Special Issue: Focus on Vaccines

- Anti-Vaccine Media: Its Impact—and Strategies to Combat It
- Immunizations Do Not Cause Autism . . . They Prevent Disease
- HPV Vaccine: Questions and Controversies
- Vaccine Costs, Compensation, and Access: Problems, Solutions

DEEPAK M. KAMAT, MD, PhD—Guest Editor
LINDA S. NIELD, MD—Co-Guest Editor
RICHARD LANDER, MD

MIRANDA O. RAMIREZ, MD
JEAN SOMESHWAR, MD
GOLDER N. WILSON, MD, PhD
Vaccines may represent the greatest advance in children’s health of the past 50 years, but they also, sadly, can frequently be a source of stress for today’s pediatricians. There is the issue of potential difficulty in recouping the cost of the vaccines from managed care organizations. There may also be struggles to convince parents who are reluctant to have their children vaccinated because of anxiety about autism, fears of other adverse effects, or concerns that their preteen daughters will get the wrong message about sex. This special issue of Consultant for Pediatricians provides a wealth of information that can help you greatly reduce these stresses.

Help countering anti-vaccine sentiment. Dr Linda Nield’s article, “Anti-Vaccine Media: Its Impact—and Strategies to Combat It,” provides concrete and practical suggestions for ways to counter the anti-vaccine sentiments and arguments you encounter from patients’ parents. Dr Nield recommends that pediatricians take time to peruse the anti-vaccine information and misinformation parents are likely to see on the Internet and elsewhere and to proactively bring up the subject with them. You may also want to consider letting parents know of your personal choice to vaccinate your own child.

Facts for allaying fears of autism. Drs Golder Wilson and Miranda Ramirez offer good, solid information that can help you combat parents’ fears that vaccines may precipitate autism (see “Vaccinations: Immunizations Do Not Cause Autism Spectrum Disorder . . . They Prevent Disease”). These authors trace the history of the Lancet article that first claimed to document a connection between the measles-mumps-rubella (MMR) vaccine and developmental regression and autism in 12 children—including the journal’s publication of a retraction when it learned that the author’s investigation had been funded by subjects’ trial lawyers. Wilson and Ramirez also provide statistics that show a continuing increase in autism rates even after thimerosal was eliminated from vaccines.

An exploration of issues surrounding the HPV vaccine. The new human papillomavirus (HPV) vaccine is perhaps the most controversial vaccine of all. In her article on the HPV vaccine, Dr Jean Someshwar discusses the various concerns that parents are likely to have about vaccinating their daughters, and she provides the facts you will need to address with sensitivity and authority the issues they raise. For example, many parents are not aware of the relatively high percentage of even young teenaged girls who are sexually active. Moreover, many adolescent girls and young women are unaware of the connections between HPV and either cervical cancer or genital warts.

Strategies to address vaccine-related financial woes. Finally, Dr Richard Lander, a crusader on behalf of more equitable physician compensation for vaccinations, outlines a variety of practical steps you can take to ensure that vaccinating patients becomes a properly remunerated part of your practice as well as a personally rewarding one. He suggests strategies for negotiating the best possible contract with a managed care organization and provides detailed information on how to code for vaccinations in order to be reimbursed all that you are entitled to.

The editors and authors hope that the information offered in the following pages will reduce vaccine-related stresses and help pediatricians move closer to the goal of protecting all of their patients from vaccine-preventable illnesses.
Introduction

Vaccines: Issues—And Answers
Deepak M. Kamat, MD, PhD
Wayne State University

Anti-Vaccine Media: Its Impact—and Strategies to Combat It
Linda S. Nield, MD
West Virginia University

Information for Parents: Vaccines Do Not Cause Autism
Golder N. Wilson, MD, PhD
Texas Tech University, Amarillo
Miranda O. Ramirez, MD
Ramirez Pediatrics, Plano, Tex

Vaccinations: Immunizations Do Not Cause Autism Spectrum Disorder . . .
They Prevent Disease
Golder N. Wilson, MD, PhD
Texas Tech University, Amarillo
Miranda O. Ramirez, MD
Ramirez Pediatrics, Plano, Tex

HPV Vaccine: Questions and Controversies
Jean Someshwar, MD
West Virginia University

Vaccine Costs, Compensation, and Access: Problems—and Solutions
Richard Lander, MD
University of Medicine and Dentistry of New Jersey

Cases in Point: Consequences of 3 Vaccine-Preventable Diseases
- Epiglottitis
- Congenital Rubella Syndrome
- Streptococcal Infection Secondary to Varicella
Anti-Vaccine Media: Its Impact—and Strategies to Combat It

LINDA S. NIELD, MD
West Virginia University School of Medicine

ABSTRACT: Harsh words, accusations, and misinformation about vaccines and vaccine providers are commonplace on the Internet, television, and radio, and in newspapers, magazines, and books. The anti-vaccine movement downplays or does not address the dangers of vaccine-preventable diseases or their prevalence abroad, and it degrades the positive image of vaccination—one of the world’s greatest public health successes. A number of strategies can help you combat negative vaccine media. Learn about current vaccine issues and controversies by reviewing the anti-vaccine media. Discuss these controversies with parents proactively. Help parents understand that the scientific evidence does not support an MMR-autism link or a thimerosal-neurodevelopmental disorders link. Relate personal accounts or share published case reports of children who have suffered from vaccine-preventable diseases. Finally, state your strong support for vaccination and consider telling parents that you have chosen to vaccinate your own children.

According to one Web site, pediatric health care providers should be arrested and prosecuted because of their involvement in the “chemical holocaust” of children. This chemical holocaust refers to vaccination—one of the greatest public health successes in the history of modern medicine. Extremely harsh words and accusations about vaccines and vaccine providers are commonplace on the World Wide Web. The Internet is a major source of negative vaccine media, along with the more traditional sources of television, radio, newspapers, magazines, and books.

Although media exposure has been found to be associated with increased levels of juvenile violence, sexual activity, obesity, and other childhood ills, fewer than one-third of pediatric residency programs in the United States teach about the effects of the media. Therefore, most pediatricians have limited formal training in dealing with harmful media influences. The true impact that fiction and nonfiction vaccine-related media stories have on the vaccine program is unknown, but the pediatric health care provider needs to be aware of the messages to which parents are exposed. Acquiring knowledge about vaccines and anti-vaccine issues highlighted in the press and the ability to effectively communicate this knowledge to the child’s caregiver are the basic tools needed to combat negative vaccine media. These issues are the focus of this article.

MEDIA AND VACCINES

The public’s experience with the media hype about true and alleged adverse effects of vaccines and lack of experience with the potential harmful effects of vaccine-preventable diseases foster an unfavorable view of vaccines in American society. Any negative publicity can degrade the positive image of vaccines. Among others, recent vaccine-related media topics with true scientific merit include:

- The withdrawal of the first licensed
rotavirus vaccine because of its possible association with intussusception.

- Reports of Guillain-Barré syndrome following vaccination with the meningococcal conjugate vaccine.
- The suboptimal effectiveness of the most recent influenza vaccine of the 2007-2008 season.

In the past decade, the most damaging media headlines concerned the alleged link of vaccines with multiple illnesses—especially neurodevelopmental disorders. The dangers of the measles-mumps-rubella vaccine (MMR) and thimerosal use in other vaccines have received the most attention. A thorough review of vaccine controversies is available elsewhere for interested readers.

As described by Danovaro-Holliday and colleagues, the lesson learned from the withdrawal of the first licensed rotavirus vaccine in 1999 is that the media can shift quickly from highly pro-vaccine to highly anti-vaccine. Before the discovery of the rotavirus vaccine—intussusception association, only 2 of 88 reviewed newspaper articles were negative toward the vaccine. During the vaccine withdrawal phase, 77% of reviewed articles were negative; the vast majority highlighted potential adverse effects. This approach by the media of “early idealization—sudden condemnation” can hurt the image of the immunization program.

