ABSTRACT

The prevention of disease via the development and application of vaccination may be the greatest public health achievement of the 20th century. Current recommendations provide that by adolescence, US children born after 2001 should have received preadolescent immunizations to protect against hepatitis B, diphtheria and tetanus toxoids, acellular pertussis, poliovirus, measles, mumps, rubella, Haemophilus influenzae type b, pneumococcal conjugate, and varicella in the absence of a previous history of chicken pox. Because immunization guidelines have changed several times in the past 10 years, it is possible that current adolescents may not have fulfilled this challenging schedule. Unfortunately, at least 1 of the basic childhood immunizations is lacking in about one fourth of America’s children, and these rates are reduced further in children who are of a racial or ethnic minority, poor, live in the inner city, or live in rural areas. It is particularly important, therefore, that patients be closely questioned concerning previous immunizations; many should receive the varicella and the hepatitis B vaccines, because these are the necessary vaccines most likely to have been omitted. In addition, certain populations of adolescents at risk for complications of infections should also be vaccinated against influenza, meningococcus, pneumococcus, and hepatitis A. In the future, vaccines for meningitis, acellular pertussis (given in combination with diphtheria and tetanus vaccine), human papillomavirus, herpes, and possibly HIV may be regularly recommended for all adolescents. Advances in routes of administration and combinations of vaccines may improve immunization rates among adolescents. Providers of healthcare for adolescents should strive to improve immunization rates for these patients who continue to be adversely affected by vaccine-preventable diseases. (Adv Stud Med. 2004;4(2B):S134-S141)

PREVENTING THE PREVENTABLE: CHALLENGES IN IMMUNIZING ADOLESCENTS

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Preventive medicine is one of the key foundations of adolescent medicine. Among the most important preventive health services that can be provided to adolescent patients is adequate immunization. It has been suggested that the prevention of disease via the development and application of vaccination may be the greatest public health achievement of the 20th century. Vaccination has resulted in the reduction—and in some instances, the disappearance—of many diseases that killed people just a short time ago. Before vaccines, the following occurred each year in the United States:

• Polio paralyzed 10 000 children.
• Rubella caused birth defects and mental retardation in as many as 20 000 newborns.
Measles infected 4 million individuals, killing 3000.

Diphtheria was a leading cause of death in school-aged children.

Haemophilus influenzae type b caused meningitis in 15,000 children, leaving many with permanent brain damage.

Pertussis resulted in death in thousands of infants.

Currently, smallpox is a disease that has been eliminated from Earth, and poliomyelitis may soon follow, with the Western hemisphere having been free of polio for more than a decade. In the United States, several vaccine-preventable diseases, such as diphtheria, tetanus, Haemophilus meningitis and epiglottitis, measles, mumps, and rubella, have been reduced to uncommon events (Table 1). In addition, a decreased incidence of pertussis, varicella, and hepatitis B has been observed.

Most emphasis regarding vaccination has been on the immunization of children younger than 35 months of age, not the adolescent or adult patient. The consequent elimination and reduction of many preventable infectious diseases during infancy and childhood, coupled with the changing epidemiology of many pediatric illnesses and the introduction of new vaccines have shifted the focus of vaccination to the adolescent population. The following is a brief review of some challenges the clinician may encounter in immunizing adolescents.

**Expected Vaccination by the Time Adolescence Is Reached**

Each year, the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians generate and approve a childhood and adolescent immunization schedule for the United States. Per these current guidelines, all infants and children should receive a series of basic immunizations before adolescence (Figure 1).

**How Successful Are We at Providing Childhood Immunizations?**

Despite the adoption of an immunization schedule, some patients are inadequately vaccinated and, as a result, vaccine-preventable diseases still occur. The reasons vary and may include missed opportunities by healthcare providers, antivaccine forces dissuading families from immunizing their children and adolescents, and parental ignorance. The AAP policy on immunization in 1997 called for universal childhood immunization; while progress has been made, this goal has unfortunately not yet been reached. In 2001, only three fourths (77.2%) of toddlers (aged 19 months to 35 months) in the United States had received the basic immunization series. Thirty-five million adolescents aged 11 years to 21 years were missing some vaccine in 2000; each year, an estimated 3.5 million adolescents enter adulthood missing some vaccines.

