Knowledge innovations about the COVID-19 pandemic

Inovações de conhecimento sobre a pandemia COVID-19

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ABSTRACT
In 2019 an acute respiratory syndrome emerged from Wuhan, China. This pandemic is caused by coronaviruses (CoV), a family of enveloped positive-stranded RNA viruses that infect birds and mammals in the intestinal and respiratory systems. This family was responsible for two previous epidemics, MERS-CoV and SARS-CoV. The COVID-19 pandemic is caused by SARS-CoV-2, a CoV with high affinity to ACE2 from humans. It binds itself with the ACE2 via spike protein, one of the five encoded proteins. SARS-CoV-2 infection causes a wide range of symptoms, including cough, fever, acute respiratory syndrome, and pneumonia. These are a result of the cytokine storm, which is mainly composed of IL-6, IL-12 and TNF-α. Due to the air droplets transmission, measures are needed to reduce the spread and transmission of the virus. These measures include the use of alcohol, proper hand hygiene, social distancing and the use of personal protective equipment (PPE), such as PFF2 masks. Our findings were made by the research of the following keywords "SARS-CoV-2", "COVID-19", "MERS-CoV", "SARS-CoV", "genome", "epidemiology" and "immunology" in PubMed, Scielo and Google Scholar during the months of February and May 2021. It is clear that the pathophysiology of the disease is complex, varying according to the immune response of each individual. Innate immunity plays an important role in the immune response against the virus, which replicates using the host's cellular machinery and antibodies neutralize and protect the body. Thus, hygiene issues must be highlighted in order to prevent new pandemics. To avoid new pandemics, caution and a multidisciplinary team are needed.

Keywords: COVID-19, Environment, Global health.

RESUMO
Em 2019, uma síndrome respiratória aguda surgiu em Wuhan, China. Esta pandemia é causada por coronavírus (CoV), uma família de vírus de RNA de fita positiva com envelope que infectam pássaros e mamíferos nos sistemas intestinal e respiratório. Esta família foi responsável por duas epidemias anteriores, MERS-CoV e SARS-CoV. A pandemia de COVID-19 é causada pelo SARS-CoV-2, um CoV com alta afinidade para a ACE2 de humanos. Ele se liga ao ACE2 por meio da proteína spike, uma das cinco proteínas codificadas. A infecção por SARS-CoV-2 causa uma ampla variedade de sintomas, incluindo tosse, febre, síndrome respiratória aguda e pneumonia. Elas são resultado da tempestade de citocinas, que é composta principalmente por IL-6, IL-12 e TNF-α. Devido à transmissão das gotículas de ar, são necessárias medidas para reduzir a disseminação e transmissão do vírus. Essas medidas incluem o uso de álcool, Nossos achados foram feitos pela pesquisa das seguintes palavras-chave "SARS-CoV-2", "COVID-19", "MERS-CoV", "SARS-CoV", "genoma", "epidemiologia" e "imunologia" no PubMed, Scielo e Google Scholar durante os meses de fevereiro e maio de 2021. É claro que a fisiopatologia da doença é complexa, variando de acordo com a resposta imune de cada indivíduo. A imunidade inata desempenha um papel importante na resposta imune contra o vírus, que se replica usando a maquinaria celular do hospedeiro e os anticorpos neutralizam e protegem o corpo. Assim, as questões de higiene devem ser destacadas a fim de prevenir novas pandemias. Também é importante ressaltar que o EPI está relacionado a menor risco de infecção. Para evitar novas pandemias, é preciso cautela e equipe multidisciplinar.
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1 INTRODUCTION

In the early 1800s in England the fast industrialization created some problems, such as stress on the bionetwork and its system, rural exodus, overpopulation, and cities pollution. Nowadays humans are in constant war against the environment, either trying to make more profit out of it or just trying to feed their families in poor regions. In the COVID-19 context, what we want to talk about is the need to obtain nutrients from foods to survive and be healthy. Food consumption changes from age, sex, physical activity level and specifically due to the culture. Cultures are what makes us different, and the Chinese food culture is probably what caused the pandemic.

