

Q. How can parents sort out conflicting information about vaccines?

A. Decisions about vaccine safety must be based on well-controlled scientific studies.

Parents are often confronted with “scientific” information found on television, on the Internet, in magazines and in books that conflicts with information provided by healthcare professionals. But few parents have the background in microbiology, immunology, epidemiology and statistics to separate good scientific studies from poor studies. Parents and physicians benefit from the expert guidance of specialists with experience and training in these disciplines.

Committees of these experts are composed of scientists, clinicians and other caregivers who are as passionately devoted to our children's health as they are to their own children's health. They serve the Centers for Disease Control and Prevention (www.cdc.gov/vaccines), the American Academy of Pediatrics (www.aap.org) and the Infectious Diseases Society of America (www.idsa.org), among other groups. These organizations provide excellent information to parents and healthcare professionals through their websites. Their task is to determine whether scientific studies are carefully performed, published in reputable journals and, most importantly, reproducible. Information that fails to meet these standards is viewed as unreliable.

When it comes to issues of vaccine safety, these groups have served us well. They were the first to figure out that intestinal blockage was a rare consequence of the first rotavirus vaccine, and the vaccine was quickly discontinued. And they recommended a change from the oral polio vaccine, which was a rare cause of paralysis, to the polio shot when it was clear that the risks of the oral polio vaccine outweighed its benefits.

These groups have also investigated possible relationships between vaccines and asthma, diabetes, multiple sclerosis, SIDS and autism. No studies have reliably established a causal link between vaccines and these diseases — if they did, the questioned vaccines would be withdrawn from use.

Q. Are vaccines still necessary?

A. Although several of the diseases that vaccines prevent have been dramatically reduced or eliminated, vaccines are still necessary:

- **to prevent common infections**

Some diseases are so common in this country that a choice not to get a vaccine is a choice to get infected. For example, choosing not to get the pertussis (whooping cough) vaccine is a choice to risk a serious and occasionally fatal infection.

- **to prevent infections that could easily re-emerge**

Some diseases in this country continue to occur at very low levels (for example, measles, mumps and *Haemophilus influenzae* type b, or Hib). If immunization rates in our schools or communities are low, outbreaks of these diseases are likely to occur. This is exactly what happened in the late 1980s and early 1990s when thousands of children were hospitalized with measles and more than 120 died. Children were much more likely to catch measles if they weren't vaccinated. Recent measles and mumps outbreaks in the United States also provide evidence of how quickly a disease can re-emerge.

- **to prevent infections that are common in other parts of the world**

Although some diseases have been completely eliminated (polio) or virtually eliminated (diphtheria) from this country, they still occur commonly in other parts of the world. Children are paralyzed by polio in Pakistan, Afghanistan and Nigeria and sickened by diphtheria in India and other countries in the southeastern region of Asia. Because there is a high rate of international travel, outbreaks of these diseases are only a plane ride away.

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Q. Do vaccines contain additives?

A. Many vaccines contain trace quantities of antibiotics or stabilizers.

Antibiotics are used during the manufacture of vaccines to prevent inadvertent contamination with bacteria or fungi. Trace quantities of antibiotics are present in some vaccines. However, the antibiotics contained in vaccines (neomycin, streptomycin or polymyxin B) are not those commonly given to children. Therefore, children with allergies to antibiotics such as penicillin, amoxicillin, sulfa or cephalosporins can still get vaccines.

Gelatin is used to stabilize live viral vaccines and is also contained in many food products. People with known allergies to gelatin contained in foods may have severe allergic reactions to the gelatin contained in vaccines. However, this reaction is extremely rare.

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Q. Are vaccines safe?

A. Because vaccines are given to people who are not sick, they are held to the highest standards of safety. As a result, they are among the safest things we put into our bodies.

How does one define the word safe? If safe is defined as “free from any negative effects,” then vaccines aren't 100 percent safe. All vaccines have possible side effects. Most side effects are mild, such as fever, or tenderness and swelling where the shot is given. But some side effects from vaccines can be severe. For example, the pertussis vaccine is a very rare cause of persistent inconsolable crying, high fever or seizures with fever. Although these reactions do not cause permanent harm to the child, they can be quite frightening.

If vaccines cause side effects, wouldn't it be “safer” to just avoid them? Unfortunately, choosing to avoid vaccines is not a risk-free choice — it is a choice to take a different and much more serious risk. Discontinuing the pertussis vaccine in countries like Japan and England led to a tenfold increase in hospitalizations and deaths from pertussis. Recently, a decline in the number of children receiving measles vaccine in the United Kingdom and the United States led to an increase in cases of measles.

When you consider the risk of vaccines and the risk of diseases, vaccines are the safer choice.

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Q. Do children get too many shots?

A. Newborns commonly manage many challenges to their immune systems at the same time.

Because some children could receive as many as 25 shots by the time they are 2 years old and as many as five shots in a single visit to the doctor, many parents wonder whether it is safe to give children so many vaccines.

Although the mother's womb is free from bacteria and viruses, newborns immediately face a host of different challenges to their immune systems. From the moment of birth, thousands of different bacteria start to live on the surface of the skin and intestines. By quickly making immune responses to these bacteria, babies keep them from invading the bloodstream and causing serious diseases.

In fact, babies are capable of responding to millions of different viruses and bacteria because they have billions of immunologic cells circulating in the bodies. Therefore, vaccines given in the first two years of life are a raindrop in the ocean of what an infant's immune system successfully encounters and manages every day.

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Q. Is the amount of aluminum in vaccines safe?

A. Yes. All of us have aluminum in our bodies and most of us are able to process it effectively. The two main groups of people who cannot process aluminum effectively are severely premature infants who receive large quantities of aluminum in intravenous fluids and people who have long-term kidney failure and receive large quantities of aluminum, primarily in antacids. In both cases, the kidneys are not working properly or at all and the people are exposed to large quantities of aluminum over a long period of time.

The amount of aluminum in vaccines given during the first six months of life is about 4 milligrams, or four-thousandths of a gram. A gram is about one-fifth of a teaspoon of water. In comparison, breast milk ingested during this period will contain about 10 milligrams of aluminum and infant formulas will contain about 40 milligrams. Soy-based formulas contain about 120 milligrams of aluminum.

When studies were performed to look at the amount of aluminum injected in vaccines, the levels of aluminum in blood did not detectably change. This indicates that the quantity of aluminum in vaccines is minimal as compared with the quantities already found in the blood.

