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mRNA Vaccines: The New Standard or a One-Hit Wonder?

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Author's Note

Prior to publication in September 2022, this paper was researched and written in April 2022. It is possible that cited facts and figures may now be considered out of date or have been updated with further research and new findings. As always, readers are encouraged to further their understanding of the presented material by conducting their own research.

Introduction

The COVID-19 pandemic brought mRNA vaccines into the spotlight when the COVID-19 vaccine was developed to combat the deadly SARS-CoV-2 virus; first being administered to health care providers in December 2020, then to the rest of the willing population soon after. The development of the COVID-19 vaccine was a monumental occurrence due to it being the first successful mRNA vaccine used in humans. mRNA vaccines are relatively new compared to other vaccine types and technologies, like the Polio vaccine. It is important to understand that when using new technologies and medical approaches to new and even existing illnesses, there are likely to be less found treatments due to the great length of time needed for research and development. Also, the mRNA is not a cure-all vaccine, special time must go into programing the vaccine to specially target what it needs to, which is not needed for other types. Unlike traditional vaccine types, the mRNA vaccine does not use a live or even a deactivated virus in its creation. It is important to understand the differences between the multiple vaccine types to comprehend just how different mRNA vaccines are. This paper will explore and analyze the

potential of mRNA vaccines, along with their downfalls in order to fully understand mRNA vaccines, its technology, and less sought-after uses. There is no surprise the COVID-19 mRNA vaccine gained so much traction; however, this poses the questions of: are mRNA vaccines better than traditional ones and will mRNA vaccines ever have another breakthrough and use as monumental as this one? These questions are ones that can only be answered with more time and research. Since the mRNA vaccination technology is still so new, it will take years before a new mRNA vaccine is produced and distributed to the public.

Due to the recently highly politicized topic discussed in this work, it is important to mention that this paper is not meant to take a political stance or make a political statement in anyway. All arguments will be solely based on facts and countless hours of research, as well as unbiased sources of clinical trials and other scientific research. This is meant to be an informative academic assignment which will contribute to the necessary understanding for others to make their own decisions.

History of Vaccines

Vaccination technology has been around longer than one may think, but this technology was not originally developed or intended for use in humans, the original intention was for animals. According to Don Nardo's book, *How Vaccines Changed the World,* in 1879, a French chemist, Louis Pasteur, began experimenting and working to find a cure for animal diseases, such as anthrax and chicken cholera. Through his research, Pasteur learned that when cultured germs age, they become weaker and less harmful, which was a considerably large breakthrough for the time period. With this information, he began injecting chickens with the weakened virus of chicken cholera to see if they would become sick. The chickens did not become sick; so, to

continue developing this theory, Pasteur injected the chickens again, this time with the full-strength chicken cholera virus. The chickens did not become sick, so Pasteur proclaimed that when a weakened virus was injected into the animal, it was not strong enough to make the chickens sick, but it was enough to create an immune response and tell the body what to target. More experiments were conducted within the scientific community to confirm Pasteur's findings, this time with sheep and the anthrax virus (2019, p. 6-9). Like most experiments in the scientific community, the testing for vaccines started on animals; however, animals are not the only thing affected by viruses and diseases, meaning humans soon became the sole focus. Developing human vaccinations followed the same development method as the animal vaccinations, however, people were more hesitant. Inoculation was a common practice at the time, but there was a severe need for a method that did not carry the risk of death as heavily. Despite vaccination carrying less of a risk, special care and consideration must be used when developing a vaccine for human use.

Making Vaccines

As mentioned, not all vaccines are made the same, the strategies used are all dependent on the function of the vaccine as well as how the "virus" will be fought inside the body. There are four approaches; the virus can be weakened, inactivated, partly used, or essentially copied at the genetic code. When the vaccine uses the weakened virus, the virus is changed so that it replicates and reproduces much slower than the normal rate when inside the body. For example, the vaccine for varicella uses this method. The advantage to this is that two doses should provide life-long immunity; however, those who have weakened immune systems should not be given this type of vaccine. In an inactivated virus vaccine, the virus is killed so it can no longer

