PARENTS PACK

MONTHLY UPDATES ABOUT VACCINES ACROSS THE LIFESPAN

April 2024

FEATURE ARTICLE — ARE mRNA VACCINES A TYPE OF GENE THERAPY?

One of the prevailing misconceptions about COVID-19 mRNA vaccines is that they are a form of gene therapy. So, is this true? The short answer is no, but let's take a closer look at why.

Why do you run?

Are you a runner? While there are many people who enjoy running as a form of exercise or for stress relief, I have never been one of them. Indeed, the only time that you are going to see me running is if I am late or if there is an emergency. Said another way, people run for different reasons. They are trying to accomplish different things.

The same can be said about vaccines and gene therapy. Both are medical interventions, but their goals are different. The goal of vaccines is to prevent, or lessen the severity of, an illness caused by an infectious agent; this includes vaccines that use genetic material, like messenger RNA (mRNA) or DNA. On the other hand, the goal of gene therapy is to treat or prevent disease caused by a person's genes. Whereas vaccines are like the people running to stay healthy, gene therapy is like the people running to resolve a situation they are in.

TRIVIA CORNER

Which U.S. president is known for having had polio?

A. James Madison

B. Franklin Delano Roosevelt (FDR)

C. Abraham Lincoln

D. Theodore Roosevelt

Vaccination: Like running to stay healthy

Vaccines protect us against infectious diseases by "training" our immune system to recognize a particular pathogen so that if we are exposed to it in the future, our immune system is ready. COVID-19 messenger RNA (mRNA) vaccines do this by delivering an RNA-based blueprint for the spike protein on the SARS-CoV-2 virus. Our cells have machinery to read mRNA blueprints and make proteins. In fact, our cells read mRNA blueprints and make proteins that our bodies need to survive every day. Of course, our bodies do not need the SARS-CoV-2 spike protein, so what happens then? Two important aspects of this question are important to consider:

1. **What happens to the protein once it's made.** When the vaccine-delivered mRNA enters the cell, it is treated the same as any other piece of mRNA — the cell reads it and makes copies of the spike protein. The difference between this and other proteins, though, is that once the spike protein is made, our body recognizes that it is not one of the proteins that is regularly present. This causes cells from our immune system to attack it, break it into pieces, and use the pieces to activate the rest of the immune system. By going through this exercise, our body will get rid of the spike protein but remember it through immunologic memory cells created during the exercise.
2. **How much of the protein is made.** Importantly, mRNA also includes a mechanism to ensure that our cells are not overrun with too much of any protein. Think of the *I Love Lucy* scene where Lucy and Ethel can't keep up on the candy wrapping line. It is the same for our cells. If pieces of mRNA remained in the cell forever, the cell would continue to produce that protein and quickly be overwhelmed by it. For this reason, strands of mRNA have mechanisms to limit how many times the "blueprint" can be used before the mRNA is destroyed. One of the main ways this happens is by the presence of "poly(A) tails" at the end of the mRNA strand. The "A" stands for adenine, one of the building blocks of mRNA. A series of several adenine molecules line up at the end of the mRNA strand — like a tail. Each time the mRNA blueprint is used to make a protein, one of the adenine molecules is removed. Eventually, the tail gets too short for the mRNA to continue being used, and it is destroyed by the cell. The same process occurs with the mRNA delivered in the vaccine. As a result, the mRNA delivered by the vaccine is gone a few days after vaccination, and once the mRNA blueprint is gone, spike protein can no longer be made.

Gene therapy: Like running to resolve a situation

While identical twins share virtually the same set of DNA, the rest of us do not. We each have a unique genetic makeup. Non-identical twins and non-twin siblings share about 50% of their DNA even though they have the same parents. This happens because of which genes are introduced by each parent, but also how the genes replicate during the process of gestational development. This is why some genetic patterns are passed from one generation to the next, but others seem to happen randomly. Sometimes, the result of either inherited genetic patterns or random changes (called mutations) can predispose a person toward development of a disease. Many conditions, some more common than others, can be caused by genetics, including sickle cell disease, hemophilia, cystic fibrosis, and some cases of diabetes, cancer, autism, blindness, and mental health conditions. Importantly, not everyone with a particular gene will develop the related condition because often other factors, like one's environment or lifestyle choices, will also contribute to whether someone develops the disease. However, when a person's condition is the result of genetics, gene therapy may offer a way to treat them or prevent symptoms from developing or worsening.

Gene therapy can take different forms depending on the condition. For example, for some immune deficiency conditions, cells from the patient's blood, called stem cells, are removed and infected with a virus that contains a working gene. Once the gene is incorporated into the DNA of the cells, the cells are purified and put back into the person, where the new gene restores the missing functionality. In other cases, after the cells are removed, the faulty DNA is deleted or fixed using a gene editing tool, like the one isolated from bacteria and known as CRISPR-Cas9. Both approaches have resulted in licensed products for people with sickle cell disease.

In some cases, the cells cannot be removed for treatment, such as in people with hemophilia. In that condition, the liver does not make a protein needed for blood clotting. In clinical trials, gene therapy has been used to successfully introduce the gene for that protein into affected individuals' liver cells. While treated individuals do not always make as much of the protein as someone without hemophilia, they are able to make some, improving the ability of their blood to clot.