In December of 2019, in Wuhan, China, a respiratory syndrome, first characterized as acute respiratory syndrome, was starting to make an outbreak. After further investigations, the World Health Organization (WHO) declared a global pandemic due to the new SARS-CoV virus, the SARS-CoV-2. On March 30th of 2021, the World Health Organization (WHO) declared that SARS-CoV-2 was transmitted to humans via bats, with another animal as an intermediary. However, it has been discovered on June of 2021, that Anthony Fauci's, one of the most famous US scientists, funded research by the Chinese military, the Wuhan Institute of Virology and American scientists to genetically manipulate coronaviruses soon before the pandemic hit. The lawsuit is under investigation.

2 METHODOLOGY

The SARS-CoV-2 outbreak made a huge boost in epidemiological, immunological and genetics studies not only to document the disease, but also to understand its beginnings, physiopathology and how we can fight against the virus. Our research was conducted taking those factors as our focus, therefore we searched the key words "SARS-CoV-2", "COVID-19", "MERS-CoV", "SARS-CoV", "genome", "cytokine storm", "epidemiology" and "immunology" in PubMed, Scielo and Google Scholar throughout February and May of 2021.
3 RESULT AND DISCUSSIONS

3.1 HISTORY/BACKGROUND/EPIDEMIOLOGY

By April 4th of 2003, WHO had recorded 2353 cases of a severe acute respiratory syndrome (SARS), the majority in China and the Asian-Pacific region. At that point around 4% of the patients died due to the alveolar damage made by this unknown microbe. After further investigation researchers pointed out that this virus main transmission was through respiratory droplets. This conclusion came after the researchers established a SARS outbreak in healthcare workers. The symptoms were usually dyspnea, fever, headache, cough, and hypoxemia. Laboratory findings were lymphopenia and mildly elevated aminotransferase level. The academic world then classified this virus as "severe acute respiratory syndrome coronavirus" (SARS-CoV). The SARS epidemic was officially controlled by July 2003 only by strict isolation of patients.

In June of 2012, the first death due to Middle East Respiratory Syndrome (MERS) was reported in a hospital in Saudi Arabia. After some time, the doctors isolated a sample of this microbe, the results demonstrated similarities with the SARS-CoV, which caused an epidemic in 2003. As the virus progressed a spike of MERS happened in the spring of 2013 and 2014, with a 44% mortality rate. That, added to the higher mortality rates in patients with comorbidities such as renal failure and diabetes, along with the respiratory droplet route of transmission, created a global concern. The clinical manifestations of MERS-CoV infection range from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome, septic shock, and multiorgan failure.

By the end of 2019, the world was starting to hear of an acute respiratory syndrome outbreak in China. The symptoms varied from asymptomatic infections to fever, cough, breathing difficulties, headache, pneumonia, and diarrhea. This outbreak put the world on high alert, shifting academic efforts to understand the microbe, how to treat and specifically, how to avoid getting infected by it. A year has passed by and we made great improvements, developed vaccines, understood the microbe, its pathogenesis and how to avoid it. However, in this meantime we lost over 2.58 million lives and still have a lot more to understand about it.
3.2 THE VIRUS ITSELF

The coronaviruses (CoVs) are a family of enveloped positive-stranded RNA viruses that infect birds and mammals in the intestinal and respiratory systems, causing even hepatitis and neurologic illness.\(^\text{10,11}\)

Previously to the SARS-CoV-2 outbreak, CoVs have been the causative agent of two large-scale pandemics in the past two decades: 1) SARS in 2002 and 2003 in the Asian-Pacific region; and 2) MERS in 2012 in Middle Eastern countries.\(^\text{5,6,8,12,13}\) After these two pandemic events researchers pointed out that this family could be the cause of a new outbreak. The researchers advert that: 1) the CoVs could undergo genetic recombination, which could lead to new genotypes; 2) the presence of a large reservoir of SARS-related coronaviruses (SARSr-CoVs) in horseshoe bats in China could be a source of this genome recombination; and 3) some bat SARSr-CoVs have the potential to infect humans.\(^\text{13}\)