The mismatch of the influenza B virus chosen for the flu vaccine in 2007 and 2008 was well publicized, perhaps leading some parents to refuse this vaccine or view it as useless. In the 2003-2004 flu season, Ma and colleagues reported that the media actually helped increase influenza vaccine rates. Physician recommendation in conjunction with media coverage was associated with higher vaccination rates in children aged 6 months to 59 months. Most of the media messages then emphasized that the flu season was early, that it was severe, and that it was associated with pediatric deaths. Sixty percent of parents reported that they vaccinated their children after physician recommendation and more than one-quarter did so following media coverage or recommendation of a friend.

The minority of parents who blame vaccines for health problems, whether valid or not, will be more inclined to believe information that supports their anti-vaccine sentiment.

The major debasement of MMR occurred in 1998 with the publication of an article by Wakefield and colleagues that alleged an association of MMR with autism. Although most of the coauthors of that report published a retraction, the damage to the vaccine program in the United Kingdom (UK) had already been done. National rates of MMR coverage dropped extensively in the UK—even as low as 50% in some areas of London.

Smith and associates reported less of an impact in the United States. The US decrease in the number of MMR vaccinations was not as drastic or long-lasting as in the UK. These authors concluded that American physicians must have tempered the potential negative impact of the media, probably by providing adequate information to their patients’ families. According to Smith and coauthors, the likely source of the negative MMR information was the Internet, since the number of negative newspaper, television, and radio reports was limited in the United States during the years immediately following publication of the Wakefield study.

The Internet is a popular source for the promotion of anti-vaccination sentiment. Anti-vaccine groups focus on several specific themes as highlighted by Wolfe and associates. According to some critics, vaccines are ineffective and harm the immune system; vaccine adverse effects are under-reported; vaccine-preventable diseases are not that serious; vaccine supporters (pharmaceutical companies, scientists, pediatricians, and others) are purely profit-driven despite vaccine dangers; mandatory vaccines are a violation of civil liberties; and vaccines are immoral. Web sites contain the disturbing stories and photographs of youngsters allegedly harmed by vaccines, and strategies are available to aid parents in obtaining vaccine exemptions.

The anti-vaccine movement downplays or does not address the dangers of vaccine-preventable diseases or their prevalence abroad. The possibility that a child’s disability may have resulted from an event in utero is rarely, if at all, mentioned on vaccine-critical Web sites. Many distortions can occur on vaccine-critical Web sites, as exemplified by the public figure “Miss America” of 1995 who is deaf. An anti-vaccine Web site implies that the deafness was indirectly caused by an adverse reaction to a vaccine. The pageant winner’s own Web site states that the deafness followed an infection with Haemophilus influenzae.Ironically, a vaccine was alleged as the indirect cause of the deafness on the anti-vaccine Web site when, in fact, one could speculate that a vaccine could have prevented the deafness. Such distortions are probably not evident to most parents, however.

May describes media as portraying vaccines in a way that promotes irrational fears. Health issues become more reportable if there is drama and personalization. Emotionally charged parental accounts of the evils of vaccines prove to be very effective in promoting fear about immunizations. The use of celebrities to promote the anti-vaccine agenda is a growing trend. Celebrities with minimal, if any, medical background appear on popular television talk shows, write books, and tout the evils of vaccinations based on experiences with their own children and heart-wrenching stories from other parents of all...
CONSULTANT FOR PEDIATRICIANS SEPTEMBER 2008 (SUPPLEMENT)

The CDC has made available a media briefing transcript about autism and mitochondrial diseases.18

**Table – Strategies to combat negative vaccine media**

- Remain current about all vaccine issues, especially vaccine controversies.
- Frequently review anti-vaccine media for information and misinformation that is being shared with public.
- Proactively discuss the vaccine controversies with parents.
- Be sure parents understand that most physicians and scientists support vaccines and that scientific evidence does not support an MMR-autism link or a thimerosal-neurodevelopmental disorders link.
- Consider disclosing your personal financial relationships or lack thereof with vaccine manufacturers and government officials.
- Be mindful not to over-sensationalize or exaggerate, but accurately describe personal accounts or share published case reports of children who have suffered from vaccine-preventable diseases.
- State your strong support for vaccinations and consider sharing your own choice to vaccinate your own children.

Legends vaccine-injured children. Physicians with vast knowledge of scientifically sound information about vaccine safety are sometimes featured alongside these celebrities, which gives the audience the impression that the medical expert and the celebrity carry equal scientific credibility. The media successfully creates the perception that the alleged vaccine controversies have extensive scientific merit. The majority of respondents to a survey believed there was equal evidence on both sides of the MMR-autism debate, and less than one-quarter knew that scientific evidence does not support a link between MMR and autism.15

It is quite easy to appreciate why parents experience confusion when the pediatrician promotes vaccine safety while the media highlights the devastation suffered by children allegedly injured by vaccines. The public is further confused with the recent awarding of financial compensation to a family of an autistic child with an underlying mitochondrial disorder; the US courts concluded that vaccinations aggravated the child’s neurodevelopmental abnormality. For further information on this topic, the CDC has made available a media briefing transcript about autism and mitochondrial diseases.18

**COMBAT STRATEGY**

Every pediatric health care provider must continually stay abreast of the latest issues concerning vaccines. Even if an issue does not seem to be of great significance, the pediatrician should be aware of it so that the parents’ questions can be answered accurately. For example, in early 2008, the Advisory Committee on Immunization Practices updated its recommendation for vaccination against measles, mumps, rubella and varicella; because of the possible minimal increase in febrile seizures after the first dose of MMRV (combination measles-mumps-rubella-varicella vaccine), MMRV is not preferred over separate vaccine components.19

Controversies should be discussed early and often so that misconceptions are not established in the parents’ minds. The importance of vaccinating one’s child should be emphasized and pro-vaccine posters and literature should be displayed in the clinic setting. Zimicki and colleagues20 describe the establishment of a “vaccine day” each month to further emphasize the strong commitment to vaccinating all eligible children.

The American Academy of Pediatrics (AAP) provides information to help pediatricians prepare for media interviews and answer parents’ questions about vaccine-related issues.21 The CDC and the AAP have posted statements to counteract a fictional plot of a recent television show about vaccine damages.22 May22 recommends the use of “packaging” information for parents, providing details from both pro- and anti-vaccine viewpoints to allow for a complete discussion. Pediatricians are encouraged to view multiple anti-vaccine Web sites, to watch and/or listen to radio and television shows, and to read articles in parent magazines where vaccines are the topic. By being aware of the alleged ills of vaccinations, one can more readily defend the pro-vaccine sentiment. A major criticism by anti-vaccine groups is that pediatricians are ignorant about vaccine composition, drug company–government connections, and parental reasons for choosing not to vaccinate.

Parents are more likely to retain information when they are touched personally, (for example, when they listen to another parent describe the difficulties of parenting a child allegedly injured by vaccines). Pediatricians who preach about theoretical dangers of non-vaccination probably leave less of a lasting impression. If the clinician has no experience with caring for children who have suffered from a vaccine-preventable disease, sharing details from published case reports may be helpful. Burgess and colleagues23 emphasize that science alone is not advancing the positive image of the vaccine program. Adding sensitivity and personal experience to the promotion of vaccines may improve the pro-vaccine campaign. Consider proclaiming your personal choice to vaccinate your own children or supporting the vaccination of your grandchildren. The
numerous scientifically sound studies that refute much of the negative vaccine publicity can ease many parents’ fears, but sharing your personal choice to vaccinate your own children will probably have an even more powerful impact.

Parents need to understand that the risks associated with non-vaccination become even greater as a larger pool of unvaccinated individuals grows in society. Exposure to the preventable disease becomes more likely when more persons are not immune. The concept of herd immunity should be explained and that choosing not to vaccinate is not without risk. Mention that encounters with some infections may only be a plane ride away. The suggestions listed in a review by Nield and Kamat21 about dealing with parental refusal of vaccines can be employed. The other suggestions in the Table will also help you counteract the anti-vaccine bias.

