VACCINE SAFETY and YOUR FAMILY

Separating Fact from Fiction

Excerpted from:

VACCINES *and* YOUR FAMILY

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INTRODUCTION

Infectious diseases have killed and maimed humans since the beginning of time. The pathogens that cause these diseases are uniquely adept at finding the most vulnerable among us. Most often, this means the youngest and oldest in our communities. The youngest because their immune systems are not yet familiar with these disease-causing agents, and the oldest because their immune systems are not as capable of defending against these agents as they once were.

Historically, these human vulnerabilities were apparent in shorter lifespans and larger families as parents had more children in the hope that some of them would survive to adulthood. Vaccines have changed all of that. Along with clean water and improved medical care, vaccines have given us a way to fight back.

Unfortunately, when vaccines work, we often don't know they protected us. As a result, some diseases are no longer seen as the enemy—because they often aren't seen at all. Conversely, because we know the day and time that vaccines are given, for some, the vaccines have become the enemy.

For most families, though, vaccines are not an enemy, but rather something they have questions about as they traverse health decisions. Many of the questions, indeed virtually all of them, have been answered using sound scientific methods, and concerns related to vaccine safety have been found to be baseless. However, often times, these findings do not find their way to the top of internet search results, social media feeds, media reports, or discussions with family and friends, leaving people confused, frustrated and outright scared to immunize themselves and their most vulnerable family members.

This booklet is designed to bring the findings of those scientific studies to families. Excerpted from the book, *Vaccines and Your Family: Separating Fact from Fiction* (©2024 Columbia University Press), the next several pages will present discussions and scientific findings related to the most common questions and concerns about vaccine safety, including about the vaccine schedule, whether vaccines cause other conditions, and what is in the vaccine vial. While these pages are not filled with references, if you are interested, you can find references for the information presented herein in the complete version of the book, available from the publisher (see form in the back of this booklet for discounted offer) or through most major booksellers.

After reading this information, we hope you will be reassured that getting vaccinated is an easy, safe, and important way to protect the most vulnerable among us from the pathogens that have been harming humanity since the beginning of time.

GENERAL QUESTIONS ABOUT VACCINE SAFETY

Are vaccines safe?

A vaccine is safe if its benefits definitively outweigh its risks. But any medical product that has a positive effect—whether a drug or a vaccine—can also have a negative effect. No vaccine is absolutely safe. All vaccines given as shots can cause pain, redness, or tenderness at the site of injection. And some vaccines can cause more serious problems. For example, the measles vaccine can cause a temporary decrease in platelets, which help the blood to clot. This happens in about one out of twenty-five thousand children who get the vaccine. This reaction, called thrombocytopenia, shouldn't be surprising since natural measles infection can do the same thing, except much more commonly and much more severely.

Other vaccine side effects can be quite severe. The chickenpox vaccine contains gelatin as a stabilizer. Some people are severely allergic to gelatin and can develop life-threatening allergic symptoms if they are given the chickenpox vaccine. The oral polio vaccine, no longer used in the United States but still in use in other parts of the world, can cause polio. It's rare, occurring in about one per 3.4 million doses, but it does happen. An influenza vaccine used in Europe during the swine flu pandemic in 2009 called Pandemrix was a rare cause of narcolepsy, a permanent disorder of wakefulness. And the yellow fever vaccine can be a rare cause of symptoms like yellow fever in older people.

But while there are rare risks to vaccines, nothing is risk free. The most dangerous aspect of vaccines is likely driving to the doctor's office to get them. Every year about forty thousand people in the United States die in car accidents. Walking outside on a rainy day isn't entirely safe; every year in the United States about thirty people are struck by lightning and killed. And tens of thousands of people die every year when they slip and fall. Even routine daily activities pose a certain degree of risk. But we choose to do them because we consider the benefits to outweigh the risks.

How do I know if a problem is caused by a vaccine?

One person's story

Anecdotal experiences can be very powerful. For example, a professor emeritus at Duke University School of Medicine tells the story about a friend's four-month-old child who was taken to a clinic to get a diphtheria, tetanus, and pertussis (DTP) vaccine. The father waited and waited in line. Finally, he tired and took the baby home without getting the vaccine. At home the father put the child to bed. Several hours later, the child was found dead in his crib, the victim of Sudden Infant Death Syndrome (SIDS). Had the child received the vaccine, no amount of statistical evidence in the world would likely have convinced him that anything other than the vaccine was the cause. *Source: Sam Katz communication with author (2000).*

Because we're human, we naturally look for reasons something happened. The process of seeking to understand what causes various problems has been crucial to our success as a species. And sometimes bad things happen, including to young children. They suffer asthma, allergies, autism, developmental delays, hyperactivity, or attention deficits, among other health problems. Worse: sometimes they die of poorly defined disorders, like sudden infant death syndrome (SIDS). Because children receive numerous vaccines during the first few years of life, some of these health conditions are diagnosed soon or immediately after receiving vaccines.

How can you know whether symptoms that follow a vaccination were caused by the vaccine? The best way is by performing scientific studies that compare a group of vaccinated individuals with a group of unvaccinated individuals who are otherwise similar. For example, in 1998, a British research group proposed that the combination measles-mumps-rubella (MMR) vaccine might cause autism. At the time, about one in two thousand children in England were diagnosed with autism, and about nine of ten were given the MMR vaccine. To determine whether the British research group's theory that the MMR vaccine caused autism was correct, researchers from around the world studied hundreds of thousands of children who did and did not receive the vaccine. If the vaccine caused autism, then the number of children with autism should be higher in the group that received the vaccine than in the group that didn't. As it turned out, the incidence of autism in children who got the MMR vaccine was the same as in those who didn't get it. (See "Do Vaccines Cause Autism?").

Importantly, when trying to determine whether a vaccine causes a particular problem, one study isn't enough; other investigators should repeat it to make sure that the results hold up across different populations of children. That was done with investigations into the MMR-causes-autism theory. Eighteen studies performed by researchers in seven countries on three continents costing tens of millions of dollars all showed the same thing: the MMR vaccine didn't cause autism. Although epidemiological studies looking at disease rates among populations are not perfect, they can be quite powerful, particularly when numerous studies by different researchers taking somewhat different experimental approaches find the same thing. Indeed, epidemiological studies can determine whether a vaccine caused a problem in as few as one in a million vaccinated children.

Many parents who read about the investigations into the MMR vaccine were reassured by the results, but some weren't. They had been compelled by individual anecdotes they had witnessed or heard about, and no study could convince them otherwise.

What systems are in place to ensure that vaccines are safe?

Before they're licensed, vaccines are tested in tens of thousands of children. These studies are large enough to determine whether vaccines cause common or even uncommon side effects, but they are not large enough to determine whether a vaccine may cause a very rare side effect. To monitor instances of very rare side effects, two post-licensure systems were put in place in the late 1980s and early 1990s: the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD).

VAERS is a surveillance system codirected by the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). If a parent, health care provider, or anyone else believes that a vaccine has caused an adverse event (i.e., a harmful or unwanted side effect), they can complete and submit a one-page form. These forms—which are easily obtained from doctors' offices or from the internet (vaers.hhs.gov/index)—are carefully evaluated by the FDA and the CDC to determine whether a particular side effect is reported more frequently than would be expected.

One example of how VAERS works occurred between 1998 and 1999 when a new vaccine to prevent rotavirus, RotaShield, was licensed by the FDA and recommended for routine use in children to be given by mouth at two, four, and six months of age. Soon after the vaccine was introduced, reports of an unusual problem, an intestinal blockage called intussusception, started coming into VAERS. Intussusception is a medical emergency that occurs when one part of the intestine telescopes into another, causing a blockage. When this happens, the blood supply to the intestinal surface can be compromised, and the intestinal lining can become severely damaged. Without medical treatment, children can suffer massive intestinal bleeding. Also, bacteria that normally live on the intestinal surface can enter the bloodstream, causing a serious infection. Either of these problems can be fatal. After RotaShield had been given for several months, fifteen cases of intussusception were reported to VAERS. This was more than had been reported for any previous vaccine. Although it was tempting at this point to conclude that RotaShield caused intussusception, VAERS data alone were not adequate to prove this. Investigators now had to determine whether intussusception following RotaShield administration was occurring at a rate greater than would be expected by chance alone (before this vaccine was first used, intussusception occurred in about one out of every two thousand infants annually). To do this, they used the VSD.

The VSD is a group of large health maintenance organizations whose computerized medical records are linked, representing about 3 percent of the U.S. population, including both adults and children. Whereas VAERS can be used to generate a hypothesis (e.g., whether a vaccine has caused a particular

problem), the VSD can be used to answer the question because it offers something that VAERS doesn't: a control group. In the case of the rotavirus vaccine, investigators could examine the medical records of children who either had or had not received RotaShield to see whether intussusception occurred more commonly in the vaccinated group. It did. RotaShield caused intussusception in about one in every ten thousand children who got the vaccine. Consequently, RotaShield was taken off the market. This was the first time a vaccine had been discontinued because of a safety problem in almost fifty years.

Seven years passed before another rotavirus vaccine was given to U.S. children. It was called RotaTeq, and it was made differently from RotaShield in that it was based on rotaviruses that infect cows rather than monkeys. This time, the VSD was immediately put into action using something called rapid-cycle analysis. As soon as children started to receive RotaTeq, VSD investigators began examining the incidence of intussusception in children who either had or had not received it. They evaluated these children's records every day, looking for any evidence that RotaTeq was causing the same problem as RotaShield. But the incidence of intussusception was the same in both groups of children.

