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Discussing Vaccination With Concerned Patients

An Evidence-Based Resource for Healthcare Providers

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ABSTRACT

Data regarding rates of vaccination among children and pregnant women show that there has been a decrease in the number of vaccinations being administered in these vulnerable populations. Surveys of parents elicit a wide variety of concerns and fears driving vaccine refusal, many of which have been refuted by research. It has been demonstrated that healthcare providers are a major source of information for patients who have questions about vaccinations. Given the established vital role of vaccinations in preventing the spread of diseases with serious morbidity and mortality profiles, it is important that healthcare providers understand and feel comfortable discussing the principles of vaccination, the recommended vaccine schedules, and the effects of vaccinations. This article provides an overview of vaccination principles, reviews the potential health and financial costs of nonvaccination, and addresses a number of common concerns cited by parents and pregnant women who are considering vaccine abstention or alternate vaccination scheduling. The information in this article will enable healthcare providers to accurately counsel patients about vaccination choices.

Key Words: alternate vaccination schedule, childhood diseases, vaccination, vaccination refusal

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Since the introduction of modern vaccination by Edward Jenner in the 1790s,[1] there has been a steady decline in the incidence, prevalence, and disease burden of vaccine-preventable diseases. Vaccination has the ability to prevent specific illnesses in individuals, leads to a reduction in long-term disability and sequelae from infection, and improves pregnancy outcomes for women who are immunized. Those who avoid infection as a result of vaccination are able to live longer, healthier, and more productive lives. Twenty-eight diseases are currently vaccine-preventable,[2] including previously common diseases with high rates of morbidity and adverse sequelae, such as chicken pox and measles. Roush and Murphy[3] demonstrated significant decreases in morbidity rates of diphtheria (100%), measles (99.9%), paralytic poliomyelitis (100%), rubella (99.9%), congenital rubella syndrome (99.3%), smallpox (100%), mumps (95.9%), tetanus (92.9%), and pertussis (92.2%) and mortality from tetanus (99.2%) and pertussis (99.3%), in direct relation to the increase in vaccination.

In addition to protecting themselves against preventable illnesses, people who receive vaccinations protect others in 2 ways. The first is through what is known as "herd immunity." If a large-enough portion of the population is vaccinated against an illness, individuals who are unable to be vaccinated will be protected because of the decreased rate of infection and the subsequent decreased likelihood of exposure.[4] Although herd immunity protects individuals who are unable to be vaccinated for any reason, parents who are vaccinated confer a similar protection specifically to infants who are too young to be vaccinated. This is one reason to ensure that pregnant women are up to date on vaccines and receive necessary vaccinations when appropriate.

In the United States, modern immunization laws, enacted in the 1960s and 1970s, require childhood vaccination before beginning school. By the 1980s, vaccination was required for entrance into public schools in all 50 states and the District of Columbia.[5] Each state law allows exemptions so that families may make individualized decisions and refuse vaccination on the basis of medical need, religion, or personal philosophy. A comparison of pre- and postvaccination rates of incidence and mortality for 11 common vaccine-preventable diseases is shown in Table 1.

Despite the evidence demonstrating significant declines in communicable diseases due to vaccination, as well as the documented safety of vaccination, rates of vaccine refusal for nonmedical reasons have increased significantly in recent years. Between 1991 and 2004, vaccination refusal rates increased from 0.98% to 1.48% nationwide, with the most significant increase of 2.54% in states that allowed for exemptions other than for religious reasons.[5] While the absolute numbers of people who are refusing all vaccinations remain low, parental requests for alternative vaccination scheduling have recently risen to as high as 13%.[9]

This increase in vaccination refusal and alternative schedules has translated into a significant increase in the rates of several vaccine-preventable illnesses. The number of pertussis cases rose from 7580 in 2001 to 16 858 in 2009.[10] The Centers for Disease Control and Prevention (CDC) reported 12 outbreaks of measles in the first 6 months of 2011, the highest incidence rates since 1996.[11] Influenza vaccination rates for pregnant women have traditionally been low, with only 15% of pregnant women reporting vaccination in the 2009-2010 influenza season.[12] While there has been a significant increase in influenza vaccination in response to the H1N1 outbreak, only 49% of pregnant women reported receiving influenza vaccination in the 2010-2011 influenza season.[13] This is still well below the Healthy People 2020 goal of 80% vaccination.[14]

SCHEDULE OF RECOMMENDED VACCINATIONS

The CDC maintains a comprehensive schedule of recommended immunizations for infants, children, and adults.[15] The schedule is reviewed annually to ensure that it is consistent with the most current evidence base as well as data from the Vaccine Adverse Events Reporting System. The CDC vaccination schedule is approved and recommended by the Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Physicians.

