VACCINE SAFETY *and* YOUR CHILD

Separating Fact from Fiction

Excerpted from:

VACCINES *and* YOUR CHILD

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INTRODUCTION

Almost immediately after a baby is born, one of the first decisions new parents face is whether to have the baby immunized. Beginning in the hours after birth with the hepatitis B vaccine and occurring frequently thereafter during the first two years of life, immunizations are a part of the parenting "to do" list. Unfortunately, for some, these decisions are wrought with emotion and fear that the vaccines may be doing more harm than good.

Many of the concerns, indeed virtually all of them, have been studied using sound scientific methods and found to be baseless. However, often times, these findings do not find their way to the top of Internet search result lists, media reports or discussions with family and friends, leaving parents confused, frustrated and outright scared to immunize their tiniest and most vulnerable family members.

This booklet is designed to bring the findings of those scientific studies to parents. Excerpted from the book, *Vaccines and Your Child: Separating Fact from Fiction* (©2011 Columbia University Press), the next several pages will present discussions and scientific findings related to the most common concerns about vaccine safety, including questions about the vaccine schedule, whether vaccines cause other conditions, and what is in the vaccine vial. While these pages are not filled with references, readers who are interested 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 book sellers.

After reading this information, it is hoped that parents will be reassured that getting their babies vaccinated is one more way of loving them.

GENERAL QUESTIONS ABOUT VACCINE SAFETY

Are vaccines safe?

A vaccine is safe if its benefits clearly and definitively outweigh its risks. But any medical product that has a positive effect—whether it is a drug or a vaccine—can have a negative effect. So no vaccine is absolutely safe. All vaccines that are given as shots can cause pain, redness, or tenderness at the site of injection. And some vaccines cause more serious problems. For example, the measles vaccine can cause a decrease in platelets, which help the blood to clot. This happens in about 1 of 25,000 children who get the vaccine. This particular reaction, called thrombocytopenia, shouldn't be surprising since natural measles infection can do exactly the same thing, except much more commonly and much more severely.

The chickenpox vaccine contains gelatin as a stabilizer. Some people are severely allergic to gelatin and develop severe allergic symptoms in response to the chickenpox vaccine. Symptoms can include hives, difficulty breathing, low blood pressure, and even shock. That's why doctors often ask patients to stick around for about fifteen minutes after they get vaccines—because this type of severe allergic reaction, although quite rare, happens very quickly.

But while there are small risks to vaccines, nothing is risk free. Probably the most dangerous aspect of vaccines is driving to the doctor's office to get them. Every year about 30,000 people die in car accidents. Walking outside on a rainy day isn't entirely safe; every year in the United States about 100 people are killed when they are struck by lightning. And hundreds of people die every year when they slip and fall in the bath or shower. So, even routine daily activities pose a certain degree of risk. 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?

Because we are all 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 to young children. They suffer asthma, allergies, autism, developmental delays, hyperactivity, or attention deficit disorder, among other health problems. Worse: sometimes they die of poorly defined disorders like Sudden Infant Death Syndrome (SIDS). Some of these problems might occur soon or immediately after receiving vaccines.

So how can you know whether symptoms that follow a vaccination were caused by the vaccine? The best way is by performing controlled studies. For example, in 1998, British investigators proposed that the combination measles-mumps-rubella (MMR) vaccine might cause autism. At the time, about 1 in 2,000 children in England were diagnosed with autism and about 9 of 10 were given

the MMR vaccine. To determine whether MMR caused autism, researchers studied hundreds of thousands of children who did or didn't receive the vaccine. If the vaccine caused autism, then the number of children with autism should be greater in the group that received the vaccine than in the group that didn't receive it. But it wasn't. In fact, the incidence of autism in children who got MMR was the same as in those who didn't get it.

However, 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. Twelve studies performed by different groups of investigators working on several different continents all showed the same thing: MMR didn't cause autism. Although no epidemiological study is perfect, they can be quite powerful, capable of determining whether a vaccine caused a problem in as few as one in a million vaccinated children.

Many parents who read about the investigations of MMR were reassured by the results, but some weren't. They had been compelled by what they had seen, and no study could convince them otherwise.

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 father actually given his child the vaccine, no amount of statistical evidence in the world would likely have convinced him that anything other than the vaccine was the cause.

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 not large enough to determine whether a vaccine causes a very rare side effect. To test for this, two post-licensure systems were put in place in the late 1980s and early 1990s: the Vaccine Adverse Events 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 someone else believes that a vaccine caused a problem, they fill out a one-page form and send it in. These

forms—which are easily obtained from doctor's offices or from the Internet (http://vaers.hhs.gov/index)—are carefully evaluated by the FDA and CDC to determine whether a particular side effect is reported more frequently than would be expected.

The best example of how VAERS works occurred between 1998 and 1999, when a new vaccine to prevent rotavirus (called RotaShield) was licensed by the FDA and recommended for routine use in children. RotaShield was given by mouth to children at two, four, and six months of age. Soon after the vaccine was introduced, reports started coming into VAERS of an unusual problem: intestinal blockage (intussusception). Intussusception, a medical emergency, 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. As a result, 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 do this. Investigators now had to determine whether intussusception following RotaShield was occurring at a rate greater than would have been expected by chance alone, since intussusception occurred in about 1 of 2,000 infants every year even before the rotavirus vaccine was first used. To do this, they used another safety system called the Vaccine Safety DataLink (VSD).

