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SARS-CoV-2-2019: emergence of a pandemic

SARS-CoV-2-2019: emergência de uma pandemia

Enio Roberto Pietra Pedroso[1]

ABSTRACT

The pandemic associated with the emergence of the SARS-CoV-2 represents a challenge imposed on human beings and their society, on a planetary basis, with repercussions yet to be determined at all levels of the biopsychosocial cultural-spiritual relationship. It represents one of the most serious challenges humankind has ever experienced, and signals the occurrence of other emergencies and reemergence's of diseases, in similar and episodic situations, which express human vulnerability and weightlessness, and requires reflection on self-knowledge and respect for limits of their dignity. This review is an effort to summarize in a simple and practical way the amount of significant aspects to the knowledge that is presented in an overwhelming way that accompanies the virology, epidemiology, clinic, diagnosis, therapy, and prevention of the disease by the SARS-CoV-2, so that its approach can be understood and facilitated.

Keywords: SARS-CoV-2; Pandemic; COVID-2019; Respiratory Disease.

RESUMO

A pandemia associada à emergência do vírus corona-2-2019 associado à síndrome respiratória aguda grave (SARS-CoV-2) representa um desafio imposto ao ser humano e sua sociedade, de forma planetária, com repercussões ainda por serem determinadas em todos os níveis da relação biopsicossocial cultural-espiritual. Constitui-se em um dos desafios mais graves já vividos pela humanidade, e sinaliza para a ocorrência de outras emergências e reemergências de doenças, em situações similares e episódicas, e que expressam a vulnerabilidade e imponderabilidade humanas, e requer reflexão sobre o autoconhecimento e o respeito aos limites da sua dignidade e da natureza. Esta revisão constitui-se em esforço para resumir de forma simples e prática a quantidade de aspectos significativos ao conhecimento que se apresenta de forma avassaladora que acompanha a virologia, epidemiologia, clínica, diagnóstico, terapêutica e prevenção da doença pelo SARS-CoV-2, para que possa ser entendida e facilitada sua abordagem.

Palavras-chave: SARS-CoV-2; Pandemia; COVID-2019; Doença Respiratória.

[1] Professor Titular da Faculdade de Medicina da Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

Editor Associado Responsável:
José Maria Peixoto

Corresponding Author:
Enio Roberto Pietra Pedroso
E-mail: eniopietra@gmail.com

Institution:
Clínica Médica, Faculdade de Medicina, Universidade Federal de Minas Gerais. Belo Horizonte, Minas Gerais, Brazil.

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Introduction

Contemporaneity has been characterized by the trivialization and transience of human relationships, and the technocratization of their activities; as if humanity was reduced to technique, and only it could save people from the difficulty of facing the natural challenges of life. The difficulty of understanding the human journey, which needs to be learned from the human being, has caused disillusionment, inattention, difficulty in perceiving oneself, agony with the evolution of technology that presents new knowledge every 48 hours, without the opportunity to his reflection, and criticism of life. The result is the maladjustment in human relationships, the difficulty of transforming information into knowledge, combined with practice and training, which provides knowledge and balance, which become wisdom. The impetus is to respond to the how to do it, in a manichean way and not the why to do it. There is increasing risk and vulnerability, and even self-destruction, as seen in the occurrence of nearly a million people who commit suicide annually in the last decade around the world; and from one to three million clandestine abortions per year in Brazil.

At this moment in which we live with such affliction, in the midst of vulnerability, weightlessness, loss of autonomy, of the perception of finitude, there remains the challenge of being solidary, resigned, active in defense of everyone's life; the perception of the grace of being alive jumps, the immense influence on the health of social goods such as education, freedom of expression, decent work, social security, housing, respect and dignity for dissimilarities, and social equality. It is evident how well-being depends on the contribution of all people. The basis for this, including that related to formal education or not, is self-knowledge, as a continuous search to understand oneself as a person and as a fellow human being, in knowing one's own limits, living with respect and dignity for oneself, for the other, for the nature, to life, to exercise compassion worthily. Health is the greatest asset that the living being has.

The destiny of Brazil, of the world, of the human being; it depends on the interruption of ignorance, misery, the uncritical absorption of information that is not translated into knowledge and knowledge; capital appreciation, to the detriment of the person. Social equality with the assets that the seven largest economies have, requires four planet Earths! Only solidarity leads to dignity, respect and care for life, citizenship, harmony with nature, solidarity that enhances affection and distributes renewable social goods with equanimity, a dignified and pleasant life, social justice and peace. This is the learning that the SARS-CoV-2 is showing.

Methods

A literature search was carried out in the PubMed database between 1/1/2020 to 6/6/2022, in English, of epidemiological, virological, clinical, diagnostic, therapeutic, prevention and prophylaxis data on the pandemic infection determined by SARS-CoV-2 through the keywords: SARS-CoV-2, pandemic, COVID-19, respiratory disease.

Articles with the largest number of cases among those associated with randomized clinical trials, meta-analyses and consensus guidelines were selected for inclusion in this trial, which resulted in 432 studies, restricted to 39 consensus guidelines, with the aim of making the subject of the largest medical publication of all times and of current impact on human existence, capable of helping to understand this challenge to which everyone is submitted.