**Who Falls Outside the System?**

Adolescent populations from diverse geographical regions, ethnic backgrounds, and social classes are not receiving full immunizations. More than at any other

<table>
<thead>
<tr>
<th>Disease</th>
<th>Maximum Reported Cases During Prevaccine Era (n)</th>
<th>Year(s) Reported</th>
<th>Reported Cases During 2001 (n)</th>
<th>Change in Morbidity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital rubella syndrome</td>
<td>20 000*</td>
<td>1964-65</td>
<td>3</td>
<td>-99.98</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>206 939</td>
<td>1921</td>
<td>2</td>
<td>-99.99</td>
</tr>
<tr>
<td>Haemophilus meningitis</td>
<td>20 000†</td>
<td>1984</td>
<td>1597</td>
<td>-92.02</td>
</tr>
<tr>
<td>Haemophilus influenzae type b</td>
<td>894 134</td>
<td>1941</td>
<td>116</td>
<td>-99.99</td>
</tr>
<tr>
<td>Measles</td>
<td>152 209</td>
<td>1968</td>
<td>266</td>
<td>-98.83</td>
</tr>
<tr>
<td>Mumps</td>
<td>265 269</td>
<td>1934</td>
<td>7580</td>
<td>-97.14</td>
</tr>
<tr>
<td>Pertussis</td>
<td>(wild)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>21 269</td>
<td>1952</td>
<td>0</td>
<td>-99.99</td>
</tr>
<tr>
<td>Rubella</td>
<td>57 686</td>
<td>1969</td>
<td>23</td>
<td>-99.96</td>
</tr>
<tr>
<td>Tetanus</td>
<td>601</td>
<td>1948</td>
<td>37</td>
<td>-93.84</td>
</tr>
</tbody>
</table>

* Estimated because national reporting did not exist in prevaccine era.
† Total number reported to the Vaccine Adverse Events Reporting System.
Data from Handal; Centers for Disease Control and Prevention.
time, global travel is easier and more affordable, and therefore more tempting, for adolescents and young adults. Vaccination rates in different countries are not uniform. Risk of new and reemerging strains of old disease is associated with not only people from the United States traveling abroad but also people from other countries traveling to the United States. As of 1998, vaccination coverage rates were the highest in the world in the United Kingdom, with morbidity and mortality from vaccine-preventable diseases approaching the lowest attainable levels. Immunization rates for developing countries are not as good as those observed in industrialized countries. The World Health Organization (WHO) has developed global immunization objectives that include goals of routine immunizations in 80% of children; however, this rate of immunization was achieved in only 26% of countries in 2001. Additional WHO goals include reduction of measles by 50% of levels in 1999, but this goal has been achieved in only 51% of countries. The eradication of polio has been an objective of WHO; the number of polio-endemic countries declined from 120 in 1988 to 10 in 2002.

Full implementation of strategies to eradicate polio have been delayed in several countries affected by war, such as the Democratic Republic of Congo. Encouraging news is that Ethiopia and Sudan have not reported wild poliovirus cases in more than 1 year, and

Figure 1. Recommended Childhood and Adolescent Immunization Schedule: United States, January to June 2004.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mo</th>
<th>4 mo</th>
<th>6 mo</th>
<th>12 mo</th>
<th>15 mo</th>
<th>18 mo</th>
<th>24 mo</th>
<th>4-6 y</th>
<th>11-12 y</th>
<th>13-18 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td></td>
<td>HepB #1 only if mother is HBsAg +</td>
<td>HepB #2</td>
<td>HepB #3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphtheria, Tetanus, Pertussis</td>
<td>DTaP</td>
<td></td>
<td></td>
<td>DTaP</td>
<td></td>
<td>DTaP</td>
<td></td>
<td></td>
<td></td>
<td>DTP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus Influenzae Type b</td>
<td>Hib</td>
<td></td>
<td></td>
<td>Hib</td>
<td></td>
<td>Hib</td>
<td></td>
<td></td>
<td></td>
<td>Hib</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inactivated Polio</td>
<td>IPV</td>
<td></td>
<td></td>
<td>IPV</td>
<td></td>
<td>IPV</td>
<td></td>
<td></td>
<td></td>
<td>IPV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, Mumps, Rubella</td>
<td>MMR #1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MMR #2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella</td>
<td></td>
<td>Varicella</td>
<td></td>
<td>Varicella</td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>PCV</td>
<td></td>
<td></td>
<td>PCV</td>
<td></td>
<td>PCV</td>
<td></td>
<td></td>
<td></td>
<td>PCV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccines below this line are for selected populations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2003, for children through age 18 years. Any dose not given at the recommended age should be given at any subsequent visit when indicated and feasible. Indicates age groups that warrant special effort to administer those vaccines not previously given. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and the vaccine's other components are not contraindicated. Providers should consult the manufacturers' package inserts for detailed recommendations.