The VSD is a group of large health maintenance organizations (HMOs) whose computerized medical records are linked, representing about 6 percent of the U.S. population, adults and children. Whereas the VAERS program can raise the question of whether a vaccine caused a particular problem, the VSD can answer it, because the VSD 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 had or hadn't received RotaShield to see whether intussusception occurred more commonly in the vaccinated group. It did. RotaShield caused intussusception in about 1 in 10,000 children who got the vaccine. As a consequence, RotaShield was taken off the market. This was the first time a vaccine had been discontinued because of a safety problem in almost 50 years.

Seven years passed before another rotavirus vaccine was given to U.S. children. It was called RotaTeq, and it was made quite differently than RotaShield. This time, the VSD was immediately put into action using something called a rapid-

cycle analysis. As soon as children started to receive RotaTeq, VSD investigators began examining the incidence of intussusception in children who had or hadn't 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 whether children had or hadn't received this vaccine.

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 like multiple sclerosis, allergies, asthma, and 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, specific immunity to a virus or bacteria can only be acquired by natural infection or immunization. And the price of natural infection is too high.

One example of why a healthy lifestyle doesn't work can be found in the life of one of America's most beloved presidents, Franklin Delano Roosevelt. FDR 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. FDR 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.

QUESTIONS ABOUT THE VACCINE SCHEDULE

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

Before the FDA can license a new vaccine, it must first be tested by concomitant-use studies, which require new vaccines to be tested with existing vaccines. The new vaccine must be shown not to interfere with the safety or immunogenicity 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 be inoculated with multiple vaccines at the same time.

Are vaccines given on a one-size-fits-all schedule?

Some parents wonder how the same vaccine can be recommended for a 10-pound baby as for a 200-pound adult. Wouldn't it make more sense to

give a baby a smaller amount of vaccine? That's exactly what is done for drugs, where the amount prescribed is often determined by weight or age.

Indeed, some vaccine dosages given to children and adults aren't the same. For example, the influenza and hepatitis B vaccines given to children contain lower quantities of vaccine than those given to adults. Sometimes the opposite is true. For example, the amount of diphtheria and pertussis vaccine contained in the DTaP vaccine given to children is actually 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 young children.

But the need to take into account weight when determining 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. Vaccines are typically injected into the arm, leg, or buttocks. The vaccine then travels to nearby lymph nodes, which are collections of immune cells located throughout the body. Once in the lymph node, the vaccine enters a type of immune cell called an antigen-presenting cell. These cells present the vaccine to other cells of the immune system responsible for making antibodies.

As a general rule, vaccines stimulate the 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 would be, how are children protected against infections that enter in different 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 infections might occur.

When vaccines are tested, children are put in groups given different doses to determine which works the best; these are called dose-ranging studies. The goal is to give the minimal amount of vaccine that is capable of inducing a protective immune response, so that the vaccine is least likely to cause side effects.

Do too many vaccines overwhelm the immune system?

Today, young children get vaccines to prevent fourteen different diseases. That could mean as many as twenty-six inoculations and five shots at one time. It's difficult for a parent to watch this and not feel that it's too much. So the question is perfectly reasonable, and can be answered in a few ways.

First, compare the number of immunological challenges in vaccines today with those in the past. Thirty years ago, in the 1980s, children received seven vaccines: MMR, DTP, and polio. Fifty years ago, in the 1950s, children received five vaccines: DTP, polio, and smallpox. A hundred years ago, at the turn of the twentieth century, children received one vaccine: smallpox. Most parents would probably be surprised to find that the number of immunological components contained in that one vaccine given a hundred years ago was greater than those contained in the fourteen vaccines given today.

To understand why this is true, let's begin by defining terms. An immunological component is that part of a bacteria or virus 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, complex sugars that surround their surface. The smallpox vaccine contained about 200 proteins. The 14 vaccines given to young children today contain about 160. So although there is no denying that 14 is greater than one, it's what's in the vaccine, not the number of vaccines, that counts. Fortunately, thanks to advances in protein chemistry, protein purification, and recombinant DNA technology, we can make vaccines today that are much purer (and consequently safer) than those in the past.

Second, compare vaccines to other immunological challenges in the environment—challenges that are unseen but much greater. The womb is sterile: no bacteria, no viruses, no parasites, no fungi. So babies' immune systems aren't required to do much. 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 10 times more bacteria live on the surface of our bodies (100 trillion) than we have cells in our bodies (10 trillion). And that's not the end of it: the food that children eat isn't sterile, nor is the dust they inhale. Most bacteria have the capacity to invade the bloodstream and cause harm, and each bacterium contains between 2,000 and 6,000 immunological components. To prevent this from happening, babies 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 aren't prevented by vaccines—like rhinoviruses (which cause the common cold), parainfluenza virus, respiratory syncytial 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, these 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 viral infections.

