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Letter to Editor

Cytokine Storm: A Coronavirus Complication

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We Did Not Return: The Serious Side Effects of Corona Healers

Even after recovering and expecting to return to normal - many corona patients report many damages that do not pass • Severe physical symptoms as well as serious mental consequences that persist over time

Post-Corona: Doctors are used to seeing people who have recovered from a viral illness, returning to their home with no effects to continue. However, the Corona has recently proven that it can leave significant damage to the adhesive in the long run, even after it has healed. Physical symptoms such as weakness, pain and changes in taste, as well as mental consequences - that accompany patients. The dimensions of damage, destruction and destruction that the virus leaves are recently discovered and are quite disturbing.

The corona can also cause brain events [1]

In many cases, the corona virus appears to send arms to many systems in the body, such as the lung system and blood clotting. Although medicine currently knows very little about the disease and its effects, it is already clear that it is causing many physical and emotional changes. "It can cause brain events, even the smallest," said Dr. Itzik Levy, an infectious disease specialist and director of the Tel Hashomer Recovery Clinic.

Afik Suissa, 24, from Ashdod became famous as the youngest in serious condition in Israel. He swung between life and death, was breathing for 50 days. Two and a half weeks ago he received a negative answer

and returned home - but even now, he cannot be defined as a healthy person. "I still have limp, leg numbness," said Afik. He added: "I have a nerve problem in my right leg, which bothers me to walk. The sense of taste is also impaired."

Memory, Dissociation and Stress Problems: The Post-Coronary Mental Disorders

He stays with high blood pressure, a relatively high pulse, and takes blood-thinning pills, which he may need to take all his life. But another thing that surprised him - looks like a change of personality: "I have less patience for things. I go into stress, to nerves."

While we all felt emotional stress during the outbreak of the virus, Corona seems to be directly causing some psychiatric effects - especially depression and suicide. It may leave a feeling of disconnection and distancing - called dissociation. "We see psychic phenomena emerging. Will they stay or not? Days will tell," said Dr. Zvi Fishel, psychiatrist and chairman of the Israeli Psychiatric Association.

The most common injury that the corona leaves in the brain is memory impairment. The recovering clinics noticed that it could happen to people who passed the disease easily, or even to those who did not feel at all ill. "It's some kind of short-term memory problem, in concentration," said Dr. Lydia Belcher, a family physician who also has coronary disease.

The same is true of 32-year-old Rona Ohayon and five of Tirat Carmel, who was left with weakness, severe fatigue and memory loss - which makes her even go to the doctors with her mother so she doesn't forget to say things and someone else will remember what they said there. "I forget to do things I wanted. I see that there is a full like me," she described.

"The phenomena in mild patients - a new phenomenon"

Maisie Avihail, also known as Patient No. 187, has experienced severe post-Corona phenomena - a language impairment, reminiscent of a stroke: "I'm trying to say something, I know which word - but I can't."

Dr. Dana Yellin, Specialist in Infectious Diseases: "The cognitive decline in people with coronary heart disease is very new to us. This is a phenomenon we are trying to understand its scope, it is still unclear how wide it is."

The damage to health is most recognized - damage left by the virus in the body after the battle. "Unlike pneumonia, which see a certain curve of recovery and improvement day by day - here you see people who are stuck in a state of being unable to do things before," emphasized Dr. On Amir, director of the Lung Institute at Sheba Hospital in Tel Hashomer. "There were also reports from China about Patients who needed lung transplants following these procedures."

Even when there is not even one virus left in the world, we have many more years of dealing with the post-corona - the epidemic after the epidemic. Only now - are we gradually beginning to discover its dimensions.