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Q. Do vaccines cause autism?

A. Carefully performed studies clearly disprove the notion that vaccines cause autism.

Because the signs of autism may appear in the second year of life, at around the same time children receive certain vaccines, and because the cause of autism is unknown, some parents wondered whether vaccines might be at fault. These concerns focused on three hypotheses — autism was caused by the measles-mumps-rubella (MMR) vaccine, thimerosal, an ethylmercury-containing preservative used in vaccines, or receipt of too many vaccines too soon.

A large body of medical and scientific evidence now strongly refutes these notions. Multiple studies have found that vaccines do not cause autism. These studies included hundreds of thousands of children, occurred in multiple countries, were conducted by multiple investigators and were well controlled.

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Q. Does my child need to still get vaccines if I am breastfeeding?

A. Yes. The types of immunity conferred by breastfeeding and immunization are different. Specifically, the antibodies that develop after immunization are made by the baby's own immune system and, therefore, will remain in the form of immunologic memory; this is known as active immunity. In contrast, antibodies in breast milk were made by the maternal immune system, so they will provide short-term protection, but will not last more than a few weeks.

These antibodies are usually not as diverse either, so the baby may be protected against some infections but remain susceptible to others. Immunity generated from breast milk is called passive immunity. Passive immunity was practiced historically when patients exposed to diphtheria were given antitoxin produced in horses; antitoxins to snake venoms are also an example of passive immunity.

Q. How can a "one-size-fits-all" approach to vaccines be OK for all children?

A. The recommended immunization schedule is not the same for all children.

In fact, recommendations for individual vaccines often vary based upon individual differences in current and long-term health status, allergies and age. Each vaccine recommendation, often characterized by a single line on the immunization schedule, is supported by about 25 to 40 additional pages of specific instructions for healthcare providers who administer vaccines. In addition, an approximately 60-page document titled "General Recommendations on Immunization" serves as the basis for all vaccine administration. The recommendations are updated as needed by the CDC and a comprehensive update is published every few years.

Q. What is the harm of separating, spacing out or withholding some vaccines?

A. Although the vaccine schedule can look intimidating, it is based upon the best scientific information available and is better tested for safety than any alternative schedules.

Experts review studies designed to determine whether the changes are safe in the context of the existing schedule. These are called concomitant-use studies.

Separating, spacing out or withholding vaccines causes concern because infants will be susceptible to diseases for longer periods of time. When a child should receive a vaccine is determined by balancing when the recipient is at highest risk of contracting the disease and when the vaccine will generate the best immune response.

Finally, changing the vaccine schedule requires additional doctor's visits. Research measuring cortisol, a hormone associated with stress, has determined that children do not experience more stress when receiving two shots as compared with one shot. Therefore, an increased number of visits for individual shots will mean an increase in the number of stressful situations for the child without benefit. In addition, there is an increased potential for administration errors, more time and travel needed for appointments, potentially increased costs and the possibility that the child will never get some vaccines.

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Aluminum is present in several vaccines to improve the immune response. Some parents are concerned that aluminum in vaccines might be harmful to babies. However, healthy babies quickly eliminate aluminum from their bodies without harmful effects.

Q. What is aluminum?

A. Aluminum is the most common metal found in nature. It is present in the water we drink, the air we breathe and the food we eat.

Q. Is aluminum in vaccines?

A. Yes. Aluminum is present in vaccines that prevent hepatitis A, hepatitis B, diphtheria-tetanus-pertussis, *Haemophilus influenzae* type b, human papillomavirus and pneumococcus. Aluminum is not present in influenza vaccines, polio vaccines or live viral vaccines, such as those that prevent measles, mumps, rubella, chickenpox, shingles and rotavirus.

Q. Why is aluminum in vaccines?

A. Aluminum is present in certain vaccines to improve the immune response. Substances used to improve immune responses are called *adjuvants*. Adjuvants often allow for lesser quantities of the vaccine and fewer doses. Aluminum salts such as aluminum hydroxide, aluminum phosphate and aluminum potassium sulfate have been used to improve the immune response to vaccines for more than 70 years.

Q. How much aluminum is in vaccines?

A. During the first 6 months of life, infants could receive about 4 milligrams of aluminum from vaccines. That's not very much: a milligram is one-thousandth of a gram and a gram is the weight of one-fifth of a teaspoon of water. During the same period, babies will also receive about 10 milligrams of aluminum in breast milk, about 40 milligrams in infant formula, or about 120 milligrams in soy-based formula.

Q. What happens to aluminum after it enters the body?

A. Most of the aluminum that enters the body is eliminated quickly. Though all of the aluminum present in vaccines enters the bloodstream, less than 1 percent of aluminum present in food is absorbed through the intestines into the blood.

However, once aluminum is in the bloodstream, it is processed similarly regardless of the source. Approximately 90 percent is processed by binding to a protein called transferrin, and about 10 percent is bound by citrate. Once bound, the majority of aluminum will be eliminated through the kidneys, a small amount through bile, and a small amount is retained in tissues of the body. About half of the aluminum in the bloodstream is eliminated in less than 24 hours and more than three-quarters is eliminated within two weeks. The ability of the body to rapidly eliminate aluminum accounts for its excellent record of safety.

Q. What happens to the aluminum retained in the body?

A. The small quantity of aluminum retained in the body accumulates over time. Most of the aluminum that accumulates (50 to 60 percent) settles in the bones, some in the lungs (about 25 percent) and some in the brain (about 1 percent). The remaining quantities are distributed in serum, skin, gastrointestinal tract, lymph nodes and glands. In fact, low quantities of aluminum can be found in most organs.

By the time children become adults, they will have accumulated between 50 and 100 milligrams of aluminum. Almost all of that accumulated aluminum comes from food.



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Aluminum in Vaccines: What you should know

Q. Is the amount of aluminum in vaccines safe?

A. Yes. The best way to answer this question is to look at people who are harmed by aluminum. These people can be divided into two groups: severely premature infants who receive large quantities of aluminum in intravenous fluids, and people with longstanding kidney failure who receive large quantities of aluminum, primarily in antacids. (The average recommended dose of antacids contains about 1,000 times more aluminum than is found in a vaccine.) Both of these groups of patients can suffer brain dysfunction, bone abnormalities or anemia because of the high quantities of aluminum that have accumulated in their bodies.

