

ROLE OF CYTOKINES AND VACCINES IN BREAK THROUGH COVID 19 INFECTIONS

ABSTRACT

Background: Despite the efforts carried out to discover corona virus disease-2019 (COVID-19) vaccines, it has been found that the vaccines do not build full immunity and long-term protection from infection and protection against COVID-19 and the newly worrisome variants of the SARS-CoV-2 coronavirus. Vaccines targeting these diverse types of infectious viral diseases may need to elicit very different types of immune responses which may require the knowledge of cytokines which play a big role in eliciting different immune responses for infectious organisms hence vital in design of vaccines.

Objective: It is vital to educate the scientific community and the general public on the importance of cytokines and how the current COVID-19 vaccines could help trigger some dormant cytokines to help build and bolster immunity even in break through infections

Materials and methods: Different literature was searched from different medical and scientific indexing sites such as PubMed, Google scholar, Medline, EMBASE, Web of Science, and Science Direct.

Results: Cytokines in the immune system can be triggered by any of the current COVID-19 vaccines within hours of vaccination and this process can help signalling molecules that can help boost the immune system to fight against the variants of new and break through COVID 19 infections.

Conclusion: Pfizer-BioNTech and Moderna vaccines are very similar, both have been found to be safe and efficacious in preventing both symptomatic and asymptomatic break through COVID-19 infections in rigorously conducted clinical trials world wide. Pfizer-BioNTech and Moderna vaccines are mRNA-based, while Johnson & Johnson's is an adenovirus.

Keywords: Cytokines, COVID-19, immunity, Pfizer-BioNTech, Moderna, Johnson & Johnson

Introduction

The immune system is regarded to be complex and pervasive with a number different cell types that either circulate throughout the body with cell playing a vital and unique role. By understanding all the details behind this network, researchers may optimize immune responses to confront specific issues, ranging from infections to cancer. All immune cells come from precursors in the bone marrow and develop into mature cells through a series of changes that can occur in different parts of the body. Immune cells for example B cells, T cells and the Natural killer (NK) are important for causing responses to specific microbes based on previous encounters (immunological memory), since they are derived from the common lymphoid

progenitor and share features of both innate and adaptive immune cells, as they provide immediate defences like innate cells but also may be retained as memory cells like adaptive cells. B, T, and NK cells also are called lymphocytes ^[1].

Break through Infections

A vaccine break through infection happens when a fully vaccinated person gets infected with Covid 19. It is a known scientific fact that vaccines are not 100% efficient that is why there are cases of fully vaccinated persons getting covid infection and developing symptoms but they tend to be less likely to develop serious illness than those who are unvaccinated and get COVID 19. It has now become known that break through infections in fully vaccinated persons makes them less likely to be hospitalised or die than people who are not vaccinated.

