Vaccines and your immune system

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-Al Vinson

As with many "medical laymen," I became interested in what would be produced by this "Operation Warp Speed." Therefore, I started a little research project. Take this for what it is ... or however you choose. But choose wisely.

Vaccines have a significant history. They started initially with a "smallpox" vaccine. People noticed youngsters who worked with dairy cattle would develop a form of pox. This pox wasn't nearly as virulent as the smallpox virus which people normally contracted. As a result, when one of those farm kids would get sick and develop pustules (from cowpox), they would take that pus and inject other people in the town who would also then have a mild case of pox. The inoculation with the pus was associated with drastic reductions of smallpox infections in the "vaccinated" population. This is a crude example of a **live attenuated virus**, where a less virulent virus or less virulent strain of the virus is used as a carrier for markers associated with the target disease in order to "train" the body to fight-off the target disease quickly and without developing symptoms or much less severe symptoms. Since then we've developed an entire suite of vaccine *types* that all serve different purposes. These include **Modified Live Virus** (or live attenuated), and some sort of subunit vaccines which would include *killed virus*, *protein segment* vaccines, and *DNA segment vaccines*. Recently, we started experimenting with DNA vaccines (not to be confused with a DNA subunit vaccine) and have not yet created more than a handful of vaccines on that principle. With the COVID-19 vaccine, Pfizer has taken this cutting-edge technology even further developing what is called a **mRNA** vaccine. mRNA has not been used in any previously made vaccine; for neither people nor animals. In fact, this type of vaccine has not even undergone animal trials of any sort. This is the first of its kind and has been expedited into distribution for injection into people.

Modified Live Virus vaccines are basically what they sound like. It's a live virus which has been attenuated or substituted somehow in place of the target disease. An example would be taking DNA fragments from the rabies virus (identifiable by the body as unique to rabies) and implanting them into something like an *adenovirus* (aka common cold) so that the individual receiving the vaccine may have symptoms of a cold but will also develop **Plasma Cells** (which are matured and activated, antibody secreting B-Cells) and **CD8 T-Cells** (the cells which control infections already inside the cells). These vaccines work by having the virus invade host cells and replicate much like a real infection would do. This produces a robust immune response which does not require a booster within 6 weeks later. In fact, MLV vaccines are often good for a minimum of a year and sometimes more (10-15 years). However, these vaccines do have their drawbacks. While in the body, there is a chance some of these vaccines undergo a process called **seroconversion**; where the disease becomes the target disease and infects the host. It's rare, and the vaccinated individual often doesn't even notice. In pregnant individuals this process can result in infection of the fetus and development of immune tolerance in the fetus. The offspring would then be chronically infected and oft times immunocompromised for the rest of their lives. For this reason, *we tend to avoid vaccinating pregnant individuals with MLV vaccines*.

For functional purposes *subunit* and *killed vaccines* can all be grouped collectively into a single category as the goal and mode of action for most of them is the same. We take a component of the target disease (cell wall in bacteria, proteins from a virus, DNA fragments from target disease) that is unique to it, and administer it to the body in order to develop antibodies against that component. When challenged with the real virus, antibodies

will already be present and can help the innate immune system stop a pathogen before it can start to replicate in the body. There are drawbacks to consider for these vaccines as well. First, a killed virus/component does not in and of itself produce an appreciable adaptive immune response. Left alone, the innate system would remove the majority of the fragments before B-Cells perform their function. For this reason, a chemical called an **adjuvant** is added to the injection. The purpose of the adjuvant is to generate inflammation at the injection site which stimulate **Dendritic Cells** to absorb this antigen and present to a B-Cell so that the B-Cell can activate, proliferate, and mature into antibody secreting plasma cells. This component of the vaccine has historically been the most concerning, citing it as the source of autism, genetic manipulation by intentionally damaging DNA, etc. In addition, this is the component of the vaccine to which most people are likely to have a reaction if they do have a reaction (this or the source of volume of the injection, such as some egg protein-based solutions). However, without this component killed/subunit vaccines would be ineffective and might as well be placebo injections. The second drawback is the nature of the immune response itself. It has two components of weakness.

