The concept of vaccinations can be considered the single most advantageous breakthrough in the history of public health and medicine, most especially in the consideration of pediatric medicine. Given the incredible downward trends in morbidity and mortality secondary to vaccine-preventable diseases since the onset of large-scale immunizations within populations, it is difficult to fathom that childhood vaccination rates are recently decreasing in many regions of the United States.
Although the National Immunization Survey, published by the Centers for Disease Control and Prevention (CDC), reports that immunization rates for many routine vaccines in 2012 were 90% or more among kids aged 19-35 months; statistics from the survey showed that “national vaccination coverage was 82.5% for ≥4 doses of the combined diphtheria, tetanus toxoid, and acellular pertussis (DTaP) vaccine, 92.8% for ≥3 doses of poliovirus vaccine, 90.8% for ≥1 doses of the measles, mumps, and rubella (MMR) vaccine, 89.7% for ≥3 doses of hepatitis B, and 90.2% for ≥1 doses of varicella vaccine.” This does represent a decline in coverage from 2011 of 1%-2% for DTaP, poliovirus, and hepatitis B. Coverage with ≥4 doses of the pneumococcal conjugate vaccine (PCV) decreased from 84.4% in 2011 to 81.9% in 2012. Coverage with the full series of the Haemophilus influenzae type b (Hib) vaccine, hepatitis A, and rotavirus vaccines remained stable from 2011 to 2012. 

Despite the seemingly ubiquitous nature of social media and opinions that oppose vaccinations in children, most parents still choose to vaccinate. But statistics show that greater than 1 in every 10 children are not receiving the recommended vaccines. Pediatricians and other primary care providers need to be well informed of the reasons more parents are requesting alternative vaccination schedules or refusing vaccines altogether. By being better informed, health care providers can better address parental concerns that commonly arise when the topic of vaccinations is being discussed, and in doing so, provide more true and accurate information.

The development and practice of vaccination has a long history. The first records of vaccines are from China around 1000 AD, where the Chinese probably practiced smallpox inoculation on a small scale by having powder from pulverized smallpox scabs blown into the nostrils or scratched into the skin. In 1661, after Emperor Fu-lin died of smallpox, his son became Emperor K’ang. He was the first to introduce smallpox inoculation into the population on a large scale. He is quoted as saying, “The method of inoculation having been brought to light during my reign, I had it used upon you, my sons and daughters, and my descendants, and you all passed through the smallpox in the happiest possible manner... In the beginning, when I had it tested on 1 or 2 people, some old women taxed me with extravagance, and spoke very strongly against inoculation. The courage which I summoned up to insist on its practice has saved the lives and health of millions of men. This is an extremely important thing, of which I am very proud.”

Throughout the 1400-1800s, epidemics raged through countries all over the world and millions died from smallpox. In the early 1800s, vaccination became an encouraged practice in the United States, and in 1813, the US Vaccine Agency was established. Of note, in the last decade of Jenner’s life, the London Bills of Mortality documented 7858 deaths resulting from smallpox, down from 18,447 the decade before vaccination.