For aluminum to be harmful, two criteria must be met: People must have kidneys that don't work well or don't work at all, and they must receive large quantities of aluminum for months or years. In these situations, a lot of aluminum enters the body and not enough leaves the body.

Q. Isn't it possible that aluminum in vaccines could be harmful to some healthy babies?

A. No. The quantity of aluminum in vaccines is tiny compared with the quantity required to cause harm. Here's another way to think about this: All babies are either breast-fed or bottlefed. Because both breast milk and infant formula contain aluminum, all babies have small quantities of aluminum in their bloodstreams all the time. The amount is very small: about 5 nanograms (billionths of a gram) per milliliter of blood (about one-fifth of a teaspoon). Indeed, the quantity of aluminum in vaccines is so small that even after an injection of vaccines, the amount of aluminum in a baby's blood does not detectably change. In contrast, the amount of aluminum in the bloodstreams of people who suffer health problems from aluminum

is at least 100 times greater than the amount found in the bloodstreams of healthy people.




This information is provided by the Vaccine Education Center at The Children's Hospital of Philadelphia. The Center is an educational resource for parents and healthcare professionals and is composed of scientists, physicians, mothers and fathers who are devoted to the study and prevention of infectious diseases. The Vaccine Education Center is funded by endowed chairs from The Children's Hospital of Philadelphia. The Center does not receive support from pharmaceutical companies.


Q. What is the harm in spacing out vaccines containing aluminum?

A. Delaying vaccines increases the time during which children are susceptible to catching vaccine-preventable diseases. Certain diseases, such as whooping cough and pneumococcus, still occur commonly in the United States. Given that aluminum is common in food and water, delaying vaccines will not significantly lessen a child's exposure to aluminum; it will only increase the child's chance of suffering a severe and potentially fatal infection.

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Vaccines and Autism: What you should know

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Some parents are concerned that vaccines can cause autism. Their concerns center on three areas: the combination measles-mumps-rubella (MMR) vaccine; thimerosal, a mercury-containing preservative previously contained in several vaccines; and the notion that babies receive too many vaccines too soon.

Q. What are the symptoms of autism?

A. Symptoms of autism, which typically appear during the first few years of life, include difficulties with behavior, social skills and communication. Specifically, children with autism may have difficulty interacting socially with parents, siblings and other people; have difficulty with transitions and need routine; engage in repetitive behaviors such as hand flapping or rocking; display a preoccupation with activities or toys; and suffer a heightened sensitivity to noise and sounds. Autism spectrum disorders vary in the type and severity of the symptoms they cause, so two children with autism may not be affected in quite the same way.

Q. What causes autism?

A. The specific cause or causes of autism in all children are not known. But one thing is clear: Autism spectrum disorders are highly genetic. Researchers figured this out by studying twins. They found that when one identical twin had autism, the chance that the second twin had autism was greater than 90 percent. But when one fraternal twin had autism, the chance that the second twin had autism was less than 10 percent. Because identical twins have identical genes and fraternal twins don't, these studies proved the genetic basis of autism. More recently, researchers have successfully identified some of the specific genes that cause autism.

Some parents wonder whether environmental factors — defined as anything other than genetic factors — can cause autism. It's possible. For example, researchers found that thalidomide, a sedative, can cause autism if used during early pregnancy. Also, if pregnant women are infected with the rubella virus (German measles) during early pregnancy, their babies are more likely to have autism.

Q. Does the MMR vaccine cause autism?

A. No. In 1998, a British researcher named Andrew Wakefield raised the notion that the MMR vaccine might cause autism. In the medical journal *The Lancet*, he reported the stories of eight children who developed autism and intestinal problems soon after receiving the MMR vaccine. To determine whether Wakefield's suspicion was correct, researchers performed a series of studies comparing hundreds of thousands of children who had received the MMR vaccine with hundreds of thousands who had never received the vaccine. They found that the risk of autism was the same in both groups. The MMR vaccine didn't cause autism.

Some parents wary of the safety of the MMR vaccine stopped getting their children immunized. As immunization rates dropped, particularly in the United Kingdom and, to some extent, the United States, outbreaks of measles and mumps led to hospitalizations and deaths that could have been prevented.

Q. Does thimerosal cause autism?

A. No. Multiple studies have shown that thimerosal in vaccines does not cause autism. Thimerosal is a mercury-containing preservative that was used in vaccines to prevent contamination. In 1999, professional groups called for thimerosal to be removed from vaccines as a precaution. Unfortunately, the precipitous removal of thimerosal from all but some multidose preparations of influenza vaccine scared some parents. Clinicians were also confused by the recommendation.

Since the removal of thimerosal, several studies have been performed to determine whether thimerosal causes autism. Hundreds of thousands of children who received thimerosal-containing vaccines were compared to hundreds of thousands of children who received the same vaccines free of thimerosal. The results were clear: The risk of autism was the same in both groups; thimerosal in vaccines did not cause autism.

For the latest information on all vaccines, visit our website at

vaccine.chop.edu

Vaccines and Autism: What you should know

Q. Is autism caused by children receiving too many vaccines too soon?

A. Several facts make it very unlikely that babies are overwhelmed by too many vaccines given too early in life.

First, before they are licensed, new vaccines are always tested alone or in combination with existing vaccines. These studies determine whether new vaccines alter the safety and efficacy of existing vaccines and, conversely, whether existing vaccines affect the new vaccine. These studies, called concomitant use studies, are performed every time a new vaccine is added to the existing vaccination schedule.

Second, although the number of vaccines has increased dramatically during the past century, the number of immunological components in vaccines has actually decreased. One hundred years ago, children received just one vaccine, for smallpox. The smallpox vaccine contained about 200 immunological components. Today, with advances in protein purification and recombinant DNA technology, the 14 vaccines given to young children contain only about 150 immunological components.

Third, the immunological challenge from vaccines is minuscule compared to what babies typically encounter every day. The womb is sterile, containing no bacteria, viruses, parasites or fungi. But when babies leave the womb and enter the world, they are immediately colonized by trillions of bacteria that live on the linings of their nose, throat, skin and intestines. Each bacterium contains between 2,000 and 6,000 immunological components. And babies often make an immune response to these bacteria to prevent them from entering the bloodstream and causing harm. The challenge that vaccines present is tiny in comparison to that from the environment.