As part of maintaining its recommended vaccination schedule, the CDC collects yearly statistics on schedule completion rates—that is, what percentage of the population receives all of the recommended vaccinations at the recommended time. Although vaccination rates for several individual vaccines meet the Healthy People 2020 goals, the rate of completion of the standard vaccine schedule for children 19 to 35 months of age is consistently below goals. These rates rose from 66% nationwide in 2002 to a high of 77% in 2007 and have trended back down to a national average of 70% in 2009 and 73% in 2010, the last year rates were published.[16,17] These rates are of particular concern because the cost of not vaccinating is so high.

To decrease rates of vaccine-preventable diseases and provide appropriate counsel to clients who may be wary of vaccines, it is important for healthcare providers to understand the basics of immunity, the best evidence for vaccination, the actual risks associated with vaccines, and the current CDC vaccination recommendations and schedule. This article identifies the current CDC vaccine recommendations, reviews the benefits of vaccination for children and pregnant women, and uses the current evidence base to answer common questions raised by vaccine-cautious parents. For an overview of disease immunity and the basics of vaccination, refer to Table 2.

BENEFITS OF VACCINATION

There are both immediate and long-term benefits of vaccination for individuals, as well as advantages for the community at large. The community benefits of vaccination stem from reduction in morbidity and mortality, as well as of reduction in cost and loss of productivity due to sick days from work and school, doctor's visits, hospitalizations, and long-term disability.[7,8] It is clear from these data that vaccination has had a staggering effect on the public health, reducing the disease burden for both individuals and communities.

Pertussis, also known as whooping cough, is a perfect example both of the success of vaccines in decreasing morbidity and mortality and of the rising rates of disease caused by decreasing vaccination rates. As noted in the introductory paragraph, before routine and mandatory vaccination for pertussis, there were 150 000 to 260 000 annual cases of pertussis and up to 9000 annual deaths reported to the CDC. In 2001, there were only 7580 reported cases of pertussis in the United States; there were 181 pertussis fatalities from 2000 to 2008, with 166 of those deaths in children younger than 6 months.[7] Such great reductions in illness and death demonstrate the significant role of vaccination in health promotion. Despite the clear benefits of pertussis

Table 1. **A comparison of pre- and postvaccination rates of incidence and mortality for 11 common vaccine-preventable diseases**

Vaccine-preventable disease (cost of vaccine)	Incidence before vaccination	Current incidence	Morbidity and mortality rates	Projected incidence if vaccination stopped
Polio (e-IPV, $11.97)	13 000–20 000	From 1980 to 1999, there were 162 confirmed cases	<1% of 20 000 polio cases each year result in paralysis of the limbs (usually the legs). Of those cases resulting in paralysis, 5%-10% of the patients die when the respiratory muscles are paralyzed.	20 000 cases per year
Measles (MMR, $18.98)	"Nearly everyone"; 450 deaths reported between 1953 and 1963	"Sporadic"	3 deaths per 1000, with 90% of those exposed getting measles and 20% hospitalized	20 million cases and 197 000 deaths each year worldwide
Type B meningitis (Hib, $8.98)	20 000	<10 fatal cases	600 deaths per year	1 in 200 children younger than 5 y
Hepatitis B ($10.35)	450 000 new infections per year; 12.5 million Americans with infection	80 000 in 1999	5000 deaths per year and >$700 million in medical and work lost costs; 25% of children infected die as a result of related liver disease.	2 billion infected worldwide; 350 million are chronic carriers
Pertussis, (DTaP, $13.25)	150 000-260 000; 9000 deaths per year	181 fatal cases from 2000 to 2008	3.8 per 1000 000 live births, and 13.1 per 10- to 100-fold increase; 1000 000 live births for infants younger than 2 mo; two-thirds of those infected hospitalized[6]	10- to 100-fold increase
Pneumococcal ($34.54)	63 000; 6100 deaths	1525 fatal cases	3000 cases of meningitis, 50 000 cases of 75% increase to prevaccination rates bacteremia, 500 000 cases of pneumonia, and 7 million cases of otitis media	Rise 75% to prevaccination levels
Rubella (MMR, $18.98)	20 000 infants with CRS, 2100 deaths, 11 250 miscarriages	6 cases of CRS in 2000	Although rubella infection is mild in children and adults, 90% of infants born to mothers infected in the first trimester will have CRS	Return to prevaccination rates
Varicella ($69.73)	"Almost all persons," 4 million cases; 11 000 hospitalizations, 100-150 deaths	400 000 cases	"Highly contagious"	Return to prevaccination rates, with virtually all susceptible persons being infected in their lifetime
Diphtheria (DTaP, $13.25)	206 000; 15 520 deaths	2 cases in 2004	5%-10% mortality, up to 20% of infants	150 000 cases and 5000 deaths reported in newly independent states of the former Soviet Union after vaccination stopped
Tetanus (DTaP, $13.25)	1314; 263 deaths	41 cases in 2000	20% mortality, vaccination does not protect community but only individuals.	300 000 newborns and 30 000 mothers die annually due to inadequate vaccination
Mumps (MMR, $18.98)	300 000 per year	266 cases in 2001	Usually mild, 1 in 20 000 children deaf, increased miscarriage rates	Return to prevaccination rates; 2006 outbreak of 6500 cases and 2010 outbreak of 3400 in unvaccinated communities