### 3.2.1 Classification

The CoVs were previously classified based on their structural protein spike (S) glycoprotein, however this classification changed to comparative sequence analysis of replicative proteins. SARS-CoV-2 is the seventh coronavirus known to infect humans. SARS-CoV, MERS-CoV and SARS-CoV-2, all β-CoVs, can cause severe respiratory disease in humans and caused a massive outbreak during their time. The other four human CoVs, α-CoVs HCoV-NL63 and HCoV-229E, and β-CoVs HCoV-OC43 and HCoV-HKU1, are known to cause mild respiratory symptoms.\(^\text{11,13,14}\)

### 3.2.2 Structure and Mechanism

The coronavirus genome encodes four to five structural proteins: envelope (E), membrane (M), spike (S), nucleocapsid (N) and hemagglutinin-esterase (HE). Trimers of the S protein make the peculiar spike structure on the virus surface.\(^\text{13}\) This trimeric S protein is a class I fusion protein that facilitates the receptor attachment.\(^\text{15}\) Thus, it is known that the spike glycoprotein from CoVs forms homodimers protruding from the viral surface and that mediate the entry of the virus into the host cells.\(^\text{16}\) Furthermore, it constitutes the main target of neutralizing antibodies after infection and hence, the focus of vaccine designing.

The viral genome is protected within the nucleocapsid. The nucleocapsid is helical in shape when relaxed and spherical when inside the virus. The coronavirus RNA
replicates in the cytoplasm of the host cell. The RNA polymerase attached itself to the primer sequence of the viral genomic RNA, and in the event of repeated attachment and detachment, a nested set of mRNAs are generated with common 3' ends.\textsuperscript{13}

The SARS-CoV-2 uses the same host receptor, angiotensin-converting enzyme 2 (ACE2), used by SARS-CoV. ACE2 is a metalloprotease expressed in the cells of the heart, lung, testis, intestine, liver, kidney, vascular endothelium, and intestine.\textsuperscript{11} In addition, the SARS-CoV-2 seems to have a receptor binding domain that binds with high affinity to ACE2 from humans and other species with high receptor homology. Six amino acids present in the receptor binding domain of the spike protein are essential for binding to host ACE2 receptors.\textsuperscript{17} Even though SARS-CoV and SARS-CoV-2 are similar, five of these six amino acids differ between them.\textsuperscript{18}

Furthermore, it is important to stress that adipocytes and adipocyte-like cells, such as pulmonary lipofibroblasts, may play an important role in the pathogenic response to COVID-19, especially in obese and diabetic individuals. It is known that obese individual has an increase of ACE2 which turns adipose tissue into a potential target and viral reservoir.\textsuperscript{19} ACE2 expression is upregulated by 8 genes and downregulated by one gene, TRIB3, which is upregulated by Irisin.\textsuperscript{19,20} Irisin is a molecule released during exercises and it is less available in obese and sedentary patients.\textsuperscript{19}

3.3 MECHANISMS OF VIRAL INVASION AND REPLICATION

3.3.1 Pathogeny of the virus

The pathogenesis of the beta-coronavirus relies on four main proteins: the S, E, N and M.\textsuperscript{21} The S protein is composed of two subunits: S1, which is responsible for binding to the human host cell, and S2, important to the protease cleavage and virus activation and penetration into the host cell.\textsuperscript{22} The invasion consists of five steps: attachment, penetration, biosynthesis, maturation, and release. The occurrence of these events is essential for the replication of SARS-CoV-2 and aggression to human tissue.\textsuperscript{23}

Firstly, the S1 subunit binds to the ACE-2. Then, the spike protein undergoes protease cleavage at the S1/S2 site, which activates this protein and allows membrane fusion and conformational changes in the host cell.\textsuperscript{22,23} The protease cleavage is mediated mostly by the type II transmembrane serine protease (TMPRSS2), along with other possible proteases, such as furin protease and cathepsin B/L.\textsuperscript{21,24}