Fourth, children have an enormous capacity to respond to immunological challenges. Susumu Tonegawa, a molecular biologist who won a Nobel Prize for his work, showed that people have the capacity to make between 1 billion and 100 billion different types of antibodies. Given the number of immunological components contained in modern vaccines, a conservative estimate would be that babies have the capacity to respond to about 100,000 different vaccines at once.

Although this sounds like a huge number, when you consider the number of challenges that babies face from bacteria in their environment, it's not.

Here's another way to understand the difference in scale between immunological challenges from vaccines and natural challenges from the environment. The quantity of bacteria that live on body surfaces is measured in grams (a gram is the weight of about one-fifth of a teaspoon of water). The quantity of immunological components contained in vaccines is measured in micrograms or nanograms (millionths or billionths of a gram).

Q. Are the studies showing that neither the MMR vaccine nor thimerosal causes autism sensitive enough to detect the problem in small numbers of children?

A. The studies showing that neither the MMR vaccine nor thimerosal causes autism, called epidemiological studies, are very sensitive. For example, epidemiological studies have shown that a rotavirus vaccine used between 1998 and 1999 in the United States caused intestinal blockage in one out of every 10,000 vaccine recipients; that measles vaccine caused a reduction in the number of cells needed to stop bleeding (platelets) in one out of every 25,000 recipients; and that an influenza (swine flu) vaccine used in the United States in 1976 caused a type of paralysis called Guillain-Barré syndrome in one out of every 100,000 recipients.

About one out of every 100 children in the United States is diagnosed with an autism spectrum disorder. Even if vaccines caused autism in only 1 percent of autistic children, the problem would have easily been detected by epidemiological studies.

Q. If I am concerned that vaccines cause autism, what is the harm in delaying or withholding vaccines for my baby?

A. A recent study by Michael Smith and Charles Woods found that children who were fully vaccinated in the first year of life were not more likely to develop autism than those whose parents had chosen to delay vaccines. Further, all of the evidence shows that vaccines don't cause autism, so delaying or withholding vaccines will not lessen the risk of autism; it will only increase the period of time during which children are at risk for vaccine-preventable diseases. Several of these diseases, like chickenpox, pertussis (whooping cough) and pneumococcus (which causes bloodstream infections, pneumonia and meningitis) are still fairly common. Delaying or withholding vaccines only increases the time during which children are at unnecessary risk for severe and occasionally fatal infections.

All of the evidence shows that vaccines don't cause autism, so delaying or withholding vaccines will not lessen the risk of autism; it will only increase the period of time during which children are at risk for vaccine-preventable diseases.

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Because autism research is continually evolving, a great way to stay up-to-date is to visit the Autism Science Foundation's research pages at www.autismsciencefoundation.org/research-year.

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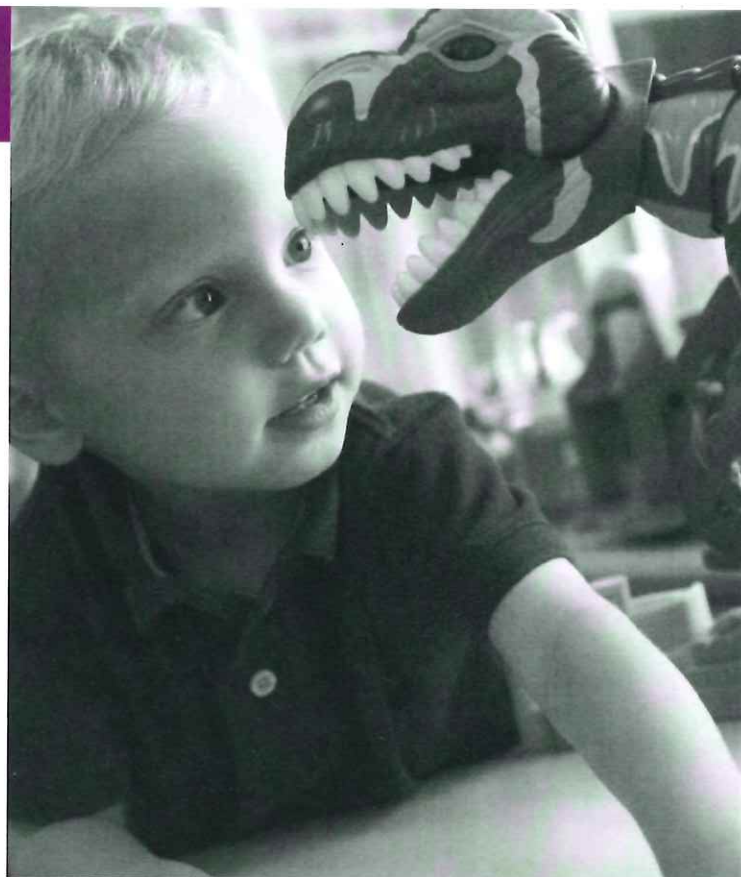
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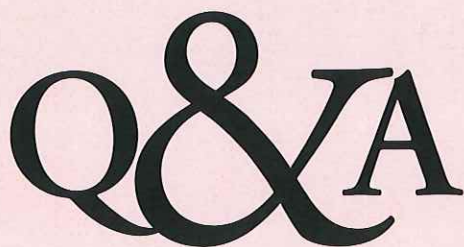
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VOLUME 1, FALL 2012

Recommended Immunization Schedule: What You Should Know

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Although only one version of the immunization schedule is endorsed by the Centers for Disease Control and Prevention (CDC), the American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP), some parents prefer to be selective about which vaccines their children receive and when. *Unfortunately, this approach can leave children susceptible to certain diseases at a time when they most need protection; worse, some children never catch up completely.*

Q. Who determines when vaccines are added to the immunization schedule?

A. Before a vaccine can be added to the immunization schedule, it must be licensed by the Food and Drug Administration (FDA). Scientists at the FDA closely monitor and review vaccine trials; sometimes they request additional studies before making a decision. The FDA determines whether the vaccine is safe and whether it works (efficacy). Studies prior to licensure often last five to 10 years and are extensive. For example, if all of the paperwork from the pre-licensure studies of one of the rotavirus vaccines was piled up, the stack would be higher than the Empire State Building.

Once a vaccine is licensed, experts from the CDC, AAP and AAFP independently review data from scientific studies to determine whether or not a vaccine should be added to the immunization schedule. Not only will they look at the safety and efficacy of the vaccine, they will also look at disease rates and susceptible populations to determine if the vaccine is needed in the community and, if so, who should get it. Their recommendations are compiled to create the immunization schedule.