Results and Discussion

There are several considerations that can be elaborated for the knowledge of the relationships between the SARS-CoV-2 and the human being, such as:

1. The coronavirus (CoVh) are found in humans and other mammals, such as dogs, cats, chickens, cattle, pigs, and birds, and can cause respiratory, gastrointestinal, and neurological problems. The most common types are 229E, OC43, NL63, and HKU1, and they cause symptoms similar to a cold in immunocompetent people[1,2];
2. This is the third time, in the last 20 years, that CoVh was responsible for serious human disease[1,2]. In previous times, CoVh-1 was associated with SARS and Middle East respiratory syndrome;
3. In 2019, emerged, through mutations or recombinations of its nucleic acid (as occurred with the influenza virus in 2009, which recombined parts of human, avian and porcine viruses, in Mexico, and became in H1N1-pdm-2009). RNA-based viruses (such as CoVh) tend to carry 100 times more mutations than DNA-containing viruses (which helps to understand why influenza immunization should be frequent, usually annually). This perspective of nucleic acid recombination made it more infective (able to spread) and to penetrate human cells through specific receptors, one of them associated with angiotensin-converting enzyme 2 (ACE2) or non-specific, when compared to its counterpart CoVh-1;
4. Bats are believed to be the natural reservoir of SARS-CoV-2, but humans may have been infected through pangolin[3];
5. Like all viruses, CoVh is an obligate parasite, and it needs cellular structures for its reconstitution. Recombination and genetic variation allow CoVh to adapt and infect new hosts, either zoonotically or anthropozoontically. SARS-CoV-2 is, so far, not anthropophilic, but anthropozoonotic. It remains in its zoonotic habitat and is apparently adapted to all planetary ecosystems, therefore capable of new and varied cycles with anthropophilic possibilities and unpredictable mutations[3];

6. The SARS-CoV-2 has a diameter of 60 to 140nm and spicules (like a spike) on the surface of its capsid (S spike protein), which varies between 9 to 12nm, with a crown appearance, which gives the name corona. It is a positive single-stranded RNA virus (linear genome) over 30,000 bases long, enveloped, incapable of accumulating frequent mutations, and very similar to SARS-CoV-1, and may make it more genetically stable[3,4];
7. Its transmission takes place through droplets expelled during conversation, coughing, sneezing, screaming, and aerosols. Exposure can occur in the presence of asymptomatic contacts located at a distance of up to 1.5 to 2m, for a prolonged period (at least for 15 minutes), or for a shorter time if they are symptomatic (cough)[3,4]. It is possible to spread through the surface of objects[3,4]. It is estimated that 48% to 62% of transmission occurs through pre-symptomatic carriers[3-5]. Its transmission speed occurs from one person to another or for more than 10; depending on the probability of their contacts (explained more than a millennium ago by the miasmatic theory). Its transmission period varies from 3 to 5 to 10 to 14 days, but the virus can persist in the oropharynx and feces for up to 50 days[4]. Vertical transmission can occur and, with few cases described, the associated changes are of mild intensity and the virus is not found in breast milk[4];
8. Protein S is its main key to penetrating host cells, as it binds with affinity to their ACE2 receptors. This binding enables two proteases, furin and serine membrane protease type 2 (TMPRLRS), to cleave the S protein, which allows the fusion of the viral capsid to the cell membrane and then the insertion of its RNA into the cells of the upper and lower airways, and the order to produce viral proteins, causing cell death, release of millions of new viruses that infect other cells, and other people. There is no evidence that drugs that act on the ACE2 receptor (hypotensives) alter its penetration process[1,2,4];
9. SARS-CoV-2, like any virus, can acquire, during its replication, mutations that are different from its origin, and that modify it, constituting a lineage that is now called a variant. The variants, despite appearing in the most diverse places in the world, have similarities in their behavior, suggesting some evolutionary convergence. The risks that accompany them are associated with reduced vaccine susceptibility, increased infectivity (spreading) and pathogenicity (disease and its severity). That is why genomic analysis is necessary so that they are identified early and analyzed in their epidemiological, clinical, therapeutic behavior, and in relation to the vaccine response. Several variants considered of human interest (variants of concern) have been identified so far, such as: Alpha (formerly B.1.1.7); Beta (formerly B.1351); Gamma (former P.1); Delta (formerly B.1.617.2); and Omicron (BA.1 and its subvariant BA.2); initially identified in the UK in September 2020; in South Africa in December 2020; in Brazil in December 2020; Delta (formerly B.1.617.2), in India, in October 2020; and Ômicron, in southern Africa by the end of 2020; whose importance stems from being more transmissible, able to escape acquired immunity (via vaccine or natural infection), or pathogenic, respectively. Alpha was the first variant with 22 mutations in all, the most important being N501Y, which enhances the link between the virus and human cells. Its transmissibility is between 30 and 50% higher than that of previous strains, with an increased risk of hospitalization and higher mortality. Its sensitivity to vaccines is equal to the original strain. It was responsible for the second wave of the pandemic in the UK, much of Europe and the US. The Beta has alterations in common with Alpha (N501Y) and two others, at the tip of the spike (K417N) that stimulates its binding in human cells, and E484K, which can help the virus escape antibodies. It is less transmissible than Alpha, and its possible association with increased mortality in hospitalized patients and the escape of the immune response, which can favor reinfection and alter the action of available immunizers, is worrying, however, the Ad26.COV 2.5 vaccines from Janssen and Comirnaty of Pfizer continue to guard against this variant in its ability to cause severe and moderate cases. Its spread reached the United States, Canada and 58 other countries. Gamma is very similar to Beta, with the same main mutations in the virus spike. It is more transmissible, spreading rapidly across Brazil, with serious repercussions between March and April 2021, with an attack rate (how many people does a sick individual infect) similar to Alpha, between 1.6 and 1.4, compared to 0.8 of the original lineage. It may escape antibodies acquired in previous contacts with other viral lineages, and may be associated with reinfection. It may be more pathogenic and increase the risk of hospitalization. It is likely to be responsible for nine out of 10 cases, and about 70% of deaths, in Brazil. The immunity obtained by the immunizers Coronavac, Covishield (AstraZeneca), and Comirnaty (Pfizer) is maintained against the Gamma variant. Delta has more than 12 mutations, of particular concern are E484Q, similar to those seen in Beta and Gamma variants, and L452R, which can help the virus evade antibodies. It appears to be the most contagious of all the variants, estimated to be between 40 and 60% more transmissible than Alfa, and capable of causing outbreaks where Alpha was predominant, with a possible higher risk of hospitalizations.