After recognition, the viral envelope merges with the host's cytoplasmic membrane, allowing it to enter the cell's cytosol. It is possible that, like SARS-CoV,
SARS-CoV-2 can also be endocited by the target cell. Once in the endosome, it goes to the cytoplasm and releases the single-stranded viral RNA with positive direction, allowing the production of polyproteins and protein structures, which initiates the viral replication process.\(^2^5\)

Viral particles are transported, joining the endoplasmic reticulum, and forwarded to the Golgi complex through the intermediate RE-Golgi compartment. Finally, vesicles containing the viral particles fuse with the cytoplasmic membrane, promoting budding release. This replication process occurs with greater intensity in type I and II respiratory epithelial cells, which are in the lower respiratory tract and present a large amount of ACE2 on the cell surface.\(^2^5\)

Considering the pathophysiology described, the tissue aggression and symptomatology depends on the ACE-2 expression on the human body. This receptor is highly expressed on lung type II alveolar cells, enterocytes of the small intestine, endothelial cells and nasal neuroepithelium.\(^2^1,2^6\) The presence of this receptor in specific cells increases the likeliness of damage on organs.\(^2^1\)

Furthermore, since SARS-CoV-2 requires priming by the TMPRSS2, the expression of this protease increases the viral capacity of damage on determined tissues. It has been shown that this protease is considerably expressed in lung cells, along with intestine cells, especially the small intestine. In addition to the TMPRSS2, the furins and cathepsins B/L were also shown in lung cells, and they could ease the viral penetration by spike protein cleavage. On the other hand, it was noticed low levels of TMPRSS2 in the heart ventricular cells, which brings uncertainty to the myocarditis injury due to SARS-CoV-2.\(^2^7\)

3.3.2 Dissemination by hematogenous route

The new viral particles can then invade the bloodstream, providing peak viremia and hematogenous spread. SARS-CoV-2 can, at this time, infect several other tissues of the host, such as liver, kidney, heart, striated muscle, endocrine glands, and any other cell that has the presence of ACE2 on its surface. However, the pathological consequences provoked in these organs are still unknown.\(^2^8\)

3.4 INNATE, CELLULAR, AND HUMORAL IMMUNITY AGAINST SARS-COV-2

The innate immunity appears to play a central role in the defense against SARS-CoV-2.\(^2^9,3^0\) Recognition of the viral molecular pattern is done through standard
recognition receptors, such as Toll-like (TLR), RIG-I-like, NOD-like (NLR) receptors, among others. Depending on the stimulated receptor, different biological responses of the host are developed. The recognition of viral antigens by TLRs, except for TLR-3, is dependent on the Toll-MyD88 pathway, leading to signal transduction that involves the activation of the NF-κB transcription factor. On the other hand, the activation of the TLR-3 pathway by the TRIF adapter molecule induces the production of type I interferon, which limits viral replication and increases phagocytosis by macrophages and cytotoxic activity by NK cells.29

However, regardless of the activation pathway, recognition culminates in the production of pro-inflammatory cytokines and chemical mediators, with the aim of providing an effective antiviral response. Different cells, monocytes, macrophages, lymphocytes, and neutrophils, migrate to the pulmonary epithelium, to contain SARS-CoV-2. When this attempt to limit an infection is exacerbated, there are non-specific oxidative and inflammatory effects that result in secondary damage to the infected and uninfected tissues.25,31

In acquired immunity, it is observed that, after the virus enters the target cell, viral peptides are presented by the main histocompatibility complex (MHC) class I to CD8⁺ T lymphocytes, which perform their function cytotoxic, leading to cell death by apoptosis of the infected cell. The presentation of viral antigens can also be mediated by antigen presenting cells by means of MHC class II molecules, promoting the activation of CD4⁺ T cells (cross presentation). This will result in the production and release of interleukin-12 (IL-12), a cytokine that will co-stimulate the production of lymphocytes with a Th1 profile.32,33

The IL-12, in addition with IFN-α, increases the expression of MHC class I and the activation of Natural Killer (NK) cells, which allows the action of antiviral mechanisms and the eradication of cells infected by SARS-CoV-2. However, even if the individual develops an immune response against SARS-CoV-2, we see that, in some cases, patients quickly evolve to more vulnerable stages.31

