. Physicians should wait at least 3 months after discontinuing high-dose steroid therapy of more than 2 weeks' duration before administering live-virus vaccines. Also, for varicella, some experts recommend withholding steroids for 2-3 weeks following vaccination if it is safe to do so.

Adolescents infected with HIV are also seen in many clinical settings. Asymptomatic individuals should receive routine vaccines with the exception of the live attenuated influenza vaccine. Both the measles and varicella vaccines are contraindicated for the severely immunosuppressed. Physicians seeking additional information and recommendations should refer to resources on specific conditions or consult individuals with expertise in the subject.

Among asymptomatic and symptomatic HIV-infected patients who are not severely immunosuppressed, MMR vaccination has been associated with variable antibody responses but not with severe or unusual adverse events. MMR vaccine is recommended for all asymptomatic HIV-infected persons who are not severely immunosuppressed and who lack evidence of measles immunity. MMR vaccination of symptomatic HIV-infected persons should be considered if they (1) do not have evidence of severe immunosuppression; and (2) lack evidence of measles immunity. MMR and other measles-containing vaccines are not recommended for HIV-infected persons with evidence of severe immunosuppression.

Household contacts of severely immunocompromised individuals

Healthy adolescents may have a household contact who is severely immunocompromised. Nevertheless, both MMR and varicella vaccines should be

administered if the adolescent needs vaccination. This prevents the adolescent from bringing measles, mumps, and rubella, or varicella wild virus home to the immunosuppressed person. MMR component viruses are not transmitted through household contact. Varicella vaccine virus transmission is uncommon but can occur when the vaccinated person develops a varicella vaccine rash. If a rash develops 7 to 21 days after vaccination, close contact between the adolescent and the susceptible person should be avoided until the rash resolves. Also, if a rash develops >21 days after vaccination and is suspicious, then contact should be avoided with susceptible persons.

Racial and ethnic populations

Disparities in adolescent health care exist among different racial and ethnic populations. Although socioeconomic status accounts for much of the gap, part of the discrepancy is due to a combination of system, provider, and patient factors. Physicians can help minimize these problems by employing a culturally diverse staff, providing linguistically diverse signage and patient handouts, and avoiding stereotypic beliefs about minority patients and adolescents. Studies show that African American and Hispanic adolescents receive fewer primary care services than non-Hispanic white youth. This highlights the importance of reviewing vaccination records and vaccinating at every possible opportunity, including acute care visits and sports physicals.

Religious and philosophical objectors

State-mandated school immunization requirements

have played a major role in achieving high vaccination rates and in decreasing disparities across different socioeconomic, racial and ethnic groups. For the general public, these requirements reinforce the role of vaccination in disease prevention, as well as provide the basis for vaccine funding by government and private institutions.

A few parents may refuse to vaccinate their teen based on religious or philosophical beliefs. Forty-eight states allow for religious exemptions, and many states have a provision for personal belief exemptions. Physicians should be aware of their state's mandates. Such information can be obtained from state health departments or through the National Network for Immunization at www.immunizationinfo.org.

It is important for practices to have a plan should parents refuse mandated vaccines for their teen. A nonconfrontational approach is best. The family should be educated, provided with informational handouts, and directed to other appropriate resources, such as Websites. Concerns and/or misconceptions should be addressed. If the family still refuses, it is important to document the refusal and the practice's attempts at education. The Childhood Immunization Support Program (CISP) offers a template to document the parent's refusal (http://www.cispimmunize.org/pro/pdf/RefusaltoVaccinate_2pageform.pdf). It is important to "leave the door open" in case the parents change their minds and are more inclined to vaccinate at some future time.

Vaccination Concerns and Issues

Vaccination is fostered through public education programs and state mandates. However, when it comes to actually having their children vaccinated, most families turn to their physician for guidance. It is important for providers to have some understanding of vaccine funding, adverse event reporting and maximizing practice immunization rates.