Third, calculate the extent to which vaccines challenge the immune system. Exactly how many different vaccines can babies respond to? The best reasoned answer to this question comes from a paper written by two immunologists at the University of California at San Diego, Mel Cohn and Rod Langman. Cohn and Langman focused on antibodies, the most important component of the immune system induced by vaccines. Antibodies are made by cells in the body called B cells, each of which has the capacity to make antibodies against only one particular 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 babies could theoretically respond to a hundred thousand vaccines at one time. Of course, we're not saying that babies should get a hundred thousand vaccines at once. We're only saying 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, examine how well newborns respond to vaccines. Probably the most dramatic example is the hepatitis B vaccine. Babies born to mothers infected with hepatitis B virus are at high risk not only of being infected with the virus but also of developing chronic liver damage (cirrhosis) or liver cancer. The greatest risk of infection and long-term problems comes at the time of delivery. When passing through the bloody birth canal of an infected mother, babies come in contact with an amazing amount of hepatitis B virus; each milliliter (about one fifth of a teaspoon) of blood contains roughly a billion infectious viruses, and the birth process exposes babies to a lot of blood. So it's no wonder that almost all children born to infected mothers contract the disease. Despite the fact that the vaccine is given after exposure, studies have shown that about 80 percent of babies are protected against infection after 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 have to be ready to respond to a tremendous microbial onslaught the minute they are born if they are to survive.

Indeed, diseases like *Haemophilus influenzae* type b (Hib), pneumococcus, rotavirus, and whooping cough all typically appear early in life. If babies are to avoid these diseases, they need to develop an immune response pretty quickly. Most mothers have antibodies directed against many of these infections and pass them on to the baby while still in the womb. But antibodies from the mother eventually fade away, leaving the child vulnerable. That's why vaccines

against Hib, pneumococcus, rotavirus, and whooping cough are given at two, four, and six months of age; when the mother's antibodies wear off, the child will already have his own protective response.

Is there any harm in using an alternative schedule?

During the first few years of life, children can receive as many as twenty-six separate inoculations and five shots at one time. For most parents, it's hard to watch children restrained against their will and injected again and again with so many shots. So it's easy to appeal to the sentiment that it might be of value to create an alternative schedule that separates, delays, withholds, or spaces out doses of vaccines.

The perceived value of an alternative schedule is that it might avoid weakening, overwhelming, or altering the immune system of the young child. However, abundant evidence shows that this is not the case. Another argument for spacing out vaccines is that they contain potentially harmful additives that might be toxic if too many are given at once, but again, evidence does not support this fear. Yet another argument is that too many vaccines are causing specific diseases like asthma, allergies, autism, diabetes, and multiple sclerosis—diseases that could be avoided by choosing a different schedule. But again, evidence refutes these contentions. Some parents (as well as 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. This isn't true for several reasons.

Increased Duration of Susceptibility to Disease

The biggest problem with an alternative 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. Population (or herd) immunity—the ability of a vaccinated community to protect those who can't or won't be vaccinated—has broken down. As a consequence, outbreaks of pertussis (or whooping cough) are common; a measles epidemic in 2008 was larger than any measles outbreak in more than a decade; and children are starting to die from bacterial meningitis because their parents are choosing to either 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 make the choice to delay vaccines are taking an unnecessary risk without deriving any benefit.

No Data to Support Safety and Effectiveness of an Alternative Schedule

Another problem with the alternative vaccine schedule is that it's 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 and 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.

More Shots

Another reasonable argument for spacing out vaccines is that it would mean fewer shots at one time, and therefore less pain for the child. Interestingly, researchers have found that children experience similar amounts of stress—as measured by secretion of a hormone called cortisol—whether they are getting one or two shots at the same visit. This suggests that although children are clearly stressed by receiving a shot, two shots aren't more stressful than one. For this reason, more visits to the doctor created by separating or spacing out vaccines will likely only increase the trauma of getting shots.

What if my child inadvertently gets an extra dose of vaccine?

The vaccine schedule is busy. In the first few years of life children can receive as many as twenty-six inoculations and five shots at one time. Also, many combination vaccines are available and often differ from one doctor's office to the next. Unfortunately, this means that occasionally mistakes are made. In some cases, a child might receive an extra dose of vaccine. Parents of these children, reasonably upset, want to know whether this is harmful. While an extra shot often causes pain, redness, tenderness, or swelling at the site of injection, it doesn't mean that the child is 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 he is given a second dose, he already has developed antibodies that limit the vaccine virus's ability to reproduce itself and travel to the skin. Children who receive an extra dose of vaccine usually develop a boost in their immune response.

Does my parent who recently had a shingles vaccine need to stay away from my baby?

Shingles typically occurs when a person has a weakened immune system due to age or disease. Because it is the reactivation of a virus that is already living in the person's body, one person cannot give another person shingles. Although a person with shingles can give chickenpox to someone who has never had chickenpox or the chickenpox vaccine, this can only happen if the non-immune person, such as your baby, comes in contact with the rash before it has crusted. It is not typically transmitted by coughing, sneezing, or casual contact. Likewise, the baby would only be exposed to the chickenpox virus if the recently-immunized parent developed a rash at the injection site *and* the baby came into contact with the rash, so it is unlikely that the baby would get chickenpox from the parent who recently had the shingles vaccine. Therefore, they do not need to be kept apart.

DO VACCINES CAUSE _____?

Do vaccines cause chronic diseases?

Some people fear that vaccines, although they have clearly extended our lives, have merely substituted chronic diseases for infectious diseases. That instead of suffering from measles, mumps, and chickenpox, we now suffer diabetes, multiple sclerosis, and arthritis, all diseases in which the body reacts against itself (autoimmunity).