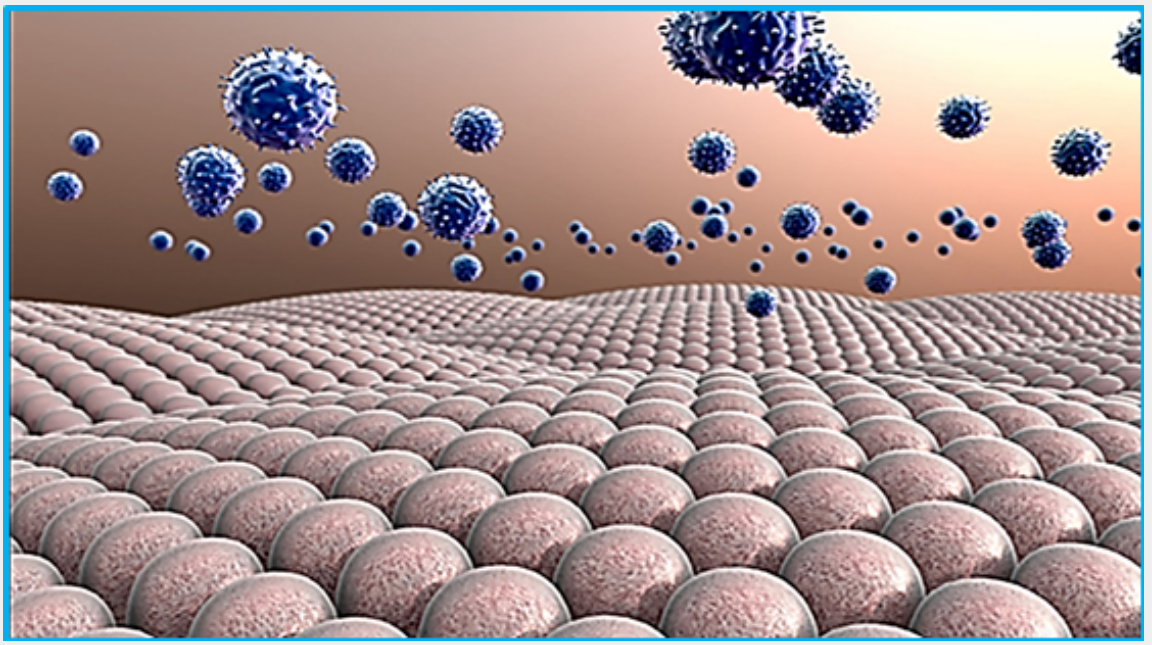

Figure 1: *Cytokines Storm (credit ref. [2])*

Survival and Programmed Cell Death by Cytokines [3]. Cytokines are a broad and released category of small proteins (~ 20-20 kDa) that are important in cell signaling. Cytokines are peptides and cannot cross the lipid bilayer of cells to enter the cytoplasm. Cytokines are shown to be implicated in autocrine, paracrine, and endocrine signaling as anti-vaccine agents. Their distinct distinction from hormones is still part of ongoing research.

A cytokine storm is a human bodily reaction in which the innate immune system releases a large number of cytokines, potentially overwhelming the body and possibly leading to fatality.

Coronavirus Virus 2019 (COVID-19) Quickly spread throughout the whole region of earth. This is significantly related mortality, especially in at-risk groups with poor prognostic features in the hour Hospitalization. The spectrum of diseases. (A disease is a particular abnormal condition that negatively affects the structure or function of all or part of an organism, and that is not due to any immediate external injury) It is broad but in constant battle, hospitalized with COVID-19, Pneumonia, Sepsis, Breathing Failure, and Acute Respiratory distress Syndrome (ARDS) often Encountered complications [4].

Inflammation is the body's first line of defense against infection or injury, responding to challenges by activating innate and adaptive responses. The microbes have developed a variety of strategies to avoid triggering inflammatory responses [5]. However, some pathogens, such as the influenza virus, and the Gram negative bacterium *Gram Francisella tularensis*, do induce life-threatening "cytokine storms" in the host which can cause significant pathology and eventually death. These diseases have been suggested to regulate

the inflammatory immune Response that may improve outcome. We are reviewing some of the current cytokine storm therapy candidates that may prove to be useful in future clinics and compare them to more traditional therapeutic candidates that target pathogen rather than host response [6].

The pathophysiology of Acute Respiratory Syndrome

Coronavirus 2 (SARS-CoV-2) induced. ARDS has similarities to this, of severe pneumonia. In the community caused by other viruses, or overproduction of Pre-inflammatory cytokines with the early Response (Tumor necrosis factor [TNF], IL-6 and IL-1β) bring about what is has been described as a cytokine drug, leading to increased risk of blood vessels over-capacity, multi-failure. Eventually, death when high. The cytokine concentrations are not significant over time [7]. Therefore, therapeutic strategies explored are focus on over-cytokine Response with anti-toxin treatments or vaccine stores. Still, it has to balance with maintaining adequate inflammatory Response for pathogen clearance.