Another example of the use of VAERS and the VSD is myocarditis (an inflammation of the heart) following receipt of mRNA vaccines to prevent COVID-19. Following the authorization of two mRNA vaccines in December 2020, reports to VAERS of myocarditis triggered studies in the VSD that found the association was real, not just a coincidence. However, while myocarditis occurs rarely after receipt of an mRNA COVID-19 vaccine (about one case per fifty thousand doses), it occurs far more commonly following natural COVID-19 infection (about one case per one hundred infections).

VAERS and the VSD are model systems to determine whether a vaccine causes a very rare side effect. They've served us well, showing that vaccines don't cause diseases or conditions like multiple sclerosis, allergies, asthma, or diabetes, among others.

Can I avoid the need for vaccines by living a healthy lifestyle?

Some people believe that living a healthy lifestyle—eating nutritious foods, getting plenty of exercise, and taking daily vitamins—is enough to avoid infections. Although good nutrition is important, immunity to specific viruses or bacteria can be acquired only by natural infection or immunization. And, as we know, the price of natural infection is often too high.

One example of why a healthy lifestyle doesn't provide enough protection can be found in the life of one of America's most beloved presidents, Franklin Delano Roosevelt. Roosevelt was an active, vigorous man. Coming from a

wealthy family, he was certainly well nourished. But in his late thirties he contracted polio, a disease that permanently paralyzed him. Roosevelt died ten years (to the day) before the polio vaccine was first licensed in the United States—a vaccine that would have been the only reliable way for him to have avoided a disease from which he suffered for most of his life.

DO VACCINES CAUSE _____?

Do vaccines cause chronic diseases?

Although vaccines have clearly extended our lives, some people fear that vaccines have merely substituted chronic diseases for infectious diseases. These people believe that instead of suffering from measles, mumps, and chickenpox, we now suffer from diabetes, multiple sclerosis, and arthritis, all of which are autoimmune conditions (in which the body reacts against itself).

It is certainly true that some infections can cause the body to react against itself. One example is strep throat, which is caused by the bacterium *Streptococcus pyogenes*. Some children infected with strep develop a disease that can severely affect the heart. This happens because proteins on the surface of strep bacteria (called M proteins) are very similar to proteins found on the cells that line the heart. When the immune system reacts to strep bacteria, it also inadvertently reacts to the heart. The result is a severe and occasionally fatal disease: rheumatic fever.

Another example is Lyme disease, caused by the bacterium *Borrelia burgdorferi*. People with Lyme disease develop a long- lived, recurrent arthritis because one of the Lyme bacterial proteins is like a protein found in joints. And intestinal infections caused by *Campylobacter* bacteria can lead to an autoimmune disease called Guillain-Barré syndrome (GBS), which causes the body to attack the lining of nerves.

If infections can cause the body to react against itself, it stands to reason that vaccines could do the same thing. But vaccines don't have what it takes to cause the autoimmunity occasionally found after natural infection. For example, multiple sclerosis is an autoimmune disease of the brain in which the body reacts against the covering of nerves. Nerves are like wires covered by a thin layer of rubber. But instead of rubber, nerves are covered by something called myelin, the principal component of which is myelin basic protein. The symptoms experienced by people with multiple sclerosis are often worse during the winter. That's because influenza infections occur most commonly during the winter, and one of the proteins on influenza virus can mimic myelin basic protein. Thus, the bodies of some people with multiple sclerosis, when making an immune response against influenza virus, also

inadvertently make an immune response to their own brain. Knowing this, a logical next question is, Can influenza vaccine do what natural influenza infections do? The influenza vaccine is like a natural influenza virus in that both contain the protein that mimics myelin basic protein. But studies have clearly shown that although natural infection can worsen multiple sclerosis symptoms, the influenza vaccine can't. That's because the influenza vaccine virus doesn't reproduce (it's not live) and therefore doesn't induce nearly the intensity of the immune response necessary to cause the body to react against itself. (Even the nasal-spray influenza vaccine, which is live and can reproduce, doesn't reproduce very well, so, like the killed influenza vaccine, it doesn't cause the body to react against itself either.)

Lyme disease is another example of why vaccines don't induce very good autoimmune responses. As mentioned, Lyme disease can cause a type of chronic arthritis based on an autoimmune response to a surface protein on the bacteria that is similar to a protein found in joints. This bacterial surface protein was used to make a Lyme disease vaccine that was available in the United States between 1998 and 2002. The obvious question is, Did the Lyme disease vaccine cause chronic arthritis? To answer this question, tens of thousands of people who had received the vaccine were compared with tens of thousands of people who didn't to see whether the risk of arthritis was greater in the vaccinated group. It wasn't. Unfortunately, however, because of unfounded safety concerns, the vaccine was not well accepted, and the company stopped making it. This is an example of an existing technology that could prevent illness and suffering but instead sits on a shelf simply because misinformation won the day.

Vaccines have demonstrated that they can't cause the cascade of immunological events necessary for autoimmunity. They have consistently been shown not to cause multiple sclerosis, diabetes, or other autoimmune diseases. Historically, one exception to this rule was the swine flu vaccine given to prevent a feared influenza pandemic in 1976, which was found to be a rare cause of Guillain-Barré syndrome in about one out of one hundred thousand vaccine recipients. Another exception to the rule was an influenza vaccine used in Europe in 2009 (Pandemrix), which was found to be a rare cause of narcolepsy, a permanent disorder of wakefulness.

Do vaccines cause autism?

The notion that vaccines cause autism was launched on February 28, 1998. That's when researchers in England published a paper claiming that the combination measles-mumps-rubella (MMR) vaccine caused autism. The British group suggested that the measles vaccine damaged the intestine, allowing brain-damaging proteins to escape the gut and enter the brain. Other scientists tried to find the same results but couldn't: no intestinal

inflammation, no brain-damaging proteins, and no clear route to the brain. The paper was later retracted, meaning it was removed from the publication, after it became apparent that the lead author, Dr. Andrew Wakefield, had been untruthful about his funding, potential conflicts of interest, and some of the report's findings. More importantly, however, eighteen subsequent studies found no evidence that children who receive the MMR vaccine are at greater risk of autism than those who don't.

In 1999, the hypothesis shifted. At that time, the American Academy of Pediatrics, together with the U.S. Public Health Service, asked for thimerosal, an ethylmercury-containing preservative, to be removed from all vaccines given to young children. These groups had become concerned that as more and more vaccines containing thimerosal were added to the schedule, babies might be exposed to harmful quantities of mercury. Those in favor of removing thimerosal argued that they were exercising caution in the absence of data because at the time, no studies had determined that the overall quantity of thimerosal received across multiple vaccines was toxic. Unfortunately, the decision to remove thimerosal was made so quickly that some parents became concerned. They reasoned that maybe thimerosal caused autism. As had been the case during the MMR scare, the science quickly followed. Six studies examined the risk of autism in those who either had or had not received vaccines containing thimerosal, and all showed that the chance of getting autism was the same in both groups. Consistent with these findings, the incidence of autism has only continued to increase even though thimerosal has been removed from all vaccines given to young infants. Three other studies found that thimerosal in vaccines didn't cause even subtle signs of mercury poisoning.

A few years later, the hypothesis shifted again. This time some parents feared that autism was caused by too many vaccines given too early. Another study was done comparing the rates of autism and other neurodevelopmental or psychological disorders in children who were vaccinated according to the recommended schedule with the rates in children whose parents had chosen to delay or withhold vaccines. Again, no difference was found between the two groups. Delaying or withholding vaccines didn't reduce the risk of autism. It only increased the risk of getting vaccine-preventable diseases.

Coincident with the studies related to vaccines and autism, other researchers were working to identify the causes of autism. While we still do not understand all the reasons that some children develop autism, we have continued to learn more. For example, we know that both genes and environmental conditions, particularly during fetal development, can play a role. Exposure to medications, such as thalidomide, or viral infections, like rubella, during pregnancy can cause an infant to have autism. Parental age, particularly that of the father, has also been found to play a role.

For the latest science on autism and for support resources and research studies for families affected by this increasingly common condition, visit the Autism Science Foundation website: https://www.autismsciencefoundation.org.

Do vaccines cause allergies and asthma?

Several types of antibodies circulate in the body. One type, immunoglobulin G (IgG), is commonly found in the bloodstream. Another type, immunoglobulin A (IgA), is commonly found at the lining of the nose, throat, and intestines. But it's the third one, immunoglobulin E (IgE), that can be particularly troublesome because it mediates most allergic diseases, like hay fever and asthma. During an allergic response, IgE binds to a type of cell in the body called a mast cell. Mast cells release inflammation mediators (such as histamine) that cause wheezing, hives, sneezing, runny nose, and itchy eyes.

Several factors control IgE. The most important is a type of immune cell called T cells. The two most important types of T cells with regard to allergies and asthma are T-helper cell type 1 (Th1) and T-helper cell type 2 (Th2). Th1 cells decrease the production of IgE, and Th2 cells increase the production of IgE. So, when talking about allergies, Th1 cells are good, and Th2 cells are bad.