Since the development of early vaccinations against smallpox, vaccines against many more diseases have been developed with massive improvements in contractions of these diseases. For instance, before Jonas Salk initiated the polio vaccine in 1952, an average of 13,000-20,000 cases of paralytic poliomyelitis was reported each year. Before the introduction of the measles vaccine, nearly everyone in the United States got measles. There were roughly 3-4 million cases each year, and an average of 450 measles-associated deaths reported every year between 1953 and 1963. Since widespread use of the MMR, measles occurrence has been reduced by 99%. Hib was recently the most common cause of bacterial meningitis in US infants and children before the vaccine was introduced in December 1987. Hib meningitis killed 600 children each year and left many survivors with severe complications, including deafness, seizures, or neurodevelopmental sequelae. As a result of routine use of the Hib conjugate vaccine since 1990, the incidence of Hib disease in infants and young children has decreased by 99% to fewer than 1 case per 100,000 children younger than 5 years. In the United States, Hib now occurs primarily in unimmunized children and among infants too young to have completed the immunization series. This disease was a common, devastating illness as recently as 1990, but now most pediatricians just completing their training have never seen a case. Before introduction of the 7-valent pneumococcal conjugate vaccine (PCV7), pneumococcal disease among children in this age was approximately 80 cases per 100,000 population. After the introduction of PCV7, rates of disease resulting from these 7 serotypes dropped dramatically to less than 1 case per 100,000 by 2007. Routine rotavirus
vaccination of US infants began in 2006. Children between the ages of 6 and 24 months are eligible for the vaccine. In another CDC study, researchers determined the impact of the vaccine among children hospitalized for vomiting and found that, in 2008, rotavirus hospitalizations among vaccine-eligible children decreased by 87%-96%.6

So, how do vaccines work to protect against diseases? The human immune system is a complex network within the body that has evolved to fight off infections. Specific and individual antigens are present within all pathogens, which trigger the immune system to mount a response and then create cellular memory of the antigens, which is protective against future infection. Immunological and medical science utilizes the concept of antigens to create vaccines. Vaccines are designed to contain either live attenuated pathogen, inactivated pathogen, toxoid antigens, acellular subunits of the pathogen, or conjugate antigens in which a molecule that causes a good immune response in the body is attached to a pathogen that the body may have difficulty mounting a response against. Administration of the vaccines is able to instigate an immune response and cellular memory formation without actually causing the disease.7

Babies begin their primary course of vaccinations at 2 months of age based on the recommended schedule. Because this is also the peak age of occurrence for sudden infant death syndrome (SIDS), the question of whether vaccines are related to SIDS has arisen. However, many studies have concluded that vaccinations are not a risk factor for SIDS. The Institute of Medicine (IOM) released a report (Immunization Safety Review: Vaccination and Sudden Unexpected Death in Infancy) in 2003 reviewing epidemiological evidence focusing on SIDS, all sudden unexpected death in infancy, and neonatal death. The purpose of the review was to investigate possible relationships between SIDS and vaccines, including the individual vaccines diptheria-tetanus-whole-cell pertussis, DTaP, hepatitis B, Hib, and polio, as well as specific combinations of vaccines. The committee did not find enough evidence to show that vaccines cause SIDS.8 Another study done by reviewing data from Vaccine Safety Datalink also found no association between immunization and deaths in young children. The study investigated deaths in children 1 month to 7 years of age between 1991 and 1995. The study compared vaccination histories for each vaccine during the week and month preceding the date of death for each child. Five hundred and seventeen deaths occurred between 1991 and 1995, most (59%) during the first year of life; but upon investigation, results did not show an association between immunizations and these childhood deaths.9

Autism spectrum disorder is a group of related neurological disorders that affect a child’s development, behavior, communication skills, and social interactions. According to the American Academy of Pediatrics (AAP), approximately 1 in 88 children are now diagnosed with autism. Over the past 15 years, the idea that development of autism spectrum disorder can be caused by immunization, in particular, immunization with the MMR vaccine, has been a growing concern for parents and health care providers. It started with the publication of Andrew Wakefield’s study in The Lancet in 1998 associating the MMR vaccine with autism. The fact that the MMR is given at 12-15 months of age and the onset of autism symptoms is usually detected at 15-18 months lends credence to this concern in the eyes of many individuals. However, since Wakefield’s study was published, 10 of the 13 authors have retracted the findings. In 2010, The Lancet retracted the study, citing ethical misconduct on the part of Wakefield. Further studies conducted in the United States and Europe have found no association between the MMR vaccine and autism. Over the years, the IOM and the AAP have organized several panels of independent scientists—all concluded that there is no association between MMR and autism. However, the fears that persist as a result of this fraudulent study have resulted in MMR vaccinations rates that are less than the targeted 90% in 15 different states.10