Abbreviations: CRS, congenital rubella syndrome; DTaP, diphtheria and tetanus toxoids and acellular pertussis; e-IPV, inactivated polio vaccine; Hib, *Haemophilus influenzae* type b; MMR, measles-mumps-rubella.

Table 2. **Basics of immunity**

Immunity: Protection from a disease-specific pathogen due to production of antibodies in response to foreign antigens.[18] Immunity can be passive or active.

Passive immunity: Results after the administration of antibodies and provides short-term immunity to specific illnesses[19]

- Infants receive passive immunity to specific diseases from their mothers during the final 2 mo of term gestation and through breast milk.[20]
- The duration of passive immunity varies between individuals, lasting between 1 mo and 1 y in infants depending on the infection.
- For some diseases, such as pertussis, passive immunity is not transmitted at all.[20]

Active immunity: Results when a person has an illness and his or her immune system responds to the antigen by producing antibodies, preventing future infection from the same disease.[19]

- Active immunity may also be acquired via the administration of a vaccine.

Both natural and vaccine-acquired active immunity cause the body to create memory cells, which enable the production of antibodies in the future, preventing future illness.

Active immunity is long term and often permanent.

Herd immunity: Refers to levels of immunity in an entire population. If a sufficient portion of the population has been vaccinated, the likelihood of exposure and subsequent infection is decreased in nonvaccinated people.[20]

- High levels of immunization within a community play a particularly important role in protecting individuals who cannot be vaccinated from exposure to vaccine-preventable diseases.[5]
- It is not possible to specify exact percentages of a population that need to be vaccinated against a particular disease in order to attain herd immunity. These vary by disease and according to demographic factors such as geographic location and population density.
- Goals for rates of vaccination in pregnancy and infancy are provided by Healthy People 2020.[14]

Types of vaccines[3]

Live antigen vaccines: Live antigens, either bacteria or viruses, are administered and cause the body to produce disease-specific antibodies and immunity.

- These attenuated antigens replicate poorly in human cells, meaning the vaccine will not cause illness in immunocompetent persons.
- Live antigen vaccines should not be administered to pregnant women because of the theoretical possibility that the antigens would harm the growing fetus.[21] This risk is purely theoretical, and there have never been any documented cases of actual harm.[22]

Inactivated antigen vaccines: Live antigens, either bacteria or viruses, are destroyed by heat and cannot replicate. The inactivated antigens are complete enough to be recognized by the immune system, causing the body to produce disease-specific antibodies and immunity.

- Inactivated antigens cannot replicate in the body and can be safely administered to pregnant women.
- Vaccines made from inactivated antigens may require "booster" doses to maintain immunity.[10]

vaccination, concerns over vaccine administration have led to a decrease in rates of vaccination. Since this decrease, the United States has seen an increase in pertussis infection rates, which rose to 16 858 in 2009, more than double the 2001 rate.

An analysis of the cost-benefit ratio of vaccination must take into account both the actual monetary cost of the vaccine and the costs of adverse events. These costs must then be weighed against the benefits of disease prevention, including the immediate and long-term costs of illness.[7,8] An excellent example of this cost analysis was performed by Carabin et al,[23] who found that the average cost per measles case (including complications such as hospitalization) in several industrialized countries was $254 to $307 whereas the average cost per postvaccination adverse event was $1.43 to 1.93. When compared with the costs of vaccine-preventable diseases, the absolute monetary cost of any individual vaccine is quite low, even when the cost of adverse events is included. This is particularly true of combination vaccines such as the measles-mumps-rubella (MMR, $18.98) or diphtheria and tetanus toxoids and acellular pertussis (DTaP, $13.25).[8]

VACCINATIONS BEFORE, DURING, AND AFTER PREGNANCY

There are several unique vaccination recommendations specific to women who are pregnant or are trying to become pregnant. There are vaccine-preventable diseases that pose special risks to fetuses and newborns; vaccination of a woman before or during her pregnancy can reduce the incidence of these diseases. There are also vaccinations that should not be given to pregnant women. Healthcare providers have the dual responsibility of understanding the impact of vaccine-preventable diseases on both mother and fetus, as well as knowing the vaccine recommendations for pregnant women and how these differ from nonpregnant adults.