At birth, babies have a predominance of Th2 cells, which bias immune responses toward allergic responses. The best way to overcome this is to enhance the production of Th1 cells. This occurs naturally by infection with bacteria and viruses, both of which prompt the body to produce more Th1 cells. The most succinct description of this phenomenon and the importance of experiencing infections in the first few years of life can be found in the subtitle of an editorial in the *New England Journal of Medicine*: "Please, Sneeze on My Child."

Some people fear that because vaccines prevent natural infections, the maturation of Th1 cells might be affected, thus causing children to develop allergies or asthma (this is often referred to as the "hygiene hypothesis"). For example, children who live in large families, attend day care, or live in low- or middle-income countries—and are therefore exposed to more bacteria and viruses than other children—are less likely to have allergies than other children. So, the hygiene hypothesis makes sense. But for a couple of reasons, it doesn't extend to vaccines.

First, vaccines do not prevent most common childhood infections. For example, a study of twenty-five thousand illnesses in Cleveland in the 1960s found that children experienced six to eight infections a year in the first six years of life, most of which were viral infections of the upper respiratory tract or intestines that aren't prevented by vaccines. They were caused by viruses, such as parainfluenza virus, rhinovirus, respiratory syncytial virus (RSV),

adenovirus, parechovirus, enterovirus, coxsackie virus, norovirus, calicivirus, and astrovirus. Therefore, vaccines are unlikely to prevent most common childhood infections and won't alter the normal balance of Th1 and Th2 cells.

Second, diseases prevented by vaccines, such as pertussis, measles, mumps, rubella, and chickenpox, are highly contagious and easily transmitted independent of the degree of hygiene in the home or the level of sanitation in the country. So, the hygiene hypothesis doesn't hold here.

Clinical studies also support the idea that vaccines don't cause allergies or asthma. One group of investigators examined computerized records of more than eighteen thousand children born between 1991 and 1997 who were enrolled in four large health maintenance organizations. Children who had received the diphtheria-pertussis-tetanus, oral polio, *Haemophilus influenzae* type b (Hib), hepatitis B, and MMR vaccines were found not to be at greater risk for asthma than those who hadn't. Another well-controlled study of more than six hundred children found that those who had received the diphtheria-tetanus-pertussis vaccine were not at greater risk for asthma, hives, or food allergies. Several other studies also found no evidence that vaccines increased the risk for allergic diseases. Taken together, these studies show that vaccines do not cause allergies or asthma.

Do vaccines cause cancer?

In the 1950s and 1960s, scientists invented two polio vaccines. One, made by Jonas Salk, involved inactivating poliovirus with formaldehyde. The other, made by Albert Sabin, involved weakening poliovirus by growing it in nonhuman cells. Both strategies shared an important feature: the vaccine viruses were grown in monkey kidney cells.

In 1960, another researcher, Bernice Eddy, found that monkey kidney cells used to make polio vaccines contained another virus: a monkey virus. Because it was the fortieth monkey virus identified, it was called simian virus 40 (SV40). This meant that children inoculated with Salk's and Sabin's vaccines had also been inadvertently inoculated with SV40 virus. This was a problem because Eddy later found that SV40 virus, when injected into newborn hamsters, caused large tumors to develop under the skin, as well as in the lungs, kidneys, and brain. At the time of this discovery, Salk's vaccine had already been injected into tens of millions of people, and thousands more were receiving it every day. Sabin's vaccine hadn't been licensed in the United States, but it had been given to ninety million people in Russia, mostly children.

During the next few years, researchers performed a series of studies that were reassuring. They found that although SV40 caused cancer when injected into hamsters, it didn't cause cancer when it was fed to them. Sabin's vaccine was

swallowed, not injected. Researchers later found SV40 in the feces of children given Sabin's vaccine, but none of those children developed antibodies to the virus. Apparently, SV40 just passed through the intestines without causing an infection. Researchers also found that although the formaldehyde used in Salk's vaccine didn't completely kill SV40, it did decrease its infectivity by at least ten-thousand-fold. The quantity of residual SV40 virus in Salk's vaccine probably wasn't enough to cause cancer. But at that point, no one was sure.

Horrified that some children had been injected with a potentially cancer-causing virus, researchers compared cancer rates in children who had received a vaccine contaminated with SV40 to the rates in unvaccinated children. Eight years after the tainted vaccines had been given, the incidence of cancer was the same in both groups, and the same was true fifteen and thirty years later. And it was true for children who had received SV40-contaminated vaccines in the United States, the United Kingdom, Germany, and Sweden. By the mid-1990s, public health officials were confident that the inadvertent contamination of polio vaccines with SV40 didn't cause cancer.

No vaccines made today contain SV40 virus.

Do vaccines cause diabetes?

In 1990, the first *Haemophilus influenzae* type b (Hib) vaccine was licensed and recommended for all children in the United States. The vaccine was designed to prevent the twenty-five thousand cases of meningitis, pneumonia, and bloodstream infection that occurred in the United States every year. And it has. But when the vaccine was first licensed, it fell under a cloud of concern when a doctor named J. Bart Classen, speaking on the national television program *World News Tonight with Peter Jennings*, claimed that it caused diabetes.

Classen had compared children in Finland who had received the Hib vaccine at three, four, six, and fourteen months of age with those who had received it only at fourteen months of age. He reported finding that children who had received four doses were more likely to have diabetes than those who had received only one dose. Classen reasoned that the Hib vaccine was the cause. Other researchers tried to duplicate Classen's findings but couldn't. For example, one group of investigators followed thousands of children who had received the Hib vaccine for ten years and found no difference in the incidence of diabetes compared with thousands of children who hadn't received the vaccine.

Another group of investigators compared 250 people with diabetes with more than seven hundred without the disease to see whether those with diabetes were more likely to have received the pertussis, MMR, Hib, hepatitis B, or varicella vaccines. They weren't.

The inability of researchers to reproduce Classen's findings caused them to take a closer look at his study. They found that his analytical methods were incorrect. Hib-vaccinated infants, whether vaccinated with one or four doses, were no more likely than unvaccinated children to develop diabetes.

Therefore, the best available evidence does not support the notion that vaccines cause diabetes.

Do vaccines affect fertility?

Vaccines would not be expected to affect fertility for two reasons. First, if a vaccine-preventable disease does not affect fertility, the vaccine, which is a weakened or partial version of the pathogen, would not be likely to affect fertility either. Second, vaccines are typically processed by immune system cells near the site of administration. Despite these facts, fertility concerns related to a couple of vaccines have persisted.

HPV Vaccine

Although human papillomavirus (HPV) can affect a person's ability to reproduce (for example, if they develop cervical cancer), HPV infection does not lead directly to infertility. Additionally, the HPV vaccine contains only the surface protein from the HPV virus. So, the HPV vaccine would not be expected to cause fertility issues. However, the HPV vaccine has been suggested as a cause of primary ovarian failure, a condition in which the ovaries stop working earlier than usual, leading to early menopause. Because of these concerns, scientists evaluated whether receiving the HPV vaccine was associated with primary ovarian failure. These studies, which evaluated hundreds of thousands of HPV vaccine recipients demonstrated no link between receipt of the vaccine and primary ovarian failure.

COVID-19 mRNA Vaccines

The fear of COVID-19 vaccines causing infertility was spawned by Michael Yeadon, a retired researcher who had worked for Pfizer, and Wolfgang Wodarg, a physician, following the release of COVID-19 mRNA vaccines in 2021. Yeadon and Wodarg argued that the SARS-CoV-2 spike protein, which is made in the body following vaccination, was virtually identical to a protein called syncytin-1, which resides on the surface of placental cells. They believed that women making an immune response to the viral spike protein in an mRNA COVID-19 vaccine might also inadvertently make an immune response to their own placenta, causing infertility. As it turned out, the SARS-CoV-2 spike protein and syncytin-1 are immunologically distinct, so an immune response to one protein isn't necessarily an immune response to another.

Given that more than two hundred million people in the United States have been infected with SARS-CoV-2 and that all of them have made an immune response to the spike protein, if Yeadon and Wodarg were right, the birth rate during the COVID-19 pandemic should have plummeted. But it didn't. It remained the same. Other studies comparing women who had or hadn't received the COVID-19 mRNA vaccines also showed no difference in pregnancy outcomes.

Do vaccines cause antibody-dependent enhancement?

Our bodies respond to viral vaccines and viral infections by making antibodies that prevent the virus from attaching to and entering cells. These types of antibodies are called virus-neutralizing antibodies. But not all antibodies neutralize the virus that they are specific for. Some bind to parts of the virus that don't prevent it from attaching to and entering cells. These types of antibodies are called virus-binding antibodies.

It's possible for certain virus-binding antibodies to attach to a virus and actually facilitate its entrance into cells. This phenomenon is called antibody-dependent enhancement (ADE). The only vaccine-preventable virus, and the only viral vaccine, for which this occurs is the dengue vaccine. As a result, recommendations regarding the use of the dengue vaccine are limited to very specific groups of individuals. The phenomenon of ADE does not occur for any other vaccine.

Do vaccines cause Sudden Infant Death Syndrome (SIDS)?

Every year in the United States, babies die of sudden infant death syndrome (SIDS), a disorder that is poorly understood and which primarily affects infants between two and four months of age. In the 1980s, some parents believed that the older version of the pertussis vaccine (called the "whole-cell" pertussis vaccine) was the cause. However, several studies compared the incidence of SIDS in babies who either had or hadn't received pertussis vaccine and found that babies who died from SIDS were not more likely to have received it.