The protection achieved for this variant by the immunizers from Pfizer (96%) and AstraZeneca (92%) is maintained after the administration of two doses of the vaccines. Ômicron did not develop from any of the more common variants, as it does not have mutations similar to Alpha, Beta, Gamma or Delta. Its epidemiological and clinical role is yet to be determined. The BA.2 suvariant is 1.5 times more contagious than the original strain. It has four sublines: BA.1 (original), BA.1.1, BA.2 and BA.3, with no evidence that it is more severe than the BA.1 lineage[5-11];

10. Epidemiological methodology makes it possible to understand the dynamics of all diseases, especially infectious ones; and, the proper use of the concept of Rt guides the taking of several decisions, which can interfere with the defense and preservation of life[4]. Understanding Rt also requires understanding what R0 is, endemic, epidemic and pandemic. Endemic is the occurrence of the specified disease, in its expected number, in a given region, in a certain period of time, based on its occurrence in previous years, and may have seasonal variations in its usual behavior. The epidemic is the occurrence of the disease beyond the expected historical average (or median). In this case, the disease usually appears suddenly, and spreads for a certain time, and in a certain region, generally affecting a large number of people. A pandemic is an epidemic that spreads across several countries on different continents, as seen with the COVID-19. The concept of R0 is associated with the contagiousness of a microorganism. The infectious disease becomes endemic when, on average, each infected person infects another person (R0=1). The presence of a disease with R0 greater than 1 indicates that the number of infected people will be exponential, which will determine the epidemic. The presence of R0 less than 1 indicates extinction of the disease at that time. At a critical moment of the pandemic, R0 reached values about 3, that is, each person infects three, and so on, on an exponential scale. It is necessary to understand, during the course of an epidemic, how the R0 (static measure) evolves, more or less, depending on the measures adopted (dynamic measure). This measure of R0 over time is described as Rt (velocity of contagion). It is necessary to understand how this evolution can be changed. The result of the measures to control the COVID-19 may take at least two weeks (which is related to the transition from the incubation period to the state, the moment of its greatest spread). By the end of May 2022, approximately 540 million and 6.4 million people had become infected and died worldwide, respectively[4];
11. SARS-CoV-2 has special tropism for airway, endothelial, gastrointestinal, neurological, and myeloid cells. Therefore, its association with all cells of similar embryological origin can be predicted, which indicates the probability of affecting almost all tissues. Viral penetration overcomes all barriers constituted by mucus secreted by goblet cells, ciliary movement, mucous membranes, and innate immunity; and continues through the incubation period and disease state. The variability of the response to infection depends on the host (innate-genetic or acquired defense, age, habits, comorbidities), and on the viral load. Human immunological defense depends on innate cellular and humoral immunity, however, several microorganisms can subvert, block, or provide permissiveness to the agent or the association of pathogens, as occurs, for example, with *S. mansoni* and *Salmonella typhi*, the virus measles and *Staphylococcus*, hepatitis B and delta viruses, human immunodeficiency virus (HIV) and opportunistic agents, and probably the blockade by CoVh-1 on the action of interferon. Cytotoxic LTCD8 are of great importance in relation to antiviral resistance. In COVID-19, there seems to be exhaustion of LT, with lymphocytopenia, as in the acquired immunodeficiency syndrome (AIDS), and phenotypic shift to LTh[4-11], which is inadequate for suppression and acquisition of immunity[4,5]. Antibody production occurs up to 20 and 15 days after exposure to SARS-CoV-2, or the onset of symptoms, respectively[11]. IgA antibodies are found in blood and saliva and may play a key role in immunity. It is observed that, despite this cytotoxicity on LT, the development of immunological memory and resistance to reinfection occurs. About half of the world's population has the immunological capacity to face SARS-CoV-2, with CoVh genome domains capable of promoting cross-reaction between them being evidenced. This immunological reserve, probably related to the human being's previous encounters with CoVh, may explain, in part, the variability of infection rates observed in various regions of the planet. Cellular immunity against SARS-CoV-2 is observed in people who were infected with CoVh-1 in 2003, and present 17 years later; exceptional evidence of lasting protection for COVID-19. Cellular immunity against SARS-CoV-2 is observed in people who were infected with SARS-CoV-1 in 2003, and present 17 years later; exceptional evidence of lasting protection for COVID-19. Viral replication mainly destroys the cells of the bronchioloalveolar and gastrointestinal units, mediated by a great variability of the immune system reaction (such as cytokines) and which can aggravate the textural lesion[12,13].

