

## Podcast: mRNA Vaccines

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My name is Ute Papkalla, I am a member of the health team of the German Institut for Medical Mission, also called Difäm. With me is my colleague, Carina Dinkel. Today we will talk about a specific kind of vaccination for Covid-19: the mRNA vaccination.

There are many different vaccines and lots of names and companies. Which ones are we talking about when we talk about mRNA-vaccines?

mRNA vaccines that are currently approved for vaccination are the ones from Pfizer-Biontech and Moderna. The vaccination developed and produced by GlaxoSmithKline, CureVac, will most likely get the approval soon. Other products from Sanofi and Providence Therapeutics are used in clinical trials but are still under development.

Okay, there are quite a number of well-known pharmacological companies producing mRNA vaccines. Nevertheless, I have never heard of mRNA vaccines before Covid-19. What is so special about them?

Yes, you are right. The mRNA technology for vaccines is fairly new, but also very clever. To trigger an immune response, many vaccines put a weakened or inactivated germ into our bodies- not so mRNA vaccines. Instead, they teach our cells how to make a protein just like a virus protein that triggers an immune response inside our bodies. Through that immune response which includes the production of antibodies and activation of different immune cells, the body is protected once the real virus enters our bodies.

You are right, this sounds clever. However, can you explain just a little more about what this mRNA actually is and what role it plays in the whole process? After all, the vaccination is named after mRNA so it must be something important.

I'll explain it to you, but first let's talk about the spike protein: coronaviruses, like the one that causes Covid-19, have their name from the crown-like spikes on their surface, called spike proteins. The spike proteins of the coronavirus are very important parts of the virus. The virus uses the spike protein like a key in a lock, to enter human cells. Only inside the cells, it can multiply and cause disease.

On the other hand, the spike protein is also the place where human antibodies bind and fight the coronavirus when someone gets Covid-19 and the body starts its immune response.

Okay, I get it, the spike protein is important: for the virus as well as for the immune response. The spike protein is used as an antigen, so that the body can built antibodies against it. But how is it possible to bring the body in contact with the antigen without infecting it with the virus or without having to produce large amounts of spike protein artificially to use it in vaccinations?

This is where the mRNA plays its part. As a method, the mRNA-vaccines are not inoculating the spike protein itself but just the genetic information of the spike protein. This information is stored on a

specific kind of ribonucleic acid. We call it messenger ribonucleic acid – in short mRNA. This mRNA is injected and enters body cells. There the mRNA works like an instruction on how to build the spike protein. With this information, the body cells know which piece to place one after the other and how to put them together, so that in the end a spike protein is built, even if they have never built a spike protein before.

This is clever: let me just explain it in my own words to see if I got it right: I want my friend to build a handwashing station like a tippy tap (this is my spike protein). My friend has never built one before. So I send him/her a very detailed message about which parts are needed and a step-by-step-instruction what to place where, in which order and so on (this is the mRNA). He/she uses the instruction and builds from the resources he/she has the tippy tap. In the end, he/she has a tippy tap, even if he/she has never built one before and not even seen how to build one before – just by the instruction I sent him/her via message.

Yes; and in the end your tippy tap – or spike protein can be used to fight the virus. The body then reacts to the built spike protein by building antibodies and the T-cells are sensitized and learn to react to the spike protein accordingly. In the end, the immune response is capable to fight not only the self-made spike protein but also a spike protein from a real coronavirus.

In addition, the body uses its own resources, no foreign protein, no external substances. That also means that there is a very low risk of allergies and side effects, and there is no risk of infection, as there is no virus involved in the whole process of building up the immune response.

This sounds really good. However, is it effective as well? I mean, only the spike protein is used to trigger the immune response, not the whole virus...

This is true. Nevertheless, the method is highly effective. Efficacy varies a bit according to the specific vaccine but is generally in the range of 95% after two doses. The efficacy to prevent severe cases of Covid-19 is even higher. It is 100%. The mRNA-vaccination has to be given twice with an interval of about one month for the vaccinations of Pfizer-Biontech, Moderna and GlaxoSmithKline-CureVac. Full immunization is expected about two weeks after the second vaccination. However, those intervals might be subject to change, as more and longer term studies are carried out.

So that is very good news, but there must be side effects, right?

Yes, no effect without side effect. However, side effects are few and harmless. There are two different types of side effects: first the ones at the site of injection, which are: pain, redness, swelling. In rare cases, the injection site will even look like an erysipelas, but there is no need for antibiotics. The redness, swelling and pain will go away on their own. You can advise the patient to apply a wet towel to the site of vaccination and to do mild exercise with the arm.

On the other hand, there are the general symptoms that might occur after vaccination. In about 60-80% of cases tiredness, headache, muscle pain, chills, fever or nausea might occur. Those side effects are more common after the second vaccination. So almost everybody feels some of those general side effects. However, they are a sign that the immune system is working well. Those side effects will not last long and go away mostly within the first three days after vaccination. To mitigate these side effects drinking plenty of fluids is advisable.

It is strictly not advised to take any prophylactic painkillers before vaccination in order to avoid the side effects!

That also sounds very good; but isn't there a downside to this type of vaccination?

If you want to call it that, yes. The building plan of the spike protein, meaning the mRNA is a substance that dissolves very quickly. The good thing is that in this way we can be sure that after having built the spike protein, it does not mess with anything in the body cells. It is absolutely not true, that the mRNA vaccines do something to our DNA or cause changes in the genetic information. The mRNA stays outside the nucleus of the cell and is broken down already in the process of building the spike protein. Therefore, once the spike protein is built, the mRNA is gone. As it dissolves so quickly, sometimes even before the spike protein can be built, it must be stored at a very low temperature to keep it stable and to avoid that it just dissolves and disappears, before it is injected. And with low temperature I mean very low temperature. We are talking of temperatures up to  $-70^{\circ}\text{C}$  or almost  $-100^{\circ}\text{F}$ . So advanced infrastructure is needed for transport and storage. This might limit the use of these vaccines to urban areas, but work is underway, to stabilize the mRNA even in milder temperatures just around the freezing point.

So let me sum it up: mRNA vaccines bring the information on how to build a spike protein of the coronavirus into body cells. The body uses this information and builds the protein against which then antibodies are built and a T-cell-immune-response is developed. With this immune response, the body is able to fight a real coronavirus once it enters the human body. The vaccine has to be given twice to establish a full response, but then the immune response is strong and effective. We are talking about efficacy of more than 95%. Adverse effects are common but mild and there is no danger of the mRNA messing with genetic information.

Yes, that is about all. mRNA vaccines are safe enough that trials with children are underway. In addition, the vaccines work against different variants of the coronavirus. In addition, if more and more mutations occur in a coronavirus the vaccine can be adapted accordingly by just adapting the „building instruction“, which is the mRNA. Production time is relatively short, this is also an advantage in times of still existing global shortage of COVID-vaccination.

Great; so, if I get the chance of getting a vaccination with an mRNA vaccine, I will take it!

Good decision! Nevertheless, if you get the chance of getting another type of vaccination, it's also very good to take it. I'll explain the advantages of the other types of vaccines to you in some other podcasts. Until then:

Be blessed and stay safe!