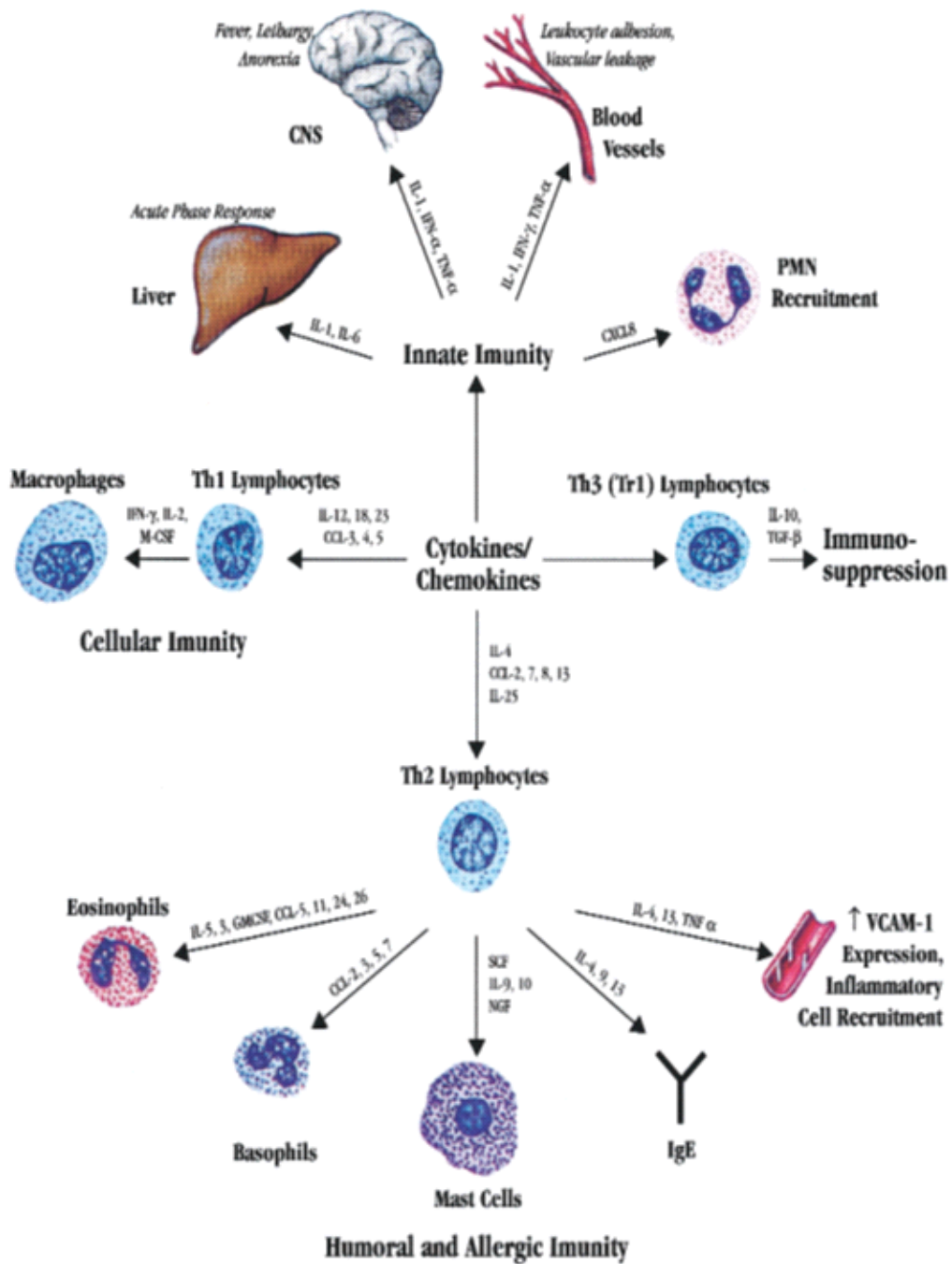
People who get vaccine breakthrough infection can still be contagious but it is know that one's immunity becomes solidly boosted after break through infection since there have been instances where fully vaccinated person who have had boosters had still be re infected with Covid 19 variants but hardly become hospitalised although that may show symptoms.

Cytokines Pathway

Cytokines are a large group of proteins, peptides or glycoproteins that are secreted by specific cells of immune system capable of signalling molecules that mediate and regulate immunity, inflammation and haematopoiesis. Cytokines are also known as small soluble proteins throughout the body by cells of diverse embryological origin that confer instructions and mediate communication among immune and non-immune cells [2]. They are made up of many cell populations with T cells and macrophages as predominant producers.

