

# **ROLE OF CYTOKINES AND VACCINES IN BREAK THROUGH COVID 19 INFECTIONS**

## **ABSTRACT**

**Background:** Despite efforts to develop a COVID-19 vaccine, it has failed to provide long-term immunity and protection against COVID-19 and the newly worrying SARS-CoV-2 coronavirus strains. Understanding cytokines, which are key in generating unique immune responses from pathogenic organisms, is important for creating vaccines.

**Objective:** In order to better understand cytokines and how the current COVID-19 vaccinations can assist reactivate latent cytokines, the scientific community and the general public must be educated.

**Materials and methods:** Medical and scientific indexing sources like PubMed and Google Scholar were used to search for relevant medical and scientific publications.

**Results:** After vaccination, cytokines in the immune system can be activated, which can help signal chemicals that can increase the immune system's ability to fight against new and break-through COVID 19 infections.

**Conclusion:** It has been discovered that both the Pfizer-BioNTech and the Moderna vaccines are safe and effective in preventing break through COVID-19 infections, regardless of whether the patient experiences symptoms or not. It is an adenovirus, not an mRNA, that Johnson & Johnson's vaccine is made of.

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

## **Introduction**

There are numerous cell types circulating throughout the body that make up the immune system, each with a distinct role to play. If researchers fully comprehend this network, they may be able to improve immune responses to infections or cancer. All immune cells begin in the bone marrow and undergo several changes before maturing in various parts of the body. Because B cells, T cells, and the Natural Killer (NK) possess properties of both innate and adaptive immune

cells, they are critical for generating responses to specific bacteria based on previous contacts (immunological memory). T-cells B, T, and NK cells are lymphocytes.