Vaccine funding

Access to medical care, including vaccinations, is largely dependent on insurance coverage. Data from 2003 reveal that 56.8% of children are covered by insurance through their parent's employment, while 27.1% are covered by government programs (Medicaid and the State Children's Health Insurance Program [SCHIP]). Millions of children fall through the gap in coverage. This is particularly true for children in low-income families, as 20.3% are uninsured compared to 11.8% of children overall. Adolescents 12-17 years old are more likely to be uninsured than children less than 12 years old (12.7% vs. 10.6%). Even when children have private health insurance, some plans do not cover vaccines or have large deductibles or copayments, placing vaccination out of reach for many families.

The Vaccines for Children Program

The Vaccines for Children (VFC) Program helps fill the gaps in vaccine coverage. The VFC program provides federally purchased vaccines for children up to and including age 18 years. Approximately 60% of children benefit from the VFC program. Children are eligible if they meet any one of the following criteria: (1) enrolled in Medicaid; (2) uninsured; or (3) American Indian/Alaskan Native. The program covers children seen in both public and private settings. Many providers are unaware that they need not be a Medicaid provider to participate in the VFC program.

VFC programs are managed jointly by the federal and state governments; consequently, the programs vary from state to state. In some states, the VFC program allows physicians in private practices to provide vaccines, not just to those who are VFC eligible but to underinsured families whose finances create a

barrier to vaccination. These states make referring the family to a federally qualified health center (FQHC) or rural health clinic (RHC) unnecessary. Underinsured children (those with some health insurance but no coverage benefit for vaccines) are eligible for VFC vaccines in RHCs and FQHCs. VFC providers are not required to take Medicaid or uninsured patients into their practice. Private physicians are not required to enroll in Medicaid in order to participate in the VFC program; however, administration fees or office visit fees under fee-for-service Medicaid will not be paid by the Medicaid program unless the child is Medicaid-enrolled and the physician is a Medicaid provider. Once providers enroll, they do not have to see children in their practice only because they are eligible for VFC; a physician is not required to accept an uninsured child into his/her practice merely because the child is eligible for immunization through the VFC program.

The vaccines are provided free of cost to the practice, while the physician is allowed to charge a fee to offset the cost of administration. The physician is not allowed to deny vaccines if the family is unable to afford the administration fee. Site visits by a VFC Immunization Educator are usually required every 2 to 3 years to monitor VFC compliance. Many practices find the training and resources available through VFC very useful. Physicians interested in additional information can access <http://www.cdc.gov/vaccines/programs/vfc/default.htm> or contact their state VFC program.

Reimbursement

To be compensated for administering vaccines it is important to properly apply Current Procedural Terminology (CPT®) codes. The CPT codes were developed by the American Medical Association in 1966 and are constantly updated to correspond with changes in medical practice. Vaccination is reimbursed through the combination of a vaccine specific-CPT code and a separate administration CPT code. Routine adolescent vaccine codes include:

- Hepatitis A two dose schedule — 90633
- Hepatitis A three dose schedule — 90634
- Hepatitis B two dose schedule — 90743
- Hepatitis B three dose schedule — 90744
- Human papillomavirus (quadrivalent) — 90649

- Influenza intramuscular — 90658
- Influenza intranasal — 90660
- Meningococcal conjugate (MCV4) — 90734
- Poliovirus (IPV) — 90713 (for subcutaneous or IM use)
- Tetanus and diphtheria toxoids (Td) — 90718
- Tetanus, diphtheria toxoids and acellular pertussis vaccine (Tdap) — 90715
- Varicella — 90716
- MMR — 90707 (live, for subcutaneous use)

There are a total of four administration codes:

- First vaccine administered by injection — 90471
- Each additional vaccine administered by injection — 90472
- First vaccine administered by intranasal or oral route — 90473
- Each additional vaccine administered by intranasal or oral route — 90474

The term “first” does not apply to the first shot in a vaccine series (e.g., the 3-shot hepatitis B series). Rather, it applies to the first vaccine administered at a visit. Only one vaccine can be coded as the first. In other words, 90471 and 90473 cannot be used in the same visit. Either the injection or an intranasal vaccine may be coded first. Reimbursement is the same in either case.

When dealing with Medicaid, a modifier for combination vaccines (U2) can be applied with the administration code for Tdap. This increases the reimbursement to help offset the extra counseling time required due to the inclusion of pertussis in the vaccine.