ACE2 and TMPRSS2 are present, particularly in the type II alveolar epithelial cell II. The inflammatory response to the virus, innate or adaptive, humoral and cellular, alters lymphopoiesis and promotes lymphocytic apoptosis. It is observed, as with other respiratory viruses such as influenza, lymphocytopenia as a result of infection and destruction of TL. These phenomena determine a change in the integrity of the endothelial barrier as viral replication increases. The inflammatory process to which the pulmonary capillary endothelial cells are submitted accentuates the inflammatory response, with the recruitment of monocytes and neutrophils[6-8]. The result is the development of interstitial mononuclear inflammatory infiltrates and edema that are expressed in the imaging study as glass matte. Alveolar spaces are filled with formation of hyaline membrane, which causes acute respiratory failure in the initial phase[12-14]. The action of bradykinin determines the appearance of pulmonary angioedema, damage to the endothelial barrier, inability to perform hematosis. These phenomena are followed by activation and consumption of coagulation elements[12,14], with the triggering of disseminated intravascular coagulation being observed in 71% of patients who died[12-15]. Thrombotic phenomena can also determine deep venous and arterial thrombosis due to peripheral ischemia, ischemic stroke, acute myocardial infarction (AMI), pulmonary thromboembolism (PTE)[12-14]. The end result is the development of multiple organ failure (MOF). The human response to this aggression seems to be individual, aggravated by several special physiopathogenetic situations, and responsible for its high lethality (50%), and which are characterized by a continuous inflammatory basis, or affected by endogenous or exogenous modulations. This unpredictable variability of the inflammatory reaction plays a central role in its severity. The inflammatory response, determined by signals of viral infection and cell injury, such as inflammasomes and TLR, stimulates the production of myeloid cell-dependent inflammatory cytokines (IL-1; IL-6; chemokines), which are amplified by the action of macrophages and cytokines. inflammatory and that in a deleterious way are responsible for the most serious cellular and textural lesions, and, consequently, for MOF. These changes can range from benign, which can affect more than 85% of people; but, in the others, it is characterized by slough and thrombosis, more intense in pneumocytes I and II, with probability of determining total loss of ventilation-perfusion and bronchiolo-alveolar function, up to 50% of the time, in special populations, with recovery at the expense of hyperplasia of the endothelial or alveolar epithelium through giant cells, of the syncytial type, followed by collagen and interstitial infiltrate; and, at the same time, destruction of red blood cells, with removal of iron from their interior, similarly to what occurs in the hepatocyte associated with malignant malaria. Pulmonary fibrosis can be expected in its course, with unpredictable results, including progressive and sustained loss of hematosis. Thrombosis is associated with a state of intense inflammation, as in any pathophysiological process, with venous-arterial thromboembolic phenomena, as seen in septicemia, postoperative periods, neoplasms, autoimmunities[13]. The direct cytopathic action of the virus on the endothelium triggers vasculitis, a prothrombotic effect[14], and the development of lung and systemic microthrombi[13-15]. The human inflammatory response can also be so intense that it can block the ability to produce delayed memory for new viral attacks, and greatly reduce the population's ability to protect itself, reflecting on the risk of determining new attacks in people already infected previously, with new epidemiological waves, or exacerbated and pathologically still unpredictable responses, as seen in tetanus, diphtheria or dengue (with different species). The speed and intensity of the pathophysiological processes observed (initial viral load or repeated inoculations), and the dependence of the specificity of the human defense response, are determining factors of lethality/mortality/morbidity/disease incidence by SARS-CoV-2, therefore, also related to the host, which can be expected for single or repeated epidemiological attacks[15-20];

12. COVID-19 presents itself in a multifaceted way, from asymptomatic to extreme and lethal severity. It has an incubation period of 5.1 days (7 to 14 days or more), progression (hours), state (14 or more days), convalescence (few days), and complete recovery or interruption of its evolution by death of the host. The average time of onset of symptoms, after exposure to the virus, is 5 days and, in 97.5% of people, it occurs up to 11.5 days later[16,17]. In about 80 to 90% of patients, symptoms are mild or absent, however, in the others, it can lead to hospital admission. The prevalence of organ dysfunction varies from 3.4% to 15% of diagnosed cases[14]. The most common complaints are fever, dry cough and dyspnea, observed in 5% and 20% of outpatients and hospitalized patients, respectively. It is observed in hospitalized patients[15]: fever (70%-90%), dry cough (60%-86%), dyspnea (53%-80%), fatigue (38%), myalgia (15%-44%); nausea, vomiting or diarrhea (15%-39%), headache, weakness (25%), rhinorrhea (7%), anosmia or ageusia (3%).