replicate or reproduce once in the body. The polio vaccine uses this method. This type of vaccine can be given to those with a weakened immune system, however, to gain immunity, several doses are needed. Using part of the virus is much like using the weakened virus, but this type of vaccine can be given to people with weakened immune systems, like the shingles vaccine. With a vaccine that uses part of a bacteria, this can include either deactivating the toxin the bacteria produces or using part of the polysaccharide in the bacteria. This is the case with the tetanus and pneumococcal vaccines. When using the genetic code from a virus, the mRNA acts as the blueprint for spike proteins. This creates an immune response and commits the "foreign" protein to memory, which allows for a rapid response the next time the protein is identified ("Making vaccines…, n.d.). This is how the COVID-19 vaccine is made.

mRNA Vaccines Explained

Due to recent events, mRNA vaccines have been the primary focus of news coverage and even household conversations. Even though these vaccines have become a commonly discussed topic, very few understand exactly how an mRNA vaccine acts and works. Messenger RNA, or mRNA, as it is commonly referred to, is naturally found in our bodies. Unlike DNA, mRNA is a single-stranded molecule, which is the complement to a gene's DNA strand. Ribosomes read this mRNA sequence and uses the genetic code to translate the codon to create an amino acid. This process is called protein synthesis (Brody, n.d.). This process is very similar to what happens when an mRNA vaccine is introduced to the body. As stated, mRNA vaccines do not use a live virus in their creation. The mRNA used in the vaccine is actually created in a lab, which is instrumental in teaching our cells what protein to make without introducing the potentially deadly virus into the body. The protein made inside the body after vaccination is the spike

protein, which is a replica of a part of the SARS-CoV-2 virus. Once this protein is placed on the cell's surface, an immune response is triggered since the spike protein does not belong. This response creates antibodies that will be ready to attack when this protein is seen again (Centers for Disease…, 2022b). Even though this may be a relatively new process it is a safe one since it was approved by the U.S. Food and Drug Administration.

Pros and Cons

Like most vaccines, mRNA vaccines have positives and negatives attached to them. mRNA vaccines have what seems to be an equal amount of these pros and cons, which is not surprising due their newness. Positives of this technology include the ability to update the technology quickly if a new mutation of the virus the vaccine was created to fight was discovered. To alter the already existing vaccine, only changing and updating the mRNA sequence present in the vaccine would be necessary. The production and manufacturing of mRNA vaccines is also quicker and more reliable than their counterparts which use viruses in their creation. Moderna only needed 66 days for their SARS-CoV-2 vaccine to be developed and used in human clinical trials (Doxzen & Prichep, 2021). The pros have led to the successful implementation and use of the mRNA COVID-19 vaccine.

The negatives to mRNA vaccines may seem trivial to the average consumer, but they pose considerable threats to the state of the vaccine and the people who would be receiving those affected doses. These cons mostly surround packaging, distribution, and storage of the vaccine one it is manufactured. The COVID-19 vaccine, specifically, must be kept at a consistent temperature of -90°C to -15°C (-130°F to 5°F) after it is made. This temperature range depends on the vaccine brand as well as how long the vaccine is to be stored for. The low storage

temperature is the case for all mRNA vaccines to prevent degradation, loss of effectiveness, and expiration (Crommelin et al., 2021, p. 997–1001). This is a problem because prior to the implementation of this vaccination technology, most hospital and other vaccine distribution centers storage freezers did not reach the low temperatures required to store the mRNA vaccine, so many facilities had to install special freezers before they could receive their COVID-19 vaccines to distribute to the population (Doxzen & Prichep, 2021). This caused delays in vaccination of frontline workers as well as the general public.