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, when they are infected with strep, develop a disease that can severely affect the heart. This happens because proteins on the surface of strep (called M proteins) are very similar to proteins found on the cells that line the heart. So when the immune system is reacting to strep, it is also inadvertently reacting to the heart. The result is a severe and occasionally fatal disease: rheumatic fever.

Strep isn't the only disease that can induce autoimmunity. Some children with Lyme disease, caused by a bacterium called *Borrelia burgdorferii*, develop a long-lived, recurrent arthritis because one of the Lyme bacterial proteins is similar to a protein that can be found in joints. And intestinal infections caused by Campylobacter can lead to an autoimmune disease called Guillain-Barré Syndrome, where the body reacts against the lining of nerves.

So 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 where the body reacts

against the covering of nerves. Nerves are like wires covered by a thin layer of rubber. Instead of rubber, nerves in the body are covered by something called myelin, the principle component of which is myelin basic protein. People with multiple sclerosis often have worse symptoms 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. Some people with multiple sclerosis, when making an immune response against influenza virus, also inadvertently make an immune response to their own brain. The logical next question would be, can influenza vaccine do the same thing that natural influenza infection does? The influenza vaccine is similar to natural influenza virus in that both contain the protein that mimics myelin basic protein. But studies have clearly shown that although natural infection can cause a worsening of symptoms of multiple sclerosis, influenza vaccine (the shot) can't. That's because 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 do so very well and, like the killed influenza vaccine, doesn't cause the body to react against itself.)

The influenza–multiple sclerosis story isn't the only example of why vaccines don't induce very good autoimmune responses. Lyme disease is another example. Lyme bacteria can cause a long-lived arthritis based on an autoimmune response to a protein that is present on the surface of the bacterium and that can be found in joints. This same protein was used to make a Lyme vaccine that was available in the United States between 1998 and 2002. So the obvious question is, did the vaccine cause chronic arthritis? To answer this question, tens of thousands of people who received the Lyme vaccine were compared with tens of thousands of people who didn't to see if the risk of arthritis was greater in the vaccinated group. It wasn't.

Vaccines don't appear to have what it takes to cause the cascade of immunological events necessary for autoimmunity. They have consistently been shown not to cause multiple sclerosis, diabetes, or other autoimmune diseases.

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 reasoned that 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. More importantly, twelve studies have produced no evidence that children who receive MMR vaccine are at greater risk of autism than those who haven't.

One year later, in 1999, the hypothesis shifted. At that time, the American Academy of Pediatrics, together with the U.S. Public Health Service, asked that thimerosal, an ethylmercury-containing preservative, be removed from all vaccines given to young children. These two 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 who favored removal of thimerosal argued that they were exercising caution in the absence of data, because at the time, no studies had determined whether thimerosal in multiple vaccines was toxic. Unfortunately, the removal was done in such a precipitous manner that parents became concerned. They reasoned that maybe it was thimerosal, not MMR, that was causing autism. As had been the case during the MMR scare, the science quickly followed. Six studies examined the risk of autism in those who had or hadn't received vaccines containing thimerosal; the chances of getting autism were 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 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, there was no difference between the two groups. Delaying or withholding vaccines didn't lessen the risk of autism.

Do vaccines cause allergies and asthma?

Several different types of antibodies circulate in the body. One type, immunoglobulin G (IgG), is most commonly found in the bloodstream. Another type, secretory immunoglobulin A (IgA), is most 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 allergic responses, IgE binds to a cell type in the body called mast cells, which release mediators of inflammation 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. Although several different types of T cells have been identified, when talking about allergies and asthma, two are most important: 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 with regard to allergies, Th1 cells are good and Th2 cells are bad.

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

Some people fear that vaccines, because they prevent natural infections, might not allow for the maturation of Th1 cells, leading to allergies and asthma. (This is often referred to as the hygiene hypothesis.) For example, children who live in large families, attend day care, or live in developing countries—and therefore are exposed to more bacteria and viruses—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 25,000 illnesses in Cleveland in the 1960s found that children experienced six to eight infections per year in the first six years of life; most were viral infections of the upper respiratory tract or intestine that aren't prevented by vaccines. They were caused by viruses such as parainfluenza virus, rhinovirus, respiratory syncytial virus (RSV), adenovirus, parechovirus, enteroviruses, 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 level of sanitation in the country. So the hygiene hypothesis doesn't hold here.

Clinical studies also support the notion that vaccines don't cause allergies or asthma. One group of investigators examined computerized records of more than 18,000 children born between 1991 and 1997 who were enrolled in four large health maintenance organizations. Children who received the diphtheria-pertussis-tetanus vaccine, oral polio vaccine, *Haemophilus influenzae* type b (Hib) vaccine, hepatitis B vaccine, and MMR vaccine were not at greater risk for asthma than those who hadn't. Another large, well-controlled study of more than 600 children found that those who received the diphtheria-tetanus-pertussis vaccine were not at greater risk for diseases like asthma, hives, or food allergies. Similarly, several other studies found no evidence that vaccines increased the risk for allergic diseases.

Taken together, these studies show that vaccines don't cause allergic diseases.

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 or 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 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 90 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 it was 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 it. Apparently, SV40 just passed through the intestines without causing an infection. Researchers also found that although formaldehyde used in the making of Salk's vaccine didn't completely kill SV40, it did decrease infectivity at least ten thousand-fold. The quantity of residual SV40 in Salk's vaccine probably wasn't enough to cause cancer. But at that point, no one was sure.