Liability for adverse events

The National Childhood Vaccine Injury Act of 1986 established the National Vaccine Injury Compensation Program (VICP). The law was passed in response to the growing number of lawsuits filed by parents against vaccine manufacturers and health care providers. The rise in liability resulted in falling vaccination rates and vaccine shortages as companies withdrew from the marketplace. VICP is a no-fault alternative to the traditional tort system. It provides compensation to people found to be injured by covered vaccines. The program covers vaccine injury claims whether the vaccine

was administered in the public or private sector. Most routine childhood vaccines are covered by the program. Adults and adolescents receiving these vaccines are covered by the program as well.

There are three ways to qualify for compensation: (1) show that an injury listed on the Vaccine Injury Table occurred; (2) prove that the vaccine significantly aggravated a pre-existing condition; or (3) prove that the vaccine caused the condition. Other legal requirements, such as the statute of limitations for filing an injury or death claim, must be satisfied in order to pursue compensation. For more information, visit the VICP Website (<http://www.hrsa.gov/vaccinecompensation>) or call 800-338-2382.

Adverse event reporting

The Vaccine Adverse Event Reporting System (VAERS) is a post-marketing safety surveillance program run jointly by the CDC and the FDA. The program collects information about adverse events that occur after the administration of vaccines licensed in the United States. It is important to recognize that VAERS serves as a surveillance tool and cannot demonstrate any causal association between an event with the administration of a vaccine. Further investigation will be needed to determine if there was any causal association.

VAERS helps identify any important new safety concerns by monitoring adverse events. Anyone can report adverse events to VAERS, including manufacturers, health care providers, state immunization programs, and vaccine recipients (or their parent/guardians). VAERS encourages the reporting of any clinically significant adverse event that occurs after the administration of any vaccine even if it is not clear whether a vaccine caused the event. Furthermore, the National Childhood Vaccine Injury Act requires health care providers to report: (1) any event listed by the vaccine manufacturer on the product insert as a contraindication to subsequent doses of the vaccine; and (2) any event listed in the Reportable Events Table that occurs within the specified time period after vaccination.

Additional information and reporting forms are available through the VAERS Website at <http://vaers.hhs.gov/> or by calling 800-822-7967.

Keys to Vaccinating Adolescents

Simply put, adolescence is the transition from childhood to adulthood. By the time they enter adulthood, adolescents should be able to obtain health care and effectively communicate with their provider. Engaging in decisions about his or her own care helps the adolescent gain confidence and mastery of these skills. In addition, adolescents who participate in their own care tend to be more receptive of medical advice, adherent to treatment regimens, and, over the long run, more invested in their own health. It is well worth the time and effort to discuss the reasoning behind a vaccine with the adolescent.

Opportunities to vaccinate adolescents should not be allowed to slip away. Many practices only address adolescent vaccinations at annual physicals, routine well visits, or “check-ups.” Unfortunately, most adolescents do not receive annual preventive services for many reasons, including lack of insurance coverage, limited transportation or because their parents do not realize the value of such visits. Still, the majority of adolescents do access medical care each year for acute illnesses or chronic problems. Recognizing this, the Society for Adolescent Medicine recommends utilizing “non-comprehensive” visits for vaccination.

It is a mistake to assume a parent’s statement that an adolescent’s vaccines are up-to-date is accurate. The parent may presume the adolescent’s immunizations are current because no one, such as the child’s school, has notified the parent otherwise. Furthermore, most parents are unaware of immunization schedules and current recommendations. Available documentation of vaccinations should be reviewed and if the adolescent appears to be behind schedule, careful questioning of the parent on why they believe the adolescent is up-to-date should ensue. Frequently, it becomes apparent that the child needs vaccination.

Vaccines can be safely and effectively administered simultaneously. There are no known adverse effects on safety or efficacy nor are there any contraindications for the concomitant administration of routine vaccines. When

administered at the same visit, each vaccine must be given in its own syringe at a different site. For example, the meningococcal conjugate can be given in one arm while the Tdap is given in the other. If vaccines must be administered in the same extremity, the injections should be at least one inch apart so that local reactions can be differentiated. The interval between live virus vaccines should be ≥ 4 weeks if they cannot be administered on the same day.