The CDC publishes vaccine guidelines for women before, during, and after pregnancy.[24] The 4 specific vaccines with unique implications for pregnant women are rubella, hepatitis B, pertussis, and influenza. These will be discussed individually later, as will specific recommendations for women who are traveling while pregnant. Live vaccines should not be given to pregnant women because there is a theoretical risk to the fetus from these types of vaccinations.[21,22] These contraindicated vaccinations include rubella, live attenuated influenza, MMR, varicella, and zoster (shingles). In addition, the human papilloma virus vaccine is "not recommended."[22]

A preconception healthcare visit is an ideal time to assess a woman's vaccination history, collect titers if necessary, and provide appropriate vaccinations if they are needed. Preconception counseling ensures that women are up to date on vaccinations and enables them to receive "missing" vaccinations before becoming pregnant. This is of particular value in the case of live vaccines such as rubella, which should not be given to pregnant women. Women who are already pregnant should be assessed for vaccination status, including titers, and counseled about which vaccines are safe in pregnancy and which should be given postpartum. Pregnant women should be assured that being up to date on their own vaccinations is the first step in protecting their infants from vaccine-preventable diseases.

Rubella

Rubella (German measles) is a viral disease that typically causes a fever and skin rash for several days. In young adults, it is usually not a serious illness and is self-limiting in duration.[25] The fetus of a pregnant woman infected with rubella is at risk for severe birth defects, including deafness, heart defects, cataracts, damage to the liver and spleen, mental retardation, and termination. The CDC recommends that women who intend to become pregnant be given the MMR vaccine if a titer result is nonimmune; these women should wait to become pregnant for at least 4 weeks after vaccination.[24] Since rubella is a live-virus vaccine, it should not be given to pregnant women because of the potential risk to the fetus. Instead, pregnant women who are found to be nonimmune to rubella should be offered the vaccine once they have given birth.

Hepatitis B

Hepatitis B is a viral infection that affects the liver. It can be either acute, lasting several weeks, or chronic and lifelong. It is spread through contact with body fluids. A pregnant woman who has hepatitis B can pass it to her infant during delivery.[26] Acute hepatitis B is more likely to develop into chronic hepatitis B the younger it is acquired. It is estimated the 90% of infants affected with hepatitis B will develop chronic infection; most people with chronic hepatitis B were infected as infants or very young children. The CDC recommends that pregnant women be tested for hepatitis B as part of preconception care or upon presenting for prenatal care. Women who are at high risk for hepatitis B and not already immune should be offered the vaccination series. The vaccination may be given during pregnancy.

The CDC also recommends the first dose of hepatitis B vaccine be given to infants within 12 hours of birth, with additional doses per the vaccination schedule for children. This is especially important if the mother has hepatitis B. Infants of these women should also be given hepatitis B immune globulin. The combination of the hepatitis B vaccine and hepatitis B immune globulin given to the infants of hepatitis B–positive women can prevent most cases of chronic hepatitis B.[26]

Pertussis

Pertussis (whooping cough) is a bacterial illness that causes severe, violent coughing spells. Complications include pneumonia and death. The CDC vaccination schedule recommends infant vaccination at 2, 4, and 6 months of age, after which time most infants are protected.[27,28] Since infant vaccination does not begin until 2 months, they are susceptible to pertussis infection before this time and are also at increased risk for complications and death. Adults who are infected with pertussis may not have symptoms, so an infected adult can pass pertussis to an infant without realizing it.[23] To protect infants who are too young to be vaccinated, the CDC recommends that all adults who are in contact with an infant younger than 12 months receive the DTaP vaccine; ideally, it should be given at least 2 weeks prior to contact. In addition, pregnant women who have not previously had a DTaP vaccine should receive it in the second or third trimester of pregnancy, which provides some passive immunity against pertussis.[27] If she is not given the vaccination during pregnancy, it should be given immediately postpartum.