In the early 1990s, the hypothesis shifted when a new vaccine—the hepatitis B vaccine—was recommended for babies. Around the time of the recommendation, the ABC news program *20/20* aired a story claiming that the vaccine caused SIDS. The reporter told the story of a one-month-old girl who had died of SIDS sixteen hours after receiving her second dose of the hepatitis B vaccine. At the time the story aired, about five thousand children died of SIDS annually. Within ten years of the introduction of the hepatitis B vaccine, about 90 percent of infants were immunized, and the incidence of SIDS decreased to about 1,600 cases a year. In other words, as the number of babies immunized against hepatitis B increased dramatically, the number

of babies dying from SIDS decreased dramatically. However, despite this correlation, the cause of the decrease in the incidence of SIDS wasn't related to the increase in hepatitis B vaccination at all. Rather, it was discovered that infants who died of SIDS were more likely to have slept face down. In response, the American Academy of Pediatrics introduced the "Back to Sleep" program, which dramatically reduced the number of SIDS deaths.

Neither the pertussis vaccine nor the hepatitis B vaccine causes SIDS.

Do mRNA vaccines change our DNA?

Because the COVID-19 mRNA vaccines were the first "genetic" vaccines, some people worried that they could alter DNA, but that is biologically impossible. Two aspects of this phenomenon have caused concerns.

The contextual biology

Our cells all have DNA and messenger RNA (mRNA). DNA is our genetic code. It is protected in the nucleus of our cells. From DNA, mRNA is made (called transcription) and released from the nucleus into the cytoplasm of the cell. Once in the cytoplasm, mRNA is processed to produce proteins (called translation). Our cells translate mRNA into proteins all the time.

Introduction of mRNA from a vaccine

The mRNA vaccines take advantage of the regular processing of mRNA by our cells, so that instead of delivering proteins via a vaccine that our immune systems respond to, our cells make the protein that our immune systems respond to. Concerns about vaccine-introduced mRNA changing our DNA are unfounded for three reasons. First, mRNA vaccines don't have the nuclear access signal that would allow mRNA to enter the nucleus of a cell where DNA resides: you can't alter DNA if you can't get to it. Second, mRNA vaccines don't have the enzyme (called reverse transcriptase) that would allow for conversion of the mRNA into DNA: you can't alter DNA if you don't have DNA. Third, even if mRNA from the vaccine could be converted to DNA, the vaccine doesn't have the enzyme (called integrase) that would allow integration into DNA: you can't alter DNA if you can't insert new DNA into existing DNA. As such, mRNA in the vaccines cannot cause changes to our DNA.

Introduction of DNA fragments from a vaccine

To make the mRNA for the vaccine, the DNA for the protein of interest (in the case of COVID-19 vaccines, the spike protein) is put into cells that reproduce and as they reproduce, more spike protein DNA is made. This DNA is then

isolated, purified, and used to make the mRNA that is delivered in the vaccine. Because DNA is part of the production process, a second concern related to whether mRNA vaccines could change our DNA emerged. Specifically, people wondered if leftover fragments of DNA from the production process could change our DNA. Like with the mRNA in the vaccine, the enzymes necessary for the DNA fragments to insert into our DNA are not present. Further, the quantity of the DNA fragments is very small (i.e., billionths of a gram). Therefore, the DNA fragments in mRNA vaccines cannot cause changes to our DNA.

WHAT'S IN THE VACCINE VIAL?

Did you know?
One raisin weighs about a gram, so a microgram is about one-millionth (0.000001) the weight of a raisin, and a picogram is about one-trillionth (0.000000000001) the weight of a raisin.

Do vaccines contain allergens?

The Centers for Disease Control and Prevention (CDC) estimates that every year several substances in vaccines cause about two hundred people in the United States to experience severe allergic reactions.

Egg Proteins

About one of two hundred people in the United States is allergic to eggs. Most are only mildly allergic, but some are severely allergic. Symptoms of a severe allergic reaction include hives, difficulty breathing, and low blood pressure. Because some influenza vaccines are made in eggs, egg proteins are present in some of the final products, usually in an amount measured in micrograms (i.e., millionths of a gram) per dose. Although current influenza vaccines contain trace quantities of egg proteins, these quantities are too small to cause an allergic reaction, even in people with severe egg allergies. Therefore, people with severe egg allergies can receive influenza vaccines safely.

The other vaccine grown in eggs is the yellow fever vaccine. Unfortunately, the quantity of egg proteins in this vaccine is large enough to cause a severe allergic reaction in people who are severely allergic to eggs. For this reason, people with severe egg allergies should avoid the yellow fever vaccine.

Some people think that if they're allergic to eggs, they can't get the measles-mumps-rubella (MMR) vaccine. But none of the viruses in the MMR vaccine are made in eggs; they're made in chick embryo cells, grown in culture in the laboratory. The quantity of residual egg proteins found in the MMR vaccine is measured in picograms (i.e., trillionths of a gram). Such a quantity is at least five hundred times less than that found in the yellow fever vaccine, so it

doesn't cause a problem. Therefore, people allergic to eggs can safely receive the MMR vaccine.

Antibiotics

Antibiotics are present in some vaccines to prevent bacterial contamination during the manufacturing process. Fortunately, the antibiotics most likely to cause allergic reactions, like penicillins, cephalosporins, and sulfa drugs, aren't contained in vaccines. Antibiotics used during vaccine manufacture include neomycin, streptomycin, polymyxin B, chlortetracycline, and amphotericin B. However, only neomycin is contained in vaccines in quantities large enough to be of potential concern. And severe allergic reactions to neomycin have not been found.

Yeast Proteins

Both the hepatitis B and human papillomavirus (HPV) vaccines contain yeast proteins. These vaccines are made by inserting the gene that makes one viral surface protein into a plasmid (a small circular piece of DNA) and putting the plasmid into baker's yeast. When the yeast cells grow, they also make the viral surface protein that eventually becomes the vaccine. The hepatitis B and HPV vaccines contain between 1 and 5 milligrams (thousandths of a gram) of yeast proteins.

Although some people are allergic to bread or bread products, it's not the yeast they're allergic to. No clear evidence exists that yeast proteins can induce the kind of immune responses necessary to cause severe allergic reactions. Therefore, the risk of experiencing a severe allergic reaction to baker's yeast is only theoretical.

Gelatin

In 1993, a seventeen-year-old girl in California developed a runny nose, hives, difficulty breathing, light-headedness, and low blood pressure within five minutes of receiving an MMR vaccine. When later describing the event, she said that it was "kind of like what happens when I eat Jell-O." Subsequent testing by an allergist found that the only substance in the vaccine to which the girl was allergic was gelatin, the main ingredient in Jell-O.

Gelatin, made by extracting collagen (the most abundant protein in the body) from the skin and hooves of pigs, is used in vaccines as a stabilizing agent, allowing small quantities of live viral vaccines to be evenly distributed throughout the vial.

The incidence of severe allergic reactions to gelatin is very low (about one case per two million doses), but it's still the most common identifiable cause of severe allergic reactions to vaccines. The gelatin in the MMR, chickenpox, and nasal spray influenza vaccines has been broken down with water

molecules, so it is less likely to cause an allergic reaction. The gelatin found in the yellow fever vaccine and one rabies vaccine (Rabavert) is in a more natural form. Because of the low incidence of reactions and the low quantities present, it is hard to know whether the gelatin in vaccines can trigger a severe allergic reaction. However, some people have a history of allergies to gelatin-containing foods and are therefore more likely to experience an allergic rection to a vaccine containing gelatin. But even in this case, the gelatin in foods comes from cows, whereas that in vaccines comes from pigs, so people with a gelatin allergy should discuss the relative risks and benefits of gelatin-containing vaccines with their health care provider or an allergist.

Do vaccines contain harmful preservatives like mercury?

The preservative in vaccines that has probably caused the most concern among parents is thimerosal. That's because thimerosal contains mercury, and large quantities of mercury can be toxic to the nervous system. The use of thimerosal in vaccines isn't new; mercury-containing preservatives have been in vaccines for decades.

Between 1900 and 1930, companies packaged vaccines almost exclusively in multidose vials, typically containing ten doses. This allowed the vaccines to be made much less expensively. Doctors kept the vials in refrigerators in their offices, often for months at a time. To give a vaccine, they would insert a needle through the rubber stopper, pull the liquid up into a syringe, and inject it. Unfortunately, by repeatedly inserting needles through the rubber stopper, doctors and nurses occasionally (and unintentionally) contaminated the vial with bacteria or fungi. In the early 1900s, many children developed local abscesses or serious bloodstream infections, including sepsis and death, caused by bacteria like *Staphylococcus* and *Streptococcus* that had contaminated the last few doses in the vial. By the 1940s, most multidose vials of vaccines contained preservatives like thimerosal to prevent contamination.

For decades, thimerosal was used in vaccines without a second thought. But as health officials added more vaccines to the routine schedule, children received more and more mercury. By the spring of 2001, the American Academy of Pediatrics and the U.S. Public Health Service decided to remove thimerosal from virtually all vaccines routinely recommended for children. While preservative levels of thimerosal are still contained in multidose preparations of the inactivated influenza vaccine, thimerosal hasn't been in vaccines routinely given to children since 2001. Unfortunately, the demand for the rapid removal of thimerosal caused some parents to wonder whether it had caused harm, specifically autism or subtle forms of mercury toxicity. Because mercury at high doses can be toxic to the nervous system, this concern was reasonable.