If a vaccine is recommended at an age when other vaccines are already given, *concomitant use studies* will be required to make sure the vaccine works and is safe when given as part of the existing schedule. If these studies reveal any negative consequences of giving certain vaccines together, restrictions will be placed on their use. For example, concomitant use studies have shown that if two live viral vaccines (for example, measles, mumps and rubella [MMR] and chickenpox vaccines) are given on the same day or separated by at least one month, no problems occur; however, if they are given between one and 28 days of each other, the immune response to the one administered later will be diminished. This is reflected on the schedule, so that healthcare providers administer the vaccines correctly.

Q. How are the amounts of immunological components in a vaccine determined?

A. Vaccine doses are not chosen arbitrarily. During the four phases of vaccine development, different doses are tested to determine the lowest effective dose for the target group. For example, the rotavirus vaccine was tested at quantities as low as one-tenth the current dose and up to 10 times the current dose.

Vaccine developers must practice good medicine and good economics. Giving larger doses of active ingredients than required would increase the side effects and giving too little of the vaccine would lessen efficacy. It's a fine balance.

Q. How can the recommended schedule be appropriate for all children?

A. A common misconception is that the recommended immunization schedule is determined using a one-size-fits-all approach. These concerns are based on misconceptions about how vaccines work and misconceptions about the schedule itself:

- Vaccines and drugs aren't distributed in the body in the same manner. Medications must be distributed throughout the bloodstream to have the desired effect, so dosing is determined by body size. This is similar to the effects of a glass of alcohol on a large man compared with a small woman. In contrast, vaccines work by introducing cells of the immune system, known as B and T cells, to the parts of a virus or bacteria that cause disease. These cells are typically "educated" near the site the vaccine is given. Once they are equipped to recognize the agent that causes illness, they travel throughout the body. These educated patrol cells are known as *memory cells*; it typically takes about a week to 10 days after immunization for the memory response to develop.
- The immunization schedule is confusing. For this reason, it is often described more simply in terms of the age at which each vaccine is given. However, healthcare providers who administer vaccines know that many rules exist regarding when and if a vaccine can be given based on individual situations. Illnesses, allergies, age and health conditions all influence whether someone is able to get a vaccine. In fact, the published immunization schedule for children from birth through 18 years of age is four pages long and is supported by a 64-page document on general recommendations as well as vaccine-specific recommendations. Documents describing specific vaccines are typically 25 to 40 pages long.

Q. How do we know who should get a vaccine?

A. A vaccine is added to the immunization schedule only after it has been studied in people who will receive it. Before a vaccine can be licensed, it must undergo rigorous scientific study to make sure that it is safe and that it works *in the age group for which it will be used*.

One might reasonably ask, then, how we know which age group might need to receive the vaccine. The answer is that scientists and public health officials perform "epidemiologic studies," which determine who gets a disease (susceptibility), when they get it (seasonality), how many people get it (morbidity), and how many people die from it (mortality). All of this information provides scientists and public health officials with a good understanding of how the disease is affecting communities and which individuals would benefit the most from a vaccine.

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Recommended Immunization Schedule: What You Should Know

Q. Why are multiple doses of some vaccines necessary?

A. Most vaccines require more than one dose. This happens for a few reasons, including the type of vaccine, the level of disease in the community and the nature of immunity:

- Vaccines that are given as live, weakened versions of the virus (e.g., MMR and chickenpox) usually require fewer doses because they reproduce at low levels in the body. The advantages are that the resulting immune response will be more robust in terms of quantity and diversity of antibodies. In contrast, when the vaccine is made from polysaccharides, individual proteins or toxoids (e.g., *Haemophilus influenzae* type B, hepatitis B, tetanus and pertussis), the immune response is limited to the specific antigens and the levels of antibody tend to be lower, so additional doses are needed to boost the immune response.
- When a vaccine is first made available, levels of disease in the community are typically high, so a child who was immunized will come in contact with the organism (i.e., virus or bacteria), but does not get sick. Even though as parents and healthcare providers, we often do not know about these encounters, they serve to boost the child's immunity to that organism. However, after the vaccine has been available for several years, the levels of disease in the community are reduced making these anonymous encounters less frequent. As a result, immunity may wane making a second dose of vaccine necessary. This is what happened following introduction of the measles and chickenpox vaccines, so children are now recommended to get one dose around 12 to 15 months of age and a second dose before starting school around 4 to 6 years of age.
- As people get older, their immune systems may not be able to fend off bacterial and viral encounters as readily as they once did. For example, most of us have the virus that causes chickenpox living silently in cells of our nervous system. This virus can also cause shingles, but shingles only occurs if our immune system fails to keep the virus "in check," such as during times of high stress, compromised immunity or with increasing age. For this reason, people 60 years and older are recommended to get a shingles vaccine. The shingles vaccine uses the same virus as the chickenpox vaccine given to children; however, to be effective, the shingles vaccine contains about 14 times the amount of virus compared with the children's version.

Q. When is it OK to use a different vaccine schedule?

A. Children who have certain health conditions or acute illnesses may not be able to get vaccines according to the routine schedule. *Contraindications* are reasons not to get one or more vaccines; they include things like having an allergic reaction to a previous dose of vaccine or not getting a live virus vaccine, such as MMR or chickenpox, when receiving chemotherapy. *Precautions* are reasons to delay getting one or more vaccines either because of an increased chance of experiencing a severe side effect or a situation that may compromise the ability of the vaccine to work. Examples of precautions can include situations such as moderate or severe illness, recent blood transfusion, uncontrolled seizures or unstable neurological condition. If you are concerned about conditions that might delay or prevent getting vaccines, talk to your healthcare provider or contact your local health department.

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Q. Why are so many vaccines necessary?

A. While it may seem like a lot of vaccines when you are watching your baby get multiple shots during the course of several office visits, the reality is that vaccines only protect babies from a small fraction of the potential disease-causing agents in the environment. The good news is that vaccines have been developed for the most deadly diseases, increasing life expectancy and decreasing infant mortality rates in the countries that use them.

Q. Wouldn't it be better for children to get some of these diseases naturally?

A. For each virus or bacteria, a specific level of immunity is needed to avoid getting sick. Once this protective level is reached, any additional protection doesn't make much difference. Vaccines are designed to introduce enough viral or bacterial antigens to induce protective immunity but not enough to cause symptoms of disease. So, while getting the disease usually creates better immune responses, not much is gained in terms of protection as compared with vaccination and the price paid for natural infection can be great in terms of suffering and, sometimes, death.