On the public level, a mass media vaccine campaign can significantly improve vaccination coverage.22 Zimicki and colleagues20 suggest that access to mass media is a key factor in promoting the vaccine program. Culturally sensitive and ethnically specific media messages about immunizations have been shown to be effective tools for positively influencing minority parents.23,24 The messages appeared as advertisements on radio, television, billboards, and printed materials. The prompt use of experts in the media when a vaccine controversy arises will help correct distorted facts from the beginning. May25 warns that as information gets further and further away from a primary scientific source, the facts have the potential to become more distorted. As recommended by Lewis and Speers,17 the individual health professional should not rely on the government alone to improve the image of the MMR vaccine. These authors contend that some citizens do not trust scientists, fearing conflict of interest from potential financial gain. Promotion by the child’s own primary care provider is likely to be more effective than from an unknown higher authority.

Be aware that alternative medical interventions are also commonly promoted by anti-vaccine supporters.2,3 Pharmaceutical companies that manufacture vaccines are readily chastised for their profit-making motives, but profit-making by the sale of alternative medications supplies and the potential conflict of interest on anti-vaccine Internet sites is not considered.2 Parents need to be reminded that alternative medicine interventions, in general, are also not without risk and have not been rigorously studied in controlled trials as vaccinations have been.

Recent strategies employed by the AAP to combat negative vaccine media include recruitment of parents of autistic children who support vaccines to serve as spokespersons.26 Parents of children who have suffered vaccine-preventable diseases are also being sought to make the dangers of these diseases more tangible to other families. Open discussions about the true risks versus benefits, expressions of concern and understanding of parental fears, and outward support of current vaccines and promotion of even safer vaccines are important to provide for all families.

REFERENCES:
Vaccines Do Not Cause Autism

Parents are understandably concerned about vaccines and autism, a relationship publicized by lawsuits, alternative therapies, and claims of government cover-up. Here we summarize the overwhelming medical evidence that most autism is genetic, that the number of children with autism did not increase after vaccines were introduced, and that cases of autism did not decline after the preservative thimerosal was removed from vaccines.\(^1,2\)

Without vaccination, your child returns to the era of primitive medicine—when children suffocated from diphtherial membranes, when chickenpox caused scarring and occasional death, when measles could produce life-long coma, and when mumps silently destroyed reproductive organs. Although some will reassure you that widespread vaccination (herd immunity) protects your child, recent epidemics in vaccine-shy areas show that risks from disease remain far greater than risks from immunizations.

WHAT IS AUTISM?

Autism disorder was first identified in 1943 by Kanner who described children with impaired communication, impaired social interactions, or repetitive movements and routines. Advances in genetics later showed that children with various forms of mental disability, including Down or fragile X syndromes, could have autism. When known genetic disorders are excluded, a diagnosis of autism still confers a 60% to 90% chance for an identical twin and a 5% chance for a sibling to be affected. These risks imply that autism, like diabetes mellitus or schizophrenia, results from the interaction of multiple abnormal genes and the environment. While novel DNA chip technologies are identifying new autism genes, increased recognition (up to 1 in 125 children) has focused attention on potential environmental factors. And while suspects abound in our chemical-laden environment, the innocence of vaccines is now established beyond any reasonable doubt.

WHY THE CONCERN ABOUT VACCINES AND AUTISM?

An article by Wakefield and 12 co-authors on measles-mumps-rubella (MMR) vaccine and autism followed use of this vaccine for 3 decades in the United States and Europe. Their 1998 article described 9 of 12 children who developed autism in addition to abdominal symptoms after having been vaccinated with the MMR vaccine. After it was discovered that the study had been funded by trial lawyers, 10 of the 12 co-authors and the journal editors retracted the article in 2004.

Subsequent attention concerned the preservative thimerosal. This preservative contains 50% ethyl mercury and has been added to vaccines since the 1930s to prevent bacterial contamination and skin infections. Episodes of mercury poisoning in fish (Japan) or grain (Iraq) have caused brain damage (not autism). However, these episodes involved methyl mercury—not the less toxic ethyl mercury found in thimerosal. Headlines also overlooked the fact that there were small amounts of mercury in thimerosal-containing vaccines (12.5 to 25 µg per dose compared to 11.5 µg found in a can of tuna) and the fact that MMR vaccine never contained thimerosal. Nevertheless, European agencies in 1995 to 1999 and the FDA in 2001 responded to concerns by removing thimerosal from all vaccines except those for influenza.

NO ASSOCIATION BETWEEN VACCINES AND AUTISM

Among studies dissociating autism from vaccines are those that found no difference in the incidence of autism in vaccinated and non-vaccinated children. One of these studies tracked more than 500,000 Danish children born between 1991 and 1998. Other studies demonstrate that autism rates have increased after thimerosal was removed from vaccines. One study from California found autism rates of 0.3 per 1000 in 1993 and 1.3 per 1000 in 2003—despite the removal of thimerosal in 2001. Nield has summarized 10 sample studies that refute any link between vaccines and autism. Several of those studies showed no relation between autism with thimerosal exposure or mercury levels.\(^1\)

The scientific elimination of vaccine-autism concerns should encourage all parents to immunize their children against devastating diseases like hepatitis and diphtheria. Affected families should take advantage of the growing ability to detect genetic changes in autism. Test results may alleviate parental guilt about prenatal or childhood exposures and can help inform relatives about risks for future children.

REFERENCES:

ABSTRACT: In response to publicity about an alleged but erroneous link between vaccination and autism, the number of children who are being immunized has decreased. This is of concern because many vaccine-preventable diseases have potentially devastating and even lethal consequences. Numerous studies have negated the role of vaccines in the environmental causation of autism. Most compelling are those studies that show no relation between vaccination status and autism. The evidence for a genetic etiology is strong. There is a 60% to 90% chance for an identical twin and a 5% chance for a sibling to have autism if a relative is affected. Studies of familial cases highlight particular chromosome regions and predisposing genes. The evidence implies that multiple variant genes and the environment interact to cross a threshold and produce autism. Pediatricians can reassure worried parents that medical science has demonstrated that there is no link between autism and vaccines, and that parents can feel safe in immunizing their children.

Case 1. An older attending physician listens during morning report to the details of the case of a child with suspected croup and decreased oxygen saturation. The resident mentions that he inspected the child’s mouth and pharynx as part of the routine examination. The attending recalls a case 20 years ago when a 2-year-old girl came to the emergency department with fever and stridor so severe that she was forced to sit erect to breathe. How different the examination was then—with observation for drooling, lateral neck radiographs for evidence of a dilated hypopharynx, and careful inspection of the throat when personnel expert at intubation were available. Examination under these conditions might demonstrate a cherry-red mass in the posterior pharynx projecting above the tongue.

Case 2. A newborn, born at full term, presents with a “to and fro” heart murmur at the upper left sternal border. The baby’s length and weight are at the 50th percentile for his age, but his head circumference is below the third percentile for age. Subsequent follow-up reveals that the infant has profound sensorineural deafness.

Case 3. A young girl presents with a peripheral vesicular rash accompanied by high fever and cough. Her health improves somewhat on the third day of illness with fluid therapy, and then worsens with increased fever, respiratory distress, and lethargy. Admission studies demonstrate hypovolemic shock and increased coagulation times, and the child is transferred to the pediatric ICU and placed on mechanical ventilation.

What is the diagnosis in each case—and how could these disorders have been prevented?
Because timely vaccination can prevent each of these infections, these presentations should remain only as night-mares in the minds of older pediatricians. We present these cases to illustrate the increased probability that they will occur because vaccination rates have decreased. This decrease is a response to publicity regarding the erroneous association between vaccines (measles-mumps-rubella [MMR] vaccine in particular) and autism.

Here we review the basic characteristics of autism disorder, its causation by genetic-environmental interaction and, most important, evidence proving that past and present vaccines have no relation to autism.

