Covid-19 pandemic: all possible effective solutions to eradicate the problem. Cross-sectional analysis of clinical, socioeconomic, political and psychological profiles

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Abstract

The present work of analysis and research prepares, starting from the biological, clinical, socio-economic and political analysis, an effective intervention plan to eradicate the pandemic problem and its direct and indirect consequences. Passing through the analysis of the therapies and treatments suggested and recommended in case of Covid-19 symptomatology, it is then suggested an integrative clinical plan according to individual needs, to finally focus on the need for socio-economic-political intervention at the community and international level, with direct and immediate effectiveness, with the preparation of a single world currency valid for the pandemic period, a plan for total homestay functional to prevent the spread of infections and a common clinical protocol, suggesting greater attention to the hypothesis of biological therapy and convalescent plasma, waiting for a monotherapy and/or pharmacological more aware and less negatively impacting on the right to individual health than the gene therapies/vaccines of which we do not know yet the medium and long term effects on human health. We analyze the individual critical issues related to vaccine/gene therapy that at the current state of the science: a) have effectiveness that is still lower than natural immunization and does not provide a lasting coverage over time, if not to the extent of 6-9 months to be repeated virtually annually like seasonal flu vaccines; b) do not provide safe immunization over time concerning potential new reactivations and variants of the virus itself. It is no coincidence that we have seen new positivity in subjects already immunized or with the inoculation carried out; c) do not guarantee certain data concerning individual health, in the medium and long term, as well as we do not know the degree of toxicity of the same; d) does not exempt the citizen from the use of the disposable surgical mask, from the social distancing and the hygienic-sanitary rules provided. Based on the evidence found and waiting to do out the fate of the use of convalescent plasma therapy and/or the effectiveness of monoclonal therapy, the most effective drug therapy appears to be the combination of dexamethasone, hydroxychloroquine, heparin (if the D-dimer is high) or salicylic acid (if the D-dimer is not high and there is a modest thrombotic risk), and azithromycin; desirable, if compatible with the clinical picture, the supplements of vitamins A, B (group), C, D and E, in addition to the use of prebiotic supplements, probiotics, omega 3-6-9, coenzyme q10, flavonoids (such as quercetin), glucosamine and lactoferrin, from the earliest moments of the morbid condition, both in preventive and in management phase of the serious patient, in addition to the necessary oxygen therapy support if the clinical conditions require it.

Abbreviations

COVID-19: (CoronaVirus Disease 19); SARS-CoV-2: (Severe Acute Respiratory Syndrome Coronavirus-2); ACE2: Angiotensin–Converting Enzyme–2; ARDS: Respiratory Failure and Thrombophilia; IL: (Interleukin); GM-CSF: (Granulocyte-macrophage Colony-stimulating Factor); IP-10: (Interferon γ-inducible Protein 10); MCP-1: (Monocyte Chemoattractant Protein 1); MIP-1α: (Macrophage Inflammatory Protein 1-α); TNF-α: (Tumor Necrosis Factor-α); CRS: (Cytokine Release Syndrome); ARDS: (Acute Respiratory Distress Syndrome); CRP: (C-Reactive Protein); LDH: (Lactate Dehydrogenase); MERS-CoV: (Middle East Respiratory Syndrome - Coronavirus); PAMP: (Pathogen-Associated Molecular Patterns); DAMP: (Damage-Associated Molecular Patterns); HLA: (Human Leukocyte Antigens); WHO: (World Health Organization); RRT-PCR (real-time Reverse Po lymerase Chain Reaction); CLIA: (Chemiluminescence); ELISA: (Enzyme Linked Immunosorbent Assay).