Influenza

Influenza is a respiratory virus that causes coughing, sneezing, fever, and body aches. It may lead to secondary infections such as ear or sinus infections or pneumonia. Because different strains of the virus are prevalent at different times, yearly influenza vaccination is recommended for everyone aged 6 months and older. As is the case with pertussis, infants younger than 6 months are at increased risk, both of getting influenza and of suffering complications. For this reason, anyone expecting contact with an infant should receive the influenza vaccine.[28]

Because of normal physiologic changes in the heart and lungs during pregnancy, a pregnant woman who contracts influenza is at a greater risk for complications, hospitalization, and death.[29] Infection with influenza also places pregnant women at higher risk of premature labor and delivery. For these reasons, any woman who is pregnant during influenza season should receive the inactivated influenza vaccination regardless of pregnancy trimester.[24] Pregnant women should not receive the live attenuated influenza vaccine, which is administered via nasal spray, because of the theoretical harm to the fetus of a live-virus vaccination.[28]

Swine influenza or "swine flu" is an influenza virus that causes illness in pigs. Although humans are not usually affected by these viruses, variant viruses have occasionally spread to humans, causing limited disease. Prior to 2009, the CDC recorded infection with these variant strains in approximately 1 person every 1 to 2 years.[30] In 2009, a strain of variant swine flu (H1N1) emerged that not only caused illness in humans but was also easily transmissible among humans. This led to a pandemic; from April 2009 to April 2010, the CDC reported mid-level estimates of 61 million H1N1 cases, 274 000 hospitalizations, and 12 470 deaths.[31] Since 2009, the seasonal influenza vaccine includes H1N1 and other similar swine influenza variants.[30]

Vaccinations for travel

International travel presents additional considerations for healthcare providers and pregnant women. There are multiple areas of the world where vaccine-preventable diseases are prevalent. In many of these areas, the prevalent diseases are not common or do not exist in the United States and travelers must be vaccinated before taking a trip. While pregnancy is a precaution against giving some pretravel vaccinations, the CDC recommends vaccination if the risk of exposure outweighs the potential risks of the vaccine. Vaccinations for Japanese encephalitis, meningococcal meningitis (the conjugate vaccine is preferred over the polysaccharide), inactivated polio, rabies, and typhoid (the polysaccharide is preferred to the live attenuated vaccine) should all be given with caution to pregnant women. However, if a woman is traveling to an area with high incidence of these diseases and exposure is likely, the CDC suggests that the benefit of vaccine administration outweighs the potential risks.[32]

The yellow fever vaccination requires that a risk-benefit analysis be made on a case-by-case basis. In some instances, the risk of vaccination outweighs that of exposure to yellow fever; in these cases, a pregnant woman may be issued a medical waiver, allowing her to travel without receiving the vaccination. If the risk of exposure to yellow fever is greater than the risk of vaccination, the vaccination may be administered.[32]

Some travel locations may require vaccination against tuberculosis, MMR, or varicella. These vaccinations are contraindicated in pregnant women because of the risks to the fetus. A pregnant woman should delay travel until after delivery rather than receiving these vaccines.[32] Women considering travel to countries that require vaccinations should be referred to a healthcare professional familiar with these vaccinations and with international travel.

VACCINE REFUSAL: BEHIND THE TRENDS

Parents and pregnant women refuse vaccinations for religious or political reasons as a result of concerns over the safety of vaccines and their ingredients. Some of the most common concerns related to vaccines have been dispelled with scientific research. Despite the evidence base supporting the safety and efficacy of vaccination, the rates of nonvaccination and of requests for alternate vaccination scheduling continue to rise. To discuss vaccine safety with parents and pregnant women, it is vital that healthcare providers be familiar with some of the more common concerns parents may present, and should explain the evidence refuting these concerns.

In August 2011, the Institute of Medicine released a consensus report titled "Adverse Effects of Vaccines: Evidence and Causality."[33] This report focused on 8 vaccinations—varicella zoster, influenza (except 2009 H1N1), hepatitis B, human papilloma virus, MMR, hepatitis A, meningococcal, and those containing tetanus—with a focus on the casual relationship between these vaccines and adverse events. This meta-analysis established that while there are links between MMR, varicella zoster, influenza, hepatitis B, meningococcal, and tetanus-containing vaccines and anaphylaxis, this is a rare occurrence. The meta-analysis found no demonstrable link between any of the vaccinations and either autism or asthma.[33] The analysis concluded that vaccines cause or are associated with few health problems. Common adverse events of vaccination include injection site reactions or localized pain, fever, and malaise, which are mild and self-limiting.

Ahluwalia et al[34] investigated the reasons why pregnant women were not vaccinated for influenza during the 2009-2010 influenza season despite the American Congress of Obstetricians and Gynecologists recommendations[35] and the Healthy People 2020 goal of 80% vaccination.[14] Using the Pregnancy Risk Assessment and Monitoring System, the most common reasons for not vaccinating for seasonal influenza were "normally don't get" (72.1%), "worried for baby" (47.7%), "worried for me" (45.2%), and "MD didn't

mention" (32.6%).[32] The high number of patients who were not vaccinated because the vaccine was not presented by their healthcare provider indicates one clear way for providers to increase vaccination rates. The percentages of women who were not vaccinated out of concerns for their own or their infant's health indicate that simple education about the benefits of influenza vaccine may be a catalyst to reaching the Healthy People 2020 vaccination goals.