Physicians frequently overestimate vaccination rates within their own practice. A chart audit, assessing the level of “current” or “up-to-date” patients can be eye-opening. The state or local health department can assist by conducting a full provider assessment and giving a “diagnostic” report to the practice, including coverage rates and missed opportunities.

There are several strategies for practices that find their vaccination rates less than desirable:

- Appoint a vaccination advocate within the practice. This is usually a member of the staff, often a nurse who firmly believes in the benefits of vaccination. It is this person’s job to ensure supplies are adequate, trouble-shoot problems, and generally remind everyone, including physicians, to vaccinate. The advocate or another individual in the practice should review medical charts, immunization records and immunization registries when possible to identify individuals who need vaccination. Reminders should be placed on charts or on patient schedules indicating which patients need vaccination. Some electronic medical records eliminate this task by automatically prompting providers and/or generating mailing lists of patients who should be sent a reminder.
- Standing orders are a strategy employed in many settings because they increase the availability of slots for vaccination while not consuming limited physician time. Standing orders allow non-physician personnel to vaccinate clients without direct physician involvement (see Table 4).
- Many physicians successfully market their practices by mailing vaccination reminders to families. It is helpful to tie these mailings to

specific events such as birthdays, the beginning of a certain season or the start of school. For instance, a practice may send a flyer to families at the beginning of summer reminding them that their children should have an annual preventive examination and review of their vaccination records before the back to school rush. Other mailings may remind them of the “12-year-old shots” or “flu-season.” It may be worthwhile to make families aware of changes in recommendations and the availability of new vaccines within the practice.

- Reducing barriers to vaccination is important as well. Some clinics offer alternative hours for families who have difficulty coming in during regular work or school hours. Still others reduce barriers by offering vaccinations at more convenient sites such as workplaces, school clinics or places of worship.

Table 4. Usual components of standing orders

1. Purpose of the orders (e.g., to prevent influenza and its complications).
2. Who can carry out the orders (e.g., eligible nurses, pharmacists).
3. Identification of eligible recipients (e.g., age, risk groups).
4. Screening for contraindications (e.g., serious egg allergy for influenza vaccine).
5. Administration directions including vaccine, dose and route.
6. Documentation requirements such as manufacturer, lot number, route and name with title of person administering the vaccine.

Case Presentation

The following case illustrates situations that may occur in practice and suggests effective ways to address them.

A mother brings her 11-year-old daughter, Monique, to the office. The medical record reveals that Monique is healthy and has had few medical visits. She has not received any vaccinations in the office since she was 4 years old. It is doubtful that her mother would have brought her this time except the school nurse directed them to see a doctor for “pink-eye.” Following a brief history and physical examination, Monique is diagnosed with mild bacterial conjunctivitis and given a prescription for ophthalmic drops.

Not wishing to miss an opportunity, the physician suggests Monique start her adolescent immunizations. The mother states that Monique’s immunizations are up to date and she doesn’t need any shots.

What should the response be to Monique’s mother?

- Inform her that the records show Monique has not received vaccinations in the office since she was 4 years old.
- Ask if Monique has received vaccines elsewhere.
- Discuss the fact that most schools do not send notices until the adolescent is past the recommended age (i.e., the tetanus diphtheria booster is recommended at age 11-12 years but many states do not mandate it for school attendance until age 14).
- Let her know that there are important vaccines recommended for protecting her daughter that are not yet required by schools.

The mother is surprised to learn that it has been years since Monique was vaccinated in the office and says she may be confusing Monique with her older sister. She does recollect that Monique was immunized for “something” at a local McDonalds 2 or 3 years ago. Wishing to include Monique in the discussion, the doctor asks her if she remembers. Monique states she recalls having fun at the event but not the type of shot she received.

How should the situation be handled?

- Tell Monique and her mother that it is unlikely that the vaccination a few years ago was one of the adolescent vaccines as it was too early to receive them.
- Check state registries if available.
- Ask the mother to bring any documentation she may have to the next visit.
- Advise them to start the recommended vaccines.