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Introduction

COVID-19 (CoVoraVirus Disease 19), also known as SARS-CoV-2 acute respiratory disease, is an infectious respiratory disease caused by the virus called SARS-CoV-2 belonging to the Coronavirus family. The origin is still uncertain, but the most accepted hypothesis is that it is a new Coronavirus from an animal source (a zoonosis). Its ideal environment is at a temperature of 4°C and in confined spaces, with little air circulation and atmospheric circumstances particularly polluting. The virus is subject to continuous mutation, and at the current state of scientific information, it is not possible to determine whether its virulence will tend to decrease in a short time frame. Instead, it has been confirmed that SARS-CoV-2 can enter the human cell through the Angiotensin-Converting Enzyme 2 (ACE2), which is more abundant in the alveolar type II cells of the lungs; in fact, the virus uses a special surface glycoprotein called peplomerin (the spines that give it the characteristic shape of a sun crown) to connect to the ACE2 receptor and enter the host cell: the density of ACE2 in each tissue correlates with the severity of the disease in that tissue (not surprisingly, some studies focus on the activity of ACE2 to cause protective effects) [1].

The first cases were recorded in China in the last two months of 2019 and currently has an apparent lethality rate of around 3% (May 2021), although the final overall figure in the opinion of the writer is overestimated, as many deaths recorded as “Covid” did not take into account the distinction between death event caused by Covid” and “independent death event in a patient also affected by Covid” [2,3].

The incubation period is about 5 days (4-7 days), with the 95th percentile of 12.5 days; for this reason, 14 days has been chosen as the quarantine or isolation period in case of suspected infection. It is currently agreed that contagion occurs via airborne route, most often through respiratory droplets, although recent studies also confirm other routes, such as contact via body fluids and oro-faecal (although recent studies have found that released SARS-CoV-2 viruses are rapidly inactivated in the gastrointestinal tract and appear to be excreted primarily in a non-infectious state) [1,4,5].

Symptomatological profiles

During the incubation period, the latent infectious state may in itself be sufficient to infect, even if during that time there is not yet the appearance of symptoms, which may remain latent or flu-like (pseudosymptomatic form) in case of low positivity or asymptomatic clinical condition, such as fever, cough, headache, dyspnea, arthralgias, myalgias, asthenia, diarrhoea, anosmia and ageusia; only in 6% of recorded cases, there is a moderate and severe symptomatic manifestation, with risk of fatal complications (ARDS respiratory failure and thrombophillia). The virus generally affects the upper and lower respiratory tract but can cause symptoms and damages affecting all organs and apparatuses by ACE-2, especially in the gastrointestinal, endocrine, vascular, neurological, cardiovascular and dermatological ones; the correlation between COVID-19 infection and psychiatric symptoms is not yet explained, although it seems to be connected with intestinal dysbiosis and vascular problems. Not surprisingly, although SARS-CoV-2 has a tropism for respiratory tract epithelial cells expressing ACE2, patients with severe COVID-19 present symptoms of systemic hyperinflammation. Clinical laboratory findings of IL-2, IL-7, IL-6, Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF), interferon γ-inducible protein 10 (IP-10), Monocyte Chemoattractant Protein 1 (MCP-1), macrophage inflammatory protein-1α (MIP-1α), and Tumour Necrosis Factor-α (TNF-α) are indicative of a cytokine release syndrome (CRS) suggesting underlying immunopathology.

In addition, people with COVID-19 and Acute Respiratory Distress Syndrome (ARDS) have classic serum biomarkers of CRS, including elevated C-Reactive Protein (CRP), Lactate Dehydrogenase (LDH), D-dimer, and ferritin [1,6-8].