Selected Resources and References

Immunization schedules are available on the CDC website at <http://www.cdc.gov/vaccines/schedules/index.html>.

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Some parents are concerned that thimerosal, a mercury-containing preservative contained in the influenza vaccine, causes autism. However, a series of biological and epidemiological studies have shown this concern to be unfounded. Here is a summary of the evidence showing that, while some things do cause autism, mercury in vaccines isn't one of them.

All mercury isn't the same: methylmercury vs. ethylmercury

Mercury is a naturally occurring element found in the earth's crust, air, soil and water. Since the earth's formation, volcanic eruptions, weathering of rocks and burning of coal have caused mercury to be released into the environment. Once released, certain types of bacteria in the environment can change mercury to methylmercury. Methylmercury makes its way through the food chain in fish, animals and humans. At high levels, it can be toxic to people.

Thimerosal — a preservative still used in some versions of the influenza vaccine — contains a different form of mercury called ethylmercury. Studies comparing ethylmercury and methylmercury suggest that they are processed differently in the human body. Ethylmercury is broken down and excreted much more rapidly than methylmercury. Therefore, ethylmercury (the type of mercury in the influenza vaccine) is much less likely than methylmercury (the type of mercury in the environment) to accumulate in the body and cause harm.



Evidence that mercury doesn't cause autism

- In 1971, Iraq imported grain that had been fumigated with methylmercury. Farmers ate bread made from this grain. The result was one of the worst single-source mercury poisonings in history. Methylmercury in the grain caused the hospitalization of 6,500 Iraqis and killed 450. Pregnant women also ate the bread and delivered babies with epilepsy and mental retardation. But they didn't deliver babies with an increased risk of autism.
- Several large studies compared the risk of autism in children who received vaccines containing thimerosal to those who received vaccines without thimerosal. The studies were consistent, clear and reproducible — the incidence of autism was the same in both groups. Denmark, a country that abandoned thimerosal as a preservative in 1991, actually saw an increase in autism beginning several years later.
- Studies of the head size, speech patterns, vision, coordination and sensation of children poisoned by mercury show that the symptoms of mercury poisoning are different from the symptoms of autism.
- Methylmercury is found in low levels in water, infant formula and breast milk. Although it is clear that large quantities of mercury can damage the nervous system, there is no evidence that the small quantities contained in water, infant formula and breast milk do. An infant who is exclusively breast-fed will ingest more than twice the quantity of mercury than was ever contained in vaccines and 15 times the quantity of mercury contained in the influenza vaccine.

Thimerosal: What you should know


What is known about the cause of autism?

- First, like cystic fibrosis or sickle cell disease, autism clearly has a genetic basis. Researchers found that when one identical twin had autism, the chance that the other twin had autism was about 90 percent; for fraternal twins, the chance was less than 10 percent.
- Second, although autism clearly has a genetic basis, environmental factors can also cause the disease. For example, children whose mothers took thalidomide during pregnancy had birth defects, including malformed ears and shortened limbs. But they also had a significantly greater incidence of autism than babies born to mothers who never took thalidomide. Thalidomide clearly caused autism, but only if mothers took it early in pregnancy. If mothers took thalidomide in the second or third trimester of pregnancy, their babies weren't at increased risk of autism.
- The thalidomide experience showed that there was a vulnerable time early in pregnancy when a drug could possibly cause autism. Echoes of the thalidomide story are found in babies infected with rubella virus. Babies born to mothers who suffered rubella early in their pregnancies develop birth defects involving the eyes, ears, brain and heart. They also are at greater risk of developing autism; but, as with thalidomide, only if the baby is exposed to rubella early during pregnancy. Babies don't develop autism if they are infected with the virus soon after birth. Taken together, these findings suggest that a virus or a drug can cause autism, and that there is a vulnerable time early during pregnancy when the baby is at risk. However, during the second or third trimester of pregnancy, or after the child is born, the window for environmental factors causing autism has apparently closed.
- Women in the United States also occasionally received mercury when they were pregnant. It happened when doctors found that the mother's blood type was not compatible with her baby's blood type. To prevent this blood mismatch from hurting the baby, mothers were given RhoGam, a product that contained thimerosal as a preservative. However, consistent with the observation in Iraq, babies exposed to thimerosal in RhoGam did not have a greater risk for autism than babies whose mothers never received RhoGam. Although thalidomide and rubella virus can cause autism in pregnancy, scientific evidence clearly indicates that mercury doesn't.

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Today, young children receive vaccines to protect them against 14 different diseases. Because some vaccines require more than one dose, children can receive as many as 27 inoculations by 2 years of age and up to five shots at one time. For this reason, some parents now ask their doctors to space out, separate or withhold vaccines. The concern that too many vaccines might overwhelm a baby's immune system is understandable, but the evidence that they don't is reassuring.

Q. What are the active components in vaccines?

A. Vaccines contain parts of viruses or bacteria that induce protective immune responses. These active ingredients are called immunological components.

Vaccines that protect against bacterial diseases are made from either inactivated bacterial proteins (e.g., diphtheria, tetanus and whooping cough [pertussis]) or bacterial sugars called polysaccharides (e.g., *Haemophilus influenzae* type b [Hib] and pneumococcus). Each of these bacterial proteins or polysaccharides is considered an immunological component, meaning that each evokes a distinct immune response.

Vaccines that protect against viral diseases (e.g., measles, mumps, rubella, polio, rotavirus, hepatitis A, hepatitis B, chickenpox and influenza) are made of viral proteins. Just like bacterial proteins, viral proteins induce an immune response.

Q. Do children encounter more immunological components from vaccines today than they did 30 years ago?

A. No. Although children receive more vaccines now than ever before, most people would probably be surprised to learn that the number of immunological components in vaccines has dramatically decreased.

Thirty years ago, children received vaccines that protected against eight diseases: measles, mumps, rubella, diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b and polio. The total number of bacterial and viral proteins contained in these vaccines was a little more than 3,000.

Today, children receive vaccines that protect against 14 diseases, but the total number of immunological components in these vaccines is only about 150. This dramatic reduction is the result of scientific advances that have allowed for purer, safer vaccines.