Horrified that children had been injected with a potentially cancer-causing virus, researchers compared cancer rates in children who had received SV40-contaminated polio vaccines with cancer rates in unvaccinated children. Eight years after the tainted vaccines had been given, the cancer incidence was the same in both groups. The same was true 15 and even 30 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 25,000 cases of meningitis, pneumonia, and bloodstream infections that occurred in the country every year. And it has. But when the vaccine was first licensed, it quickly fell under a cloud of concern when a doctor named Bart Classen, speaking on the national television program *World News Tonight with Peter Jennings*, claimed that it caused diabetes.

Classen had studied children in Finland who had received the Hib vaccine at three, four, six, and fourteen months of age and compared them with those who had received it at fourteen months of age only. He found that children who had received four doses of Hib vaccine 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 studies but couldn't. One group of investigators followed thousands of children who 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 examined 250 people with diabetes and compared them to more than 700 people who didn't have the disease. They wanted to see whether those with diabetes were more likely to have received vaccines like pertussis, MMR, Hib, hepatitis B, or varicella. They weren't. People with diabetes were not more likely to have received these vaccines than people who didn't have diabetes.

The inability of researchers to reproduce Classen's findings caused them to take a closer look at his original study. They found that the analytical methods used were incorrect; no significant differences in the incidence of type 1 diabetes in Hib-vaccinated infants were found ten years later. Indeed, Finnish children who had received four doses of Hib weren't more likely to have diabetes than those who had received one dose.

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

Do vaccines cause mad cow disease?

Mad cow disease was a problem in the United Kingdom in the 1990s. Caused by a unique infectious agent called proteinaceous infectious particles or prions, it could also spread to humans. The human form of mad cow disease is called variant Creutzfeld-Jacob Disease (vCJD), a rapidly progressive, debilitating form of dementia. During the mad cow scare, some people became concerned that vaccines, which may contain trace amounts of animal products used during the manufacturing process, could cause vCJD.

Vaccines are grown in laboratory cells that require many factors for maintenance, some of which are obtained from animals. An excellent source of these growth factors is serum from the fetuses of cows (fetal bovine serum).

Because of concerns about vCJD, the FDA prohibited the use of bovine-derived materials obtained from countries known to have a problem with mad cow disease. This raised the question of whether children inoculated with vaccines prior to the ban were at risk for vCJD. Newspapers reported this possibility in the late 1990s. However, several features of mad cow disease should reassure parents that vaccines don't cause vCJD.

First, prions that cause mad cow disease are detected in the brain, spinal cord, and retina of cows, not in blood, serum, or other organs. Therefore, trace quantities of fetal bovine serum that might be present in liquids that support the growth of cells used to make vaccines don't contain prions. Indeed, no cases of vCJD have been caused by exposure to blood or blood products, and a history of blood transfusion does not increase a person's risk for vCJD.

Second, even in England, products used in vaccines that were derived from cows didn't cause vCJD. Studies clearly showed that children who received vaccines were not more likely to develop vCJD than those who hadn't.

Third, transmission of prions occurs through either eating brains from infected animals or, in experimental studies, directly inoculating preparations of brains from infected animals into the brains of healthy animals. Transmission of prions has not been documented after inoculation into the muscles or under the skin (routes used to vaccinate).

Taken together, the chance that currently licensed vaccines cause vCJD is zero.

Do vaccines cause multiple sclerosis?

Multiple sclerosis is a chronic disease of the brain caused when the immune system reacts against the covering of nerves.

Nerves are like electrical wires surrounded by thin rubber tubing. The sheath covering nerves is made of myelin, and the main component of myelin is myelin basic protein. People develop multiple sclerosis when one part of their immune system (called T cells) reacts to myelin basic protein and destroys it. Although the root cause or causes of multiple sclerosis remain unclear, the fact that it is an autoimmune disease involving an abnormal response to the body's myelin is quite clear.

In the mid-1980s, some people became concerned that hepatitis B vaccine could cause an immune response against myelin resulting in multiple sclerosis. This fear became so widespread that the French government temporarily suspended their school-based program of hepatitis B vaccination.

However, the idea that hepatitis B vaccine caused multiple sclerosis was flawed for several reasons. First, there is only one protein in the hepatitis B vaccine (called hepatitis B surface protein) and it doesn't mimic myelin basic protein, so an immune response to the vaccine shouldn't cause an immune response

to myelin. Second, natural infection with hepatitis B virus is associated with production of large quantities of hepatitis B surface protein—about ten thousand times more than that contained in the vaccine—but is not associated with an increased risk of multiple sclerosis.

Further evidence that vaccines don't cause multiple sclerosis can be found in two large studies, both reported in the *New England Journal of Medicine*. The first involved hundreds of thousands of nurses observed for more than a decade. Nurses who developed multiple sclerosis were not more likely to have received hepatitis B vaccine than those who didn't develop the disease. The second study involved hundreds of patients with multiple sclerosis in Europe to see whether the hepatitis B, influenza, or tetanus vaccines caused a worsening of symptoms. They didn't. Therefore, vaccines don't cause or worsen symptoms of multiple sclerosis.

Do vaccines cause Sudden Infant Death Syndrome (SIDS)?