Compared to SARS-CoV and MERS-CoV, SARS-CoV-2 is less lethal but more contagious despite the latter presenting unique pathological features, namely Acute Respiratory Distress Syndrome (ARDS), Cytokine Release Syndrome (CRS) and lymphopenia despite excessive dominant inflammation of myeloid cells (correlated with COVID-19 severity). In fact, COVID-19 patients revealed the existence of the viral genome in immune cells suggesting that the immune system is a biological target of the virus showing a necessary pathogenic signature of immune dysregulation: normally a viral infection leads to a coordinated immune response, from immune activation by Pathogen-Associated Molecular Patterns (PAMP) and Damage-Associated Molecular Patterns (DAMP) along with activation of numerous cytokines and chemokines (in particular, it has been shown that in asymptomatic and mild after about 10 days patients reduce cytokine levels, while in severe patients there is an increase, thus clarifying the role of the inflammasome); in the case of SARS-CoV-2 infection and potential immunological asynchronies may result in aberrant hyper inflammation that is the cause of heavy infiltration of mononuclear cells in affected areas, including lung, heart and kidney, associated with cytokine storm and lymphopenia; antibodies in SARS-CoV have also been shown to be pathological by distorting macrophage responses, leading to fatal acute lung injury through severe hypercytokinemia. In addition, it has been noted that: neuropilin-1 potentiates SARS-CoV-2 infectivity suggesting the need for additional receptors to ACE-2 for SARS-CoV-2 cell entry; the high glycosylation profile of SARS-CoV-2 would provide a glycan mask to reduce viral immunogenicity; the greater extent of SARS-CoV-2 pathogenesis compared with SARS-CoV can be explained by the role of furin in cleaving the viral spike protein once the virus is inside the infected cell. Overall, therefore, SARS-CoV-2 reduces adaptive immunity by causing ineffective viral clearance along with failure to temper innate immune responses; indeed, patients infected with SARS-CoV-2 often lose antibody titers within weeks or months after recovery [9,10].

Genetically, research has pointed out that in 15% of severe forms of Covid-19 they have immunogenetic causes: the results suggest that there may be mutations in type I IFN-related...
genes in patients with COVID-19 pneumonia; furthermore, neutralizing IgG against IFN-α, IFN-γ and IFN type I were found (this would suggest that inborn errors of type I IFN immunity underlie COVID-19 pneumonia); yet, in another study, two alleles were identified, among the seven altered HLA susceptibility alleles (mutated alleles that could represent markers of disease susceptibility [9–13].

The mechanism of correlation between positivity, severity, and Covid-19 infection is not yet fully understood: however, several studies would show that patients in group 0 and Rh- (negative) have lower risks of being exposed to SARS-CoV-2 infection, but there are no correlations regarding the severity of the clinical condition [14–25].

Clinical laboratory and instrumental investigation profiles

Since the beginning of the pandemic state, there have been several diagnostic protocols approved by the WHO (World Health Organization), all aimed at carrying out a real-time reverse polymerase chain reaction (RT-PCR) test on biological samples (sputum and saliva), taken from the patient, with a result available in a few hours, or even through an antibody investigation (through the blood), waiting for the result of at least two non-consecutive samples but a few days apart (usually three, in case a negative result of the first test) [26].

Therefore to date, the tools used to diagnose the positive or negative state of COVID-19 are: [26].

a) “molecular swab test”: this is a molecular reverse transcription (rt) – Real–Time PCR investigation for the detection of the SARS-CoV-2 virus genome (RNA) in the biological sample; this method allows to identify in a highly specific and sensitive way one or more target genes of the virus present in the biological sample and to measure in real-time the initial concentration of the target sequence.

b) “The rapid antigenic test”: using nasal, laryngopharyngeal, salivary swab: unlike molecular tests, however, antigenic tests detect the presence of the virus not through its nucleic acid but its proteins (antigens). Unfortunately, to date, there are not enough published studies that, in the face of specific contexts and a large number of cases, provide indications on the sensitivity and specificity of these rapid tests in all situations. At present, the available data of the various tests for these parameters are those declared by the manufacturer: 70–86% for sensitivity and 95–97% for specificity.

c) “The serological test”: they detect exposure to the SARS-CoV-2 virus but are unable to confirm or not an infection in progress. For this, positivity requires a molecular swab test for confirmation. It is strongly recommended to use CLIA and/or ELISA type tests that have a specificity of not less than 95% and a sensitivity of not less than 90%, to reduce the number of false-positive and false-negative results. Below these thresholds, the reliability of the result obtained is not adequate for the purposes for which the tests are performed.