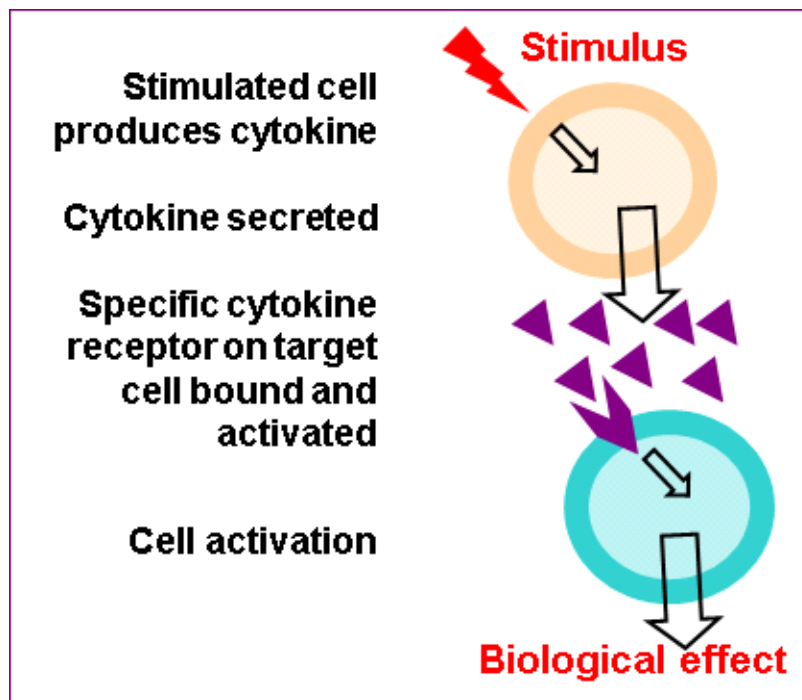
Cytokines are known to be key regulators of the immune system that shape innate and adaptive immune responses. A portfolio of cytokines is central to the role of macrophages as sentries of the innate immune system that mediate the transition from innate to adaptive immunity. For protective immunity and less immunopathology to be achieved, there should be an appropriate equilibrium in the cytokine environment. Cytokines, including IL, IFN and TGF, are proteins, peptides or glycoproteins secreted by immune cells, which could aid cell to cell communication in immune responses.

As part of the immune system, cytokines regulate the body's response to disease and infection, as well as mediate normal cellular processes in your body. The immune system is complex different types of immune cells and proteins do different jobs. Cytokines are among those proteins.



Cytokines play a vital role in controlling the cell, and hence tissue, growth, migration, development and differentiation these include a group of inflammatory cytokines such as the interleukins and interferons, growth factors such as epidermal and hepatocyte growth factor and chemokines such as the macrophage inflammatory proteins, MIP-1 α and MIP-1 β .

Cytokines made by lymphocytes can also be referred to as lymphokines. Many of the lymphokines are also known as interleukins (ILs), since they are not only secreted by leukocytes but also able to affect the cellular responses of leukocytes. Cytokines can have endocrine activity by traveling through circulation and acting on target cells in distant parts of the body. Cytokines are a broad group of signalling proteins that are produced transiently, after cellular activation, and act as humoral regulators which modulate the functions of individual cells, and regulate processes taking place under normal, developmental and pathological conditions.



The biological activities of cytokines are mediated by specific membrane receptors which can be expressed on virtually all cell types. The mechanism by which receptor occupation by cytokines results in the generation of a signal through the receptor is not completely understood. It is likely that on binding to the extra-cellular portion of the receptor the cytokine induces a conformational change, or oligomerization of multiple receptors, resulting in an activation event in the intracellular domain itself or in receptor-associated elements such that signal transduction to elicit subsequent intracellular events occurs. Small antagonist molecules that bind to cytokine receptors do not activate subsequent events probably because they do not deform the extra-cellular receptor sufficiently to excite subsequent events.

Basics of Vaccines

Vaccines contain weakened or inactive parts of a particular organism (antigen) that triggers an immune response within the body. Newer vaccines contain the blueprint for producing antigens rather than the antigen itself. Regardless of whether the vaccine is made up of the antigen itself or the blueprint so that the body will produce the antigen, this weakened version will not cause the disease in the person receiving the vaccine, but it will prompt their immune system to

respond much as it would have on its first reaction to the actual pathogen. Some vaccines require multiple doses, given weeks or months apart. This is sometimes needed to allow for the production of long-lived antibodies and development of memory cells. In this way, the body is trained to fight the specific disease-causing organism, building up memory of the pathogen so as to rapidly fight it if and when exposed in the future^[9]