3.4.1 Covid-19 cytokine storm

It has been reported that a cytokine storm is associated with many infectious diseases, SARS and MERS.32,33 The cellular entry of SARS-CoV-2 depends on the binding of the S proteins that cover the surface of the virion to the cellular ACE2 receptor
and to the S protein. After entering the respiratory epithelial cells, SARS-CoV-2 elicits an immune response with the production of inflammatory cytokines.\textsuperscript{34,35}

Pathogenic Th1 cells and CD14 + and CD16 + monocytes are mediated by receptors that activate signaling pathways. This is followed by the infiltration of macrophages and neutrophils into the lung tissue, which results in a cytokine storm.\textsuperscript{34,36} Particularly, SARS-CoV-2 can rapidly activate Th1 cells to secrete pro-inflammatory cytokines, as a stimulating factor for granulocyte-macrophage colonies (GM-CSF) and interleukin-6 (IL-6).\textsuperscript{34,35} GM-CSF also activates the inflammatory monocytes CD14 + CD16 + to produce large amounts of IL-6, tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)) and other cytokines. The same study demonstrated that the cytokine storm in COVID-19 is mainly characterized by high expression of IL-6 and TNF-\(\alpha\).\textsuperscript{34}

\textbf{3.4.2 Mechanisms of the cytokine storm in COVID-19}

The mechanism of the cytokine storm is caused by the angiotensin 2 pathway. Studies have shown that levels of IL-1\(\beta\), IL-6, IL-8, IL-12, inducible protein 10 (IP-10), MCP-1 and IFN-\(\gamma\) are increased during SARS-CoV infection. In contrast, low levels of Th2 cytokine IL-4 were also observed.\textsuperscript{34}

Furthermore, it is known that severe COVID-19 patience’s express significantly decreases in lymphocyte counts (CD4 + cells and CD8 + cells), especially CD8 + T cells, but increases in neutrophil counts when compared to mild patients.\textsuperscript{34,36}

A study found that the levels of most cytokines, except IL-1, peaked after the nadir of respiratory function, indicating that cytokine expression may not be the primary cause of impaired respiratory function in patients with COVID-19. Dynamic cytokine storms and T-cell lymphopenia are associated with COVID-19 severity.\textsuperscript{35} These findings are of clinical importance for doctors today. After all, it is possible to identify patients at risk of developing severe COVID-19 as early as possible, by monitoring dynamic cytokine storms and NLR. Below, changes in the major cytokines induced by SARS-COV, MERS-COV, SARS-COV-2 are shown in Table 1 and the patterns of cytokine secretion based on the severity of COVID-19 are shown in Table 2.

<table>
<thead>
<tr>
<th>Virus</th>
<th>SARS-CoV</th>
<th>MERS-CoV</th>
<th>SARS-CoV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated cytokines</td>
<td>IL-18; IL-6; IL-8; IL-12; IP-10; MCP-1; IFN-γ</td>
<td>IL-15; IL-17; IFN-γ; TNF-α</td>
<td>IL-2; IL-4; IL-6; IL-7; IL-10; IP-10; G-SCF; MIP1A; IFN-γ; TNF-α</td>
</tr>
<tr>
<td>Downgraded cytokines</td>
<td>IL-4</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>COVID-19 status</th>
<th>Uninfected</th>
<th>Mild and moderate COVID-19 infection</th>
<th>Severe COVID-19 infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comum symptoms</td>
<td>No symptoms</td>
<td>Fever, myalgia, fatigue and dyspnea</td>
<td>Fever, myalgia, fatigue, dyspnea, ARDS or MOF</td>
</tr>
<tr>
<td>Cytokines patterns</td>
<td>No cytokines</td>
<td>Elevated IL-16, IL-10 and TNF-α</td>
<td>Elevated IL-1, IL-6, IL-10, TNF-α and MCP-1</td>
</tr>
</tbody>
</table>

3.4.3 The immune evasion

The nicotinic cholinergic system may also be related to immune evasion by SARS-CoV-2. The nAChR α7 receptor was highly expressed along with ACE2 receptors in the airway epithelial and may also bind to the virus’ spike protein. This receptor is relevant to the anti-inflammatory pathway from the cholinergic system since it is responsible for regulating pro-inflammatory cytokine production, such as TNF-α. The nAChR α7 receptor also participates in naive T cell differentiation into effector T cells. As a result, by binding to the nAChR α7 receptor agonist, the virus would act as an antagonist, impair an anti-inflammatory pathway, and favor the cytokine storm from COVID-19.