**WHAT IS AUTISM?**

Autism disorder is a combination of behavioral symptoms that fall into the category of pervasive developmental disorders (PDDs) according to the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*. In 1943, Kanner described children with 3 types of behavioral problems:

- Impaired verbal as well as nonverbal communication.
- Impaired social interactions.
- Repetitive movements and routines.

Autism disorder and the relatively mild Asperger disorder comprise autism spectrum disorder; these 2 conditions share features with the other 3 members of the PDD category: Rett syndrome, childhood disintegrative disorder, and pervasive developmental disorder not otherwise specified. Autistic behaviors can occur in most disorders that manifest with cognitive disability—including genetic syndromes such as Down or fragile X and environmental disorders such as fetal alcohol or thalidomide syndromes or rubella. In this discussion, the term “autism” includes all members of the PDD category except for Rett syndrome and excludes other...
Among the genes suspected to be affected are those identified by changes within chromosome material (equivalent to 1 million small extra or missing chromosome bases or several genes) as exemplified by high-resolution chromosomes that can be observed using fluorescent DNA probes to employ fluorescent in situ hybridization (FISH). Recently, novel telomere fluorescent in situ hybridization techniques have been developed to study telomeres, which are located at the ends of chromosomes and play a crucial role in cell function. These techniques allow for the identification of telomere length variations that may be associated with various diseases, including those that involve chromosome instability.

Even when children with known genetic-developmental conditions are excluded from studies of autism, evidence for genetic factors is compelling. There is a 60% to 90% chance for an identical twin and a 5% chance for a sibling to have autism if a relative is affected. Studies of familial cases have highlighted particular chromosome regions and predisposing genes. Risks for siblings are analogous to those for disorders such as diabetes, mental illness, cleft palate, and other isolated birth defects that follow the model of multifactorial determination. Such risks imply that multiple variant genes and environmental factors interact to cross a threshold and produce autism. Those with a family history of autism or with underlying genetic-developmental disorders require lower amounts of environmental exposure (lower thresholds) to produce autism.

Baseline genetic testing is usually considered when autism is diagnosed. This includes routine and high-resolution chromosomes that employ fluorescent DNA probes to study multiple chromosome regions (subtelomere fluorescent in situ hybridization [FISH]). Recently, novel microarray analysis or DNA chip technology can search for very small extra or missing chromosome material (equivalent to 1 million bases or several genes) as exemplified by changes within chromosome 16. Among the genes suspected to cause autism, only that for fragile X syndrome is amenable to routine analysis.

Although relaxed diagnostic criteria, justifications for therapy, and physician awareness undoubtedly contribute to the increase in autism prevalence (currently said to be 1 in 125 children), recent increases would necessarily point to environmental changes rather than to genetic factors.

**WHY THE CONCERN ABOUT VACCINES AND AUTISM?**

Wakefield and colleagues published an article in 1998 on the MMR vaccine and autism. These investigators had followed up the use of this vaccine for 3 decades in the United States and Europe. The MMR vaccine was initially given to children at age 12 to 15 months; its efficacy was high and the incidence of the vaccine’s component diseases dropped by 99%. A second dose of MMR is now given to children aged 4 to 6 years after some localized outbreaks of measles or mumps in older children suggested incomplete immunity.

Wakefield, a gastroenterologist, described 12 children in whom abdominal pain, diarrhea, and inflammation by endoscopy developed after MMR vaccination. Nine of these children also exhibited developmental regression and autism. Wakefield posited a gut-brain interaction in which the MMR vaccine produced persistent measles infection and gut inflammation with increased absorption of CNS toxins.

After realizing that Wakefield’s investigation had been funded by trial lawyers claiming damage from the MMR vaccine, 10 of his 12 coauthors and the journal editors published a retraction in 2004. Nevertheless, concerns about MMR and/or mercury in vaccines were inflamed by Wakefield’s article and have led to lower vaccination rates along with the expected disease outbreaks in the United Kingdom, Europe, and the United States.

Much of the scare over vaccines and autism centered on the preservative thimerosal, a compound containing 50% ethyl mercury that has been added to vaccines since the 1930s. Preservatives in vaccines were initially mandated by the FDA to prevent bacterial contamination and skin infections. Legitimate concerns about mercury grew after reports of ingestion of contaminated fish surrounding Minimata Island in Japan and of contaminated grain in Iraq. Higher mercury levels caused cerebral dysfunction, ataxias, and potential death in adults. The offspring of exposed women suffered from severe mental deficiency, seizures, impaired hearing, and vision (but not autism).

These well-documented cases of mercury toxicity involved very high levels of methyl mercury, a compound that is more toxic than the ethyl mercury in thimerosal. Furthermore, the amounts of mercury from thimerosal preservative in other vaccines ranged from 12.5 to 25 µg per dose. By comparison, a can of tuna contains 11.5 µg of mercury. A final irony is that the MMR vaccine contained 0.02 µg of ethyl mercury in thimerosal. As we will discuss, the discontinuation dates proposed in the Wakefield study never did contain thimerosal.

In response to increasing media articles and lawsuits relating to vaccines and autism, the FDA Modernization Act of 1997 specifically considered mercury and noted that multiple vaccines exposed children to levels of mercury that could exceed safety limits established by the Environmental Protection Agency. The FDA and American Academy of Pediatrics then urged removal of thimerosal from vaccines in 1999 because it would decrease concerns; this took effect in 2001 in the United States. Only certain influenza vaccines now contain small amounts of thimerosal. Most other Western countries have discontinued thimerosal in vaccines. As we will discuss, the discontinuation dates pro-
Vaccinations:

Immunizations Do Not Cause Autism Spectrum Disorder... They Prevent Disease

vid good markers for comparing autism among thimerosal-exposed and non-exposed children.

Despite the removal of thimerosal from vaccines, media coverage continues to emphasize this concern—illustrated by this year’s television episode of Eli Stone in which a plaintiff recovered damages for vaccine-related autism. The controversy continues in real life as the first of more than 4800 damage claims went to the US Court of Federal Claims and concerned a 12-year-old child with autism and GI symptoms. A special legal defense has been formulated with 3 special masters presiding over 9 tests cases divided among 3 hypotheses; MMR in combination with other vaccines causes autism; MMR alone causes autism; or combination vaccines cause autism. This first case has now been settled and some damages were awarded to the plaintiff. The outcome served to reinforce the disproven association between vaccines and autism.

NO ASSOCIATION BETWEEN VACCINES AND AUTISM

Numerous studies have negated the role of vaccines in the environmental causation of autism. Most compelling are those that show no relation between vaccination status and autism. Madsen and colleagues did a retrospective population study of all children (more than 500,000) born in Denmark between 1991 and 1998. They found no difference in the incidence of autism between those who were and those who were not vaccinated. There was also no correlation between autism and the presence or absence of thimerosal in vaccines.

Other studies have shown that autism rates have continued their general increase since thimerosal was eliminated from vaccines. Schecter and Grether analyzed records of children in California born between 1989 and 2003 in whom autism had been diagnosed between 1995 to 2007. Overall, the prevalence of autism increased from 0.5 per 1000 in 1995 to 1.3 per 1000 in 2003 despite removal of thimerosal in 2001. Niedt summarizes 10 sample studies that refute the link between MMR vaccine and autism—including several showing a constant rate of autism and several showing no link with thimerosal or mercury levels.

Medical science has, therefore, demonstrated that there is no link between autism and vaccines. Parents should feel safe in immunizing their children and realize the far greater risks from contracting disease (as illustrated in the opening cases). Families with members who have autism should also recognize that alternative therapies based on chelation to remove heavy metals have lost their major justification: thimerosal is no longer used in vaccines and never contained the demonstrated toxin methyl mercury. Heavy metals are thus one of many environmental factors to be considered in autism, but there is no compelling evidence for any particular agent as yet. Parents should also be made aware of the growing ability to detect genetic changes in autism: results may alleviate parental guilt about prenatal or childhood exposures and can help to inform relatives about risks for future children.