Herd immunity

When someone is vaccinated, they are very likely to be protected against the targeted disease. But not everyone can be vaccinated. People with underlying health conditions that weaken their immune systems (such as cancer or HIV) or who have severe allergies to some vaccine components may not be able to get vaccinated with certain vaccines. These people can still be protected if they live in and amongst others who are vaccinated. When a lot of people in a community are vaccinated the pathogen has a hard time circulating because most of the people it encounters are immune. The more people are vaccinated, the less likely people who are unable to be protected by vaccines are at risk of even being exposed to the harmful pathogens. This is called herd immunity. This is especially important for those people who not only can't be vaccinated but may be more susceptible to the diseases we vaccinate against. No single vaccine provides 100% protection, and herd immunity does not provide full protection to those who cannot safely be vaccinated. But with herd immunity, these people will have substantial protection, thanks to those around them being vaccinated. Vaccination does not only protect oneself, but also protects those in the community who are unable to be vaccinated^[9]

Make up of COVID-19 Vaccines

Competent vaccines take 10 to 15 years to be fully developed and the immunity effect well known. Poliomyelitis, measles, small pox, yellow fever vaccines were all developed with much years of clinical trials and at times genetic modulations. The current COVID-19 vaccines be with Pfizer AstraZeneca, Moderna, Sputnik V, Oxford vaccine and Johnson and Johnson vaccines are barely 2 years old and although its competency is not well documented, it has shown to reduce death rate and this is a progressive step for the human race in relation to the COVID-19 pandemic which is now been endemic.

Pfizer – BioNTech vaccine

The first COVID-19 messenger-ribonucleic acid (mRNA) vaccines currently authorized for emergent use in the United States and around the world were the Pfizer-BioNTech and the Moderna vaccines. Conventional vaccines rely on weakened and inactivated pathogens or a fragment of the pathogen to trigger an immune response. In contrast, the COVID-19 mRNA vaccines use a novel approach by which mRNA is delivered into our cells to provide the genetic instructions for our own cells to “temporarily” make a “specific” viral protein that triggers an immune response^[10]. The Pfizer-BioNTech COVID-19 vaccine is composed of only one active ingredient which is the mRNA, this is protected by a group of lipids known as (4-hydroxybutyl) azanediyl) bis(hexane-6,1-diyl) bis (2-hexyldecanoate), 2 [(polyethylene glycol)-2000]-N, N-ditetradecylacetamide 1,2-Distearoyl-snglycero-3-phosphocholine cholesterol.

The vaccine also contains salts such as Potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dehydrate which help in balancing the acidity in the

body. The last ingredient in this vaccine is the sugar component known as sucrose which helps the molecules maintain their shape during freezing ^[11].

Moderna Vaccine

This contains mRNA just like the Pfizer BioNTech vaccine, lipids such as SM-102, 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 [PEG2000-DMG] cholesterol 1,2-distearoyl-sn-glycero-3-phosphocholine which help to deliver the mRNA to the cells.

Some other ingredients include acetic acid, acid stabilizers, salt and sugar which all work together to maintain the stability of the vaccine after it's produced ^[12].

Mechanism of MRNA COVID 19 Vaccines (Moderna and PfizerBioNTech vaccines)

Injections given from Pfizer and Moderna vaccines give the body genetic instruction manuals to safely learn how to fight the coronavirus. Pfizer's and Moderna's vaccines train the body to fight COVID-19 by injecting mRNA, or messenger RNA, into a person's deltoid, the rounded muscle that hugs the upper arm and shoulder. The mRNA that's injected into the muscle codes for the spike protein. The coronavirus' spike protein is what allows the virus to latch on to and invade the human cells. The mRNA vaccines train the human bodies to immunologically move in a determined pace ^[13]. The body sees that protein and makes an immune response against it, giving the body the protection that has been shown with both of the mRNA vaccines. ^[14]

Mechanism of ADENO VIRUS (cold virus) COVID 19 Vaccines (The Johnson & Johnson vaccines)

The Johnson and Johnson vaccine injects viral DNA and not mRNA. This is a key reason why Johnson and Johnson's vaccine is much easier to manufacture and can be stored in the normal fridges in our homes and clinics. The DNA inside is not as fragile as the single-stranded mRNA in Pfizer's and Moderna's vaccines. The DNA in the Johnson and Johnson vaccine is encapsulated in a harmless, non-replication-competent virus. The adenovirus is called Ad26 and is a common cold virus that has had its illness-causing genes removed, so it can't get the human system sick. Once the vaccine is injected into a person's arm, the virus injects its DNA into cells, where it's copied into messenger RNA. That mRNA then codes for coronavirus spike proteins in the same way as Pfizer's or Moderna's shots ^[14]