3.5 THE VIRAL REPLICATION

The infection is created by the interaction of the viral particle with specific proteins on the cell surface. After a genetic material of the virus is inserted into the host cell, a cell vesicle is formed, retaining the virus inside, starting its multiplication, occurring due to the replicase enzymes already existing in the incoming virus. Subsequently, to produce viral proteins, there is a participation of ribosomes connected to the endoplasmic reticulum in the presence of the Golgi complex. Sequentially, as RNA
+ molecules produced within endosomes are released, and viral protein synthesis takes place.\textsuperscript{39}

At the 5' end, the viral RNA translation will encode the ORF 1a and 1b proteins that will give rise to the polyproteins called pp1a and pp1b containing 16 NSP (16 non-structural proteins) 1-11 and 1-16, being cleaved into the individual NSP by papain-type proteases and 3CL-protease, forming a replicase-transcriptase complex, of paramount importance for genome transcription and translation, generating genomic and sub-genomic RNAs in the form of batch transcription. Other ORFs proteins, which are located at the 3 'end, will encode the structural proteins (E, N, M, and S). The E protein is responsible for the assembly and release of virions, the N protein for the formation of the viral N, the M protein for the formation of virions and the S protein that will be the receptor for adhesion and replication in host cells.\textsuperscript{3}

The RNA - molecule produced from the RNA + molecule will be the model for producing more RNA + molecules, which will compose the virus that invaded the cell. Once viral proteins are produced, virions are assembled by the inclusion of RNA + molecules in protein capsids. As they approach the cell plasma membrane, virions - with their capsids and protein spikes - are surrounded by a lipid bilayer, that opens at the end of the process and releases the viruses to the outside. It is important to understand that SARS-CoV-2 is released from the cell by budding and not by cell lysis.\textsuperscript{39}

3.6 THE ROLE OF THE IMMUNE RESPONSE IN WORSENING THE INFECTION

Antibodies, in addition to the ability to neutralize and provide other functions that protect the organism, can also interact with other components of the immune system, such as factors of the complement system, phagocytes and NK cells, thus causing an infection of the target cells and consequently worsening of diseases. We call this type of antibody-mediated response an antibody-dependent enhancement (ADE).\textsuperscript{40}

Regarding the disease caused by SARS-CoV-1, the virus-antibody complexes can amplify the inflammatory response, activating myeloid cells through the crystallizable fragment receptors.\textsuperscript{41}

Associated with this, there is also a greater uptake of macrophages by means of ADE, which can lead to an increase in the production of TNF and IL-6.\textsuperscript{42}

Thus, the importance of analyzing the occurrence of ADE in SARS-Cov-1 infection is highlighted.
3.7 PREVENTION OF THE INFECTION

In the face of new outbreaks of contagious diseases, the spread of information related to the importance of personal hygiene, hand sanitizing in particular, becomes more frequent. Thus, it is known that products with active ingredients containing molecules capable of acting on the membranes of microorganisms, causing their breakdown and inactivation, are used.

When talking about hygiene, alcohol appears as a product of expressive capacity to fight SARS-CoV-2. In biological terms, alcohols have a broad-spectrum action and can act on several microorganisms. Due to their chemical compositions, one of the explanations about the way in which alcohols act is related to the denaturation of proteins that make up the pathogens. In the fight against SARS-CoV-2, the intermolecular forces of alcohols act on the polypeptide chains of viruses shaping the proteins to form functional and active three-dimensional structures in the biological species to which they belong. Thus, the presence of alcohols can interfere in these interactions and break hydrogen bonds, for example.