REFERENCES:
HPV Vaccine: Questions and Controversies

ABSTRACT: The human papillomavirus (HPV) vaccine Gardasil (Merck) has been shown to be almost 100% effective in preventing infection from the 4 strains of HPV (types 6, 11, 16, and 18) that cause 70% of cervical cancers and 90% of genital warts. The CDC and the Advisory Committee on Immunization Practices recommend that 11- to 12-year-old girls routinely receive the vaccine. Barriers to immunization include vaccine cost, families’ cultural or religious beliefs, and concerns about safety and efficacy. Factors that may influence acceptance of the vaccine by patients and parents are the provision of anticipatory guidance about HPV and sexuality and consideration of the financial and logistical burden of needing 3 separate visits for the vaccine.

The approval of Gardasil (Merck)—a recombinant vaccine providing protection against human papillomavirus (HPV)—in 2006 sparked instant controversy. Because HPV infection is a sexually transmitted disease, the use of a vaccine for such a disease brought the following political, medical, and moral questions to the forefront:

- Is this vaccine safe, efficacious, and cost-effective?
- Should only girls be vaccinated?
- Will the vaccination of preadolescents increase promiscuity?
- Should this vaccine, as many legislators are suggesting, join the ranks of the mandatory vaccines needed for school entry?
- Are these legislators influenced by drug company lobbyists or moralists?
- Are health care providers supportive of the vaccine?

This review provides the clinician with information to help answer some of these questions and clarifies some of the controversies surrounding the HPV vaccine.

OVERVIEW

More than 6 million persons aged 14 to 44 years are newly infected with HPV annually in the United States; almost 75% of these infections occur among male and female adolescents and young adults aged 15 to 24 years. More than 25% of American women aged 14 to 59 years are estimated to have HPV at any given time. More than 100 types of HPV cause infections; a large proportion of these infections resolve on their own without sequelae. Gardasil protects against 2 of the high-risk types associated with persistent disease that leads to cervical cancer (types 16 and 18), and against 2 of the types that most often cause genital warts (types 6 and 11). In clinical trials, the vaccine was almost 100% effective in preventing infection from these 4 strains of HPV, which cause 70% of cervical cancers and 90% of genital warts.

The HPV vaccine has been approved for use in girls and young women aged 9 to 26 years. The CDC and the Advisory Committee on Immunization Practices currently recommend that 11- to 12-year-old girls routinely receive the HPV vaccine. Administering the vaccine at

Dr Someshwar is assistant professor of pediatrics at West Virginia University School of Medicine in Morgantown.

JEAN SOMESHWAR, MD
West Virginia University
Human Papillomavirus Vaccine: Current Recommendations

- Gardasil is approved for use in girls and young women aged 9 to 26 years.
- Routine vaccination is recommended for girls aged 11 to 12 years.
- No baseline Papanicolaou (Pap) test or pelvic examination is required before vaccination.
- Regular Pap tests are still recommended for women who have received the human papillomavirus vaccine.
- The vaccine should not be given to girls or women who are pregnant.

this age before the initiation of sexual activity is preferable for maximum preventive benefit. The initial dose of the vaccine is followed with boosters at 2 months and 6 months. Vaccination is not limited by previous Papanicolaou test history or history of previous sexual activity.

GIRLS ONLY?

Although the current vaccine recommendations are for girls and women only, boys and men are equally likely to become infected with HPV. According to a 2007 study, the cancers associated with HPV infection in men include penile, anal, and certain kinds of oral cancers. HPV type 16 has been linked to head and neck cancers in both men and women; these cancers are actually more prevalent in men. Both men and women who report having 6 or more oral-sex partners during their lifetime have been shown to increase their risk of tonsil/tongue cancer 9-fold. Researchers are collecting data to determine whether HPV vaccination will show a benefit in reducing these oropharyngeal cancers.

The vaccine has been shown to have an equally strong immune response in both sexes and therefore should confer equal protection in both. In Europe and Australia, boys and men are vaccinated along with girls and women. Studies are also under way to address the issue of whether the inclusion of boys and men in routine vaccination will indirectly protect girls and women by providing herd immunity.

Parental attitudes toward the vaccine may become even more negative if boys are included in the vaccine-eligibility pool. Based on the predictors of intention to vaccinate reported in a recent study from Cincinnati, the major impetus of cancer prevention, while a valid argument in men as well as women, may not resonate as strongly among the male population because of a lack of public recognition of risk. Without a compelling belief in personal risk, male patients and their parents may be less likely to agree to voluntarily undergo the 3-shot series.

HOW SAFE IS IT?

Gardasil has a safety profile similar to those of many other childhood vaccines. In the 2 years after its approval, 9749 side effect reports were submitted via the Vaccine Adverse Events Reporting System (VAERS). These included 20 deaths subsequent to vaccination; however, the deaths were not proved to be related to the HPV vaccine. The most commonly documented complaint was soreness at the injection site. Only 6% of all events reported were deemed serious.

There have been reports of Guillain-Barré syndrome after vaccination, although the data currently do not suggest an association with the vaccine. There is also no clear evidence that vaccination altered the course of HPV-16 or HPV-18 infection that was present before administration of the first dose. Parents need to be informed that reports to VAERS do not prove cause and effect and that a temporal association does not confirm a causal connection.

IS IT COST-EFFECTIVE?

The potential clinical benefits of the vaccine do come with a significant financial burden. The cost for each injection is $360 for the complete 3-dose series. Most private insurance companies will cover the cost of the HPV vaccine. Free vaccination is also available for children through the following programs:

- Vaccines for Children. This federal health program provides free vaccines to children and teens younger than 19 years who are uninsured, Medicaid-eligible, Native Americans, or Alaska natives.

- Merck Vaccine Patient Assistance Program. This is available for young women 19 years and older living in the United States whose family income does not exceed 200% of the poverty level.

For the US population, the estimated annual cost for HPV-related diseases tops $3 billion. However, analysis of the financial burden of the disease versus the cost of universal HPV vaccination of 12-year-old girls, computed in many different countries including the United States, suggests that the HPV vaccine would indeed be cost-effective.

PROMISCUITY INCREASED?

Will adolescent girls engage in sexual intercourse earlier or more readily after being vaccinated against HPV? Previous research has focused on whether the availability of contraceptive care to teens affects their rates of sexual activity. It has been hypothesized that by discussing methods of contraception and prevention of sexually transmitted diseases, teens will feel uninhibited and free to pursue sexual encounters. In reality,
the opposite seems true, according to research. One study from the University of Pennsylvania showed that only the comprehensive sex-education approaches, which include contraceptive training, will delay initiation of sexual intercourse, reduce the frequency of unprotected sex, and reduce the number of sexual partners.\textsuperscript{14}

Perhaps one reason that parents object to their middle school-aged children being vaccinated is their belief that teens are unlikely to become sexually active in the near future. However, CDC statistics report that 13\%, 43\%, and 70\% of US girls are sexually active by age 15, 17, and 19 years, respectively.\textsuperscript{1,15} Even if parents realize that their teen may be statistically more likely to initiate sexual activity than they thought, neither parents nor teens may link this fact with the risk of contracting HPV. In a study conducted by Mays and coworkers,\textsuperscript{16} most of the adolescent girls and young women surveyed were unable to identify HPV infection as the major cause of cervical cancer or as a sexually transmitted disease, specifically genital warts. This lack of knowledge may have a substantial impact on vaccination rates.

Currently, 4 in 10 girls and women within the indicated age range are vaccinated.\textsuperscript{1} Recent data collected nationally by researchers at Cincinnati Children’s Hospital Medical Center note that mothers are less likely to pursue HPV vaccination for their daughters at age 11 to 12 years, as recommended, and more likely to vaccinate their teens at older ages.\textsuperscript{17} Specifically, of the mothers who intended to have their daughters vaccinated, 48\% said they would have their daughters vaccinated at age 11 to 12 years, 68\% at 13 to 15 years, and 86\% at 16 to 18 years.