First, the vaccine cannot generate a satisfactory response on the first injection therefore requires one and sometimes even 2 booster shots spaced about 4 weeks apart. Second, the cells involved in the response. B-Cells are a part of what is called humoral, or systemic, immunity. They can release antibodies that can actively bind to antigens present OUTSIDE the cells of the host. This is effective for keeping early stage viral and extracellular bacterial infections in check. However, *when infections happen inside the cell* (such as all viral infections, and intracellular bacterial infections) where the pathogen replicates inside the cell until it bursts, this response is weak. With only this response and innate responses, a viral infection would eventually overrun the immune system which is what occurs with HIV, or the response would take a significantly longer time to clear the infection.

The second part of the adaptive response is called a **Cell Mediated** response. This is where our aforementioned CD8 T-Cell's become players. These cells bind to a component called an MHC. MHC loads an antigen. The antigen/MHC complex can then be bound to and recognized by a T-Cell with an affinity for that same antigen. All cells in the body express MHC-1's, which pair with CD8 T-Cells. CD4 T-Cells are called helper T-Cells and bind with other immune cells in the body to amplify their function; a "force multiplier" if you will. These are associated with MHC-2's, which only a select few immune cells express (such as the aforementioned Dendritic Cells). The CD8 T-Cell will then kill the cell that to which it has bound when it binds with a cell expressing its antigen on an MHC-1 molecule. The reason for this is because in order to bind, antigen must be present. If antigen is present, it means the cell has been invaded by the source of that antigen and the pathogen is likely replicating inside of it. This prevents millions of viral particles from escaping the cell and slows the rate of replication considerably by saving nearby healthy cells from infection.

This CD8, Cell-Mediated response is lacking during vaccination with a subunit/killed vaccine. Without antigens replicating inside the cell, there can be no stimulation of a CD8 response. As a result, if someone gets sick there will be a delay between onset of symptoms and development of a T-Cell response. Usually, the individual will clear the infection naturally without CD8 T-Cell help. This is the source of "reduced symptoms" from vaccination in many cases. The vaccine produces an antibody response that keeps the infection in check, but still takes a long time to clear the infection. On the next exposure, both Humoral and Cell-Mediated responses will be present and a much stronger immune response can be fielded against viral and intracellular bacterial infections. This drawback, of generating humoral but not cell-mediated immunity, is only relevant for viral and intracellular bacterial infections. For vaccines against parasites, toxins, extracellular bacteria, etc. this type of vaccine does not have that drawback because cell mediated immunity doesn't occur with those types of infections.

DNA vaccines are a relatively new technology, being used and researched only within the last 5-8 years or so. The concept is similar to a Modified Live Virus, but with several important distinctions. First, a bacterium is the carrier of the DNA sequence instead of a virus. This is not a drastic difference. However, the amount of genetic manipulation used to obtain a **plasmid** (ring of DNA) from the target disease and implant it into the bacteria is more extensive than what is done for an MLV. This ability is owed primarily to our advancements in genetic engineering as well as the ability to map gene segments. With increased mapping efficiency, we are able to identify strings of DNA unique to the target disease easier and design a set of DNAses (enzymes that degrade DNA) that can cut out the desired segment. From there, we inoculate a bacterium that is accustomed to accepting DNA plasmids so that the plasmid will be replicated as the bacterium replicates. At that point, the bacteria are injected where it infects host cells, replicates, and causes disease. The body recognizes the DNA plasmid as foreign (like many other components) and develops Plasma Cells and CD8 T-Cells with receptors unique to that antigen. So, while the development technique is more advanced, it is in practice very similar to an MLV.

A common and important element to all of these vaccines (as opposed to an mRNA vaccine, which we'll address a moment), is that more or less all of the foreign material that gets into the body is *from the syringe*. Once all of the injected material is broken down, it's gone (an exception being the limited replication of MLV and DNA vaccines. However, those are live organisms that the body WILL kill in short order). This means that any damage a vaccine can do is limited because the foreign material is only in the body for a limited time. *The antigen will go away*, the *adjuvant will be broken down* (if it has one), and the carrier solution will be degraded and either utilized as base components (amino acids from proteins used to build your proteins) or excreted.