At the time of thimerosal's removal from vaccines, several facts about mercury were reassuring. Mercury is part of the earth's surface, released into the environment by burning coal, rock erosion, and volcanoes. After it's released, it settles onto the surface of lakes, rivers, and oceans, where it is converted to methylmercury by bacteria. Methylmercury is everywhere—in the fish we eat, the water we drink, and the infant formula and breast milk we feed our babies. There is no avoiding it. Because everyone drinks water, everyone has small amounts of methylmercury in their blood, urine, and hair. In fact, a typical breast fed infant will ingest almost 400 micrograms (millionths of a gram) of methylmercury during the first six months of life. That's more than twice the amount of mercury than was ever contained in all childhood vaccines combined. And because the type of mercury in breast milk (methylmercury) is excreted from the body much more slowly than that contained in vaccines (ethylmercury), mercury ingested through breast milk is much more likely to accumulate in the body. This doesn't mean that breast milk or infant formula are dangerous. It means only that anyone who lives on the planet consumes small amounts of mercury all the time.

To address parents' concerns about whether thimerosal in vaccines caused harm, investigators in several countries compared children who had received thimerosal-containing vaccines with those who had received the same vaccines with smaller amounts of thimerosal or no thimerosal. They found no difference in the risk of autism among these groups. Further, children who had received thimerosal-containing vaccines didn't develop even subtle signs of mercury toxicity.

The use of a mercury-containing preservative in vaccines harkens back to a statement made by a seventeenth-century chemist named Paracelsus: "The dose makes the poison." In other words, although large quantities of a particular substance might be harmful, small quantities aren't. Indeed, we all have very small quantities of a variety of heavy metals in our bodies, including arsenic, cadmium, thallium, beryllium, and lead. All these substances can be harmful in large quantities, but the small quantities we encounter from typical exposure to these metals don't pose a risk.

Do vaccines contain harmful adjuvants like aluminum?

Adjuvants, which have been used in vaccines since the 1930s, were added to vaccines to enhance the immune response, allowing for lesser quantities and fewer doses of vaccine. (*Adjuvant* comes from the Latin *adjuvare*, meaning "to help.") The DTaP, hepatitis A, hepatitis B, Hib, RSV, pneumococcal, shingles, and one of the one of the COVID-19 vaccines (Novavax), all contain adjuvants.

Aluminum

Historically, vaccines contained only one type of adjuvant: aluminum salts. So, the safety of aluminum in vaccines has been assessed for more than eight decades. Some parents, however, are concerned that excess aluminum might cause harm. The facts are reassuring.

The amount of aluminum contained in vaccines is far less than that which babies typically face every day. That's because aluminum, the third most abundant element on Earth, is everywhere: in the air we breathe, the food we eat, and the water we drink. The most common source of aluminum is food. It's present naturally in teas, herbs, and spices. It's also added to leavening agents, anticaking agents, emulsifiers, and coloring agents. Large quantities of aluminum are found in pancake mixes, self-rising flours, baking powder, processed cheeses, and corn bread.

Because aluminum is everywhere, adults typically ingest between 5 and 10 milligrams (thousandths of a gram) of it every day. Babies are no different; all are exposed to aluminum in breast milk and infant formula. Those exclusively breast fed will ingest about 10 milligrams of aluminum by six months of age; those fed regular infant formula, 30 to 40 milligrams; and those fed soy formula, about 120 milligrams. These quantities are much greater than those contained in vaccines: babies who get all the recommended vaccines will receive about 4 milligrams of aluminum in the first six months of life.

Large quantities of aluminum—much greater than those contained in vaccines—can be harmful, causing brain dysfunction, weakening of the bones, and anemia. But harm from aluminum occurs in only two groups: severely premature infants who receive large quantities of aluminum in intravenous fluids and people on chronic dialysis for kidney failure who receive large quantities of aluminum in antacids. So, the only way babies can be harmed by aluminum is if their kidneys work poorly or not at all and if, at the same time, they are receiving large quantities of aluminum from intravenous fluids or medications like antacids. A typical antacid contains about 350 milligrams of aluminum per teaspoon.

Some people worry about the aluminum in vaccines because while only a small amount of aluminum that is ingested makes it into the bloodstream, all of the aluminum that is injected ends up in the bloodstream. However, when our body is processing chemicals, it does not distinguish where the chemical came from, so aluminum in the blood is processed the same regardless of whether it was eaten or injected. And even though the amount may be higher after vaccination, the body is capable of processing it, except in rare instances when, as previously described, the kidneys are not functioning properly and the quantities of aluminum are significant and introduced regularly over long periods of time (months or years).

Studies of aluminum in vaccines have also been reassuring. Because aluminum is unavoidable, everyone has it circulating in their bodies, even babies who have between 1 and 5 nanograms (billionths of a gram) per milliliter of blood. Researchers have studied whether vaccines containing aluminum increase the amount of aluminum in the blood. They don't. The quantity of aluminum in vaccines is so small that the amount in blood is unchanged after vaccination. Other studies have shown that the body eliminates aluminum quickly; in fact, about half of it is eliminated in just one day.

Monophosphoryl Lipid A and Saponin

Other adjuvants are also used in vaccines. The shingles vaccine and one of the RSV vaccines (AREXVY) contain a combination of adjuvants called monophosphoryl lipid A (MPLA) and saponin. Saponin is a soap. MPLA is a substance found on the surface of bacteria. When our body identifies something that resembles bacteria, our innate immune system springs into action. Both MPLA and saponin, when used as adjuvants, can cause low-grade fever and pain and redness at the injection site.

CpG

Another adjuvant, used in one of the hepatitis B vaccines (Heplisav-B), is called CpG, which stands for "cytosine and guanine linked by a phosphodiester." Cytosine and guanine, along with adenine and thymine, are building blocks of DNA. Bacterial DNA is composed of repeated units of cytosine and guanine, which do not occur in human DNA. Like MPLA, CpG stimulates the innate immune system, making for a powerful and safe adjuvant.

Do vaccines contain harmful chemicals like formaldehyde?

Vaccines are complicated to make. They're not like other pharmaceuticals for which the synthesis of small molecules can be performed relatively easily in a laboratory. Vaccines are biologicals, meaning they are made from organisms, so they are more complex to manufacture. Viruses can be grown only in cells; bacteria need nutrients to grow, and even for vaccines made using recombinant DNA technology—like the hepatitis B and HPV vaccines—cells are still required to make the viral proteins used in the vaccine. Vaccines must also be sterile, so the process often involves the use of antibiotics (see "Do Vaccines Contain Allergens?").

Even after vaccines are made, they might require stabilizing agents, like gelatin, to ensure that the vaccine virus is equally distributed throughout the vial and doesn't stick to the sides. And vaccines require buffering agents to keep them stable across a wide range of temperatures.

Because of these requirements, vaccines may contain small quantities of fetal bovine serum, monosodium glutamate, polysorbate, phenoxy ethanol, ethylenediaminetetraacetic acid (EDTA), polyethylene glycol, sodium borate, octoxynol, and sodium deoxycholate. However, these chemicals are present only in very small amounts, and similar or greater quantities of them are found in foods, beverages, toothpastes, and over-the-counter medicines. But one particular chemical in vaccines has drawn much attention: formaldehyde.

Formaldehyde is used to inactivate viruses (like polio and hepatitis A) and bacterial toxins (like diphtheria and tetanus toxins); therefore, small quantities of formaldehyde are found in the final products. In addition to the chemical's use by morticians conjuring up images of death, concerns have centered on the fact that large quantities of formaldehyde can damage cellular DNA, causing cancerous changes in cells grown in laboratory flasks.

Studies evaluating the potential for formaldehyde to cause cancer in people have had mixed results; however, the studies tended to focus on individuals exposed to large amounts of formaldehyde for long periods of time (years), typically resulting from occupational exposures, such as in the case of embalmers. In such individuals, the associated types of cancers include those of the nasopharynx and leukemia, specifically myeloid leukemia. Importantly, even in people with regular exposure over many years, the link between formaldehyde and cancer has not been found consistently. Although these studies led to formaldehyde being categorized as a carcinogen (a cancer-causing agent), the quantities used in vaccines are nowhere near those to which the study populations were exposed. Further, animals exposed to quantities of formaldehyde exponentially greater than those contained in vaccines don't develop malignancies. Indeed, quantities of formaldehyde at least six hundred times greater than those contained in vaccines have been given safely to animals.

The quantity of formaldehyde in individual vaccines does not exceed one-tenth of a milligram (thousandths of a gram). This amount is safe for several reasons. First, formaldehyde is one of the intermediary products of human metabolism and a necessary component in the synthesis of thymidine, purines, and amino acids, which are necessary for the formation of DNA and proteins. Therefore, everyone has detectable quantities of formaldehyde in their bloodstream, about 2.5 micrograms (millionths of a gram) of formaldehyde per milliliter (one-fifth of a teaspoon) of blood. Assuming an average two-month-old weighs 5 kilograms (about eleven pounds) and has a blood volume of 85 milliliters per kilogram, the total amount of formaldehyde found naturally in their circulation would be about 1 milligram—a value at least ten times that contained in any individual vaccine. In other words, there is far more formaldehyde circulating naturally in our bodies than contained in vaccines.

Do vaccines contain animal products?