Every year in the United States, babies die from a disorder that is poorly understood, called Sudden Infant Death Syndrome or SIDS. The disorder primarily affects children 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 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—to prevent hepatitis B virus—was recommended for young 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 died of SIDS 16 hours after her second dose of hepatitis B vaccine. At the time the story aired, about 5,000 children died every year from SIDS. Within 10 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 each year. In other words, while the number of babies getting hepatitis B vaccine dramatically increased, the number of babies dying from SIDS dramatically decreased. In fact, the cause of the decrease in SIDS wasn't related to vaccines at all. Rather, it was discovered that children who died from SIDS were more likely to have slept face down. So the American Academy of Pediatrics introduced the Back to Sleep program, which dramatically reduced the number of deaths from SIDS. Therefore, the hepatitis B vaccine—like the pertussis vaccine—doesn't cause SIDS.

Do vaccines cause Guillain-Barré Syndrome (GBS)?

Guillain-Barré Syndrome (GBS) is a disease characterized by weakened muscles, burning or tingling of the legs or arms, loss of muscle tone, and sometimes paralysis. GBS occurs when a person's immune system attacks the proteins that line nerves. Although the exact cause is not known, some people get the disease after having a viral infection that affects the lungs or digestive tract. GBS is very rare, occurring in about 1 of 100,000 people every year.

Some adolescents have been diagnosed with GBS shortly after receiving meningococcal vaccine, so their parents have wondered whether the vaccine caused the disease. By the end of 2008, thirty-three people reported GBS following meningococcal vaccine to the Vaccine Adverse Events Reporting System (VAERS). So the CDC performed studies to determine whether GBS occurred more frequently in the vaccinated group. It didn't. The incidence was the same in people who did or didn't receive the vaccine.

WHAT'S IN THE VACCINE VIAL?

Do vaccines contain products to which children could be allergic?

The Centers for Disease Control and Prevention (CDC) estimates that every year several substances in vaccines cause about 200 people to suffer severe allergic reactions. Because severe allergic reactions happen quickly, parents are encouraged to keep children in the doctor's office for about fifteen minutes after getting any vaccine. Remaining in the doctor's office will assure access to medical care should it be needed.

Egg Proteins

About 1 of 200 people in the United States is allergic to eggs. Most are only mildly allergic, but some are severely affected. Two vaccines are made in eggs–yellow fever and influenza vaccines. The recommendations regarding whether egg-allergic people should get these vaccines differ slightly:

- Yellow fever vaccine - The quantity of egg proteins present in the final product can be measured in micrograms (millionths of a gram) per dose, and although these quantities are quite small, they might be sufficient to cause allergic reactions, including hives, difficulty breathing, and low blood pressure. People with egg allergies who think they need the yellow fever vaccine should see an allergist.
- Influenza vaccine - Studies have shown that people with egg allergies can still safely receive the influenza vaccine.

Some people think that if they're allergic to eggs they can't get the measles and mumps vaccines. But those vaccines aren't made in eggs; they're made in chick embryo cells in culture. The quantity of residual egg proteins found in measles and mumps vaccines is measured in picograms (trillionths of a gram). This quantity is at least five hundred times less than that found in influenza vaccines, so it doesn't cause a problem. Therefore, children allergic to eggs can receive the MMR vaccine safely.

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, chlortetracyline, and amphotericin B. However, only neomycin is contained in vaccines in quantities large enough to be detectable. And severe allergic reactions to neomycin have not been found.

Yeast Proteins

Both hepatitis B vaccine and one of the human papillomavirus (HPV) vaccines (Gardasil) contain yeast proteins. These vaccines are made by inserting the gene that makes one viral surface protein into a plasmid (small circular pieces of DNA) and putting the plasmid into baker's yeast. When the yeast cells grow, they also make the viral proteins that eventually become the vaccine. Hepatitis B and HPV vaccines contain between one and five 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 severe allergy due to baker's yeast is theoretical.

Gelatin

In 1993, a seventeen-year-old girl in California developed a runny nose, hives, difficulty breathing, lightheadedness, 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.

Gelatin, which is made by extracting collagen (the most abundant protein in the body) from the bones and hides 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 1 case per 2 million doses), but it's still the most common identifiable cause of severe allergic reactions to vaccines. Gelatin is contained in the MMR, chickenpox, shingles, influenza (nasal spray), and rabies vaccines. And it's hard to know whether children are allergic to gelatin. Some people who are allergic to gelatin have a history of allergies to gelatin-containing foods and therefore are allergic to gelatin in vaccines. But this isn't always the case, because the gelatin in foods comes from cows whereas that in vaccines comes from pigs.

Do vaccines contain harmful preservatives like mercury?

The preservative in vaccines that has 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 suffered local abscesses or serious bloodstream infections, including sepsis and death, caused by bacteria like staph and strep that had contaminated the last few doses of the vial. By the 1940s, most multidose vials of vaccines contained preservatives like thimerosal, which prevented severe and occasionally fatal infections caused by contaminated vials.

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. As a consequence, the American Academy of Pediatrics and the U.S. Public Health Service decided to remove thimerosal from virtually all vaccines by the spring of 2001. (Preservative levels of thimerosal are still contained in multidose preparations of the inactivated influenza vaccine.) This meant that vaccines containing thimerosal would no longer be given to young infants. 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

by bacteria to methylmercury. 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 child 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), breast milk mercury is much more likely to accumulate. This doesn't mean that breast milk is dangerous, or that infant formula is dangerous. It means only that anyone who lives on the planet consumes small amounts of mercury all the time.