The duration of antibody production will depend on the lifespan of the differentiated plasma cells. This can vary from less than a year to well over 10 years. Several factors influence this, including the strength of the initial response, the individual's health (if energy is constantly going somewhere else, such as fighting other illnesses or repairing injuries, then those cells will not persist for as long), and specifics to the individual disease response itself.

If antibody production has stopped from a previous illness, it is likely that a new primary adaptive response will have to be made. Antibody production typically begins about one week to 10 days into a sickness and reaches its peak somewhere around 3-4 weeks later. If production doesn't stop (meaning memory B-Cells are still present), then an antibody response will be immediate and levels will begin to rise within a day of exposure. This is called a secondary adaptive response.

mRNA Vaccines. I've detailed what we have been using in vaccine types and how they work. I've outlined their strengths and weaknesses. Hopefully I've given enough explanation to show why they are relatively safe to use in practice if used wisely (e.g. only given when needed, given in the appropriate manner/route, given to appropriate individuals; such as abstaining an MLV injection to a pregnant individual, etc.) mRNA vaccines will work on an entirely different set of principles than previous vaccines. They have the potential in a slim set of controlled circumstances to provide a form of immunity that would be permanent and never require a booster. The immune system would constantly be at the ready and a robust response always on standby. These vaccines, however, have many potential pitfalls. I'll detail those after I explain how they are supposed to work.

mRNA vaccines work, as you may have guessed, by using mRNA. The "m" stands for "messenger", and mRNA is what the body uses to "program" ribosomes to produce a desired protein. The normal process in the body is for special enzymes in the nucleus to first unwind the **double helix DNA,** then another set "reads" the DNA by copying from half of it. This half copy is what ultimately becomes mRNA. After mRNA is released from the nucleus, it is no longer regulated. Any ribosome which encounters it will read it and produce a protein. This

process goes on and on until the mRNA degrades and goes away (which can be a really very long time). As a result, the presence of mRNA is often a tightly regulated system inside the cell. mRNA is injected and then absorbed, via the carrier into which the mRNA is placed, into the cell. Inside the cell the mRNA's presence is unregulated and ribosomes will begin to read it and produce proteins. The theory, is that this mRNA is programed to produce proteins when read that are associated with the target disease. In this way, we're really doing a double programing of the body. *We're programing the cells to produce the antigen* (normally supplied in the vaccine syringe, with a limited supply), and then allowing the immune system to identify these foreign proteins and destroy them.

There are a couple potential issues with this. First, as they're being produced by your cells there is a real chance of developing *an autoimmune disorder* if the body develops CD8 T-Cells against the cells producing this foreign protein. This could mean systemic muscular atrophy, bone atrophy, etc. Also, any tissue *in or near the injection site could be identified as foreign*, and ALL the cells of that type targeted inside the body. Imagine your heart cells being attacked because the immune system identified muscle cells as foreign! Another potential pitfall is that the body actually becomes TOLERANT of the foreign proteins. This would mean that when challenged with the real disease (COVID-19) the immune system wouldn't respond at first. This could WORSEN symptoms rather than alleviate them. Paired with this is the potential for a *severe overreaction post vaccination*. This is not unique to the mRNA vaccine, but rather to the development of Coronavirus vaccines in general. During the early days of development of coronavirus vaccines for animals, there was an astronomically high number of fatalities in vaccinated populations because of this *hypersensitivity* when challenged with the real disease, and it was due to the vaccine itself. We had reports of rare occurrence by young/healthy people contracting COVID-19 and their immune system overreacting in a similar fashion. This risk factor is added BY the mRNA vaccine type but we do not yet know the increased degree of this risk factor.