Further detail is included on the Centers for Disease Control and Prevention Web site (www.cdc.gov/nip/recs/child-catchup.pdf).

DTaP = diphtheria, tetanus, pertussis; Td = tetanus and diphtheria toxoids; Hib = Haemophilus influenzae type b; IPV = inactivated polio; MMR = measles-mumps-rubella; PCV = pneumococcal conjugate vaccine; PPV = pneumococcal polysaccharide vaccine.

Adapted from Centers for Disease Control and Prevention.
Somalia is approaching 1 year without evidence of transmission of wild poliovirus. At least 1 of the basic childhood immunizations is lacking in about one fourth of America’s children. These rates are even lower in children who are of a racial or ethnic minority, poor, live in the inner city, or live in rural areas. The rates of vaccination are also shown to be lower in children who do not have health insurance or are not eligible for free vaccination clinics. Adolescents are the most poorly insured age group in the United States.

What to Do When the Adolescent Is “Behind”

In 2000, Handal reported several reasons why adolescents may not receive their immunizations regularly. These reasons clearly involve a mix of social factors, including poor access to care, inadequate insurance status, inadequate funding for immunizations, and educational status (Table 2). Another factor related to missed vaccinations involves the changes in some of the recommendations for childhood vaccinations that occurred after current adolescents entered late childhood. These changes necessitate that some adolescents need to “catch up” to the new standards. Table 3 gives the catch-up schedule and minimum intervals between doses for children who have delayed immunizations. There is no need to restart a vaccine series regardless of the time that has elapsed between doses (Table 3).

In order to improve vaccination coverage, a routine visit to healthcare providers is recommended for adolescents aged 11 years to 12 years. These visits ensure vaccination for hepatitis B, varicella, tetanus-diphtheria (Td booster); review of vaccination records; and provision of other preventive services.

Expected Vaccination During Adolescence

Varicella

Varicella vaccine became available in 1995, and the AAP and ACIP provided recommendations for varicella vaccination in 1995 and 1996, respectively. The vaccine is currently underused, however, resulting in hospitalizations, serious complications, and deaths.
despite the recommendation that a physician’s diagnosis of varicella, a reliable history of the disease, serologic evidence of immunity, or receipt of varicella vaccine be a prerequisite for enrollment in childcare centers and schools. Some barriers to varicella immunization include misconceptions about disease severity, concerns about vaccine efficacy, waning immunity, and a shift of disease burden to older age groups. Overall, routine immunization is recommended for all susceptible children and adolescents that do not have a contraindication. Annualized estimates from July 1997 to June 1998 provided that the US varicella vaccine coverage for children aged 19 months to 35 months was 34%. This rate of vaccination varied widely in state and urban areas (ranging from 6% to 52%). More recent data (January 2002 to December 2002) from the Centers for Disease Control and Prevention (CDC) US National Immunization Survey show an increase in these rates to 80% (ranging from 64% to 92%).

HEPATITIS B

Hepatitis B is transmitted primarily via sexual contact, intravenous drug use, regular household contact with a chronically infected person, or occupational exposure. In the United States, most infections with hepatitis B are acquired as young adults or as adolescents. Vaccination against hepatitis B is therefore an appropriate strategy for eliminating the transmission of this infectious disease. Adolescents who have not previously been immunized should receive 3 age-appropriate doses of hepatitis B vaccine according to the manufacturer’s recommendations. A schedule of 0, 1 to 2, and 4 to 6 months is suggested. If interrupted, the second dose should be given as soon as possible and the third dose at least 2 months later. The CDC directs that the first dose of hepatitis B vaccine be given soon after birth as the monovalent vaccine. The series can be completed with either monovalent or combination vaccine. As with most healthcare visits for the adolescent patient, it is important to be flexible when vaccinating adolescents.