The most common complications seen in hospitalized patients include[15]: pneumonia (75%); SARS (15%); acute liver injury characterized by elevation of aspartate/alanine and bilirubin enzymes (19%); elevation of troponin (7%-17%), acute heart failure (HF), dysrhythmias and myocarditis; venous and arterial thromboembolism (TE) (10%-25%); acute kidney injury (9%); neurological injuries, including altered consciousness (8%), acute cerebrovascular disease (CD) (3%); and shock (6%). Rare complications in critically ill patients include an acute inflammatory response with macrophage elevation and activation, with secondary hemophagocytic lymphohistiocytosis. Elderly people with comorbidities have a higher risk of lethal evolution, especially due to acute ventilatory failure and mechanical ventilation (MV), due to SARS and FOM[15];

13. The observation of very low blood oxygen saturation and absence of dyspnea sensation, named as "happy hypoxemia" is intriguing. Dyspnea is reported in only 19% of patients with SARS; and, 62% of those with severe disease; and 42% of intubated, ventilated, deceased; respectively, they did not have the sensation of dyspnea, but had tachycardia, tachypnea, and respiratory alkalosis. These data indicate a disconnection between the hypoxia state identified by the brain, expressed as a sensation of "shortness of breath". There are still no explanations for these anatomopathological correlations, but they may be associated with lesions in hypoxia afferent neuronal sensors, due to the direct viral effect on mitochondria or nerve fibers and the intense action of cytokines[16];
14. Recovery to the previous level of health occurs within 14-21 days in 65% of people who test positive for SARS-CoV-2. It can evolve, in about 10% of patients, after 21 days of its state period, in a prolonged manner (post-acute) or exceed more than 12 weeks (chronic), similar to infectious mononucleosis, CoVh-1 and Middle East respiratory syndrome. This evolution may result from: persistent viremia, recurrence, reinfection, inflammatory or immunological reactions, physical deconditioning or mental factors (post-traumatic stress). Prolonged symptoms result from alterations: a) general: feverish syndrome, exanthema (maculopapules, vesicles, hives), lack of control of underlying diseases (diabetes mellitus, HF, systemic arterial hypertension, bronchial asthma), malnutrition; b) cardiorespiratory: prolonged dyspnea, cough; sequelae of ET, myocarditis, pericarditis, AMI, arrhythmias; c) locomotor: asthenia, myalgia, sarcopenia; d) neuropsychiatric: changes in cognition, depression, delirium, headache, encephalitis sequelae, cranial neuropathies; e) gastrointestinal: diarrhea, dyspepsia. Recovery occurs, in most cases, spontaneously and slowly, based on general clinical support, family and psychological support, diet, exercise (including specific ventilation techniques), and symptoms. The basis for evaluating these patients is clinical surveillance, which does not always require additional tests. Care must be taken to exclude the presence of: anemia, fever, inflammation or chronic infection (elevated C-reactive protein, leukocytosis, elevated ferritin), cardiovascular alterations (troponin, D-dimer), pleuropulmonary alterations (chest teleradiography). Pulmonary rehabilitation is often needed to aid recovery[17];
15. The clinical-epidemiological basis of the diagnosis is constituted by the evaluation of the viral RNA, through tests that detect the virus, obtained through the collection with a swab (swab) in an oronasal or bronchoalveolar clinical specimen. The identification of the virus with high sensitivity and specificity is essential for epidemiological control (contact tracing, social isolation, identification of viral mutants/variants), diagnosis, cure, vaccine response, identification of blood donors and hyperimmune plasma. The tests available that can detect the virus are: a) RCP-RT (real time polymerase chain reaction): considered the gold standard for diagnosing COVID-19. This test identifies the presence of SARS-CoV-2 genetic material in a clinical specimen collected from the patient's naso-oropharynx. The ideal is to be performed in the first week of the onset of symptoms, preferably before the 12th day, when the viral load is higher, which means it is easier to detect your RNA. This exam, performed at the right time, has a reliability above 90%, and rarely presents a false positive result. The exam result is usually delivered within two days. The positive result of RT-CPR results in the determination of strategies, such as patient isolation, and therapeutic plan, and indication of the exam in symptomatic or asymptomatic contacts; b) POCT-PCR (point of care test for PCR): the clinical specimen is collected from nose and throat secretions using a cotton swab, in hospital laboratories, with the advantage that the results come out in minutes, which speeds up the clinical management in the hospital; c) genetic sequencing, Sanger: uses the sequencing methodology, without the need for reagents to extract the RNA from SARS-CoV-2, making it very practical and agile. It has the same accuracy as CPR-TR; d) Crispr (clustered regularly interspaced short palindromic repeats): consists of the technique of analyzing a set of regularly interspaced short palindromic repeats, and refers to a region of the genome characterized by the presence of short and repeated DNA sequences.