Along with concerns regarding a possible connection between the MMR vaccine and autism, the concern of thimerosal in vaccines has also been raised as a reason to withhold childhood vaccinations because of concerns of neurotoxicity and an autism link. Thimerosal is a mercury-containing organic compound. It was widely used in vaccines as a preservative and antimicrobial agent starting in the 1930s. There are case reports of clinical neurotoxicity following accidental poisonings with ethyl mercury or suicide attempts using thimerosal. However, doses in these cases ranged from 0.5 to 83 mg/kg (250-fold higher than in US influenza vaccines).11

A study published in the American Journal of Preventive Medicine in 2003 by Paul Stehr-Green found that more children in Sweden and Denmark were diagnosed with autism after removal of thimerosal from vaccines in those countries.12 A study published by Jon Heron in 2004 looked at more than 14,000 children in the UK and found no evidence of increased autism relative to exposure to thimerosal.13 Another study in the same issue of Pediatrics by Nick Andrews studied the records of more than 100,000 children who received different amounts of thimerosal and did not find evidence that exposure to thimerosal led to neurodevelopmental disorders.14 Since then, many epidemiological studies have shown that the levels of thimerosal in vaccines are not associated with increased risk of neurodevelopmental problems or autism.15 However, with the increasing awareness of potential neurotoxicity related to even low levels of mercury, the US Food and Drug Administration has worked with vaccine manufacturers to eliminate thimerosal from vaccines. Because of the possibility of infants and very young children receiving amounts slightly in excess of the recommended limits of 0.1 μg/kg/day per the US Environmental Protection Agency, thimerosal has now been removed from, or reduced to trace amounts in, all vaccines routinely recommended for children aged 6 years.
or younger, with the exception of inactivated influenza vaccine.\textsuperscript{16} Parents are also worried about the presence of aluminum in vaccines. Aluminum is present in hepatitis A, hepatitis B, DTaP, Hib, human papillomavirus, and pneumococcus vaccines. Aluminum is used as an adjuvant in order to improve the immune response to vaccines. Aluminum is a very common metal in nature and is ingested in both food and water. Most of aluminum that is ingested is quickly eliminated from the body. It is true that during the first 6 months of life, infants could receive approximately 4 mg of aluminum from vaccines. But, during the same 6 months, infants will also receive approximately 10 mg of aluminum in breast milk, approximately 40 mg in infant formula, or approximately 120 mg in soy-based formula.

Aluminum is harmful only if given in much larger amounts to premature infants or persons with compromised renal function.\textsuperscript{17} There are also people who have the concern that vaccines contain tissue from aborted fetuses; and for those who are strongly prolife, this may create an ethical dilemma, casting the development of vaccines in an immoral light. But is it true? No. Vaccines do not, in and of themselves, contain cells from aborted fetuses. However, this is one of those half-truths about vaccines. The truth, which has been distorted by many antivaccine and prolife groups, is that the hepatitis A vaccine, the MMR vaccine, and the chickenpox vaccine all contain attenuated or inactivated viruses that were grown in human cells. The specific cell lines used in vaccines are the MRC-5 and WI-38 cell lines, and both of these cell lines were cultured from cells taken from 2 abortions performed in the 1960s. The cells being used today are not actual cells from any fetus, but they have been propagated from that line. That is where the grain of truth in this lie comes from.\textsuperscript{3} And, although many religions support the prolife position, most do not prohibit or even discourage the practice of childhood vaccination. In fact, the statement from the National Catholics Bioethics Center regarding this issue is: “One is morally free to use the vaccine regardless of its historical association with abortion. The reason is that the risk to public health, if one chooses not to vaccinate, outweighs the legitimate concern about the origins of the vaccine. This is especially important for parents, who have a moral obligation to protect the life and health of their children and those around them.”\textsuperscript{3}

The vaccine refused more than any other is the influenza vaccine. Parents each have their own reason for refusing this vaccine, but the reason encountered most often is that the influenza vaccine makes their children or other family members sick. The concept of a vaccine causing illness is not far-fetched. There are indeed some vaccines that can cause illness, although it happens very rarely and usually in immune-compromised individuals. But whether or not a vaccine has the capacity to cause illness is based on the type of antigen it utilizes. Only vaccines with live attenuated viruses can actually cause illness.