The rationales cited by parents for decreasing rates of completed vaccination for their children are more complex. Kennedy et al[36] examined parental beliefs and concerns regarding vaccination. The primary concerns cited by parents who did not vaccinate their children or elected to follow an alternate vaccination schedule were "pain" (38%), "receiving too many vaccines at one time" (36%), "too many vaccines in the first 2 years" (34%), "potential for fever" (32%), "potential for learning disabilities and autism" (30%), and "unsafe ingredients" (26%). Localized pain and swelling, as well as mild fever and the potential for anaphylaxis, are part of the informed consent and should be discussed with parents and pregnant women. However, it is appropriate and important to emphasize that these are not the reasons to delay or withhold vaccination and the sequelae of infection are more significant and more frequent than those resulting from vaccination. Clients with concerns about learning disabilities, vaccine ingredients, and safety should be reassured and provided evidence demonstrating vaccine safety. In addition, current CDC data about rising rates of vaccine-preventable diseases in the community and the role of vaccination can be useful information for parents.

When making decisions about infant vaccination, Kennedy et al[36] found that the most frequently cited sources were trusted healthcare providers (85%), family (46%), and friends (22%), government and professional organizations (28%), the Internet (10%), and traditional media (11%). Omer et al[5] emphasized that parents who delay vaccination or select alternate scheduling, such as "Dr Bob's Selective Vaccine Schedule"[37] (see further discussion on alternative vaccination schedules later), often do so at the suggestion of their healthcare providers. These reviews indicate that trusted healthcare providers can have a great deal of impact on rates of vaccine administration for infants, children, and pregnant women and on preventing disease outbreaks.

TALKING POINTS FOR PROVIDERS IN RESPONSE TO COMMONLY ASKED QUESTIONS

Most parents with concerns about vaccinations are asking similar questions. Some common questions and concerns patients bring to providers are presented, followed by a discussion of the evidence and talking points for providers.

Do vaccines cause autism and developmental delays?

This concern gained momentum and publicity after the publication of an article in *Lancet* by Wakefield et al[38] in 1998. The article featured interviews with the parents of 12 children with a diagnosis of autism spectrum disorder (ASD). The parents of 8 of these children recalled that symptoms of developmental delays had begun with the administration of the MMR vaccine. The article speculated that the MMR vaccine had, in fact, been the cause of these delays and of the children's autism.

As this purported link gained momentum, many in the medical field pointed to the inherent flaws in the article of Wakefield et al, including the very small study population and the reliance on interview and parent recollection as its main data sources. Further research was conducted to examine the suggested causal link between MMR vaccination and ASD. One notable study was performed by Thompson et al in 2007.[39] In a large-scale cohort study, 1107 children 7 to 10 years of age were given a series of neurophysical tests designed to assess 42 characteristics, including speech ability, memory, hyperactivity, and tics. These results were compared with levels of thimerosal each child had received in vaccines. There were no associations found between the level of thimerosal exposure and any of the neurophysical outcomes.[39]

All of these subsequent studies culminated in an Institute of Medicine review, "Immunization Safety Review: Vaccines and Autism,"[40] and a 2005 Cochrane Database review, "Vaccines for Measles, Mumps and Rubella in Children."[41] At the highest level of scientific evidence, neither review found any evidence of a causal linkage between MMR vaccination and ASD. After review of these findings, *Lancet* ultimately retracted the original article of Wakefield et al.

The American Psychological Association diagnostic criteria for ASD outline a range of symptoms, varying in severity from "mild" to "requiring very substantial support."[42] The onset of symptoms coincides with the recommended age for MMR vaccine administration,[43] which has led some parents to infer a causal relationship between receipt of the vaccination and the development of ASD. Concerned parents should be assured that although these events are *correlated* (ie, occur at similar points in time), there is no evidence showing *causation* (ie, one event, having autism, happens because of the other event, receiving a vaccination). While acknowledging parent's concerns, healthcare providers

can succinctly present the information from the Institute of Medicine and Cochrane Database reviews to sufficiently demonstrate that the evidence demonstrates no connection between vaccination and the development of ASDs.

Do vaccines have lots of chemical additives?

One common criticism of vaccinations is that they contain unknown or unusual ingredients. Those commonly cited by concerned parents and patients include thimerosal or mercury (which is discussed earlier), aluminum, formaldehyde, and antifreeze. Information distributed by antivaccination groups and individuals cites the industrial uses of these chemicals and the adverse effects of exposure in large amounts or over long periods of time as reasons to question the safety of vaccines containing these ingredients.