Mother and daughter are told that the recommended vaccines at Monique’s age are the Tdap, MCV4 and HPV. The mother readily agrees to the tetanus shot but wants to hear more about the meningitis and cancer shots.

What are the important points to share about the meningococcal vaccine?

- Meningococcal disease is rare. It can occur in outbreaks but most cases are random.
- There are two common manifestations of the disease; meningococemia and meningitis. Both have rapid onset, cause serious illness and can be deadly. People who survive meningococcal disease may suffer permanent disabilities such as hearing loss or amputations.
- The symptoms of meningitis can include severe headache, sensitivity to light, neck stiffness, irritability and confusion, while meningococemia causes flu-like symptoms and sometimes a rash of little red or purple spots.
- The vaccine covers many but not all of the types of bacteria that cause meningitis and meningococemia. If Monique ever has worrisome symptoms, it is important to seek medical attention immediately.
- There have been concerns about the vaccine and Guillain-Barré syndrome (GBS). GBS is a rare disease of unknown origin, with symptoms of weakness and sometimes tingling of the arms and legs. Some people become so weak that they may need a respirator to breathe. The majority of people recover from this disease.
- The CDC is closely monitoring GBS and the vaccine. If indeed the vaccine is associated with GBS, the risk is extremely low; about one case in a million doses. The risk appears similar to that of the flu vaccine.

Monique and her mother think MCV4 sounds like a good idea, but Monique's mother wants to hear more about the HPV vaccine.

What are the keys to discussing HPV vaccination with families?

- Sensitivity to any discomfort about discussing sexual matters. Parents may not be used to thinking about their child's sexuality.
- Education about HPV. Many people are unaware of the ubiquitous nature of the virus and its association with cervical dysplasia and cancer.
- Universality of the recommendation. Tell them that it is recommended for **all** females in this age group. They may feel stigmatized if they feel singled out.

The mother questions why the vaccine is given at such a young age. She asks if vaccinating doesn't send her daughter the wrong message.

What should Monique's mother be told?

- The vaccine is unlikely to increase sexual activity. Young people rarely base decisions about sex on fear. It is clear that fear of HIV and pregnancy dissuade very few from sexual activity.
- The most important ways to decrease unwanted adolescent sexual activity are communication and parental monitoring. Parents need to communicate their values and expectations to their children. In addition, parents should know who their child is with and what they are doing so the child can be kept from "risky" situations.
- At a minimum, it takes 7 months to be completely immunized. It is best to get vaccination out of the way so they don't have to worry later.

Monique's mother is advised to view the vaccine as similar to a car seatbelt. Both are there just in case something unexpected happens. When teens begin driving, parents often remind them to wear their seatbelt. Telling them to wear a seatbelt is not the same as giving approval to drag race. Satisfied, Monique's mother indicates her desire for her daughter to start the series.

How can this be wrapped up?

- Educate Monique and her mother that women still need routine gynecologic examinations even after vaccination.

- Point out that it is advisable for Monique to have a comprehensive check-up to fully examine her and look at her growth and development. The mother should schedule an appointment 2 months from now for the second vaccine and a routine examination.
- Remind the mother that her older daughter also likely needs a comprehensive examination and a review of her immunization record.

What if the discussion doesn't go well?

Everyone has had experiences with families that are less than enthusiastic about vaccination. Some are wary of certain vaccines while others are skeptical of all. The physician should ensure that nothing said can be mistaken for mockery or scorn. It is best to have the family verbalize concerns so their worries can be addressed from the start. Their views should be heard and any misconceptions corrected. The safety and efficacy of the vaccine should be reviewed in terms they can understand. The family should be given informative handouts and information about appropriate resources. If they do refuse, be sure to leave the door open for them to change their minds. Given time to think without pressure, many decide at a later date to have their child vaccinated.

Sometimes parents are hostile or become angry when vaccination is discussed. Some physicians admit they shy away from uncomfortable encounters and are hesitant about discussing the HPV vaccine with parents. Of course, these feelings are natural but it is important to remember that most families will want to hear about the vaccine. When discussions do go awry, it is best to reflect and see if there might have been a better way to approach the family. In this way, we can all learn from such experiences and further hone our vaccine counseling skills.