It is a gene editing technique, with an accuracy similar to RT-RCP, and requires about an hour to identify the RNA of the virus. Biological material is collected in the same way as RT-CPR. The tests available that can detect the presence of antibodies, identify who has had contact with SARS-CoV-2 or who has had the disease. It is performed in a blood sample, which must be collected after seven or 10 days from the onset of symptoms. Serological tests for COVID-19 detect the presence of antibodies of the IgA class, IgM (which appear earlier, generally around 10 days after infection) and IgG (after about 15 days). In COVID-19 these different types of antibodies appear at the same time (called synchronism). There are several technologies available, such as: a) enzyme immunoassay (ELISA): which reveals the presence of IgA and IgG; b) chemiluminescence (CLIA): it is based on the emission of light produced by chemical reactions and discriminates IgM (acute phase of the disease) and IgG (memory antibodies); c) electrochemiluminescence (ECLIA): identifies total antibodies without differentiating between them. Serological tests are less sensitive for the diagnosis of the disease when compared to RT-CPR, so it is not recommended for diagnosis. There is a greater risk of false negative results if they are performed early in the symptomatology, since the production of antibodies may not be sufficient to be detected. It can also cross-react with the presence of antibodies against other viruses, such as H1N1, and therefore false positive for COVID-19. They are useful tests, however, for the evaluation of previous exposure to the virus late after the onset of symptoms or in asymptomatic patients, which makes them useful for determining the degree of exposure of groups or populations, in epidemiological assessment, and helps in the decision on disease control measures. Results usually come out in two or three days; d) rapid tests (lateral flow immunochromatography test): its name is related to the fact that its result corresponds to a color change when the collected blood comes in contact with the reagent. The blood sample is obtained by puncturing the fingertip and placed by drop on an appropriate plate, which has a visual indication of the result. The reliability of the result is variable, and the false negative rate is high, with lower sensitivity. There is a risk of interpretation, that is, the person may have been exposed to the virus, but the result is negative, especially in populations with low prevalence. Its advantage is that it does not require equipment that can only be carried out in laboratories, and the results come out in a few minutes. health managers the most appropriate time to deactivate population isolation measures and reopen social activities. The control of the pandemic can be carried out with the substantial help of rapid tests for viral or antibody evaluation in the person with or without symptoms so that they can be quickly identified as a carrier of the virus and adequately isolated, in addition to detecting viral spread in a given location, to create strategies capable of containing the spread of COVID-19[20-27];

16. There are still no data that allow defining that a certain level of antibody is associated with protection against subsequent exposure to SARS-CoV-2[15]. The most common laboratory alterations among hospitalized patients are lymphocytopenia (83%); elevation of: erythrocyte sedimentation, C-reactive protein, ferritin, tumor necrosis factor α, IL-1, IL-6; and hemostasis (prolonged prothrombin time, thrombocytopenia, elevated D-dimer, hypofibrinemia)[16-29];
17. Imaging is a valuable diagnostic aid, revealing predominant pulmonary alterations in the lower lobe, peripheral, in ground glass, that is, ill-defined, with air bronchograms, interlobular or irregular septal thickening[17,18]. The first images obtained by computed tomography (CT) or chest teleradiography are approximately normal 15% or 40% of the time, respectively[22]. The rapid evolution of abnormalities may occur in the first two weeks after the onset of symptoms, and gradually disappear[29-32]. CT are nonspecific compared to other infections;
18. Therapeutic measures depend on the following observations: dietary requirements and water intake must be normal, until complications that require modification occur; more than 75% of hospitalized patients need supplemental oxygen therapy[24-29]; movement should be encouraged, even if the patient is in isolation, with mechanical measures to protect against edema and stasis in the lower limbs. The administration of Remdesivir (antiviral)[25] reduces the recovery time (discharge from hospital or not supplemented with oxygen) from 15 to 11 days, however it requires venous infusion, and is of little benefit. Administration of hyperimmune plasma does not reduce recovery time[24,25]; and methylprednisone (within 28 days of observation) and dexamethasone (6mg/day for up to 10 days) reduce the risk of death in patients with pneumonia and SARS[25-32], with greater benefit in the face of symptoms for more than seven days, and requiring MV; no benefit (and even the possibility of harm) is observed if used in patients with shorter duration of clinical manifestations and need for supplemental oxygen[2]. Low molecular weight heparin should be administered to all hospitalized patients,[24] and to those with increased D-dimer. In severe cases, therapy is essentially