The most powerful determinants of intention to vaccinate found in this study were, in order of importance, the mothers’ beliefs:

- That HPV vaccination would provide protection against cervical cancer.
- That vaccinated girls would not engage in riskier sexual behavior after having been vaccinated.
- That their personal clinician recommended the HPV vaccine.
- That their own daughter was at risk for HPV infection.\textsuperscript{17}

**Mandatory Vaccination?**

HPV vaccination has become a political issue.\textsuperscript{14,17} In Texas, a gubernatorial executive order mandating HPV vaccination of all girls before entry into sixth grade was rescinded by the state legislature. This legislative rebuke—passed by an overwhelming majority—was not vetoed by the governor; it prevents any mandatory HPV vaccination for the next 3 years in Texas. Opponents of the executive order complained that the governor was unduly influenced by his close ties with a pharmaceutical lobbyist, a former chief of staff.

Only the state of Virginia has passed a law that mandates HPV vaccination of girls entering the sixth grade; the statute takes effect in 2009.\textsuperscript{15,18} Parents are allowed to opt out if they have objections. A similar statute had passed in New Mexico but was subsequently vetoed by the state’s governor. Several other states have introduced related legislation.

**Are Pediatricians Recommending HPV Vaccination?**

Health care professionals may have ambivalent feelings regarding the push for HPV vaccination. Barriers that may prevent pediatricians from recommending immunization include:

- Vaccine cost.
- Anticipated frustration with addressing families’ cultural or religious beliefs regarding the vaccine.
- Anticipated reluctance of families to accept the new vaccines because of concerns about safety and efficacy.\textsuperscript{20-24}

In a study using interviews with primary care providers, some of the factors that positively influenced acceptance of the vaccine by patients and parents were the provision of anticipatory guidance about HPV and Human Papillomavirus Vaccine Facts

- More than 6 million persons aged 14 years to 44 years are newly infected with human papillomavirus (HPV) annually in the United States, and almost 75\% of these infections occur among male and female adolescents and young adults aged 15 to 24 years.\textsuperscript{1,15}
- Although only girls and women are formally recommended to receive the vaccine, boys and men are equally as likely to become infected with HPV.\textsuperscript{1,17}
- HPV type 16 has been linked to head and neck cancers in both men and women; these cancers are actually more prevalent in men.
- Most adolescent girls and young women surveyed were unable to identify HPV as the major cause of cervical cancer or as a sexually transmitted disease, specifically genital warts.
- In one study, among mothers who intended to have their daughters vaccinated, 48\% said they would have their daughters vaccinated at age 11 to 12 years, 68\% at 13 to 15 years, and 86\% at 16 to 18 years.
- Currently, 4 in 10 girls and women within the indicated age range are vaccinated against HPV.
- Only the state of Virginia has passed a law that mandates HPV vaccination of girls entering the sixth grade, beginning in 2009.\textsuperscript{14,17} Parents are allowed to opt out if they have objections.
Vaccines are perhaps the single most important contribution the 20th century made to civilization. They have been responsible for saving untold numbers of lives and for vastly improving the quality of many more. Although vaccines have had some bad press of late, they are still strongly recommended by the medical community. However, financial issues, difficulties with managed care organizations (MCOs) and other parts of our health care system, and problems with the manufacture and delivery of vaccines prevent optimal use of this crucial preventive service. Here I discuss the problems associated with vaccine delivery and administration and suggest several practical solutions.

MY 30 YEARS IN PEDIATRICS: THE IMPACT OF VACCINES

I began practicing on July 1, 1978. I felt privileged to be a pediatrician in the golden age of vaccines. I felt confident that there were several infectious diseases that I would probably never have to treat because of the fine array of vaccines in the physician’s arsenal. I had seen occasional cases of measles, mumps, rubella, tetanus, and pertussis during my training—but far fewer than were seen by pediatricians who had begun to practice in 1958 or even in 1968. I had studied diphtheria, polio, and smallpox but had seen not a single case of any of these diseases throughout my medical school and residency years.

Despite the wonders of lifesaving vaccines, patients were still dying of diseases caused by Streptococcus pneumoniae and Haemophilus influenzae. Like all other pediatricians of the time, I lived in fear of the middle-of-the-night phone call from parents concerned about their child’s unusual cough. Was it croup caused by a virus or could it be epiglottitis caused by H influenzae? My son suffered with croup and I spent many a night under our “army tent” (sheets placed over a bridge table with two vaporizers working), fearful that I might miss the diagnosis of epiglottitis.

Newborn nursery and pediatric unit beds were still occupied by patients with bacterial meningitis. I remember as if it were yesterday informing the parents of children with meningitis that even after survival there were potential complications that could occur—complications such as brain abscess, loss of vision or hearing, learning disabilities, motor impairments, and more.

Today, in 2008, we have cut the number of cases of H influenzae infection significantly, and annual cases of S pneumoniae pneumonia in the United States are down to about 40,000.1 Meningococcal disease has also been radically reduced to fewer than 1000 cases a year.2 The annual
incidence of hepatitis A is down to about 20,000 cases and varicella to about 32,000 cases; the numbers of cases of rotavirus infection and polio have fallen even more dramatically. Today we have influenza virus vaccines that have diminished the risk of vaccine-induced Guillain-Barré syndrome. Soon we will have the pleasure of seeing a significant drop in the incidence of cervical and anogenital cancers as a result of the recent introduction of a vaccine to protect against human papillomavirus (HPV) infection, currently the most prevalent sexually transmitted disease in the United States.

USE OF VACCINES STILL FAR FROM OPTIMAL

However, despite the availability of these vaccines, they are not reaching enough people. There are still 15 million to 60 million cases of influenza reported annually in the United States alone. Vaccines save approximately 3 million lives a year. This is a wonderful statistic, but it is not good enough. Close to 2 million lives a year are still lost to vaccine-preventable diseases.

Suboptimal use of vaccines is the result of a variety of problems with vaccine delivery. These include problems related to the cost of vaccines, inadequate physician compensation by MCOs, the manufacture of vaccines, effects of new types of health insurance, changing patterns of use of the health care system, and the fractured nature of health care delivery to poor children. Each of these problems is discussed in greater detail below, and possible solutions are outlined.

EROSION OF THE MEDICAL HOME

In times past, it was primarily underprivileged persons who had difficulty establishing roots in a medical home. The local hospital’s emergency department was often their primary source of medical care. Today, however, many families have 2 working parents who must seek medical care after normal business hours. These families turn to urgent care centers, emergency departments, and retail-based clinics. Some of these facilities are open 24 hours a day, 7 days a week, and are being used for this convenience.

Many retail-based clinics make it possible to pick up a gallon of milk or a box of tissues while obtaining medical care from a nurse practitioner or physician’s assistant. Retail-based clinics also offer short waiting times, plenty of parking, and the convenience of proximity to patients’ homes. The benefits of a medical home include being examined and treated by a physician or by a nurse practitioner who is working under the close supervision of a physician; being able to speak directly to one’s physician after hours in the event of an emergency; and being able to rely on the physician to keep track of such things as drug allergies, significant aspects of medical or family history, and vaccinations received or needed.

THE RISE OF HIGH-DEDUCTIBLE HEALTH PLANS

Another recent phenomenon, high-deductible health plans, also impedes the optimal administration of vaccines. These plans require the patient to pay for the first $1100 to $3000 of health care each year. Now families must decide how to spend their health care dollars. Patients arrive in doctors’ offices sicker than they did previously because they want to save money by waiting to be seen.

Although some high-deductible health plans cover preventive care received before the deductible has been met, about two-thirds do not do so. Some patients are electing to skip the yearly health maintenance exam in an effort to save money. As a consequence, conditions such as developmental problems, diabetes, and heart issues may be missed. There is also a real fear that vaccinations will be skipped because of patients’ efforts to keep out-of-pocket costs to a minimum.