Q. Can too many vaccines overwhelm an infant's immune system?



A. No. Compared to the immunological challenges that infants handle every day, the challenge from the immunological components in vaccines is minuscule. Babies begin dealing with immunological challenges at birth. The mother's womb is a sterile environment, free from viruses, bacteria, parasites and fungi. But after babies pass through the birth canal and enter the world, they are immediately

colonized with trillions of bacteria, which means that they carry the bacteria on their bodies but aren't infected by them. These bacteria live on the skin, nose, throat and intestines. To make sure that colonizing bacteria don't invade the bloodstream and cause harm, babies constantly make antibodies against them.

Colonizing bacteria aren't the only issue. Because the food that we eat and the dust that we breathe contain bacteria, immunological challenges from the environment are unending. Viruses are also a problem. In the first few years of life, children are constantly exposed to a variety of different viruses that cause runny noses, cough, congestion, fever or diarrhea.

Given that infants are colonized with trillions of bacteria, that each bacterium contains between 2,000 and 6,000 immunological components, and that infants are infected with numerous viruses, the challenge from the 150 immunological components in vaccines is minuscule compared to what infants manage every day.

Too Many Vaccines? What you should know

Q. How many vaccines can children effectively handle at one time?

A. A lot more than they're getting now. The purpose of vaccines is to prompt a child's body to make antibodies, which work by preventing bacteria and viruses from reproducing themselves and causing disease. So, how many different antibodies can babies make? The best answer to this question came from a Nobel Prize-winning immunologist at the Massachusetts Institute of Technology named Susumu Tonegawa, who first figured out how people make antibodies.

Tonegawa discovered that antibodies are made by rearranging and recombining many different genes, and found that people can make about 10 billion different antibodies. Given the number of antibody-producing cells in a child's bloodstream, and the number of immunological components contained in vaccines, it is reasonable to conclude that babies could effectively make antibodies to about 100,000 vaccines at one time. Although this number sounds overwhelming, remember that every day children are defending themselves against a far greater number of immunological challenges in their environment.

Q. How do we know that multiple vaccines can be given safely?

A. The Food and Drug Administration (FDA) requires extensive safety testing before vaccines are licensed. Before a new vaccine can be licensed by the FDA, it must first be tested by something called "concomitant use studies." Concomitant use studies require new vaccines to be tested with existing vaccines.

These studies are performed to make sure the new vaccine doesn't affect the safety or effectiveness of existing vaccines given at the same time, and vice versa. Because concomitant use studies have been required for decades, many studies have been performed showing that children can be inoculated with multiple vaccines safely.

Q. What is the harm of separating, spacing out or withholding vaccines?

A. Delaying vaccines can be risky. The desire by some parents to separate, space out or withhold vaccines is understandable. This choice, however, is not necessarily without consequence.

First, delaying vaccines only increases the time during which children are susceptible to certain diseases, some of which are still fairly common. Chickenpox, whooping cough (pertussis), *Haemophilus influenzae* type b, influenza and pneumococcus still cause hospitalizations and deaths in previously healthy children every year. And, for example, before the chickenpox vaccine, every year about 70 children died from the disease.

Second, spacing out or separating vaccines will require children to visit the doctor more often for shots. 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 study 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 actually increase the trauma of getting shots.

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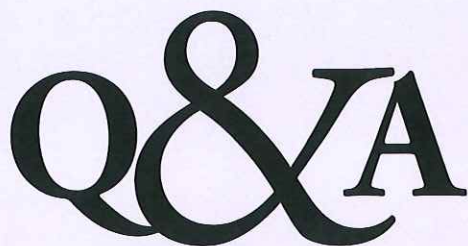
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VACCINE EDUCATION CENTER

Some parents are concerned about ingredients in vaccines, specifically aluminum, mercury, gelatin and antibiotics. However, parents can be reassured that ingredients in vaccines are minuscule and necessary.

Q. Why is aluminum in vaccines?

A. Aluminum is used in vaccines as an *adjuvant*. Adjuvants enhance the immune response by allowing for lesser quantities of active ingredients and, in some cases, fewer doses. Until recently, aluminum salts were the only class of adjuvants approved for use in the United States. In 2009, a second adjuvant, known as monophosphoryl lipid A, was also approved for use in the United States.

Aluminum

Aluminum salts have been used as adjuvants in vaccines in the United States since the 1930s. Some people wonder whether aluminum in vaccines is harmful — the facts are reassuring.

First, aluminum is present in our environment; the air we breathe, the water we drink and the food we eat all contain aluminum.

Second, the quantity of aluminum in vaccines is small. For example, in the first six months of life, babies receive about 4 milligrams* of aluminum if they get all of the recommended vaccines. However, during this same period they will ingest about 10 milligrams of aluminum if they are breastfed, 40 milligrams if they are fed regular infant formula, and up to 120 milligrams if they are fed soy-based infant formula.

Some people wonder about the difference between aluminum injected in vaccines versus aluminum ingested in food. Typically, infants have between 1 and 5 nanograms (billionths of a gram) of aluminum in each milliliter of blood. Researchers have shown that after vaccines are injected, the quantity of aluminum detectable in an infant's blood does not change and that about half of the aluminum from vaccines is eliminated from the body within one day. In fact, aluminum causes harm only when kidneys are not functioning properly or at all (so aluminum cannot be effectively eliminated) AND large quantities of aluminum, such as those in antacids, are administered.

Monophosphoryl lipid A

Monophosphoryl lipid A was isolated from the surface of bacteria and detoxified, so that it cannot cause harm. This adjuvant has been tested for safety in tens of thousands of people.

*A milligram is one-thousandth of a gram, and a gram is the weight of one-fifth of a teaspoon of water.

Q. Why is formaldehyde in vaccines?

A. Formaldehyde is a by-product of vaccine production. Formaldehyde is used during the manufacture of some vaccines to inactivate viruses (like polio and hepatitis A viruses) or bacterial toxins (like diphtheria and tetanus toxins). While most formaldehyde is purified away, small quantities remain.

Because formaldehyde is associated with the preservation of dead bodies, its presence in vaccines seems inappropriate. However, it is important to realize that formaldehyde is also a by-product of protein and DNA synthesis, so it is commonly found in the bloodstream. The quantity of formaldehyde found in blood is 10 times greater than that found in any vaccine.