Summary

The main components in the Pfizer-BioNTech and Moderna vaccines are very similar, both vaccines have been found to be safe and efficacious in preventing symptomatic COVID-19 disease in rigorously conducted clinical trials. Pfizer - BioNTech and Moderna vaccines are mRNA-based, while Johnson & Johnson's is an adenovirus. These COVID-19 mRNA and Adenovirus vaccines are safe and have gone through the same rigorous testing process as other vaccines before being approved for emergent use in the United States and now worldwide. In clinical trials and experiments it has showed that Moderna and Pfizer Vaccines when administered were more effective overall than the Johnson and Johnson vaccine in the trials, but it was observed and noticed that all these vaccines share two very important statistics that is zero hospitalizations and zero deaths among fully vaccinated and also now with those who have taken booster shots although they are all prone to break through infections. ^[15].

Either the adenovirus and mRNA COVID-19 vaccines are the same as all vaccines ultimately result in a spike protein in the right conformation that gives the body the opportunity to feel that this is the it's the protein that it is moving with. The protein prepares a vaccinated person's body to fight off a COVID-19 infection if the person comes into contact with the virus. Both the mRNA and the adenovirus vaccines appear to prevent the most severe COVID-19 infections very well ^[15].

Research and case reports has showed that Pfizer and Moderna two shot courses were more than 94% effective in their trials, while Johnson and Johnson (J&J) vaccine were 85% effective in preventing severe disease and death. Adenovirus vaccines like J&J's might give people a more robust form of immunity against viral variants, with antibody and T-cell responses. mRNA vaccines may provide only narrower antibody protection but that remains to be seen as more people get vaccinated and variants continue to spread [14].

When taking the vaccines, the population should take note that the vaccine vial or seal is not already broken, the vaccine does not change to any colour or does not develop colours while in the vial, vaccines should be opened in the face of the receiver, syringes to be used for vaccination must new per each person and opened in the face of the receiver, vaccine should be taken from the cold chain storage box.

Conclusion

Any of the arms of people receiving the vaccines could be used; there is no scientific or medical reason for using or injecting only the left arm. It could be the right arm or left depending on the preference of the person receiving the vaccine. Most developing countries insist people are vaccinated in their left arm which is medically and scientifically wrong and of no purpose. The now incorporation of cytokines as molecular adjuvants in some vaccines has been attempted to strengthen vaccine-induced immune responses, and as a rational approach to modulate cytokine milieu in vivo and tailor host immunity for specific situations. These approaches have been tried in experimental models and veterinary species, and a few of them have entered into clinical trials. However, manipulating the cytokine network to modulate immune responses is not a simple task, because cytokine functions are complex and the final effects on the immune response will depend on timing and length of exposure, cell(s) targeted and other cytokines present in the same microenvironment [3].

Recommendation

Although most literature do not state or know the exact immunity duration or even any immunity of the COVID-19 vaccines been developed and rolled out, the population should still take the vaccines since most components of the vaccines may trigger cytokines and in the normal state and can build some undefined form of immunity so the need for the population to take the vaccines. Also, it is recommended that severe adverse reactions or even subtle adverse reactions from the vaccine that doesn't resolve or go away within 72hrs should be urgently reported to health authorities and accredited health centres for such purpose.

There are rumours that mRNA vaccines will alter our DNA because the RNA molecule can convert information stored in DNA into proteins. That's simply, not true. It's critical to note that the mRNA vaccines never enter the nucleus of the cell, where our DNA is stored. After injection, the mRNA from the vaccine is released into the cytoplasm of the cells. Once the viral protein is

made and on the surface of the cell, mRNA is broken down and the body permanently gets rid of it, therefore making it impossible to change our DNA. Furthermore, it is extremely important for the population to keep on masking, using the hand washing techniques regularly, using the alcohol hand sanitizers and physical or social distancing approach to help achieve a competent prevention even after taking the prescribed doses of any of the COVID- 19 vaccines since the world has not yet achieved herd immunity [15].

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