Some viral vaccines are made in animal cells (for example, monkey kidney cells). Although the vaccine virus is purified away from the cells, small amounts of animal cell proteins or DNA sometimes remain. The remaining amounts are so small that they are measured in nanograms (billionths of a gram) or picograms (trillionths of a gram). It is fair to say that we are all exposed to far greater quantities of nonhuman proteins or DNA when we eat food.

Gelatin

One animal product in vaccines, however, is present in fairly large quantities: gelatin (see "Do Vaccines Contain Allergens?"). Gelatin used in vaccines, derived from the skin and hooves of pigs, is highly purified and hydrolyzed (broken down by water) to make much smaller molecules than are found in nature. Unlike animal cell proteins and DNA, the amount of gelatin contained in vaccines isn't small. For example, the chickenpox (varicella) vaccine contains about 8 milligrams (thousandths of a gram) of gelatin. Some religious groups, such as Jewish people, Muslims, and Seventh Day Adventists follow dietary guidelines that oppose the ingestion of pig products. However, religious leaders from all three of these groups have sanctioned the use of gelatin-containing vaccines for several reasons. First, vaccines are injected, not ingested (only the rotavirus vaccine is ingested, and it doesn't contain gelatin). Second, the gelatin in vaccines is modified enough to render it sufficiently different from natural gelatin. Third, the benefits of receiving a vaccine outweigh adherence to the religion's dietary principles.

Are vaccines made using aborted fetal cells?

Viruses and bacteria are different. Whereas bacteria can grow on the surface of the skin, nose, or throat, viruses can grow only inside cells. So, when making viral vaccines, cells are a required part of the process. One of the advantages of using human fetal cells is that they are essentially immortal; they can reproduce many, many times before dying. This is in direct contrast with cells obtained from organs that are fully developed; such cells reproduce about fifty times before they can no longer be used. Because fetal cells are longer-lived, they can be used to make viral vaccines for centuries.

Other aspects of human fetal cells also make them attractive for vaccine use. First, human cells are much more likely to support the growth of human viruses than are animal cells. Second, because the fetus is in a sterile environment, human fetal cells are sterile, meaning they're not contaminated with other viruses. This typically isn't the case with cells obtained from live animals or humans after birth.

In the early 1960s, cells used to make vaccines were obtained from two elective abortions—one performed in Sweden, the other in England. The human fetal cells obtained from Sweden were sent to the Wistar Institute in Philadelphia, where Dr. Stanley Plotkin was working on a rubella vaccine and Dr. Tad Wiktor was working on a rabies vaccine. These cells were called Wistar Institute-38 or WI-38 cells. The cells obtained in England were studied at the United Kingdom's Medical Research Council; they're called MRC-5 cells. These two sources of human fetal cells have been used to make vaccines against rubella, rabies, chickenpox, and hepatitis A.

More recently, the adenovirus-based COVID-19 vaccines (like the one made by Janssen/Johnson & Johnson) were also made using fetal cells. The adenovirus strain used in vaccine production cannot replicate in people, so to produce the vaccine, the adenovirus containing the gene of interest (in this case the SARS-CoV-2 spike protein) must be grown in a cell line that includes a gene that will enable it to reproduce. A retinal cell line, called PER.C6, was isolated in the mid-1980s and adapted to include the necessary gene for this application. (The Janssen/Johnson & Johnson vaccine is no longer used in the United States because of some rare but severe side effects and the availability of other COVID-19 vaccines.)

To some, using human fetal cells to make vaccines is abhorrent, an act against God. In July 2005, in response to pressures from a pro-life group in the United States, the Vatican's Pontifical Academy for Life ruled on whether using vaccines derived from human fetal cells was wrong. The ruling was made by Cardinal Joseph Ratzinger, then the head of the Catholic Church's Congregation for the Doctrine of the Faith. Ratzinger was a well-known theologian and prolific author. He later became Pope Benedict XVI, the 265th pope (until he retired in February 2013). Ratzinger reasoned that those involved in the original abortion had "formally cooperated with evil." But he decided that the doctors and nurses who give vaccines made from human fetal cells are engaged in only a "very, very remote" form of cooperation with evil, so remote that "it does not indicate any [negative] moral value" when compared with the greater good of preventing life-threatening infections.

The National Catholic Bioethics Center agreed with the Vatican's decision: "Clearly the use of a vaccine in the present does not cause the one who is immunized to share in the immoral intention or action of those who carried out the abortion in the past ... Human history is filled with injustice. Acts of wrong-doing in the past regularly redound to the benefit of descendants who had no hand in the original crimes. It would be a high standard indeed if we were to require all benefits that we receive in the present to be completely free of every immorality in the past."

Are package inserts useful?

Package inserts contain important information about vaccines: for example, a list of ingredients, details of the studies performed to determine whether a vaccine is safe and effective, dosage information, special considerations for various groups, contraindications (i.e., who shouldn't get the vaccine), precautions (i.e., who might be at risk from the vaccine), and possible adverse reactions.

Unfortunately, one aspect of package inserts can be misleading. Studies to determine whether a vaccine is safe and effective typically include two groups: those who have received the vaccine and those who haven't. This is done so that researchers can determine whether the vaccine causes a problem. If more people who received the vaccine experience a particular side effect than those who didn't get the vaccine, the vaccine probably caused the problem. Conversely, if about the same number of people in each group experience a side effect, then the vaccine probably didn't cause the problem. Unfortunately, package inserts often state that a vaccine might cause a particular side effect even when it occurred with the same frequency in both vaccinated and unvaccinated study participants. This is probably because package inserts are written by pharmaceutical company lawyers who want to make sure that they haven't failed to warn people about possible side effects. For this reason, inserts are more like legal documents than medical ones and can be misleading to people trying to determine whether a vaccine may cause certain side effects.

PRACTICAL CONSIDERATIONS

How do we know that different vaccines can be given at the same time?

Before the Food and Drug Administration (FDA) will license a new vaccine, it must first be tested in concomitant-use studies in which the new vaccine is given with existing vaccines at the same time. The new vaccine must be shown not to interfere with the safety or immunogenicity (the immune response) of existing vaccines, and existing vaccines must be shown not to interfere with the safety or immunogenicity of the new vaccine. These studies take years to complete and cost millions of dollars. Because concomitant-use studies have been required for decades, hundreds of studies have been performed showing that children can safely be inoculated with multiple vaccines at the same time.

Are vaccines given as one size fits all?

Some people wonder how the same vaccine can be recommended for a ten-pound baby and a two-hundred-pound adult. Wouldn't it make more sense to give a baby a smaller amount of vaccine? That's what is done for drugs, where the amount prescribed is often determined by weight or age.

Indeed, some vaccine doses given to children and adults aren't the same. For example, the hepatitis B vaccine given to children contains less vaccine than the one given to adults. But sometimes the opposite is true. For example, the amount of diphtheria and pertussis vaccine in the DTaP vaccine given to children is more than is in the Tdap vaccine given to adolescents and adults. That's because adolescents and adults often have more serious local reactions to the diphtheria and pertussis components of the vaccine than children do.

But the importance of weight in relation to dose isn't the same for vaccines as it is for drugs. Drugs enter the bloodstream and are distributed throughout the body. That's not true for vaccines. With a few exceptions, such as the intranasal influenza vaccine and the orally administered rotavirus vaccine, most vaccines are typically injected into the arm, leg, or buttocks. Regardless of how a vaccine is administered, the part that generates immunity, called the antigen, is transported to nearby lymph nodes, which are collections of immune cells located throughout the body. Transport occurs via cells called antigen-presenting cells. In the lymph node, these cells present the antigen to other cells of the immune system responsible for making antibodies and creating immunologic memory.

As a rule, a vaccine stimulates an immune response in the area where the vaccine is given, not throughout the body. Adjuvants, which are substances occasionally added to vaccines to enhance the immune response, also act only locally (see "Do Vaccines Contain Harmful Adjuvants Like Aluminum?"). All of this means that, for the most part, how much someone weighs doesn't matter because vaccines aren't distributed throughout the body.

The next logical question is, How are children protected against infections that enter through other places, like the nose, throat, or intestines? The answer is that although immune cells, like those that make antibodies, are typically generated where the vaccine is given, they travel throughout the body, offering protection at the many sites where infection might occur.

When vaccines are tested, dose-ranging studies are used. In this type of study, groups of participants are given different doses to determine which works best. The goal is to give the smallest amount of vaccine that can induce a protective immune response so that the vaccine is both effective and unlikely to cause side effects.

Can too many vaccines overwhelm the immune system?

Today, young children get vaccines to prevent fifteen different diseases. That can mean as many as twenty-seven inoculations altogether and as many as five shots given at one time. It's difficult for a parent to watch this; they might wonder if it is too many. So, the question is perfectly reasonable and while the answer is no, the reasons why are worth understanding.

First, let's compare the number of immunological challenges in vaccines today with those in the past. In the 1980s, children received vaccines against seven diseases: measles, mumps, and rubella (combined as MMR vaccine); diphtheria, tetanus, and pertussis (combined as DTP vaccine); and polio. In the 1950s, children received vaccines against five diseases: diphtheria, tetanus, and pertussis (combined as DTP); polio; and smallpox. At the turn of the twentieth century, children received just one vaccine: smallpox. Most parents today would probably be surprised to learn that the number of immunological components contained in that one vaccine given a hundred years ago was greater than the number contained in all vaccines given to prevent fifteen diseases today.