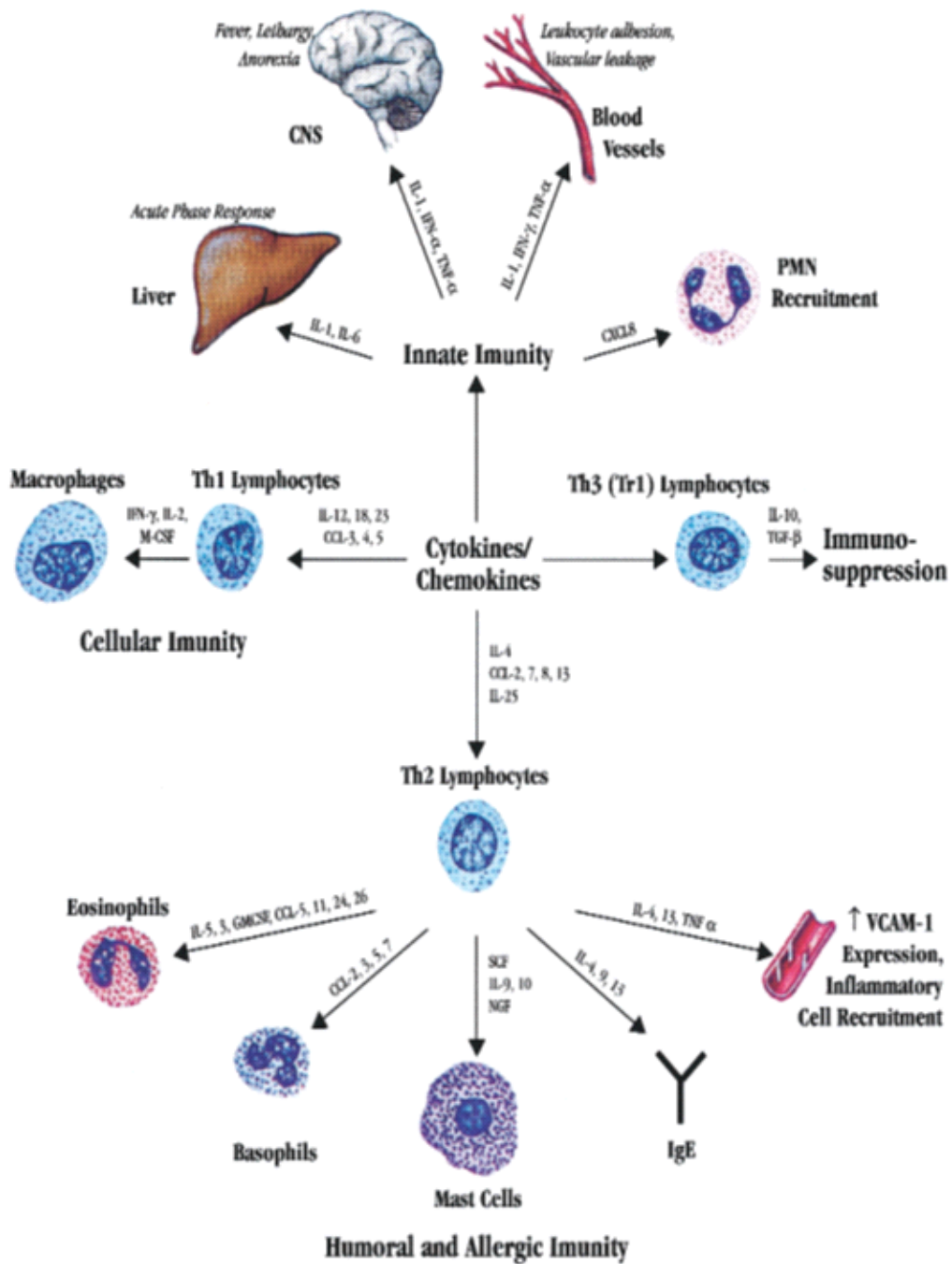
### **Overcoming Infections**

A "vaccine break through infection" occurs when a person who has had all of their vaccines gets Covid 19. Although fully vaccinated persons can show signs of COVID 19, they are less likely to get sick than unvaccinated ones. Vaccines do not always work. Preventing hospitalisation or death from break-through infections is now possible with full immunisation.

Because fully vaccinated persons who had boosters were still infected with Covid 19 variations but did not become hospitalised despite showing symptoms, it is known that immunity is boosted after the infection.

### **Cytokines Pathway**

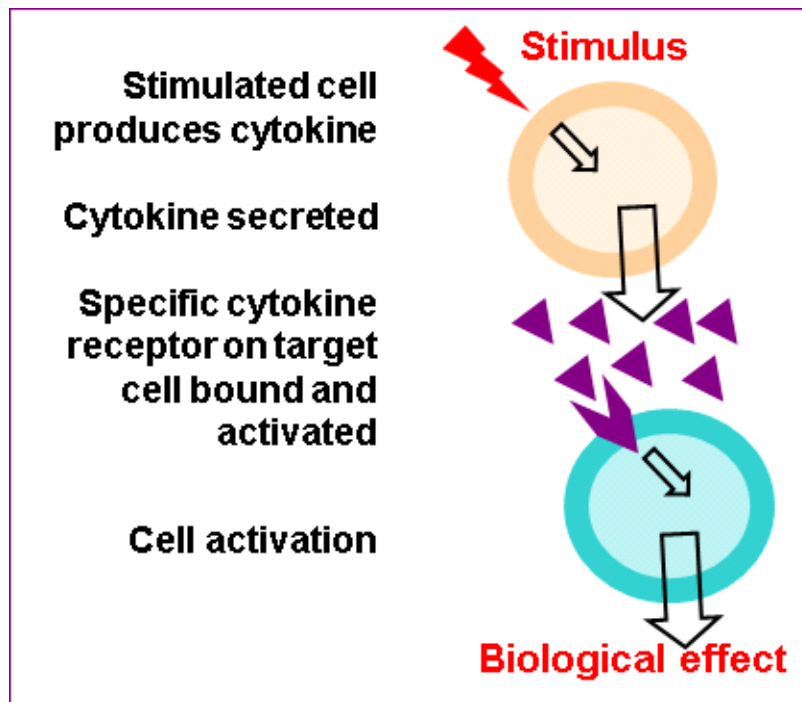
Immune cells create many proteins, peptides, and glycoproteins that govern immune response, inflammation, and haematopoiesis via signalling molecules. Immune and non-immune cells communicate via cytokines, which are small soluble proteins found in all types of cells [2]. T-cells and macrophages are two primary immune cell types. Cytokines, long recognised as essential immunological regulators, regulate the innate and adaptive immune responses. Macrophages release a number of cytokines that help bridge the innate and adaptive immune systems. Cytokine equilibrium is essential for a healthy immune system. Interleukin (IL), interferon (IFN), and tumour growth factor (TGF) are among the cytokines secreted by immune cells (TGF). Cytokines are proteins that play a role in both the immune system's response to illness and infection as well as cell function. (fig:1) The immune system uses a wide range of immune cells and proteins. Among them are cytokines.