Aluminum salts are included in vaccines to increase efficacy. They increase the body immune response to the antigen, which decreases the number of shots needed to create immunity. Because aluminum is present in the earth crust, we are exposed to it in food and water and it is present in both breast milk and infant formula. It is estimated that the amount of aluminum found in vaccines is about that present in 33 oz of infant formula.[44]

Formaldehyde is another vaccine component that often causes concerns because of its better-known uses in industrial trades and as an embalming agent. It is used in vaccines to inactivate viruses and detoxify diphtheria and tetanus. The amount that is left in the actual vaccine is smaller than the amount of formaldehyde found naturally in the human bloodstream. It is also worth noting that formaldehyde can be found in household products such as paper towels and cosmetics and is not harmful in these amounts.[44]

Antifreeze is often cited as a worrisome vaccine component, although this is based on a misunderstanding. Antifreeze is made up of ethylene glycol, whereas the vaccine component is polyethylene glycol, which is often used in cosmetics and toiletries such as lotion and toothpaste. Safe amounts of polyethylene glycol are used in vaccines to inactivate viruses and as a purifier.[44]

Concerned parents should be told that small amounts of these preservatives and stabilizers are used in manufacturing vaccines to ensure their safety and sterility. In a 2003 review of the evidence, Offit and Jew[45] found that these chemical additives, in the amounts present in vaccinations, are likely not harmful to humans. For parents with more specific concerns related to individual vaccines or individual ingredients, the CDC outlines the ingredients found in each vaccine, as well as the evidence for the safety of these ingredients, in its "Ingredients of Vaccines Fact Sheet."[46] Healthcare providers may wish to share this fact sheet with parents to help them make fully informed choices about vaccinating their children.

Of course, persons with known allergies to any vaccine component should not receive vaccines containing these components.

Do vaccines have a lot of adverse effects?

Some common adverse effects of vaccine administration are irritation and redness at the injection site, low-grade transient fever, cold-like symptoms (malaise, cough, stuffy nose, etc), and diarrhea. All of these adverse effects are considered mild and will, unlike the diseases prevented by vaccines, resolve without intervention or long-term sequelae.[45] There is a potential for more severe reactions and adverse effects following vaccine administration. These adverse effects most notably include autoimmune reactions (rheumatoid arthritis and Guillain-Barre syndrome), complications of high fevers (encephalopathy and seizures), and anaphylaxis or other allergic responses.[47] The potential for these serious adverse effects should be considered in context: the Vaccine Adverse Events Reporting System has received so few reports of these reactions that it is difficult to determine a causal relationship between vaccinations and these extremely rare adverse effects.

The exception for vaccine refusal in the face of potential adverse effects is for the case of patients who are immunocompromised. Live vaccines should not be given to those who are immunocompromised, and their family members should discuss the situation with a healthcare provider before being vaccinated themselves. The most important point to remember and emphasize with patients and families is that the adverse effects from vaccinations are typically mild and transient whereas the diseases they prevent have higher rates of debility and death.

Are these diseases really that bad?

There is a misunderstanding among many parents and pregnant women that vaccine-preventable diseases are not serious illnesses or are not common enough to warrant vaccination. The perception of the benign nature and infrequent morbidity of these diseases ironically stems from the success of vaccination. Since polio has been completely eradicated in the United States and the prevalence of other vaccine-preventable diseases has decreased so significantly, the public health risks of these diseases are not as visible or widespread as they once were. Adults who remember having measles or chickenpox when they were children may not realize the rates of disability and death associated with

these diseases, thinking of them instead as routine and harmless childhood illnesses.

Misconceptions about the seriousness and transmissibility of vaccine-preventable diseases may prompt patients to question the relevance of vaccinations based on an erroneous risk-benefit ratio. It is important for healthcare providers to be able to explain how sufficiently high enough levels of vaccination in the community ("herd immunity") work to prevent a rapidly spreading outbreak. Providers can also discuss the prevaccination morbidity and mortality rates for vaccine-preventable diseases to counsel patients on the continued importance of vaccinations for individual health and in the larger social context.

Can the vaccines be given on a different schedule?

Many parents with concerns about vaccines may ask about alternatives to the CDC-recommended vaccine schedules. These "alternate schedules" aim to spread the course of vaccination over a longer time period. This is usually accomplished by giving fewer vaccinations at one time, requires more office visits to give all of the recommended vaccinations, and results in finishing the full vaccination course at a later age. Although alternate schedules may seem to be a good compromise, giving all of the recommended vaccinations while assuaging some fears of vaccine-cautious parents, alternate vaccine schedules create gaps in coverage and are not recommended or endorsed by any expert committees.[48] It is important that healthcare providers be able to discuss these schedules and correct misconceptions about their value as substitutes for the CDC-recommended schedule.