mRNA Shortcomings

The COVID-19 pandemic set the precedent for the use of mRNA vaccines; however, there may be more areas this vaccine type can assist in. Chemically modified mRNA vaccines have the potential to treat and even correct multiple types of diseases, illnesses, and disorders. These new uses are not to be taken for granted, even though the COVID-19 vaccine was developed and approved for use in what seems like record time, there are a few areas of concern surrounding these vaccines that are being identified and corrected, if possible. For example, “naked” mRNA is difficult to work with because its susceptibility to degradation is extremely high when the large molecules are being transported through the cellular membranes. These combined create the difficulty of mRNA molecule delivery and inadequate stability of the molecules. Through several different experiments with varying trials, the standard method to counteract these occurrences was developed and is continually used with this vaccine type (Elkhalifa et al., 2022, p. 112385). Since these obstacles were able to be overcome, researchers were able to begin experimenting with other uses for mRNA vaccines. mRNA vaccine use for the treatment of HIV showed hopefulness, however, the execution fell short. Even with the

correction of delivery and stability, there are several other problems specific to what the vaccine is to be developed for. In the case of an HIV vaccine, “high HIV antigenic variations, the presence of a latent HIV reservoir, and difficulty obtaining a broad neutralizing antibody response” are all struggles being faced (Kahlid et al., 2021, p. 16197). Due to these shortcomings, the clinical trials and studies working on a vaccine for HIV were not able to produce a functional vaccine. There are several problems surrounding the function of mRNA vaccines which are making development and implementation a challenge for researchers, developers, and scientists. With the additional problems coming to light with every new trial and study, the uses for mRNA vaccines, aside from COVID-19, is becoming unlikely.

Confirmation

New mRNA vaccines to fight other diseases and illnesses are still in their development stages. There have been considerable improvements and breakthroughs in several clinical trials and other studies. This includes promising results in cancer and infectious diseases being treated and even cured with an mRNA vaccine. Before these vaccines can be made and experimented with, the problems previously mentioned with the mRNA vaccine were corrected. Several modifications were made to correct the degradation of the mRNA within the cellular process, the *in-vivo* half-life, the initial immunogenicity, stability, and delivery. These were done with down-regulations and other modification types to achieve the desired level of each needed to reach the highest effectiveness of the vaccine.

Since the use of traditional vaccines have failed in the fight against infectious diseases, scientists started looking for a different approach. These traditional vaccine methods failed because a more versatile and potent treatment was needed to attack the complex viruses. Thus,

the mRNA method was thought to aid in development. Two types of vaccines were tested in these trials: self-amplifying RNA and non-replicating mRNA, with both communicating positive results. In the case of influenza type A, specifically the H10N8 subtype, a breakthrough in its mRNA vaccine clinical testing was found (Pardi et al., 2018, p. 261-279). H10N8 is a particularly severe and fatal form of the flu causing severe respiratory issues. Similarly, to the SARS-CoV-2 virus, H10N8 has also crossed species barriers, once affecting birds and now humans. According to Bahl et al. results were promising in both animal and human trials. Results were measured by hemagglutination inhibition in order to understand effectiveness and adequate delivery. It was determined that in both the cases of animals and humans there was a considerable rate of immunogenicity, meaning an immune response was provoked inside the body's tissues and cells (2017, p. 1316-1327). Although more trials and testing will be needed, this study shows promising results in vaccination against H10N8, which can be applied to other infectious diseases.

Cancer is the abnormal growth of cells, which starts in one part of the body and then spreads to other healthy tissues. It has plagued our world since the beginning of time and there is no cure, only therapies which may stop the growth. Cancer is one of the leading causes of death, so a cure is needed. In the beginning stages, the various mRNA cancer vaccines had the same problems as most other mRNA vaccines in their development. The vaccine would target tumor-associated and tumor-specific antigens to attack and kill the malignant cancer cells. The appeal of mRNA vaccines as a cancer treatment is their ability to be taken on by dividing and non-dividing cells and mRNA does not enter the genome sequence, so there is no possibility of a DNA mutation (Miao et al., 2021). Clinical trials have begun for testing and treatments with

malignant metastatic melanoma, which is a particularly deadly form of skin cancer. Several of these trails are in their later stages and they have show promising results, however, it is important to note these mRNA cancer vaccines must be used in conjunction with other therapy types and therapy drug cocktails to ensure complete targeting of cancer cells. BioNTech saw considerable success with their FixVac vaccine when used in melanoma patients. It was advantageous in boosting immune response in at least one melanoma-associated antigen in a large majority of clinical trial patients (Bidram et al., 2021, p. 1060). Many of the vaccines in their clinical trial phases have shown positive results in stopping cell and tumor mutation and growth, but these therapies are going to require large amounts of time and testing before they will become available to the public. The testing and trials are meant to ensure upmost efficiency in the vaccine before the FDA can approve the treatment.