**Fig: 1 Signaling Pathways of the Gamma-Chain Family of Cytokine Receptors**

Cytokines regulate cell proliferation, migration, development, and differentiation. Interleukin-1 (IL-1) and interferon (IFN-) cytokines, growth factors (EGF and HGF), and chemokines (such as macrophage inflammatory proteins, MIP-1 and MIP-1)

Lymphokines are cytokines produced by lymphocytes. Interleukins (ILs) are lymphokines that can alter leukocyte cellular responses. Cytokines can serve as endocrine agents by interacting with cells throughout the body. In normal, developmental, or pathological settings, stimulated cells secrete a broad family of proteins known as cytokines.



**Fig: 2 Cytokine mode of action**

Cytokines' biological actions are mediated by membrane receptors found on practically all cell types.(fig: 2) The process by which cytokines occupy receptors and generate signals through them is unknown. This activation event happens in the intracellular domain itself or in receptor-associated components, culminating in signal transduction to evoke subsequent intracellular activities. They don't work because they don't distort the extracellular receptor enough to excite following processes.

### **Basics of Vaccines**

An immune reaction is triggered by weakened or inactive components of an organism (antigen). Newer vaccines contain a blueprint for making the antigens they protect against. While a vaccination that contains an antigen or a blueprint for how the body manufactures an antigen does not cause illness, the weakened form encourages the immune system to respond as it would

if exposed to the pathogen. Some immunizations require multiple doses over time. This may be required for long-lasting antibodies and memory cells. As a result, the body is better equipped to fight the illness and respond promptly to future exposures [9].

### **Herd immunity**

Vaccines against specific diseases usually protect against them. But not everyone can get vaccinated. Certain vaccines may be inaccessible to people with immune system illnesses (such as cancer or HIV) or substantial sensitivities to vaccine components. They can be kept secure if they are near other immunised people. A pathogen has a hard time spreading in a community where most people are vaccinated. Anti-vaccine immunity reduces exposure to harmful bacteria as vaccination rates climb. Herd immunity is the term. Notable exceptions include those who cannot be vaccinated or are more susceptible to infections. Even if herd immunity protects everyone, those who cannot be vaccinated are still at risk. However, the immunizations of individuals around them will provide significant protection. Vaccination protects not just the individual but also others who cannot be vaccinated [9].

### **Make up of COVID-19 Vaccines**

A fully effective vaccine with a documented effect on immunity takes 10–15 years to create. Vaccines against poliomyelitis, measles, smallpox, and yellow fever took years of clinical trials and genetic tweaking. The COVID-19 vaccines from Pfizer AstraZeneca are only 2 years old, and while their efficacy is unknown, they have shown to reduce mortality rates in the context of an endemic COVID-19 pandemic. This is a positive move for the human race in the face of the COVID-19 epidemic.

### **Pfizer – BioNTech vaccine**

Pfizer-BioNTech and Moderna were the first COVID-19 mRNA vaccines approved in the US and globally. Conventional vaccinations employ weakened or inactivated pathogens or a portion of the pathogen to trigger an immune response. The COVID-19 mRNA vaccines, on the other hand, instruct our own cells to "temporarily" create a "exact" viral protein that induces an immune response [10]. The Pfizer-BioNTech COVID-19 vaccine's active ingredient, 4-hydroxybutyl azanediyl bis(hexane-6,1-diyl) bis(2'-hexyldecanoate), 2 [(polyethylene glycol)-2000] protects the mRNA. N-ditetradecylacetamide, 1,2-distearoylsnglycero-3-phosphocholine

So the vaccine contains potassium chloride and monobasic potassium phosphate to balance the body's acidity. This vaccine contains sulphate, a chemical that helps molecules retain shape when frozen [11].

### **Moderna Vaccine**

Such the Pfizer BioNTech vaccine, it contains mRNA and lipids that help transfer mRNA to cells, like SM-102, 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG). Acetic acid, along with other acid stabilisers, salt, and sugar, helps maintain the vaccine stable after manufacture.