Q. Why is gelatin in vaccines?

A. Gelatin is used in some vaccines as a *stabilizer*. Stabilizers are added to vaccines to protect the active ingredients from degrading during manufacture, transport and storage. Gelatin, which is made from the skin or hooves of pigs, is concerning because some people (about 1 of every 2 million) might have a severe allergic reaction to it.

Also, because religious groups, such as Jews, Muslims and Seventh Day Adventists, follow dietary rules that prohibit pig products, some parents are concerned about using vaccines that contain gelatin. However, all religious groups have approved the use of gelatin-containing vaccines for their followers for several reasons: First, vaccines are injected, not ingested (except the rotavirus vaccine, which does not contain gelatin). Second, gelatin in vaccines has been highly purified and hydrolyzed (broken down by water), so that it is much smaller than that found in nature; therefore, religious leaders believe it to be different enough that it does not break the religious dietary laws. Finally, leaders from these religious groups believe that the benefits of receiving vaccines outweigh adherence to religious dietary laws.

Q. What about the cumulative effect of vaccine ingredients when my child receives multiple vaccines in a single day?

A. Questions about the cumulative effect when multiple vaccines are given on the same day are reasonable. However, several sources of information provide reassurance:

- A study by Michael Smith and Charles Woods showed that 7- to 10-year-old children who had received vaccines according to the recommended schedule as infants did not have neuropsychological delays, such as speech and language delays, verbal memory, fine motor coordination, motor or phonetic, and intellectual functioning.
- If a new vaccine is added to the schedule at a time when other vaccines are given, studies must be completed to show that neither vaccine interferes with the safety or ability of the other to work. Known as concomitant use studies, these studies are numerous and extensive, offering additional information regarding interference of vaccine ingredients or effects caused by too much of an ingredient.
- Studies of the immune system estimate that we can respond to about 10,000 different immunologic components at any one time; the number of immunologic components contained in all of the vaccines recommended for young children today is less than 200 immunologic components.
- Finally, additives in vaccines, such as aluminum, have been studied regarding how they are processed in the body as well as what levels are toxic. For example, people who suffer toxic effects of aluminum must have had long-term exposure to aluminum (months or years) as well as non-functioning or improperly functioning kidneys.

With all of this information, we can conclude that multiple vaccines given in one day are not overwhelming an infant's immune system.

For the latest information on all vaccines, visit our website at

vaccine.chop.edu

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Vaccine Ingredients: What you should know

Q. Why is mercury in vaccines?

A. Mercury is contained in some multidose preparations of influenza vaccine as a preservative. Preservatives prevent contamination with bacteria. Early in the 20th century, most vaccines were packaged in vials that contained multiple doses. Doctors and nurses would draw up a single dose and place the vaccine back in the refrigerator. Unfortunately, sometimes bacteria would inadvertently enter the vial and cause abscesses at the site of injection or bloodstream infections that were occasionally fatal. Preservatives, originally added in the 1930s, solved this problem.

The most common preservative used was thimerosal, a mercury-containing compound. As more vaccines were given, children received greater quantities of thimerosal. By the late 1990s, the American Academy of Pediatrics and the Public Health Service requested that mercury be removed from vaccines to make "safe vaccines safer." No evidence existed to suggest that thimerosal was causing harm, but they wanted to be cautious. Unfortunately, their caution worried parents who wondered whether mercury in vaccines was causing subtle signs of mercury poisoning or autism. Addressing these concerns, scientists performed several studies, all of which showed that thimerosal at the level contained in vaccines hadn't caused harm.

Further, because mercury is a naturally occurring element found in the earth's crust, air, soil and water, we are all exposed to it. In fact, infants who are exclusively breastfed ingest more than twice the quantity of mercury than was contained in vaccines. Today, breastfed infants ingest 15 times more mercury in breast milk than is contained in the influenza vaccine.



Q. Are some vaccines made using fetal cells?

A. Fetal cells are used to make five vaccines: rubella, chickenpox, hepatitis A, shingles and rabies. Fetal cells used to grow the vaccine viruses were isolated from two elective abortions performed in Sweden and England in the early 1960s. Further abortions are not necessary as the cells isolated in the 1960s continue to be maintained in laboratory cultures.

Some parents wonder why scientists would choose to use fetal cells at all. There are several reasons for this. First, viruses, unlike bacteria, require cells to grow, and human cells are often better than animal cells at supporting the growth of human viruses. Second, fetal cells are different from other types of cells in that they are virtually immortal, meaning they can reproduce many, many times before dying. Other cells reproduce only a limited number of times before they die.

Some questions have been raised regarding the use of vaccines grown in fetal cells by people whose religious beliefs are against abortions. In 2005, when Pope Benedict XVI was head of the Catholic Church's Congregation of the Doctrine of Faith, this question was addressed; it was determined that because of the life-saving nature of vaccines, Catholic parents could reasonably give these vaccines to their children. Similarly, the National Catholic Bioethics Center determined that use of vaccines grown in fetal cells isolated from historic abortions was morally acceptable.

Q. Do ingredients in vaccines cause allergic reactions?

A. In addition to gelatin, other ingredients in vaccines such as egg proteins, antibiotics and yeast proteins might cause an allergic reaction. Latex used in vaccine packaging is also a concern related to allergies.

Egg proteins

Because the influenza and yellow fever vaccines are grown in eggs, the final products may contain egg proteins. Advances in protein chemistry have resulted in significantly lower quantities of egg proteins in the influenza vaccine; therefore, people with egg allergies can now get influenza vaccine. However, it is recommended that severely egg-allergic vaccine recipients remain in the office for 15 minutes after getting the influenza vaccine in case of any reaction.

Antibiotics

Antibiotics are used to prevent bacterial contamination during production of some vaccines. However, the types of antibiotics used in vaccines, such as neomycin, streptomycin, polymyxin B, chlortetracycline and amphotericin B, are not those to which people are usually allergic.

Yeast proteins

A couple of viral vaccines are made in yeast cells; these include hepatitis B vaccine and the human papillomavirus vaccine. Although the vaccine is purified away from the yeast cells, about 1 to 5 millionths of a gram remain in the final product. The good news is that people who are allergic to bread or bread products are not allergic to yeast, so the risk of allergy from yeast is theoretical.

Latex packaging

A small number of vaccines are packaged with materials that include latex. While it is rare that patients have a reaction to latex in vaccine packaging, people with latex allergies should consult with their allergy doctor before getting any vaccines packaged in this way.

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
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