To answer parents' concerns about whether thimerosal in vaccines caused harm, investigators in several countries examined children who had received thimerosal-containing vaccines and compared them to those who had received the same vaccines containing lesser quantities of thimerosal or no thimerosal. They found that there was no difference in the risk of autism among these groups. Further, children receiving thimerosal-containing vaccines didn't develop even subtle signs of mercury toxicity. Now, thimerosal is contained in only one preparation of one vaccine that could be given to older infants (multidose preparations of the inactivated influenza vaccine). However, parents should be reassured that studies of babies less than six months of age who received quantities of thimerosal eight times greater than those contained in the current influenza vaccine showed that thimerosal was not harmful.

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, everyone living on the planet has very small quantities in their bodies of a variety of heavy metals including arsenic, cadmium, thallium, beryllium, and lead. All of these substances can be harmful in large quantities. But the small quantities we all encounter from 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 of vaccine and fewer doses. (The word "adjuvant" comes from the Latin adjuvare, to help.) The DTaP, hepatitis A, hepatitis B, Hib, and pneumococcal vaccines all contain adjuvants.

For the past eighty years, vaccines have 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 cornbread.

Because aluminum is everywhere, adults typically ingest between five and ten 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 10 milligrams of aluminum by six months of age; those fed regular infant formula, 30 milligrams; and those fed soy formula, 120 milligrams. These quantities are much greater than those contained in vaccines: babies who get all of the recommended vaccines will receive 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 very 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.

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 one and five 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 completely eliminated in one day.

In 2009, another adjuvant, monophosphoryl lipid A, was licensed for use in children in the United States. This substance is contained in one of the human papillomavirus (HPV) vaccines (i.e., Cervarix). Lipid A, from which

monophosphoryl lipid A is derived, is a natural product, found on the surface of certain types of bacteria. Taking advantage of the natural adjuvant effect of lipid A, researchers detoxified it so that it couldn't cause harm.

Do vaccines contain harmful chemicals like formaldehyde?

Vaccines are complicated to make. They're not like other pharmaceuticals, for which synthesis of small molecules can be performed relatively easily in a laboratory. Vaccines are biologicals: viruses can only be grown in cells; bacteria need nutrients to grow; and for vaccines made using recombinant DNA technology—like hepatitis B and human papillomavirus vaccines—cells are still required to support the expression of viral proteins. Vaccines must also be sterile, so the process often involves inclusion of antibiotics (see "Do vaccines contain products to which children can be allergic?").

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 (see "Do vaccines contain products to which children can be allergic?"). 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 (see "Do vaccines cause mad cow disease?"), monosodium glutamate, polysorbate, phenoxyethanol, ethylenediaminetetraacetic acid (EDTA), polyethylene glycol, sodium borate, octoxynol, and sodium deoxycholate. All of these chemicals are present in very small amounts. Similar or greater quantities of these substances are found in foods, beverages, toothpastes, and over-the-counter medicines. But one chemical in vaccines draws the most attention: formaldehyde.

Formaldehyde is used to inactivate viruses (like polio and hepatitis A) and bacterial toxins (like diphtheria and tetanus toxins); as a consequence, small quantities of formaldehyde are found in the final product. Besides the chemical's use by morticians (so its name conjures up images of the deceased), concerns have centered on the fact that large quantities of formaldehyde can damage cellular DNA, causing cancerous changes in cells grown in laboratory flasks. Fortunately, formaldehyde doesn't cause cancer in man, and animals exposed to quantities of formaldehyde exponentially greater than those contained in vaccines don't develop malignancies either. 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 is considered to be safe for the following reasons: formaldehyde is an essential intermediate in human metabolism and is required for the synthesis of thymidine, purines, and

amino acids, all 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 weight of a two-month-old of 5 kilograms (about 11 pounds) and an average blood volume of 85 milliliters per kilogram, the total quantity of formaldehyde found naturally in an infant's 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 naturally circulating in our bodies than contained in vaccines.

Do vaccines contain ether or antifreeze?

The concern that vaccines contain ether and antifreeze has been propagated on the Internet as well as by anti-vaccine celebrities on national television shows.

Ether is the popular name given to the chemical diethyl ether, an anesthetic no longer used in hospitals, in large part because it is highly flammable. Vaccines don't contain diethyl ether. It is hard to know where this myth started, but it might be because manufacturers use small amounts of a mild detergent to break open the cells used to grow vaccine viruses. This mild detergent has the chemical name polyethylene glycol pisooctylphenyl ether. Ethers are commonly found in nature, linking carbohydrates via a central oxygen atom. We are exposed to these harmless linkages every day.

Antifreeze is used to prevent water from freezing, primarily in car engines. Quaker State AntiFreeze and Coolant is typical of most products, containing ethylene glycol and diethylene glycol. Sometimes antifreeze products also contain methanol, also known as wood alcohol. Vaccines don't contain any of these substances. Again, it's hard to figure out where this notion came from, but it may have to do with the presence of trace amounts of the harmless product polyethylene glycol, which is not antifreeze and is often found in over-the-counter medicines and toothpastes.

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 only grow inside cells. So if you are going to make a viral vaccine, you need cells to be part of the process. One of the advantages of using fetal cells is that they are essentially immortal; they can reproduce forever. This is in direct contrast with cells obtained from organs that are fully developed; such cells reproduce about fifty times, then die out. Because fetal cells are immortal, they can be used to make viral vaccines for centuries.