Besides the use of alcohol and hygiene, it is also important to implement social distancing and the use of personal protective equipment (PPE) to halt the SARS-CoV-2 transmission. Firstly, it has been shown across studies that increased distance between people is associated with lower risk of infection. A minimum of 1 meter physical distance was considered an effective one to prevent onward transmission, while 2 meters may be even more effective. This was noticed not just in COVID-19, but also in other coronaviruses.

Furthermore, as mentioned previously, usage of PPE was also related to less coronaviruses’ infection. Masks and respirators, such as N95, were associated with reduced events of transmissions. In health-care settings, which may be considered a higher risk environment due to aerosol-generating procedures and greater incidence of COVID-19 patients, N95 respirator was still effective and relevant to reduce SARS-CoV-2 infection. Finally, eye protection was also associated with lower virus’ infection, and it may be relevant, especially in health-care settings.

Thus, the use of masks shall be remembered as an important way to decrease viral, and consequently it may impact the clinical symptoms and severity of the disease. Studies have shown that high viral load during the first infection and repeated exposure to virus especially in healthcare workers can be an important factor for severity of disease. In addition, the virus exposure may also influence lymphocyte responses.
infection may lead to appropriate effector T and B-cell response, neutralizing antibodies, and rapid viral clearance, high-dose exposure may cause severe disease and delayed viral clearance. This may be related to inefficient T and B-cell immunity, subsequently the cytokine storm and destructive tissue inflammation.45

It is important to understand that these measures prevent the spread of the virus and the infection itself, but do not help the immune system combat the virus and develop a memory. Therefore, we shall keep a community effort to develop vaccines. As of right now most of the COVID-19 vaccines are being developed with the protein subunit strategy, making the vaccines available, and safe, to immunosuppressed patients.46 In conclusion, behavioral changes, such as personal hygiene, and vaccination are efforts that are necessary to manage the COVID-19 pandemic, and they shall be used for years to come.

3.8 RISKS AND CONSEQUENCES IN THE COVID-19 PANDEMIC

As outlined throughout the year, the economic scenario for the global industry in 2020 was reduced. The latest report released recently by UNIDO indicated that global manufacturing production fell 4.1%.47 Industrialized countries were exposed to a new wave of contamination by COVID-19 from October of 2020, which changed dynamism and remained below the production average at the end of 2019, evidencing of the vulnerability of the industrial sector in relation to the evolution of the pandemic.

The World Economic Forum (WEF) Global Risk Report analyzed the risks and consequences of the COVID-19 pandemic.48 Emphasizing the increase in inequalities in terms of access to health, technology, and employment opportunities. In addition to the fragmentation of society, amplified by the dynamics of the COVID-19 pandemic.

Among the immediate threats, most likely in the next two years, are social risks (such as illness, unemployment, etc.), but also risks of cybersecurity failures, digital inequality, prolonged economic stagnation, terrorist attacks and man-made environmental damage.48,49

From a 3 to 5 year perspective, economic risks are prevalent. They include price instability, commodity shocks and debt crises. In addition to geopolitical risks, including around natural resources.49

In the horizon of 5 to 10 years, environmental risks predominate, such as loss of biodiversity, natural resource crises and failure of climate action, associated with
geopolitical risks. Along with this scenario, there is the possibility of adverse effects on technology.49

It cannot be denied that the acceleration of the fourth industrial revolution was one of the effects of the COVID-19 pandemic, expanding the digitalization of human interaction, e-commerce, online education, and remote work. These changes promise enormous benefits, but the WEF points out that they can also accentuate digital inequalities, ruining the prospects for a comprehensive recovery.

Failure to tackle economic inequalities and the division of society can further paralyze actions on climate change, which constitute an existential threat to humanity.47 However, in the WEF assessment, if environmental risks are not addressed in the short term, environmental degradation will intersect with social fragmentation, causing drastic consequences.