To understand why, let's begin by defining terms. An immunological component, or antigen, is that part of a virus or bacterium that induces an immune response (like making specific antibodies). For viruses, immunological components consist of viral proteins; for bacteria, they consist of bacterial proteins or polysaccharides, which are complex sugars that surround the bacterial surface. The smallpox vaccine contained about two hundred proteins. The vaccines given to protect young children against fifteen diseases today contain a total of about 160 proteins. So, although there is no denying that fifteen vaccines are more than one, it's what's in the vaccines, not the number of vaccines, that counts. Fortunately, thanks to advances in protein chemistry, protein purification, and recombinant DNA technology, vaccines today are much purer (and consequently safer) than those used in the past.

Second, let's compare vaccines with other immunological challenges in the environment—challenges that are unseen but much greater than those in vaccines. The womb is sterile: no bacteria, no viruses, no parasites, no fungi. So, fetal immune systems aren't required to do much. But as the baby passes through the birth canal and enters the outside world, that changes quickly; the baby is immediately confronted with trillions of bacteria. These bacteria live on the lining of the nose, throat, skin, and intestines. Indeed, about ten times more bacteria live on the surface of our bodies (about one hundred trillion) than we have cells in our bodies (about ten trillion). And that's not the end of it: the food that children eat isn't sterile, nor is the air they inhale. Most bacteria have the capacity to invade the bloodstream and cause harm, and each bacterium contains between two thousand and six thousand immunological components. To prevent this from happening, babies' bodies make large quantities of antibodies every day. Grams of them. That's a tremendous commitment by the baby to make one type of protein (antibodies). In addition, soon after they're born, babies encounter a variety of viruses that can't be prevented by vaccines—like rhinoviruses (which cause the common cold), parainfluenza virus, adenovirus, norovirus,

calicivirus, astrovirus, echovirus, coxsackie virus, human metapneumovirus, parechovirus, parvovirus, and enterovirus. And unlike vaccine viruses, which reproduce poorly or not at all, natural viruses reproduce thousands of times, causing an intense immune response. Studies have shown that healthy children experience between six and eight viral infections every year during their first few years of life. Vaccines don't prevent most of these.

Third, let's calculate the extent to which vaccines challenge the immune system. Exactly how many vaccines can a baby respond to? The best reasoned answer to this question comes from a paper written by two immunologists at the University of California San Diego, Mel Cohn and Rod Langman. Cohn and Langman focused on antibodies, an important component of the immune response induced by vaccines. Antibodies are made by B cells, each of which has the capacity to make antibodies against only one immunological unit, called an epitope. By calculating the number of B cells in the bloodstream, the average number of epitopes contained in a vaccine, and the rapidity with which a critical quantity of antibodies could be made, we know that a baby could theoretically respond to one hundred thousand vaccines at one time.

Of course, we're not saying that babies should get a hundred thousand vaccines at once. We're saying only that they could handle it. Indeed, given that babies are constantly confronted with trillions of bacteria and that each bacterium contains thousands of immunological components, this shouldn't be surprising. In a sense, babies are responding to such an assault every day.

Fourth, let's examine how well newborns respond to vaccines by looking at the hepatitis B vaccine. Babies born to mothers infected with hepatitis B virus are at high risk of not only being infected with the virus but also developing cirrhosis (chronic liver damage) or liver cancer. The greatest risk of infection and long-term problems comes at the time of delivery. Hepatitis B virus is present in large quantities in the blood of infected people. So, when passing through the bloody birth canal of an infected mother, a baby encounters an incredible amount of hepatitis B virus. Each milliliter (about one-fifth of a teaspoon) of blood from someone infected with hepatitis B contains roughly one billion infectious viruses, and the birth process exposes a baby to a lot of blood. So, it's no wonder that almost all children born to infected mothers contract the disease.

The hepatitis B vaccine is given shortly after birth, and in cases where the baby was exposed to the virus during delivery, studies have shown that about 80 percent of babies are protected against infection after just one dose of hepatitis B vaccine, which contains only 20 micrograms (millionths of a gram) of one protein from the virus. That's amazing. And it speaks to the remarkable resiliency and strength of the newborn's immune system. But it shouldn't be surprising. Given the natural onslaught from challenges in the environment,

babies must be ready to respond to a tremendous microbial onslaught the minute they are born if they are to survive.

Indeed, babies are typically exposed to diseases like *Haemophilus influenzae* type b (Hib), pneumococcus, rotavirus, and pertussis (whooping cough) early in life. If they are to avoid these diseases, they need to develop an immune response quickly. While maternal antibodies directed against many of these infections are passed on to babies while still in the womb, these antibodies eventually fade away, leaving the child vulnerable (this is an example of passive immunity). That's why vaccines against Hib, pneumococcus, rotavirus, and pertussis are given at two, four, and six months of age, so when *passive immunity* fades, the child will have developed their own immunity, which is called *active immunity*.

Is there any harm in using an alternative schedule?

During the first few years of life, children may receive as many as twenty-seven separate inoculations and up to six shots at one time. For parents, it can be hard to watch their children restrained against their will and injected several times. Therefore, it's easy to see why some might prefer an alternative vaccine schedule that separates, delays, withholds, or spaces out vaccine doses.

The perceived value of an alternative schedule is that it might avoid weakening, overwhelming, or altering the young child's immune system. However, abundant evidence shows that vaccines do not cause these untoward effects, so changing the schedule would not add value.

Another argument people use for spacing out vaccines is that they contain potentially harmful additives that might be toxic if too many vaccines are given at once. But again, the evidence does not support this fear so changing the schedule will not increase the safety of vaccines.

Yet another specious argument is that getting too many vaccines is causing chronic conditions or diseases like asthma, allergies, autism, diabetes, and multiple sclerosis—which presumably could be avoided by choosing a different schedule. But again, no evidence supports these contentions of causality, so changing the schedule does not offer an advantage.

Some parents (and some doctors) argue that even if it's true that children's immune systems can easily handle the challenge of vaccines, there's no harm in spacing them out. However, there are several reasons that this is not true.

More Time Being Susceptible to Disease

The biggest problem with an alternative vaccine schedule is that it increases the time during which children are susceptible to vaccine-preventable

diseases. If immunization rates across the United States were about 95 percent, this wouldn't be a problem.

Parents could hide their children within a highly protected population knowing they wouldn't be hurt by bacteria and viruses. But that's not the case. Herd (or community) immunity—the ability of a vaccinated community to protect those who can't or won't be vaccinated—has broken down. Consequently, outbreaks of pertussis are common; a measles epidemic in 2019 was larger than any year since the early 1990s; and children are starting to die from bacterial meningitis again because their parents are choosing either to delay or withhold vaccines. (For example, outbreaks of Hib meningitis caused the deaths of four unvaccinated children in Minnesota and Pennsylvania in 2008 and 2009.) Parents who choose to delay vaccines are taking an unnecessary risk without deriving any benefit.

No Data to Support the Safety or Effectiveness of an Alternative Vaccine Schedule

Another problem with alternative vaccine schedules is that they're untested. Every time a new vaccine is added to the recommended schedule, it's tested to make sure that it doesn't interfere with the immune response or safety of the existing vaccines or vice versa (see "How Do We Know That Different Vaccines Can Be Given at the Same Time?"). Making up a schedule that is untested takes an unnecessary risk, again without benefit. The irony of an alternative schedule is obvious: parents who opt out of the recommended schedule because of unfounded safety concerns are trading a schedule based on published studies in millions of children for one that has been formally tested in no children.

More Visits to the Doctor

Another reasonable-sounding argument for spacing out vaccines is that it would mean fewer shots at one time and therefore less pain for the child. However, researchers have found that children experience similar amounts of stress—as measured by the level of a hormone called cortisol—whether they are getting one shot or two at the same visit. This finding suggests that although children are clearly stressed by receiving a shot, two shots aren't more stressful than one. For this reason, separating or spacing out vaccinations, thus requiring more doctor's visits, would likely increase children's stress, could increase the risk of vaccination errors and missed vaccinations, and could result in greater out-of-pocket expenses for doctor's visits.

Is an extra dose of vaccine harmful?

The vaccine schedule is busy. In the first few years of life, children are recommended to receive several inoculations, some of which are given at the same time. Also, many combination vaccines are available and often differ

from one doctor's office to the next. Unfortunately, this complexity means that mistakes are occasionally made. In some cases, a child might receive an extra dose of vaccine. When this happens, parents of these children wonder whether the extra dose is harmful. While an extra shot may cause pain, redness, tenderness, or swelling at the injection site, the child is not more likely to suffer worse side effects. That's because the child has already started to make an immune response to the vaccine virus.

For example, suppose that a child who receives MMR vaccine develops a mild measles rash about a week later. This is an uncommon reaction that happens when measles vaccine virus travels to the skin. A parent could reasonably ask whether a child who develops a rash after the first dose of vaccine is more likely to develop a rash after the second dose. The answer is probably not because the child makes an immune response after the first dose. So, when given a second dose, the child has already developed some antibodies that limit the vaccine virus's ability to reproduce and travel to the skin.

Children who receive an extra dose of vaccine usually develop a boost in their immune response. The same is generally true for adults who get an extra dose of vaccine. For example, someone who has lost their immunization record might wonder whether they should get a blood test done first to see if they've already been vaccinated. Often, their health care provider will recommend getting the vaccine rather than a blood test because the extra dose of vaccine will boost any existing immunity. Also, blood tests aren't always accurate and, in some cases, may not be available.