Other aspects of human fetal cells make them attractive for vaccine use. First, human cells are much more likely to support the growth of human viruses than 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 isn't always the case with cells obtained from live animals (see "Do vaccines cause cancer?").

In the early 1960s, cells used to make vaccines were obtained from two elective abortions, one performed in Sweden, the other in England. Human fetal cells obtained from Sweden were sent to the Wistar Institute, where Stanley Plotkin was working on a rubella vaccine and Tad Wiktor was working on a rabies vaccine. These cells were called Wistar Institute-38 or WI-38 cells. The other source of human fetal cells was an abortion performed in England and studied at the 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.

To some, using human fetal cells to make vaccines is abhorrent, an act against God. In July 2005, in response to pressures from a prolife group in the United States, the Vatican's Pontifical Academy for Life ruled on the issue of whether using vaccines derived from human fetal cells was wrong. The ruling was made by Cardinal Joseph Ratzinger, then head of the Catholic Church's Congregation of the Doctrine of Faith. Ratzinger was a well-known theologian and prolific author. He became Pope Benedict XVI, the 265th pope, until he retired in February 2013. Ratzinger reasoned that those involved with 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 Vatican reasoned that because vaccines saved lives, parents who chose not to give those derived from human fetal cells would be in "much more proximate cooperation with evil" than if they had accepted a morally questionable vaccine.

The National Catholic Bioethics Center, based in Boston, 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 wrongdoing in the past regularly rebound to the benefit of descendents 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 all the ingredients, details of the studies performed to determine whether the vaccine was safe and effective, dosage information, special considerations

for use of the vaccine in various groups, vaccine contraindications (who shouldn't get the vaccine), precautions (who might be at risk from the vaccine), and possible adverse reactions.

Unfortunately, one particular aspect of package inserts can be misleading. When studies are performed to determine whether a vaccine is safe and effective, they typically include two groups of children: those who received the vaccine and those who didn't. Studies are performed in this manner so that researchers can determine whether the vaccine caused a problem. If the percentage of children with a side effect is greater in the group that got the vaccine, then the vaccine probably caused the problem. Conversely, if the percentage of children with a side effect is the same in both groups, 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 children. This is probably because the insert is written by pharmaceutical company lawyers who want to make sure that they haven't failed to warn parents about possible side effects. For this reason, inserts are more legal communication documents than medical ones and can be misleading to parents trying to determine vaccine side effects.

> "In 1736 I lost one of my sons, a fine boy of four years old, by the small-pox, 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 baby to go out into the world without all of the protection available to him or her. Therefore, it is imperative that parents 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 truths 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 parents are choosing to immunize their babies. As a result, you probably don't know a family who lost a child to diphtheria or pneumococcus or one that lives with a child crippled by polio or congenital rubella. And, amazingly, if you go to a younger physician, he or she 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 watching children suffer these infections.

Vaccines have not only eliminated some of these diseases, they've eliminated the memory of these diseases.

Questions for the doctor:

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Notes:

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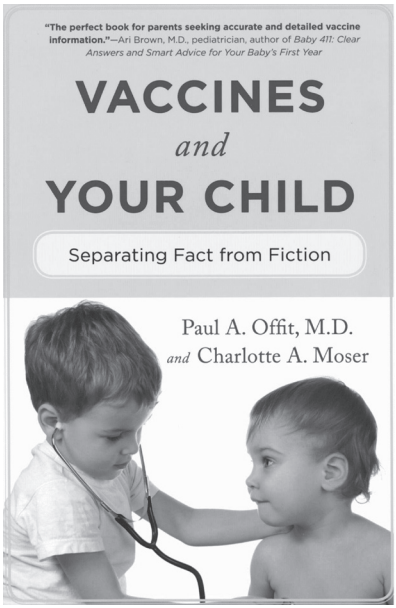
Did you find this booklet to be helpful? Do you want more information about vaccines and the diseases they prevent? If so, you might be interested in the full version book:



Divided into two main sections, "Questions parents have about vaccines" and "Individual vaccines," the book addresses not only common questions that parents are asking about vaccines, but also describes each vaccine and the disease(s) it prevents. Highlighted boxes throughout the book offer readers personal anecdotes, interesting facts, and things they can do to make sure everyone in their family is up to date. The back of the book also offers a place to record immunizations from birth through 18 years of age and is easily photocopied for keeping track of multiple children's immunizations.

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VACCINE EDUCATION CENTER

Vaccine Safety and Your Child was excerpted from the book for parents, *Vaccines and Your Child: Separating Fact from Fiction*, published by Columbia University Press in 2011. Authored by the Director and Assistant Director of the Vaccine Education Center at The Children's Hospital of Philadelphia (VEC), the book was written as a guide for parents.

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 at
vaccine.chop.edu
and
vaccine.chop.edu/parents

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Founded in 1855, The Children's Hospital of Philadelphia is the birthplace of pediatric medicine in America. Throughout its history, a passionate spirit of innovation has driven this renowned institution to pursue scientific discovery, establish the highest standards of patient care, train future leaders in pediatrics, and advocate for children's health. A haven of hope for children and families worldwide, CHOP is a nonprofit charitable organization that relies on the generous support of its donors to continue to set the global standard for pediatric care.

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