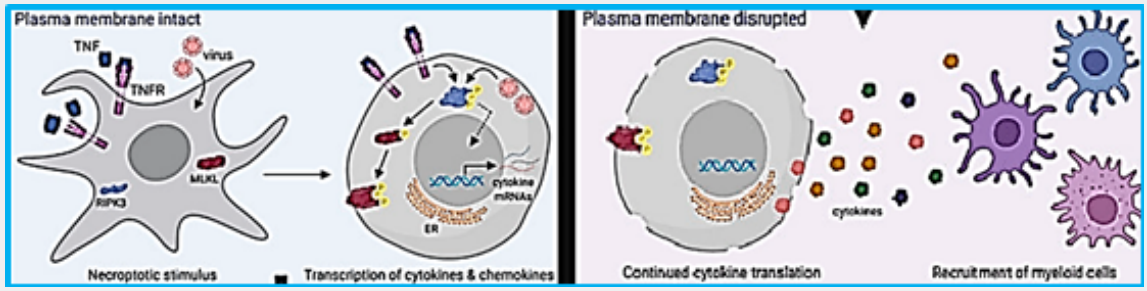

Figure 2: *Cytokines (credit ref. [8])*

RNA viruses like the influenza virus, or coronavirus, are toxic to most cell types in which it replicates. IAV activates the RIPK3 (Receptor-interacting serine/threonine-protein kinase 3 is an enzyme that in humans is encoded by the RIPK3 gene) host kinase, which induces cell death through parallel pathways of necrosis, driven by the MLKL pseudokinase, and apoptosis, depending on the RIPK1 and FADD (Fas-associated protein with death domain (FADD), also called MORT1, is encoded by the FADD gene on the 11q13.3 region of chromosome 11 in humans correlation proteins). How IAV runs RIPK3 remains unknown. We report that DAI (ZBP1 / DLM-1), previously assimilated as a cytoplasmic DNA sensor, is essential for RAVK3 activation by IAV. Upon infection, DAI recognizes genomic RNA from IAV, is linked to RIPK3 and is required to recruit MLKL and RIPK1 to RIPK3. DAI-deficient cells or containing nucleic acid-deficient DAI mutants are resistant to IAV-induced necrosis and apoptosis. DAI-deficient mice fail to control IAV replication and succumb to respiratory infection. These results identify DAI as a link between IAV replication and RIPK3 activation and affect DAI as an RNA virus sensor [9].

"Cytokine storm" refers to the role of the living immune system in producing an uncontrolled and generalized inflammatory response [10].

Five of the processes regulate the onset of host-graft disease, a condition characterized by an impressive potent activation of the immune system [11]. Cytokine storms describe a broad spectrum of infectious and non-infectious diseases, and since 2005 it has been linked to avian influenza H5N1 infection [12].

Apart from the immediate significance of the term cytokine storm, the biological and clinical consequences of this immune system hyperactivity are by far less known, making it worthwhile a brief overview.

One can find similarities in clinical features between COVID-19 and infections previously identified with the beta-coronavirus. The typical clinical findings include: most patients are with fever, dry cough, dyspnea, and bilateral refractory glass opacity on chest CT scans [13].

The physio-pathology, the various mechanisms through which SARS-CoV or MERS-CoV produce high pathogenicity have not yet fully revealed. Since the first reports of COVID-19 disease, acute respiratory distress syndrome (ARDS) appears to be a significant number of deaths in infected patients and that ARDS should become viewed as a SARS-CoV-2 immunosuppressive clinic, similar to what described in the infection. SARS-CoV and MERS-CoV [14]. Acute respiratory distress syndrome (ARDS) is a devastating event, with an estimated mortality of approximately 40%, defined as the presence of bilateral lung infiltrates and severe hypoxemia. ARDS can occur in a variety of clinical situations, including pneumonia, sepsis, pancreatitis, blood transfusion. Acute respiratory distress syndrome (ARDS) involves inflammatory damage to the Albiol-capillary membrane, leading to an increase in lung permeability and the removal of protein-rich lung edema fluid, which eventually leads to respiratory failure [15]. As shown by previous data in the literature, increased circulating levels of pro-inflammatory cytokines (eg, Interferon γ, interleukin (IL-) 1B, IL-6, IL-12) and chemokines (CXCL10, and CCL2) are associated with pulmonary inflammation and extensive lung involvement in SARS patients, similarly to what happens in MERS-CoV infection [16]. As far as COVID 19 infection is concerned, Huang *et al*. recently reported that infected patients also show high levels of pro-inflammatory cytokines and chemokines [17]. The demonstration of increased levels of IL-1B, IFN, CXCL10, and CCL2 firmly pointed toward the activation of T-helper-1 (Th1) cell function [18].

More importantly, the so called “cytokine storm” emerged as a main factor driving a more severe clinical course. This concept originated from the observation that COVID-19 patients requiring ICU admission displayed higher concentrations of CXCL10, CCL2 and TNFα as compared to those in which the infection was less severe and did not require an ICU admission. To further complicate the issue, it should be highlighted that, in patients with SARS-Cov-2 disease, at the difference from SARS-CoV infection, there is also an increased secretion Th2-immune-oriented cytokines such as IL-4 and IL-10, whose main effect is to suppress inflammation [19].

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18. The T helper cells (Th cells), also known as CD4+ cells, are a type of T cell that play an important role in the immune system, particularly in the adaptive immune system. They help the activity of other immune cells by releasing T cell cytokines. These cells help suppress or regulate immune responses. They are essential in B cell antibody class switching, in the activation and growth of cytotoxic T cells, and in maximizing bactericidal activity of phagocytes such as macrophages.

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