Informative Websites for parents:

- American Medical Association (AMA)
<http://www.ama-assn.org/ama/pub/category/1824.html>
- American Academy of Pediatrics
<http://www.cispimmunize.org/>
- National Network for Immunization Information
<http://www.immunizationinfo.org>
- National Immunization Program
<http://www.cdc.gov/vaccines/>
- Immunization Action Coalition
www.immunize.org

Selected References

American Academy of Pediatrics. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006.

Bruce, MG; Rosenstein, NE; Capparella, JM; Shutt, KA; Perkins, BA; Collins, M. Risk Factors for Meningococcal Disease in College Students JAMA. 2001;286:688-693. An update on human papillomavirus infection and Papanicolaou smears in adolescents. MMWR. March 23, 2007;56(RR02); 1-24.

Centers for Disease Control and Prevention. Immunization of adolescents: recommendations of the Advisory Committee on Immunization Practices, Academy of Pediatrics, the American Academy of Physicians, and the American Medical Association. MMWR. 1996;45(RR-13):1-16.

Centers for Disease Control and Prevention. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2006;55(RR-3):1-34.

Centers for Disease Control and Prevention. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2005;54(RR-7):1-21.

Centers for Disease Control and Prevention. Update: Guillain-Barré syndrome among recipients of Menactra® meningococcal conjugate vaccine—United States, June 2005-September 2006. MMWR. 2006;55(41):1120-1124.

Centers for Disease Control and Prevention. Youth risk behavior surveillance—United States 2005. MMWR. 2006;55(No. SS-5).

Centers for Disease Control and Prevention. Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2006;55(RR10):1-42.

Centers for Disease Control and Prevention. Using live, attenuated influenza vaccine for prevention and control of influenza: Supplemental Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2003;52(RR13):1-8.

Centers for Disease Control and Prevention. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2005;54(RR16):1-23.

Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2006;55(RR-7):1-23.

Centers for Disease Control and Prevention. National Vaccination Coverage Among Adolescents Aged 13-17 years -United States, 2006 MMWR. August 31, 2007 / ;56(34);885-888.

Centers for Disease Control and Prevention. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2006;55(RR15):1-48

Centers for Disease Control and Prevention. Recommended Adult Immunization Schedule: United States, October 2006-September 2007. Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR. October 13, 2006 :55(40);

Centers for Disease Control and Prevention. Prevention of pneumococcal disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 1997;46(RR-08):1-24.

Centers for Disease Control and Prevention. Guide to Contraindications to Vaccinations. Accessed: <http://www.cdc.gov/nip/recs/contraindications.htm>.

Centers for Disease Control and Prevention. Measles, mumps, and rubella - vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*. 1998;47(RR-8):1-57

Cherry JD. The epidemiology of pertussis. *Pediatrics*. 2005;115;1422-1427

Dunne EF, Unger ER, Sternberg M, McQuillan G, Swan DC, Patel SS, Markowitz LE. Prevalence of HPV infection among females in the United States *JAMA*. 2007 Feb 28;297(8):813-9;297(8):813-819

Guttmacher Institute. U.S. Teenage Pregnancy Statistics: National and State Trends and Trends by Race and Ethnicity. Updated Sept 2006. Accessed: <http://www.guttmacher.org/sections/adolescents.php?pub=stats>.

Health Canada. *CCDR*. 2000;26(ACS-1): 1-8.

Kandola K. Abstract. *Can J Infect Dis Med Microbiol*. 2004;15;351.

Khan, JA. An update on human papillomavirus infection and Papanicolaou smears in adolescents. *Curr Opin Pediatr*. 2001; (Aug13)(4):303-309.

Koutsky L. Epidemiology of genital human papillomavirus infection. *Am J Med*. 1997 (May 5);102(5A):3-8.

Marin, M, Güris, D, Chaves, SS, Schmid, S, Seward, JF. Prevention of Varicellavariella: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*. June 22, 2007. 2007:56(RR04);1-40

Markowitz, LE, Dunne, EF, Saraiya, M, Lawson, HW, Chesson, H, Unger, ER. Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*. March 23, 2007. 2007:56(RR02);1-24

American Medical Association
515 N. State St. • Chicago, IL 60610