What can I do to make vaccinations less stressful?

Whether you're taking a member of your family for a vaccination or getting your own, there are several things you can do before, during and after the appointment to make the visit less stressful.

Before the visit

- Find out which vaccines are due.
- Bring the person's immunization record.
- Write down any questions you have.
- Bring along a favorite book, electronic game, toy, or blanket, depending on the age of the person receiving the vaccination.

During the visit

- Read the Vaccine Information Statements (VISs) that are available in doctors' offices. If you are not provided with these, ask an office staff member.

- Ask the healthcare team any questions you have about vaccines before they bring them into the room.
- If your infant or young child is getting immunized, hold them on your lap. Preteens, teens, and adults should be seated or lying down during immunizations.
- If you are there supporting a family member, talk reassuringly, make eye contact, smile, and offer physical comfort, such as holding an older person's hand or cuddling a young child before and immediately following the shots. It's important to realize that if you demonstrate apprehension, your family member will likely pick up on that and react accordingly, particularly young children who rely on their parents and caregivers for comfort.

After the visit

- If the area where the shot was given is red, tender, or swollen, apply a cool, wet cloth or ice to the area.
- Some people develop fever following vaccination, which is an indication that their body is responding to the vaccine. As such, treating fever after vaccination is not typically recommended, but if you have questions, talk with your health care provider. Importantly, if a pregnant person develops a fever following vaccination, it should be treated since a fever can harm the unborn baby.
- Ensure that the vaccinated individual drinks plenty of fluids and realize that they may be less interested in food during the next 24 hours.
- Watch for signs of severe reactions, such as prolonged fever, unusual behavior, or new, severe, or unexpected symptoms. If you have any concerns, call the health care provider where the vaccine was administered for guidance.

Most reactions to vaccines are mild. However, if someone experiences a more severe reaction, they should report it to the Vaccine Adverse Event Reporting System (VAERS): vaers.hhs.gov/index. Anyone can submit a report to VAERS.

Are vaccines free?

Insurance companies typically pay for recommended vaccines. For children who are uninsured or underinsured, the Vaccines for Children (VFC) Program (cdc.gov/vaccines-for-children/vfc-information-for-parents) pays for vaccines. For adults who are uninsured or underinsured, public health departments will sometimes cover the cost of certain vaccines, or they may know of programs in the area that will do so.

Vaccines for international travel may not be covered by insurance or government programs, so it's a good idea to look into which vaccines may be needed well in advance. Seek advice from travel clinics when possible because they often stock these types of vaccines, and they can also provide information about how to prepare for and stay healthy during travel as well as what to watch for when you return.

What should I expect or watch for after a vaccination?

Vaccines sometimes cause a knot, or hard area, at the site of inoculation, usually as a result of a vaccine adjuvant. This knot usually goes away in a few days, but if it doesn't, it would be reasonable to have your health care provider look at it.

Vaccines induce an immune response. Some of the proteins made by the immune system in response to a vaccine (with names like cytokines and interferons) can themselves cause symptoms, like muscle aches, joint pain, joint stiffness, headache, and fever. These symptoms are normal and should go away within a few days. However, if you're not sure if a reaction is normal or if you have concerns about the severity or length of symptoms, contact the health care provider where the vaccine was given.

Should I treat a fever that develops after vaccination?

For all mammalian species (including humans), fever is part of the immune response. We develop a fever because our immune system works better at a higher temperature than at normal body temperature. Indeed, some studies have shown that giving fever-reducing medications (called antipyretics) before or immediately after vaccination can reduce the immune response, and indeed, many studies have shown that treating fever can prolong or worsen a variety of bacterial and viral illnesses by weakening the immune response. So, unless you or your family member are very uncomfortable, you should try to embrace the day or two of low-grade fever following vaccination.

As mentioned, one exception when it comes to treating fevers is during pregnancy. Pregnant people who develop fever following vaccination should be treated as maternal fever can harm the unborn baby.

How can I talk to those with different ideas about vaccines?

When it comes to vaccines, we ask a lot from parents in the United States. During the first few years of life, children can receive as many as twenty-seven inoculations to prevent diseases that most people don't see using biological fluids that most people don't understand. It's not

hard to understand why some parents could fear all these shots. So, the most important thing when talking to friends or family members is to be understanding. It is perfectly reasonable to be skeptical of anything that we put into our bodies, especially vaccines given to healthy young children.

When people have fears about vaccines, it's usually because they're worried about vaccine safety. For example, after the scare about the MMR vaccine potentially causing autism in the late 1990s (see "Do Vaccines Cause Autism?"), thousands of parents refused to have their children receive the MMR vaccine, resulting in hundreds of hospitalizations and several deaths from measles. Despite the millions of dollars that went into research that confirmed there was no evidence that the MMR vaccine caused autism, some people remained skeptical. And some had crossed the line from skepticism to cynicism, believing in a vast international conspiracy of researchers hiding the truth. Likely nothing will reassure those who have fallen into this group.

However, people hearing the concerns of others should evaluate the arguments for themselves and consider whether the individual sharing it is someone who is unwilling to be convinced by high-quality evidence or if the individual may be motivated by something other than a true concern for people's health.

The Vaccine Education Center at Children's Hospital of Philadelphia provides helpful resources to address people's vaccine concerns, including the following:

- "Evaluating Information": media.chop.edu/data/files/pdfs/vaccine-education-center-evaluating-info-qa.pdf
- "Families and Vaccines: When Opinions Differ": media.chop.edu/data/files/pdfs/families-vaccines.pdf
- "Logical Fallacies and Vaccines": media.chop.edu/data/files/pdfs/vaccine-education-center-logical-fallacies.pdf

"In 1736 I lost one of my sons, a fine boy of four years old, by the smallpox, taken in the common way. I long regretted bitterly, and still regret that I had not given it to him by inoculation. This I mention for the sake of parents who omit that operation, on the supposition that they should never forgive themselves if a child died under it; my example showing that the regret may be the same either way, and that, therefore, the safer should be chosen. — *Benjamin Franklin*

Vaccines are among the best tested medical products, held to a high standard of safety. That's because they are given to people who are healthy, often young babies. While concerns about vaccine safety might make a decision to forego immunizations seem easier, and safer, this is not the case. In fact, doing nothing is still doing something—in this case, allowing your loved one to go out into the world without all of the protection available to them. Therefore, it is imperative to evaluate vaccine safety information with logic and not emotion. Those who don't believe that vaccines are safe can be quite convincing in their arguments. They share anecdotes; they parade celebrities, and even doctors, through the media with their messages; and, yes, they even share their own "scientific findings."

It makes discerning the truth much more difficult, but for every anecdote, every celebrity, and every "study," at the end of the day realize that most doctors, most scientists, and even most families are choosing to be immunized. As a result, you probably haven't seen disease or death caused by diphtheria or pneumococcus or polio or congenital rubella. And, amazingly, if you go to a younger physician, they may only recognize a measles rash or diagnose epiglottitis caused by *Haemophilus influenzae* type b, a swelling of the membrane that covers the voice box and can cause suffocation and death, based on lessons in textbooks and not from diagnosing these infections.

Vaccines have not only eliminated some of these diseases, they've also eliminated the memory of these diseases. Let's keep it that way.

Questions for the health care provider:

1. _____

2. _____

3. _____

4. _____

5. _____

6. _____

7. _____

8. _____

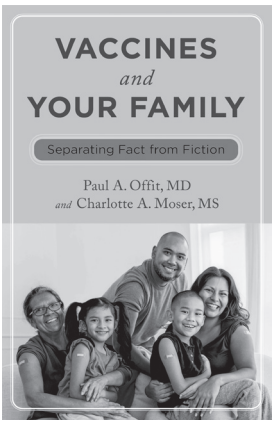
9. _____

10. _____

ORDER THE BOOK

Did you find this booklet to be helpful? Do you want more information about vaccines and the diseases they prevent? If so, you might be interested in the full version book.

Divided into two main sections, "Questions people have about vaccines" and "Individual vaccines," the book addresses not only common questions about vaccines, but it also describes each vaccine and the disease(s) it prevents. Highlighted boxes throughout the book offer personal anecdotes, interesting facts, and things to do to make sure everyone in your family is up to date. The back of the book also offers a place to record immunizations and is easily photocopied for keeping track of immunizations for multiple family members.



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Notes:

Notes:

Vaccine Safety and Your Family was excerpted from the book for families, *Vaccines and Your Family: Separating Fact from Fiction,* published by Columbia University Press in 2024. Authored by the Director and Co-Director of the Vaccine Education Center at Children's Hospital of Philadelphia (VEC), the book was written as a guide for families.

The VEC was founded in October 2000 to provide accurate, comprehensive and up-to-date information about vaccines and the diseases they prevent. The Center is funded by endowed chairs from the Children's Hospital of Philadelphia and does not receive support from vaccine companies.

For more information about vaccines, visit the Vaccine Education Center websites:

- Science-based vaccine information: **vaccine.chop.edu**
- Vaccine safety references: **vaccine.chop.edu/safety-references**
- Tools and resources: **vaccine.chop.edu/resources**
- Program for families: **vaccine.chop.edu/parents**
- Program for healthcare providers: **vaccine.chop.edu/vaccineupdate**
- Program for classrooms: **vaccinemakers.org**
- Scientists and their work: **hillemanfilm.org**
- Game and info for children: **vaxpackhero.org**

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