based on basic and advanced life support. MV should be performed with protection of the lungs with a low tidal volume (4-8ml/kg, predicted body weight), and a plateau pressure of less than 30mmg/Hg[32]; in the prone position, brief positive expiratory pressure, and with neuromuscular blockade so that ventilation is facilitated by means of cisatracurium or other muscle relaxants. About 8% of hospitalized patients have bacterial or fungal co-infection, and up to 72% antibiotic therapy is broad-spectrum, including a potential prevalence of mycoplasmosis. The application of several measures are under evaluation, such as: antivirals (favipiravir), antibodies (convalescent plasma, hyperimmune immunoglobulins), statins, immunomodulatory therapies and with monoclonal antibodies (tocilizumab, sarilumab, anakinra, ruxolitinib, pioglitazone), and antifibrotics (inhibitors of tyrosine kinase)[31-34]. Some antiviral drugs were initially shown to be useful, such as: casirivimab/imdevimab (Roche-Regeneron) with a probable effect of reducing hospitalization and consequently deaths in the unvaccinated population, with no previous history of previous COVID-19, and with risk factors, with very low level of certainty in the evidence, with no data on safety and efficacy in previously vaccinated people; molnupiravir (Merck) an orally administered protease inhibitor that reduces hospitalizations by 30%, but is controversial in its potential risk of determining viral and human genetic modifications; paxlovid (PF-07321332, Pfizer) associated with ritonavir, viral protease inhibitors, administered orally, every 12 hours, for five days, to be started as soon as symptoms appear, with an 89% reduction in hospitalizations and deaths. There is no evidence that chloroquine, hydroxychloroquine, ivermectin are beneficial in mild (preventive) or severe cases; and requires validation of the use of hyperimmune plasma (as seen in hepatitis B virus, tetanus, snakebite)[34-39];

19. The most appropriate preventive measures are the same recommended for all airborne diseases (miasmatic theory), that is, care with respiratory secretions, hand hygiene, social isolation. The most successful strategies associated: efficient tests to detect the presence of the virus in all people, which identifies carriers and isolates them, and recognizes strains and their variation; adequate knowledge about the disease; and efficient quarantine (including travel bans, and crowding). These precautions allow: early identification of the virus in the naso-oropharynx, even before the onset of symptoms, which allows for quarantine, reduction of social movement and viral dissemination and genetic modification; training everyone for early identification of disease symptoms; health education, which enables awareness of the importance of personal distance, of at least 150cm, with greater distances, providing greater protection; the use of masks, N95 and surgical ones, which are more protective than cloth ones; hand washing, disinfection of living spaces. The most stringent measures, such as total social isolation, should only be used when all else fails[12,32,33];
20. There are disagreements about the best way to apply insulation, vertical or horizontal. In the vertical strategy, people considered at risk are isolated, such as: the elderly, or those with diabetes mellitus, overweight; comorbidities such as cardiorespiratory, autoimmune, auto-inflammatory, neoplastic, genetic diseases; or, under corticosteroid therapy, immunomodulation, antiblasts, radiotherapy. In the horizontal strategy, the measures are comprehensive for social isolation, restricting the mobility of all population groups, including the obligation of total quarantine, and even imposing fines and imprisonment in case of disobedience. Vertical isolation can increase the risk of significant contamination and death in regions, such as Brazil, where the availability of measures is limited: examination of all people, for early identification of the virus, in the upper airways and its recognition genetic; isolation of the infected, and provision of hygiene and cleaning products; and the need for daily work without isolation for the economic survival of families. Understanding the evolution of the epidemic is facilitated by the understanding of Rt depending on the prevention measures adopted. This parameter makes it possible to establish the speed of viral dissemination, the influence of the control measures instituted, which may take at least two weeks to express themselves (due to the incubation period of the virus), and allow the necessary adjustments for its control. The presence of 2% Rt for the Brazilian population of 200 million people means that about 4 million will be in a serious condition, in need of intensive care, and potentially dependent on 60,000 ventilators for use at the same time, which means the death of many without adequate care[11];
21. Active immunization is based on the knowledge of how the stimulation of human defenses against SARS-CoV-2 can be done, however, little is yet known, and it assumes that it can be carried out by the action of antibodies or activity of lymphocytes[34]. There are several immunizations available, either from: a) subunits of viral proteins, being used, in general, the S protein (Novavax, Anhui Zhifa Longcom and Chinese Academy of Medical Sciences);

b) viral genetic material the RNA that will instruct the formation of viral protein S covered by liposomes (Modera, Pfizer/BioNTech, Bayer/Curevac, Zydus Cadila); c) viral vector such as the adeno virus that carries part of the genetic material of the SARS-CoV-2 to the human body and that will give the human immune system the instructions to make the S protein that will activate the LB and LT (Oxford/AstraZeneca, CanSino, Sputnik, Johnson/Jansen); d) inactivated virus as in Influenza (Coronavac). It is also necessary to search for processes capable of preventing viral penetration into cells, avoiding inappropriate inflammatory response and thrombosis, excluding and preventing the participation of opportunistic agents, and replacing, when relevant, the function of main functional organs[5,27,37,39];