Special Populations, Special Situations

Hepatitis A. Person-to-person transmission is responsible for most cases of hepatitis A virus (HAV), and the highest rates of disease occur in those aged 5 years to 14 years. Certain populations who are at a greater risk of becoming infected with HAV should be vaccinated. People traveling to or living or working in an area that has high or intermediate endemicity of HAV infection (eg, Asia, Central America, South America, the Mediterranean Basin, the Middle East, Southern Europe, and Mexico) should receive the vaccine or immune globulin. If a trip to one of these areas is for a long duration, the vaccine should be administered rather than the immune globulin.

Unvaccinated adolescents who live in communities that have a high rate of HAV infection (at least 2 times the national average) should be vaccinated. Communities in the following states are included in this recommendation: Arizona, Oklahoma, Alaska, South Dakota, Oregon, Nevada, New Mexico, California, Utah, Idaho, and Washington. In addition, all adolescents, regardless of where they live, who fit any of the following descriptions should receive the HAV vaccine: those with chronic liver disease, those receiving clotting factors, illicit drug users (including intravenous and noninjectable drugs due to high-risk factors associated with such behavior), or males who have sex with males.

Figure 2. Distribution by Sex for HIV Infection Cases Reported Among Persons Aged 13 to 19 Years and 20 to 24 Years, 2000

Adapted from the Centers for Disease Control and Prevention.
Influenza. Risk of complications of influenza infection is greatest in the young; the elderly; those with underlying health conditions, such as chronic disorders of the pulmonary or cardiovascular systems, chronic metabolic diseases, renal dysfunction, hemoglobinopathies, or immunosuppression; and those who use aspirin long-term.20 More than 8 million children and adolescents in the United States (including 2.2 million with asthma aged 10 to 18 years) have at least one medical condition placing them at high risk for complications associated with influenza. The CDC recommends that these patients receive an annual vaccination for influenza; however, immunization rates for these at-risk adolescents range from 5% to 79%.20

Meningococcal Vaccine in Adolescents. Meningococcal infections, caused by Neisseria meningitidis, most frequently target children who are younger than 1 year of age.3 The fact that the incidence of infection with this bacterium rises again at around 15 years of age makes meningococcal vaccination logical at age 11 years to 12 years when other vaccinations are given. Currently, the vaccine is recommended for children and adults older than 2 years of age who are at increased risk. High-risk populations include those with asplenia, those with selective complement deficiencies, college freshman living in dorms, those exposed to infection during an outbreak (for vaccine groups A, C, Y, or W135), and those traveling to sub-Saharan Africa. It is now required that students entering college in some states be offered meningococcal vaccine.

Pneumococcal Vaccine. It is estimated that among Americans aged 2 years to 18 years, 340 000 are at risk for pneumococcal disease or its complications due to chronic illness.17 Adolescents with anatomic or functional asplenia, nephrotic syndrome, cerebrospinal-fluid leaks, or immunosuppressive disease (such as HIV infection) should be vaccinated with the 23-valent pneumococcal polysaccharide vaccine. Additionally, revaccination is recommended if the period since administration of the first dose of vaccine was 5 or more years earlier. Vaccination against the pneumococcus is becoming even more important as strains of the bacteria have developed resistance to many of the broad-spectrum antibiotics used over the past decade.

EXPECTATIONS FOR THE FUTURE

The evolving field of vaccine development may produce a number of improvements to vaccines, including vaccines for illnesses not included in current recommendations and vaccines for the prevention and treatment of noninfectious diseases.4

Meningococcal Vaccine

The current meningococcal vaccine protects against 4 serogroups of meningococci that commonly cause disease (types A, C, Y, and W135). It is of value for those adolescents at highest risk for disease.1 A continuing limitation of this vaccine, however, is its lack of protection against group B meningococcus, the strain that causes a large proportion of meningococcal disease in children. Several conjugate vaccines, including a multiserogroup (types A, C, Y, and W135) conjugate vaccine, for meningococcal disease are being studied. Conjugate vaccines, in which a carrier protein is attached to the oligosaccharide antigen formed from the bacteria, typically induce a longer-lasting immune response compared with polysaccharide vaccines. These improved conjugate vaccines, however, will not solve the dilemma of lack of protection against group B meningococcus.