Counterargument

mRNA vaccines are showing huge successes across several areas of both infectious diseases, cancers, and other illnesses. This could lead to more mRNA vaccines being available to the public, in addition to the COVID-19 vaccine. With most treatments and vaccines, the long-term effects are not revealed until the therapy has been used on a vast population and a considerable amount of time has passed. mRNA vaccines are no different, it is a new technology and scientist are not completely sure what those effects will look like. Since the COVID-19 vaccine was the first mRNA vaccine approved by the U.S Food and Drug Administration and the first mRNA vaccine to be distributed to the public, its research is the only base for findings. Severe side effects are still very rare, with most showing up within two months. This was the case with the Johnson & Johnson COVID-19 vaccine, which was found to cause blood clots

within a small population of those individuals who received the Janssen Pharmaceutical Company's vaccine. Only 28 out of nearly 7.4 million people who received the vaccine experienced this life-threatening side effect, this equates to roughly a 0.0004% risk (University of Missouri, n.d.). The vaccine was considered safe for continued production and administration since the benefits outweighed the risk of the severe side effect.

Other severe side effects have been reported when receiving the COVID-19 vaccine, regardless of brand. These long-term side effects can target multiple areas of the body and are not specific to any particular organ or organ system. These rare, but still present side effects include anaphylaxis, Thrombosis with Thrombocytopenia Syndrome, myocarditis, pericarditis, Guillain-Barré Syndrome, and even death (Centers for Disease…, 2022a). Although the risk of severe side effects may be low, they are still possible and should be properly documented to allow consumers to be made aware. The previously mentioned side effects are just the ones that scientists and the Center of Disease Control and Prevention have knowledge of, there could still be others which are temporarily dormant.

Other concerns with the COVID-19 vaccine have begun to be raised by scientists within the pharmaceutical community. The SARS-CoV-2 vaccine uses a polyethylene glycol (PEG) adjuvant to reach the desired level of distinctive immunological profiles within the vaccine. These PEG molecules are known to cause anaphylaxis and cardiovascular collapse in animals, however, when blood samples of humans were examined, 42% had a presence of PEG antibodies. Of those who had the antibody, 72% had not been previously exposed to PEG. Having this antibody and receiving a vaccine which uses PEG could pose serious health risks to the individual (Seneff & Nigh, 2021, p. 38-79). This is just one of the effects on the cellular level

of not only the COVID-19 vaccine but possibly all future mRNA vaccines. Several other potential consequences of mRNA vaccines are present and are just as dangerous to the human body.

Conclusion

Without the use of mRNA vaccines, COVID-19 would still be at full strength and have would still have considerably overwhelming infection and death rates in the United States and the rest of the world. Knowing a vaccine works is only half the battle when a new technology is being considered and actively used. It is important to know how a vaccine works in order to understand why the vaccine is successful. A good practice is to be somewhat skeptical of new scientific findings and developments, especially when those new developments have the ability to significantly impact our lives if they are found to not be “safe” after they were introduced into people's bodies. Every vaccine is different, however, the newness of mRNA vaccines and their technological complexity, makes them unlike any other vaccine ever used. When discussing mRNA vaccines, many do not know the complete scientific standings and innerworkings of the technology, leading to misconceptions, incorrect information, and fallacies to be spread. Ignorance should not be present in debates surrounding vaccination, those debates should only be based on trusted, published scientific findings. Vaccines will not disappear; they will only become more prevalent in our society as the world and its illnesses evolve and become more complex.

mRNA vaccines have not had enough time to reach their full potential. They are still a new vaccination technology which was thrown into the general public's eye with little priming due to the rapid development and need for the COVID-19 vaccine. This caused several people to be less curious and more unwavering in their opinion of mRNA vaccines. There are several promising studies and clinical trials in the works that will undoubtedly produce an effective mRNA vaccine targeting their specific illness or disease. It is just a matter of time before mRNA vaccines become just as common as traditional vaccines. With every new technology comes setbacks and breakthroughs, but these are all discovered with time, which is exactly what mRNA vaccines need.

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