Unfortunately, there is no way to predict who will have a mild case of chickenpox and who will have serious or even deadly complications. Influenza vaccines that are administered via injection are currently made in 2 ways: The vaccine is either made with inactivated influenza virus and is therefore not infectious or with no influenza viruses at all, as is the case for recombinant influenza vaccine. The intranasal vaccine is made with live attenuated influenza virus, which, in otherwise healthy individuals, can only cause a localized reaction in the cooler temperatures of the nares and are inactivated by higher core body temperatures. However, the intranasal vaccine is not recommended for extremely immune-compromised persons.\textsuperscript{15}

Another question parents ask is, “Why give the chickenpox vaccine? Isn’t chickenpox just a normal childhood disease? After all, we all had it and we are just fine.” It is true that before the introduction of the vaccine, nearly everyone in the United States contracted the disease at some point in their lives and most cases are mild. The problem lies in the possible complications, which include severe skin infection, scabs, pneumonia, brain damage, or even death. And, unfortunately, there is no way to predict who will have a mild case of chickenpox and who will have serious or even deadly complications. The chickenpox is extremely contagious, so preventing the spread of the disease with vaccination also helps to protect vulnerable populations, such as the very young, the very elderly, and chronically ill or immune-compromised children. Since the introduction of the varicella vaccine in 1995, the number of children who contract chickenpox is dramatically reduced, and, more important, the number of hospitalizations and deaths from chickenpox has gone down more than 90%.\textsuperscript{19} Some parents also want to know if the varicella vaccine will prevent the sequelae of shingles. The answer is that chickenpox vaccines contain a weakened live strain of varicella, which may cause latent infection. The vaccine-strain varicella can reactivate later in life and cause shingles. However, the risk of getting shingles after chickenpox vaccination is much lower than getting shingles after natural
Infants currently receive 14 different vaccines, sometimes requiring as many as 5 shots at a single visit and should have 26 inoculations by 2 years of age, so parents’ concern that their children might be overwhelmed by too many vaccines is understandable. Parents often express concern that an infant’s immune system is unable to process this many vaccines at a time, as well as concern for increased problems, irritability, and side effects. However, the idea of overwhelming the immune system and rendering it incapable of mounting a good response when multiple vaccines are given at the same time is just a common myth.

Babies, starting the day of birth, encounter immumerable new antigens and their immune system is built to be able to prioritize and respond to extremely large numbers of new antigens at once. In studies on the diversity of antigen receptors, with estimations of the numbers of antigens and epitopes in each vaccine, immunology experts calculate that an infant’s immune system has the capacity to respond to approximately 10,000 vaccinations at any one time. Or, looking at it another way, if 11 vaccines were given to an infant at 1 visit, the response would require only approximately 0.1% of the immune system. Studies have also shown that infants and children are unlikely to suffer any more-intense side effects with multiple vaccines than with a single vaccine. Rather, by giving vaccines one at a time, children are more likely to experience common side effects, such as pain, irritability, and/or fever, on several occasions instead of just one time, as with multiple vaccine administration. It is also important for parents to know that there are expert committees whose sole purpose is to review and investigate all studies and data related to vaccine science—the Advisory Committee on Immunization Practices (ACIP), which advises the CDC and the Committee on Infectious Diseases, which advises the AAP. These committees, after reviewing all of the data, came up with the currently recommended vaccine schedule, secure in the knowledge that studies have found it to be safe and effective for infants and young children, as well as protecting them from vaccine-preventable diseases as early as possible.