22. The case fatality rate varies markedly by age, from 0.3 to 304.9 deaths/1,000 cases, among patients aged 5 to 17 and 85 years or older, respectively. The lethality is up to 40% among those admitted to the Intensive Care Unit[2,10,14];
23. The repercussion of the infection on the population effectively determines effects on the health system, due to the number of patients affected simultaneously, with loss of their pulmonary functional capacity, need for MV, and occupation of hospital beds;
24. Infection by SARS-CoV-2 should be considered, from now on, in every patient with respiratory complaints, in which increased temperature, rhinorrhea, dyspnea are predominant complaints, being necessary in the entire system of elective or emergency health care, the performance of a differential complementary diagnostic panel, through RT-CPR, in the third to fifth initial days of symptoms, or the rapid test for the identification of IgM or IgG, after 10 to 14 days of its start;
25. The pandemic cannot neglect the various serious public health problems, such as: a) ecological changes, including those related to economic development and land use, with repercussions on agriculture, dams, change in water ecosystems, deforestation and reforestation, floods, droughts, hunger, inadequate eating habits, climate change, environmental pollution, which favors the expression of schistosomiasis, hemorrhagic fevers, leishmaniasis, arboviruses (dengue, yellow fever, sabiá, rocio, mayaro, oropouche, chikungunya, zika); b) demography, human behavior: disorderly population growth, migrations, wars and civil conflicts, deterioration of urban centers, population density, sexual behavior, use of illicit drugs through the venous route, which is associated with HIV, other sexually transmitted diseases (human papilloma), spread of dengue, resurgence of tuberculosis, violence, psychiatric disorders; c) international trade and travel, movement of goods and people, which are associated with: malaria, spread of vector mosquitoes, re-introduction of cholera and dengue, introduction of chikungunya and zika; influenza, corona, and arena viruses; d) industry and technology: the globalization of food supply, changes in its processing and packaging; organ and tissue transplants, use of immunosuppressants and antibiotics, including in foods, and the emergence of bovine encephalitis, hemolytic uremic syndrome (*E. coli*), transfusion diseases (hepatitis, Chagas), infection in immunosuppressed patients; d) evolution of microorganisms, with selective pressure and development of resistance: natural variations and viral mutations (HIV, influenza and corona) and bacteria (Brazilian purpuric fever caused by *H. influenzae*), resistance to antibiotics, antivirals, antimalarials, pesticides; e) collapse of public health measures: inadequate sanitation and vector control, cuts in disease prevention programs (cholera, dengue, diphtheria, chikungunya, zyka); f) economic model, which considers the person as a piece and not a subject-essence of development, which incites to greed, indelicacy, the search for a quick patrimony and a lot; exploitation of work, competition, loneliness, less affective capacity, stress, predatory action on the environment, malnutrition and overnutrition, unemployment, precarious housing conditions, urbanization, sanitation; g) industrialized foods, with control of the production chain of seeds, fertilizers, herbicides, insecticides, hormones, antibiotics, which is potentially associated with transgenics, production control, exploitation of land and water sources; h) predominance of domesticating, non-libertarian education; and health disconnected from biopsychosocial cultural and spiritual well-being, which is associated with: acritical society, limited in self-knowledge, discriminatory; unable to break through harassment, stigma, greed capital;
26. The safety of resuming activities after quarantine also requires the question: "Is it safe to reopen schools? Is any activity that includes people gathered and unknown safe?" Safety issues are fluid when they involve family members and acquaintances, subjectivism and emotion predominate and there are no statistics to resolve, the feeling of guilt for having allowed the risk predominates. Complete security does not exist in any situation, not even at home. Many people die from a fall from their own height without any noticeable provoking factor, in their own home.

The risk of contracting infectious disease, or of trauma and physical or psychological violence are common, whether controlled or not, in schools, markets, pharmacies, and other places. It depends on the priority and essentiality given to the activity; and if it is not yours, it will be someone else's. Schools, especially "Home School", constitute a special phenomenon, conferring discrimination on social categories lacking learning resources and families less apt in terms of equipment and necessary skills. In everything is the widening of inequalities, in the short and long term, of what is established and in the future. It is therefore a complex risk assessment. The decision, therefore, depends on science, but also on the sensitivity that interprets risks and advances in challenges, even if they are unpredictable[31].

Conclusion

The cost that the pandemic is imposing on human beings and their society, whether of lives, the economy and social organization, requires broad reflection from the whole of society. Does the value of the economy (which is human, but values some human lives more) outweigh that of human life in general? Isn't it time for economic development agencies to sustain life, without the intermediation of market logic, so that life can be recomposed? The Spanish flu followed with the Great Depression, and the Second World War. Will the war declared by Russia on Ukraine, with the participation of the European Community and the United States, promote a new global geopolitical and economic-financial revolution?

It is evident and astonishing that no country, however dominant it may be, is prepared to face such a challenge, be it the organization of health services, political-ideological, economic-financial integration. Imponderability invites solidarity as the only form of a better world perspective and signals that there will be no human possibility without thinking about the world in a broad, interactive way, with common perspectives of actions for the protection of life and nature. It is evident how the role of education, research, freedom of criticism and creation, solidarity and compassion, continue to underpin the meaning of human existence. The Unified Health System showed what it came to, in all its social importance, even with its underfunding and spasmodic risks of privatization. It was not necessary for any extraterrestrial to show the human being how much he needs to be supportive.

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