One of the most popular variations on the vaccine schedule is "Dr Bob's Alternative Vaccine Schedule," which was created by Dr Robert Sears and explained in his 2011 *The Vaccine Book*.[37] The book has sold more than 40 000 copies and Dr Sears' vaccination schedule has been shared on numerous blogs and Web sites. *The Vaccine Book* presents 2 vaccination schedules of Dr Sears's creation. The first is an "alternative" schedule that gives all of the CDC-recommended vaccinations over a longer period of time—for example, hepatitis B vaccination is begun at 2.5 years rather than at birth. The second schedule is a "selective" schedule that eliminates the MMR, varicella, hepatitis A, and polio vaccinations and delays the influenza vaccination until 21 months of age.[37] In their 2009 article, Offit and Moser[48] review the statements made in Dr Sears' book and provide evidence countering these claims. The main arguments in *The Vaccine Book* are those covered previously in this article—that the safety of vaccinations is suspect, that vaccinations contain toxic ingredients, and that vaccines prevent diseases that are no longer a concern in the United States. In addition to providing evidence against these claims, Offit and Moser[48] point to the negative effects of following one of Dr Sears' alternate schedules. While parents may feel that the alternative schedule is an acceptable alternative to the CDC-recommended schedule, a delay of months or years in receiving vaccinations leaves children unprotected at a time when they are most vulnerable. Since children are among the groups more likely to experience severe illness or death when infected with vaccine-preventable diseases, an alternative vaccine schedule that leaves the youngest children unvaccinated increases the risk of illness and disease outbreak.[46]

CONCLUSION

Rates of vaccination for children and pregnant women continually fall short of the Healthy People public health campaign goals, and patients are declining or delaying vaccinations because of fears and misunderstandings with increasing frequency. The decrease in vaccination rates is leading to increasing disease rates. Given the enormous body of evidence supporting vaccination as a highly effective weapon against multiple diseases, it is clear that increasing vaccination rates and meeting the Healthy People 2020 goals will have a marked effect on public health.

Evidence also shows that patients look to their healthcare providers for information and guidance when they have questions or concerns about the necessity and safety of vaccination. Healthcare providers are in the position of trusted resource for the families and communities they serve. As such, providers have an obligation to know and understand the basic principles of immunity, the evidence base about vaccination safety, and the current vaccination recommendations from government and professional organizations. They must then be able to use this knowledge to discuss vaccinations with parents and pregnant women, answer their questions, and guide them through the large volume of information available. In the digital age, patients are able to assemble information from a wide body of sources, from evidence-based research articles to personal opinion blogs. While acknowledging and respecting patients' right to autonomy and self-efficacy, healthcare providers are under professional responsibility to correct erroneous information and calm unfounded fears and guide patients in safe, rational, and evidence-based decision making.

Table 3 provides a list of further evidence-based resources about vaccines, their purpose, their adverse effects, and their safety, suitable for sharing with patients who desire more information.

Table 3. **Vaccination resources for parents and patients**

Resource	Description
Childhood vaccines: what they are and why your child needs them[49]	A brief overview of how vaccination creates immunity and information about common vaccinations and the diseases they prevent
10 reasons to get vaccinated[50]	Simple information about seasonal influenza vaccination, covering herd immunity and vaccination safety
What if you don't immunize your child?[51]	Pamphlet explaining consequences of influenza, pertussis, measles, and chickenpox; lists links to other resources
2012 CDC vaccination schedule[15]	Single-page graph listing recommended vaccinations and the ages these should be administered
Instant childhood immunization schedule[52]	Interactive Web site that lists the dates each CDC-recommended vaccination is due on the basis of a child's birth date.
Vaccination FAQ[53]	American Academy of Pediatrics site giving further information on topics ranging from why vaccination is important to what the ingredients in vaccinations do; includes information about vaccination coverage for children without insurance or whose insurance will not pay for vaccinations
IAC vaccine information for the public and healthcare professionals[54]	In-depth information from the Immunization Action Coalition about specific vaccinations and frequent concerns [*Note*: links to photographs of people with various vaccine-preventable diseases, which may be disturbing to some patients or children]
Need help responding to vaccine-hesistant parents?[55]	List of evidence-based Web sites, handouts, and videos from several reputable organizations
Questions and answers about vaccine ingredients[44]	American Academy of Pediatrics handout answering concerns about various vaccine ingredients, explaining the purpose and safety of a number of common ingredients

Abbreviations: CDC, Centers for Disease Control and Prevention; FAQ, frequently asked questions; IAC, Immunization Action Coalition.

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