The final issue is the ongoing/indefinite presence of antigen itself. In normal vaccines, everything goes away relatively shortly. We established that. However, with an mRNA *vaccine the body itself becomes the source of the antigen.* mRNA is not regulated. It will persist for a very long time. This is the source of the potential advantage, by constantly keeping the immune system on its toes for the antigen. However, this also means that any vaccine complications that develop because of the antigen will be with you for a very long time, and there's no known treatment for this condition. Nor do we know the implications of indefinite presence of the antigen (for COVID-19) in the body. It could be as benign as running a warm engine with the choke "ON;" not the best operation technique but no damage would result. It could also inhibit the body's ability to produce those plasma cells to defeat a disease other than COVID-19 … again, a sort of auto-immune against one/many diseases other than COVID-19.

Vaccines have been used safely and effectively for a long time. We started with a crude version of a modified live virus, and then developed true MLV's, subunit vaccines, and recently DNA vaccines. All of these vaccines are fully degraded in a short period of time, and pose mild to moderate risk to specific individuals in a narrow range of circumstances. In addition, extensive research has been done on these types of vaccines and they have been peer reviewed and passed extensive sets of animal/clinical trials before being used in the general population. mRNA vaccines are an untested and unresearched, cutting-edge vaccine type that should have taken years to develop and test before being used in the general population. They function by programming the body to produce antigen, instead of the antigen being supplied in the syringe. The potential adverse impacts of this are untreatable reactions, autoimmune disease generation, and hypersensitivity reactions that could be fatal when challenged with the live virus. Individuals receiving this vaccine will be producing COVID antigens for a very long time inside their bodies, and the impacts of this have not been researched. Related research (on repeated and extended exposure to a specific antigen) points to immune tolerance (bad) and hypersensitivity (also bad).

Because of all of these potentially harmful side effects, I find it extremely unwise that Pfizer and the other pharmaceuticals chose to develop this mRNA vaccine to be the answer to a pandemic that demands an immediate and reliable response. A standard subunit or MLV vaccine would have been faster to develop, cheaper to make, and much easier to ensure its safety since it would work the same as vaccines we have used for decades. For these reasons (and associated, but unproven, concerns about possible sterility being a side effect) it is my recommendation that no one receive this vaccine until it can be thoroughly tested, and proven to function as intended. As a great football coach once said: "3 things can happen to a pass, and 2 of 'em ain't good." mRNA is very much a pass play in a "playbook" surrounded by proven run plays.

My final concerns about this vaccine are unrelated to the fact that it is mRNA (though they are amplified by that fact). Pfizer has yet to complete their analysis of their clinical trial data. The clinical trials themselves were shallow in comparison to previous test on all other vaccines/types. So, the trial was shallow, and our analysis of that trial is not yet complete. Despite the 12/11/20 certification, the FDA has yet to finish their analysis. How could they when Pfizer itself hasn't had time to do so (remember, 5-7 years on a new vaccine type?) The development of this vaccine has been rushed, it's peer review actively blocked by Pfizer. Even though we don't yet know what we have (because analysis isn't finished), we're mass producing it and presumably about to inject every man, woman, and child with it starting today with great fanfare: "It's a shot of hope." The circumstances of this distribution are highly suspect. The possible consequences (hypersensitivity, tolerance, sterility, untreatable reactions) are even worse than the virus itself in the VAST majority of active cases. **It has been stressed in medical schools that before you give a vaccine you need to consider the risk the disease poses, the likelihood of infection without the vaccine, the risks that the vaccine poses, and the risk of infection with the vaccine**. For this vaccine the disease risk is certainly substantial, given the apparent degree of contagiousness in COVID-19, but unlike other vaccines the risk associated with the vaccine is astronomically high and the efficacy is questionable because we have yet to complete data analysis. This equation is therefore shifted heavily in favor of rejecting the vaccination.

My review of our COVID-19 state/vaccination offered freely. I will not argue with any who object, but will entertain honest and civil discussion. As I would always recommend, do your own research and make your own decisions based upon what you think you should do. For anyone that does receive the vaccine I pray that all of my misgivings are unfounded, that you are protected from COVID-19, and that despite all of the abnormal circumstances of development and distribution, the vaccine works as intended without any significant long-term side effects.

—- Al Vinson