FRACTURED CARE FOR LOW-INCOME CHILDREN

There are also problems associated with the administration of vaccines to patients who are uninsured and underinsured. There are wonderful programs, such as Vaccines for Children and the Children’s Health
Insurance Program (CHIP)/State Children’s Health Insurance Program (SCHIP), which supplement Medicaid programs. However, access problems arise because patients’ eligibility status can change from month to month. It can also be challenging to convince these patients to keep appointments. Record keeping can be problematic because for many of these children, trips to the doctor’s office are interspersed with trips to the emergency department and the local clinic. All of these issues can lead to lower vaccination rates.

Some states have begun to address the problems involved in providing vaccines to low-income children by implementing vaccine registries.

MANUFACTURER- AND SUPPLY-RELATED PROBLEMS

Recently, plant shutdowns have given rise to problems with maintaining adequate supplies of vaccines. Inadequate supplies have also resulted from unexpected demand. In addition, the delivery of vaccines given to prevent a seasonal disease has at times been too late to permit optimal vaccination of the population. If a vaccine is given to prevent a seasonal disease, it is important that it be released long enough before the season begins to both educate physicians and patients and to distribute the vaccine to the appropriate sources.

VACCINE COSTS

There are significant problems involved in the cost of supplying vaccines. Manufacturers incur costs associated with research and development that can reach hundreds of millions of dollars. The manufacture of vaccines is a business and manufacturers need to recoup expenses and earn a profit. The costs of vaccine development are passed on to the physicians who purchase vaccines. This problem is compounded by the fact that some of the vaccines that have been recently released are quite expensive. Some cost between $85 and $120 per dose.

It is not uncommon for a pediatrician to have more than $100,000 worth of vaccines stored in its refrigerator for future use. The money invested in the purchase of the vaccines is not making money. Would it save a practice money to carry a smaller inventory of vaccines? It would certainly require less of an investment in inventory, but it also would increase the chance of running out of a vaccine and not being able to immunize a patient when needed. Covering that eventuality would require a recall system to notify patients when an out-of-stock vaccine once again became available. Yet, when a patient returned for the vaccine, would you collect another co-pay? The patient might feel that it was unfair to incur the cost of this second co-pay. On the other hand, if you didn’t collect the co-pay, you would lose between $10 and $25 because the MCO would subtract it from the amount due you for the encounter, assuming that it had been paid by the patient. Worse still, patients might not return to the office and you might not be able to maintain their vaccine schedules.

One solution to the problem of the up-front cost of purchasing vaccines is to use a universal supplier—either the state or federal government. However, some states have already tried this approach and it has not been 100% effective. Massachusetts, for example, is experiencing fiscal problems trying to provide complete vaccine coverage for all the children in that state. Furthermore, although a universal supply system would ensure that physicians did not lose money on vaccines, neither would they make money with such a system, since they would lose the profits currently derived from vaccinating patients.

INADEQUATE PHYSICIAN COMPENSATION

While preventing disease and saving lives are the primary goals of every pediatrician, vaccinating patients also provides an important source of income. Certainly, no physician should lose money vaccinating a patient. Vaccines are a product purchased by physicians and, as in any business, there is profit involved when the product is sold. In the case of vaccines, profit is realized when payment is received after administration. The amount of payment will vary depending on the payer. If a vaccine is administered to a patient who is insured by an MCO, the amount of money received is determined by the contract that the physician has negotiated with the MCO. Some physicians can receive more than 35% above cost, while others with poorer contracts might receive as little as 1% to 2% above cost. Unfortunately, some physicians are even paid below cost.

Certainly, no physician should lose money vaccinating a patient... Some physicians can receive more than 35% above cost, while others with poorer contracts might receive as little as 1% to 2% above cost. Unfortunately, some physicians are even paid below cost.
waiting several weeks after the administration of a vaccine to be paid—means that during all this time the money invested in the purchase of the vaccine has not been making money.

For physicians who treat patients who are insured by MCOs, still other problems arise. MCOs do not incorporate new vaccines or price increases for existing vaccines until the manufacturer’s cost has been published. Some MCOs have been known to take as long as 90 days to adjust their computer systems to recognize and pay for new vaccines or new price increases. During this period, the physician has no idea what his or her payment will be or if he will be paid at all. Once the decision has been made to pay for a new vaccine, some MCOs retroactively pay physicians, but this is rare. A physician has the right to wait to offer a vaccine until the amount of the payment is known. However, if such a strategy were adopted, both patients and physician might suffer. Patients could be exposed to and contract the disease in question; in addition, the physician who did not provide the vaccine might then be open to a lawsuit.

Estimating accurately what you must receive for vaccines. In an effort to help pediatricians, the American Academy of Pediatrics has devised a vaccine business plan; this plan advises that in order to break even on a vaccine purchase a physician must receive 17% to 24% above the cost of that vaccine. This figure takes into account several factors: the cost of the vaccine, the cost of storage (including refrigeration and electricity), wastage, whether or not the product is returnable, and the cost of money.

Negotiating for better contracts with MCOs. Income also derives from the service performed at the time of the patient’s visit. This is the vaccine administration fee, which is dependent on the physician’s managed care contract. Physicians can and must advocate for higher payments. We must remind MCOs that vaccinating people saves money. It costs far less to vaccinate than it does to treat disease. When dealing with capitated plans, request that vaccines be carved out instead of included as part of the capitated rate.

When negotiating, remember that there is strength in numbers. Physicians must speak up for what they want. The more physicians who speak up for what they want and need, the greater will be their success. In addition, remember that pediatricians are important to families as they shop for insurance coverage. It is the rosters of pediatricians and obstetrician-gynecologists that are most often checked by young families. This fact can give pediatricians leverage with MCOs—although it can only do so if it is brought to the MCO’s attention.

Using proper CPT codes to maximize reimbursement for vaccinations. To generate profit, one must use the appropriate CPT codes. These codes clearly identify the specific product used; correctly identifying the product should guarantee proper payment. For example, there are multiple CPT codes for hepatitis

---

Table – Vaccine administration codes for children

<table>
<thead>
<tr>
<th>Codes for children younger than 8 years who have received vaccine counseling from a physician:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 90465—first intramuscular vaccine</td>
</tr>
<tr>
<td>• 90466—second and subsequent intramuscular vaccine given</td>
</tr>
<tr>
<td>• 90467—first oral or intranasal vaccine</td>
</tr>
<tr>
<td>• 90468—second and subsequent oral or intranasal vaccine given</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Codes for children younger than 8 years who have received vaccine counseling from a non-physician, or for any child older than 8 years who has received a vaccine:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 90471—first intramuscular vaccine</td>
</tr>
<tr>
<td>• 90472—second and subsequent intramuscular vaccine given</td>
</tr>
<tr>
<td>• 90473—first oral or intranasal vaccine</td>
</tr>
<tr>
<td>• 90474—second and subsequent oral or intranasal vaccine given</td>
</tr>
</tbody>
</table>

*If an intramuscular vaccine and an oral or intranasal vaccine are given at the same time, although only one oral or intranasal vaccine is being given, the oral or intranasal vaccine is still considered to be the second vaccine administered. Thus, the codes to use in this situation are 90465 and 90468 or 90471 and 90474.
B vaccines. Use code 90743 when giving hepatitis B vaccine to an adolescent if you are using the 2-dose series. If you are giving the 3-dose series to an adolescent, the appropriate CPT code is 90744.

The correct use of CPT codes is also helpful with Healthcare Effectiveness Data and Information Set (HEDIS) reporting. With the explosion of pay-for-performance programs among MCOs, rate of vaccination is one of the few measures that an MCO can use to assess performance in pediatrics.

Pediatricians must also remember to advocate for appropriate payment for the administration of vaccines. Some MCOs contend that if they pay fairly for the vaccine they should not have to pay fairly for its administration. This is utter nonsense. There must be proper payment for both product (the vaccine) and service (the administration of that vaccine). The various vaccine administration codes along with an explanation of their proper use, are provided in the Table.

In addition to CPT codes for vaccine administration, there are also evaluation and management CPT codes for the visits themselves. For a well-child visit for an established patient use the 99391-99395 series codes. If a patient comes into the office for a sick visit and you notice that the child is behind in his or her vaccine schedule, use this opportunity to play catch-up; the appropriate CPT codes are 99212-99215 for such encounters are 99211 and the ICD-9 diagnosis code v64.06.