Acellular Pertussis Vaccine

In a somewhat different pattern from other infectious diseases of childhood, pertussis is often passed from adolescents and adults to children as well as from child to child.3 It is estimated that each year in the United States, between 600 000 and 900 000 adults and adolescents become infected with pertussis. The erstwhile version of the pertussis vaccine was a whole cell vaccine that contained a killed form of the whole pertussis bacteria and was associated with a high rate of adverse reactions among those aged 7 years and older. In 1996, a modern version of the pertussis vaccine was introduced that does not contain the whole killed pertussis bacteria. This acellular vaccine is currently administered in combination with tetanus and diphtheria toxoids in children younger than 7 years. An adolescent formulation is being tested and appears to be associated with a dramatically lower rate of side effects than the previous version. Pending the results of these studies, recommendation of vaccination (as a combined vaccination with diphtheria and tetanus toxoids) in those aged 7 years and older may be forthcoming.

Human Papillomavirus Vaccine

Molecular evidence of human papillomavirus (HPV), a sexually transmitted disease, has been found in almost all cases of cervical cancers worldwide
(99.7%) and implies the highest worldwide attributable fraction reported to date for a specific cause of any major human cancer.21 Approximately 100 subtypes of HPV have been identified. Of the 40 that infect the genital tract, about 15 are linked to cervical cancer (high-risk subtypes: HPV 16, 18, 31, and 45); others are linked to genital warts (low-risk subtypes).22 The prevalence of high-risk HPV infection is highest in women 20 to 24 years of age (24.0%), and when followed longitudinally, most cases (90%) will spontaneously resolve in 2 years.23 HPV vaccines currently available provide protection against specific types of HPV rather than HPV infection in general. The immunogenic specificity of the HPV-16 vaccine was demonstrated by the prevention of HPV-16 infection in a double-blind controlled study of 2392 women aged 16 to 23 years of age.24 Further study addressing the duration of effect, potential need for booster shots, and development of multivalent vaccines is currently under way and may lead to the routine immunization of female adolescents. The possibility of eradicating high-risk HPV responsible for 80% of cervical cancers has been met with much enthusiasm; however, the impact of HPV vaccination on the total number of cervical cancer cases in both developed and developing countries may not be fully realized for many decades.25

**HIV Vaccine and Adolescents**

Despite a decline in the incidence of AIDS from 1996 to 1999 in the United States, there has not been a comparable decline in the number of newly diagnosed HIV cases among adolescents.26 HIV infection diagnosed in those aged 13 years to 24 years may indicate subsequent overall trends in HIV and AIDS and in young people. A relatively higher incidence of HIV infection has been reported in females aged 13 years to 19 years (Figure 2). For those aged 16 years to 21 years, young African American women have the highest rate of HIV infection.27 Prevention of HIV/AIDS in young people and clear communication about risky sexual behaviors are important. These efforts include education about gay and bisexual behavior, sexual and drug-related risk, and sexually transmitted diseases and the evaluation of factors that influence adolescent behavior. If a successful HIV vaccine is found, perhaps a recommendation for vaccinating adolescents against HIV will be made in the future.

**Novel Ways of Administering Vaccines**

In 2003, a new influenza vaccine that is administered via nasal inhalation rather than injection was introduced.28 Because the nasal spray formulation contains weakened live influenza virus, it is not recommended for persons with medical conditions that place them at high risk for complications from influenza, persons aged 5 years or younger, persons aged 50 years or older, children or adolescents taking long-term aspirin, persons with a history of Guillain-Barré syndrome, or pregnant women. It is also not recommended for persons with a history of allergy to eggs. The inhaled influenza vaccine is recommended only for healthy persons aged 5 years to 49 years.

Other novel vaccine delivery approaches being evaluated include needle-free epidermal powder and aerosol delivery.29,30 Needle-free technologies may improve compliance for those adolescent patients who may be afraid of needles. Perhaps one of the most important advances in current immunization practice is development of multicomponent vaccines.2

**Conclusion**

We currently enjoy a more disease-free environment due to advances in vaccination technology and immunization guidelines. Great emphasis placed on appropriate immunization of children has resulted in the decrease or elimination of many infectious diseases. Such emphasis, however, has left many adolescents in the United States and around the world in an “immunization gap.” Efforts should be made to document the vaccination records of adolescents at age 11 years to 12 years; if any immunizations are missing or lagging, they should be brought up to date. Immunizations can also be given at times other than well-care visits. Delivery of immunizations also provides opportunities for counseling/screening/preventive medicine efforts for adolescent patients. Future advances in immunization technology and evolution of disease epidemiology may bring more vaccination recommendations for the general adolescent population. Providers of healthcare for adolescents should strive to improve immunization rates for these patients, who continue to be adversely affected by vaccine-preventable diseases.
REFERENCES