3.9 HOW TO AVOID NEW PANDEMICS OUTBREAKS

Transmission of a virus is also related to the food products, in a way that viruses can contaminate an extensive variety of that and can last contagious until four weeks. Several viruses are transmitted by foods, Norovirus and hepatitis A are examples of that.50,51

Moreover, there are other viruses, such as, Rotavirus, enterovirus, sapovirus, astrovirus, adenovirus and hepatitis E virus that can be passed on to humans from contaminated food or water.52 CoV is a zoonotic disease, which means it may be transmitted from animals to humans. It is not just in bats that the CoV has been recognized. Several other animals can transmit the virus to humans, such as cattle, cats, rats, chickens, swine, dogs, rabbits, turkeys and horses. These animals may origin respiratory tract and gastrointestinal diseases.53

China has been known as a country that consumes wild and exotic animals, such as bats, marmots, pheasants, dogs, among other species.53,54 Moreover, this country is the most populous in the whole world.54 One of its cultures is slaughtering wild animals because they are considered more nutritious. The habit to not just consume wild and exotic animals, but keep them, alive or dead, near, contact or cross-contamination is simply easier to occur and by consequence, that can spread the virus. Furthermore, the quality and cleanliness of the seafood tanks, body fluid of live and dead animals or insufficient air quality conditions may disseminate the transmission of SARS-CoV-2 to humans53.
As shown by the WHO-convened Global Study of Origins of SARS-CoV-2: China Part, wildlife bats studied did not find SARS-CoV-2 infection, nor colonization. Whereas 7% of the bats tested in the Huanan market were positive for SARS-CoV-2 contamination.⁵⁵ Therefore, the existence of the virus is directly associated with the Homo sapiens interaction with the environment. Thus, WHO implied that a key point in the prevention and management of cross-species transmission is the control of environmental factors and being aware of possible mutations in places where the environment and society collides.

With that in mind some articles have pointed out that the monitoring of the environment is a multiprofissional task, demanding a collective and real time effort. This is already being done in East Africa, specifically Kenya, where the El niño phenomenon is observed, hence when this phenomenon is active the cases of Rift Valley Fever elevate, giving more time for the government to take actions; and in Guinea and Congo, where they use EBO-SURSY and EbOHealth projects to foresee new possible outbreaks.⁵⁶ These observational programs may have government influence, but they can be useful not only for the country itself, but also to his neighbors. It is clear these projects have a cost and maintenance, therefore it is important to abandon socioeconomics and geopolitical deadlocks to have a cooperative effort, investment and maintenance.

One of the challenges that need to be worked on to reduce the risk of food contamination is the possibility that products or packing can also contain the SARS-CoV-2. So, food contamination with pathogenic microorganisms needs to be studied and addressed. ⁵⁰,⁵⁴ This issue must be attended to because studies have found that the viruses can survive on the surfaces, such as food packages or on surfaces that have been in contact with contaminated food, so this hazard should also be considered for the COVID-19. This risk has been already outlined by the EU Commission.⁵⁷

When it comes to non-developed countries, the consumption of animals, particularly exotic and wild ones, should be tested to eliminate the rapid spread of COVID-19. The U.S. Food and Drugs Administration suggests that cleaning, separating, cooking, and freezing can be addressed to lower the risk of contamination. Another proposal is to consume more canned and packaged foods, at least when the chance to get an infection is likely to occur, rather than noncanned and unpacked foods. Furthermore, even canned, and packed products should be boiled.⁵⁷
Therefore, the COVID-19 outbreak has spread worldwide, but precautions related to the food industry must be taken at the international level. The outcomes of these precautions should be disseminated globally.

4 CONCLUSION

In our study we observed that SARS-CoV-2 can alter the host’s immune response, in addition to also causing systemic repercussions. CoV immunology is considered complex and, above all, versatile, because in addition to the damage caused, it can stimulate autoimmunity against the host is also observed.

Thus, attention is drawn to the need to prevent this pathology. The analysis of prevention methods already shows the effectiveness of social distance, avoiding the crowding of people, in addition to encouraging the use of masks. Furthermore, the emergence of the coronavirus can be explained by considering the cultural habit of the Asian population and the interaction of Homo sapiens with the environment. With that in mind, it is important to see culture and environment management as key points to avoid new pandemics.
REFERENCES