Keep a watchful eye on charges made and monies received. Even if you have employed the correct CPT codes, you must still determine whether you have been paid correctly. Regularly review your explanation of benefits to determine its accuracy. Did the MCO pay your contracted amount? Or did they pay too much, too little, or not at all? Have you stayed current regarding the amount you are charged by the vaccine manufacturers?

One effective method for tracking charges is to employ a grid for every vaccine given, listing the CPT code, the purchase price, and the amount you are charged by the vaccine manufacturers.

The public’s fear of autism caused by vaccines continues, and physicians are spending significantly more time explaining the value of vaccines and trying to dispel parents’ fears. In such a situation, use the CPT code 99211 and remember to document in your notes the extra work involved. If after you have spoken with the parents, they still refuse the vaccine, use the code 99211 and the ICD-9 diagnosis code v64.06.

For a patient who comes to the office for a sick visit and you notice that the child is behind in his or her vaccine schedule, use this opportunity to play catch-up; the appropriate CPT codes are 99212-99215 for established patients or 99201-99205 for new patients (in addition to the codes for the vaccines given). If a patient comes to the office for a vaccine only, use the CPT code for that vaccine but do not code for an office visit. However, an exception to the foregoing rule may be made if the time spent in counseling far exceeds what you would normally spend.

The public’s fear of autism caused by vaccines continues, and physicians are spending significantly more time explaining the value of vaccines and trying to dispel parents’ fears. In such a situation, use the CPT code 99211 and remember to document in your notes the extra work involved. If after you have spoken with the parents, they still refuse the vaccine, use the code 99211 and the ICD-9 diagnosis code v64.06.

The correct use of CPT codes is also helpful with Healthcare Effectiveness Data and Information Set (HEDIS) reporting. With the explosion of pay-for-performance programs among MCOs, rate of vaccination is one of the few measures that an MCO can use to assess performance in pediatrics.

Pediatricians must also remember to advocate for appropriate payment for the administration of vaccines. Some MCOs contend that if they pay fairly for the vaccine they should not have to pay fairly for its administration. This is utter nonsense. There must be proper payment for both product (the vaccine) and service (the administration of that vaccine). The various vaccine administration codes along with an explanation of their proper use, are provided in the Table.

In addition to CPT codes for vaccine administration, there are also evaluation and management CPT codes for the visits themselves. For a well-child visit for an established patient use the 99391-99395 series codes. If a patient comes into the office for a sick visit and you notice that the child is behind in his or her vaccine schedule, use this opportunity to play catch-up; the appropriate CPT codes are 99212-99215 for such encounters are 99211 and the ICD-9 diagnosis code v64.06.

Keep a watchful eye on charges made and monies received. Even if you have employed the correct CPT codes, you must still determine whether you have been paid correctly. Regularly review your explanation of benefits to determine its accuracy. Did the MCO pay your contracted amount? Or did they pay too much, too little, or not at all? Have you stayed current regarding the amount you are charged by the vaccine manufacturers?

One effective method for tracking charges is to employ a grid for every vaccine given, listing the CPT code, the purchase price, and the amount of money received from all the major MCOs. Review this information quarterly.

REFERENCES:
Epiglottitis

JEFF ALLEN BECK, MD
Grand Rapids Medical Education and Research Center, Mich

JERI WEYHER KESSENICH, MD
Helen DeVos Children’s Hospital, Grand Rapids, Mich

A 17-month-old girl awoke with drooling, cough, respiratory distress, and a muffled cry and was brought to the emergency department. She had no nausea, vomiting, or diarrhea and no history of choking, aspiration, or airway problems.

On examination, the patient was in significant respiratory distress with audible stridor during inhalation and exhalation. While in an upright-seated position, the infant was noted to be leaning forward. Rectal temperature was 40.5°C (105°F); respiration rate, 40 breaths per minute; and pulse rate, 202 beats per minute. Oxygen saturation on room air was normal. Inhalation treatments were administered.

Anteroposterior and lateral neck radiographs demonstrated an enlarged epiglottis with effacement of the vallecula and thickening of the aryepiglottic folds and pharyngeal edema. Laryngoscopy demonstrated a severely edematous and erythematous epiglottis. The true vocal cords were normal. Aerobic and anaerobic culture specimens from the surface of the epiglottis were obtained.

The patient was transferred to the pediatric critical care unit in stable condition and placed on a mechanical ventilator. A review of systems at this point was normal. The mother reported that the patient had no significant medical or surgical history and no sick contacts. The infant was born at term via spontaneous vaginal delivery without complications. She had not yet received her final Haemophilus influenzae type b (Hib) or pneumococcal conjugate vaccinations; all other immunizations were up-to-date. She lived at home with her mother and 2 siblings.

Laboratory data revealed an elevated peripheral blood white blood cell count of 16,700/µL, with 38 segmented neutrophils, 1 band, 51 lymphocytes, 8 monocytes, and 2 eosinophils on manual differentiation. The culture was positive for a few Streptococcus pyogenes colonies. A nasal swab was negative for viral antigens (adenovirus; influenza A and B; parainfluenza viruses types 1, 2, and 3; and respiratory syncytial virus). A peripheral blood culture was negative.

Since the routine administration of Hib conjugate vaccine, the incidence of epiglottitis, a presentation of invasive Hib disease in children younger than 5 years, declined from 100 cases in 100,000 children in 1988 to 0.3 cases per 100,000 children in 2000.1 In 2006, 93% of children aged 19 to 35 months had received at least 3 doses of the Hib vaccine.2 Bacteria other than Hib have been associated with epiglottitis in children. These include Haemophilus influenzae types A and F; Streptococcus pneumoniae; Staphylococcus aureus; and β-hemolytic streptococci groups A, B, C, and F.2 Viral causes of epiglottitis are rare and associated with infection by herpes simplex
virus type 1, parainfluenza virus type 3, and influenza virus type B. Thermal injury also may cause epiglottitis. Most children with epiglottitis recover without residual airway effects when the appropriate antibiotics are administered and the airway is secured. Most deaths result from failure to secure the airway once the condition is suspected.

This patient was extubated on hospital day 3 after receiving ceftriaxone (50 mg/kg/d) and a total of 6 doses of dexamethasone given every 6 hours. Intravenous ceftriaxone was continued for a total of 7 days. After 48 hours of normal oral intake, the child was discharged with a prescription for a 5-day course of extended-release amoxicillin/clavulanate (45 mg/kg bid). The child was completely well at the follow-up visit 5 days later.

REFERENCES:
Cases In Point

Consequences of 3 Vaccine-Preventable Diseases

**Streptococcal Infection Secondary to Varicella**

KATHRYN S. MOFFETT, MD
West Virginia University

This 7-year-old boy was hospitalized because of vomiting, dysuria, fever (temperature, 40°C [104°F]), and generalized rash. Vesicles had appeared 2 days earlier, and new lesions were erupting on his abdomen, perineum, back, face, throat, and urinary meatus. The child had trouble drinking because of a sore throat, and he refused to void secondary to pain.

There were vesicular lesions on the patient’s eyelids, throat, anterior nares, external ear canals, and urinary meatus in addition to the more than 3000 ruptured vesicles on the rest of his body. Few of the vesicles had crusted. The skin around many of the lesions was red and inflamed; no pus was noted.

Blood was drawn for culture, and intravenous fluids were administered. On the basis of the clinical presentation, a diagnosis of varicella was made. Cultures were positive for secondary bacterial infection from group A β-hemolytic streptococci (Streptococcus pyogenes). No throat culture was performed.

The patient’s older brother had “brought home chickenpox” (according to the patient’s father) from school 18 days before his 2 younger brothers became infected. None of the 3 siblings had received immunization with the varicella vaccine.

The patient was given a 10-day course of ampicillin. He became afebrile on day 5, and the pox began to crust.