The current vaccine schedule recommended by the CDC and AAP is designed to protect infants and children from dangerous and possibly life-threatening diseases as early as possible in their lives, at the time when they are the most vulnerable. Every vaccine in the schedule has been tested during the licensing process to ensure that it is safe and effective for children to receive at the recommended ages. Then the ACIP

### Figure 1. CDC childhood immunization schedule

The current vaccine schedule recommended by the CDC and AAP is designed to protect infants and children from dangerous and possibly life-threatening diseases as early as possible in their lives, at the time when they are the most vulnerable. Every vaccine in the schedule has been tested during the licensing process to ensure that it is safe and effective for children to receive at the recommended ages. Then the ACIP

**NOTE:** The recommendations in this schedule must be read along with the detailed footnotes provided by the CDC on http://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-schedule.pdf. The related CDC footnotes as a reference are provided within this chart.

This schedule includes recommendations in effect as of January 1, 2014. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at http://www.cdc.gov/vaccines/hcp/acip-recs/index.html. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (http://www.vaers.hhs.gov) or by telephone (800-822-7967). Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for vaccination, is available from CDC online (http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm) or by telephone (800-CDC-INFO [800-232-4636]). This schedule is approved by the Advisory Committee on Immunization Practices (http://www.cdc.gov/vaccines/acip), the American Academy of Pediatrics (http://www.aap.org), the American Academy of Family Physicians (http://www.aafp.org), and the American College of Obstetricians and Gynecologists (http://www.acog.org).
works throughout the year to review all new and available data regarding all existing vaccines as well as potential new vaccines. The current recommended schedule can be seen in Figure 1. Other than physicians, who else influences parents’ decisions on whether or not to vaccinate their children? Certainly, friends and family can influence parents, but what about other health professionals? Many Americans are turning to alternative medicine specialists, most notably chiropractors. Because nearly one-fourth of all Americans use chiropractic services, chiropractors have a growing influence on the popular opinions regarding medical concepts and practices such as vaccination. Although the majority of modern, evidence-based chiropractors embrace the practice of vaccination, given the overwhelming evidence of the benefit and efficacy of vaccines, there is a minority in the chiropractic profession that vocally oppose vaccines. The basis of this opposition may be rooted in early chiropractic philosophy, which rejected the concept of infectious disease caused by germs and rather considered disease the result of spinal nerve dysfunction caused by misplaced vertebrae. Parents are the primary advocate for their children, but they have a lot of contradicting information coming at them from variable sources. When we take our oath as physicians, we take on the responsibility to advocate for the children who become our patients as well. The information we give to parents and the ease with which we are able to dispel unfounded fears regarding childhood vaccinations truly matters. Not all parents will have a change of heart or abide by our recommendations, but at least they are making a better-informed decision. In addition, it is important to continue to give the best possible medical care and work to build a trusting relationship with families, even when they refuse vaccines for their children. The official position of the AAP is: “Families with doubts about immunization should still have access to good medical care, and maintaining the relationship in the face of disagreement conveys respect and at the same time allows the child access to medical care. Furthermore, a continuing relationship allows additional opportunity to discuss the issue of immunization over time.” Physicians are on the front lines in the battle against childhood disease, and vaccines are one of our greatest weapons. We cannot just throw our hands up and give up the fight when the media, celebrities, and others are telling parents not to vaccinate their children. Because we know vaccines save lives. We know better.

References

Heather M. DiCross, MD, is in private practice in Livingston, Montana. She can be reached at heatherdicros@yahoo.com.

Michael E. Ryan, DO, FAAP, FACOP, is associate chief medical officer and chairman of pediatrics; associate in pediatric infectious diseases at Geisinger Medical Center in Danville, Pennsylvania. He can be reached at mryan@geisinger.edu.