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

By injecting Pfizer and Moderna vaccines, the body receives protective genetic instructions. Pfizer and Moderna's vaccines help train the body to fight COVID-19 by injecting them into the deltoid muscle. The spike protein is encoded by the injected mRNA. The coronavirus spike protein allows it to connect to and infect human cells. The mRNA vaccinations train the body to move at a specific rate [13]. To defend itself, the body recognises the protein and mounts an immunological reaction. [14]

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

Rather than mRNA, the Johnson & Johnson vaccination administers viral DNA. Johnson and Johnson's vaccine is easier to create and can be stored in standard refrigerators in our homes and clinics because of this. ' The single-stranded mRNA in vaccines made by Pfizer and Moderna is more brittle than the DNA within. Capsulated in an innocuous, non-replicating virus, Johnson and Johnson's vaccination contains DNA. Ad26 is an adenovirus that has had its sickness-causing genes removed, so it can't infect the human body and cause illness. Following an injection into the arm, the virus injects its DNA into cells where it is translated to messenger RNA and spreads throughout the body. It is this mRNA that codes for coronavirus spike proteins like Pfizer or Moderna injections [14].

## **Summary**

Both the Pfizer-BioNTech and the Moderna vaccines have been shown in rigorous clinical trials to be safe and effective in preventing COVID-19 disease symptoms. Pfizer's mRNA-based vaccines, BioNTech and Moderna, outperform Johnson & Johnson's adenovirus vaccine. Due to their safety and rigorous testing, these vaccines have been approved for use in the United States and now globally. In clinical trials and experiments, Moderna and Pfizer vaccines outperformed Johnson and Johnson vaccines, but it was noted that all of these vaccines share two very important statistics: zero hospitalizations and zero deaths among those fully vaccinated and those who have received booster shots, despite the fact that they are all susceptible to break through infections. [15].

This is because the adenovirus and mRNA COVID-19 vaccines produce the same spike protein in the correct conformation, which simulates movement in the body when exposed to the virus or the mRNA vaccine. A person who has been immunised with the protein is better able to fight off infection when exposed to the virus. [15] Less severe COVID-19 infections seem to be prevented by adenovirus and mRNA vaccines.

These vaccines were found to be 88% effective in preventing severe disease and death in Pfizer and Moderna trials. For example, J&J's Adenovirus vaccine may boost viral immunity with antibody and T-cell responses. Although mRNA vaccines provide less antibody protection, more people will get them, and new versions will be developed [14].

When administering vaccines, remember to open the vial or seal in front of the recipient, and to remove the vaccine from the cold chain storage box.

## **Conclusion**

There is no scientific or medical reason to only use or inject vaccines in the left arm. The vaccination can be given to either the right or left arm. In most impoverished nations, the left arm should not be vaccinated. Some vaccines contain cytokines as molecular adjuvants to boost immune responses and tailor the host's immune response to specific situations. These methods have been tested on animals and in clinical trials. However, manipulating the cytokine network to alter immune responses is difficult due to the complexity of cytokine functions and the effects

of timing and duration of exposure, targeted cells, and other cytokines in the same microenvironment [3].

## **ETHICAL APPROVAL**

This study was carried out according to the guidelines of National Research Council Guide and in accordance with the principles of Good Laboratory procedure (GLP) following approval of the Institutional Ethical Committee on the Use and Care of Animals.

## **Recommendation**

Despite the lack of specific evidence on vaccine immunity duration or even immunity, the public should still receive immunizations because most vaccine components stimulate cytokines and in a normal condition can create some undefined type of immunity. Vaccine-related severe or minor adverse effects should be reported immediately to health authorities and licenced health centres. Because RNA may translate DNA information into proteins, MRNA vaccines are thought to change our DNA. I'm stunned you say that. It is vital to stress that mRNA vaccines do not enter the nucleus because human DNA is kept there. Vaccination releases it into the cytoplasm of cells. Once on the cell surface, the viral protein breaks down mRNA, preventing it from changing our DNA. Even after receiving the recommended doses of either COVID-19 vaccination, persons must continue to wear masks, wash their hands often, use alcohol hand sanitizers, and keep a physical or social distance from each other [15].

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