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A few considerations are important when it comes to gene therapy:

- The term "gene therapy" represents a host of approaches. They can involve DNA or mRNA. As previously described, cells can be treated inside the body or taken out of the body, altered and replaced. And efforts can be direct or indirect in how they aim to help an individual or group of individuals affected by a particular condition, meaning what a particular therapy does to alleviate a condition once delivered to the recipient can differ. For example, the therapy can directly target cancer cells or it may work by helping the person's own immune system better target cancer cells.
- The science of gene therapy, like all lines of scientific inquiry, is evolving. Despite working on potential uses for gene therapy for a few decades, we are continuing to learn. The array of opportunities is vast, but each potential application is unique. COVID-19 mRNA and DNA vaccines provided humanity with a significant step toward progress because they generated information that can be applied to gene therapy, but many potential therapies (and other vaccine applications) are only in early stages of development and not all of them will work. So, it's important to realize that every study will not result in a product that will be used in people and that is OK. These efforts help us learn and hopefully, along the way, some of them produce safe and effective vaccines or therapies.
- For these reasons, general statements about gene therapy should always be evaluated with caution because someone may be using examples that are not comparable — either because they don't understand the nuances of the science themselves or simply because they are trying to provoke fear and anxiety among others.

In sum

We don't often think about our genes, so hearing that vaccines or therapies deliver genetic material can be scary. However, realizing that genetic material, like mRNA, can be used in different ways for different reasons can help remove some of that fear. The notion that we can harness our knowledge to prevent people from dying with a vaccine or delay someone from going blind with gene therapy is quite incredible to consider. So, when you hear something scary about an mRNA vaccine or therapy, remember the runners — and then start sorting through what you heard to see if it is as scary as it sounds.

For links to resources in the Feature Article, please visit *bit.ly/April2024FA*.

DR. HANDY'S CORNER: MMR AND CHICKENPOX VACCINES: TOGETHER OR SEPARATE?

Dr. Lori Handy talks about the differences between the MMR and MMRV vaccines and considerations for parents deciding between these two vaccines for their children.

Watch the video: *bit.ly/MMR-chickenpox*.

NEWS & NOTES

A little discussed effect of COVID-19 infection in children

About two to six weeks after a COVID-19 infection, a very small number of children experience a condition called multisystem inflammatory syndrome in children, or MIS-C. (Adults can also experience this syndrome in whom it's called MIS-A.) Affected patients experience fever and one or more symptoms like stomach pain, vomiting or diarrhea; bloodshot eyes; skin rash; or dizziness or lightheadedness. Some symptoms requiring emergency medical attention can also appear, such as trouble breathing, chest pain or pressure, severe abdominal pain, inability to wake up or stay awake, or pale or grayish-blue skin color. MIS-C typically affects multiple organs, including eyes, brain, heart, lungs, kidneys, skin or organs associated with digestion.

MIS-C can occur following any COVID-19 infection (mild, moderate or severe). Early in the pandemic, it became clear that a recent COVID-19 infection increased one's risk for this condition, so medical professionals have been monitoring cases ever since. A recent report offered some important updates:

- While cases had decreased from their height in late 2020 and early 2021, reports recently increased — coincident with a spike in COVID-19 infections in the fall of 2023.
- During 2023, 117 children were diagnosed with MIS-C. About half of them were admitted to the intensive care unit. Three children died.
- About 8 of every 10 children affected with MIS-C were not vaccinated against COVID-19 even though they were old enough to have been vaccinated.
- Of the vaccinated children who experienced MIS-C, about 6 of 10 had received their vaccine more than one year prior.
- Almost 6 of every 10 children affected had no underlying medical conditions.
- The functioning of the child's heart was affected in about 3 of every 10 cases. Likewise, about 3 or 4 of every 10 children suffered shock, meaning their organs were not getting enough blood for a period of time.

These findings are important for families to consider, particularly given that many children remain unvaccinated against COVID-19.

17 states have had cases of measles in early 2024

Measles, probably the most contagious vaccine-preventable disease, continues to circulate throughout the U.S. As of the mid-March 2024, 17 states have reported 64 cases of measles — already surpassing the number reported in all of 2023 (58 cases). Adding to this concern is the steady drumbeat of cases each week. Every week since the beginning of December 2023, at least one case of measles has been reported to the Centers for Disease Control and Prevention (CDC).

70 years spent in an iron lung

Have you heard of Paul Alexander? Chances are you have not. Paul passed away on March 11, 2024, at the age of 78. Since the age of 6, Mr. Alexander survived with the use of an iron lung. His story is one of inspiration for all he accomplished during his life, including completing college and becoming a lawyer. But his life is also a reminder of a disease that rarely affects children in the U.S. today because of effective vaccinations.

For links to resources, please visit bit.ly/April2024NN.

TRIVIA ANSWER

The correct answer is B. Franklin Delano Roosevelt was diagnosed with polio at age 39, 12 years before becoming President of the United States. As President, Roosevelt accomplished many things during his term, including spearheading a campaign to raise money to make a polio vaccine and creating a program known as the New Deal.

Go to vaccine.chop.edu/trivia to play Just the Vax, the Vaccine Education Center's trivia game, where you can find this question and others like it.

Children's Hospital of Philadelphia
Vaccine Education Center

Contact us: contactPACK@chop.edu

Learn more: vaccine.chop.edu/parents

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