Individual clinical management profiles: treatments and therapies. Best practices

Since the beginning of the pandemic state, treatments and therapies have evolved considerably, based on clinical experience, recommendations, protocols and symptomatic manifestations, often different from country to country and sometimes even from different geographical regions of the same country. To clarify, in a systematic way, it is necessary to divide the hypotheses according to the level of severity, and therefore:

a) in the “asymptomatological” hypothesis, there are no particular indications, if not the obligation of quarantine (in the case of the accidental discovery of one’s positive state) up to the complete state of negativization [27].

b) in the hypothesis of “mild symptoms”, there are no particular indications other than maintaining the right hydration, rest, social isolation and the use of Paracetamol, 500 mg (2 times a day, for a maximum of 3–5 days) if the febrile state is between 38° C and 38.9° C, 1000 mg (twice a day, for a maximum of 3–7 days) if the febrile state is higher than 39° C, always taking care to report the symptoms, the values of body temperature, blood pressure and saturation to your doctor [27,28].

c) in the hypothesis of “moderate symptoms”, the indications are the same as for the previous hypothesis, but paying particular attention to the profiles already listed, because it may be necessary to supplement the therapy with an antiplatelet agent (eg salicylic acid), to the entire period of positivity, after checking the thrombophilic and hematochromic values in the serum. Until a few months ago, the integration of Vitamin D and low-dose dexamethasone was recommended, but currently, they are not recommended [27–30].

d) in the hypothesis of “severe symptoms”, the clinical indications have alternated and spaced. At the beginning of the declaration of a pandemic state in the West (March 2020), a corticosteroid and antiviral approach (especially Remdesivir) was preferred [31], but over time there was a need not to use antivirals and to prefer betamethasone [32] in a protocol with an anticoagulant (eg low molecular weight heparin) and a double or triple antibiotic therapy, especially in the presence of patients with bilateral interstitial pneumonia, immunodeficiency, autoimmune diseases and coagulopathies. Towards the second half of 2020, the indications and protocols changed, advising against the use of vitamin D [33] and dexamethasone (if not due to their scarce contribution to healing or in some cases due to the excessive presence of contraindications), exclusively combined with oxygenation therapy and in combination with Baricitinum or Remdesivir [34].

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Currently, the best approach, other than vaccine therapy, despite the insistence of governments to adhere to the antiviral vaccination campaign as the only truly effective tool, involves one of the following 2 scenarios:

1) The use of corticosteroids (eg. betamethasone, dexamethasone, methylprednisolone, prednisone, hydrocortisone) [35] and antimalarials (hydroxychloroquine) [36], for patients in the early stages of infection and those hospitalized and on oxygen therapy, combined with heparin only if the D-dimer is elevated [37] (otherwise an antiplatelet such as salicylic acid is sufficient, also in terms of prevention) [38] and with adenosine by aerosol for severe patients with respiratory symptoms, to extinguish uncontrolled inflammation [39]. To the ternary therapy of “hydroxychloroquine - dexamethasone - heparin / salicylic acid” it seems extremely useful to add also azithromycin [40], especially to anticipate infectious complications arising from Covid-19 (and the resulting cytokine storm), precisely in terms of prevention and clinical management of the patient, from the very first symptoms. This general protocol should also, be supplemented (in an adjuvant mode) with intravenous vitamin C at 1000-1500 mg [41], vitamin D, at a dose of 500-1000 mg [42-44], to promote the timely reaction of the immune system, to be supplemented with vitamin K2 at a dose of 50-100 mcg [97]. Lactoferrin in a dose of 300-1000 mg [45], to promote natural immunity and reduce serious complications, glucosamine in a dose of 500 mg to 1500 mg [46], to promote the anti-inflammatory and reconstructive power of cartilage, glutathione in a dose of 400 mg to 800 mg [94-96], to promote a powerful antioxidant intervention, and quercitin in a dose of 500-1000 mg [46,47], as a flavonoid, to inhibit viral duplication.

2) The use of “convalescent (or super-immune) plasma” turned out to be extremely interesting and less dangerous than a vaccine and combined drug therapies (in terms of administration complications) in the light of published research results and possible correlations with the immunity of family ancestors who contracted one of the three pandemic infections of the last century and survived it. In this hypothesis, however, two factors must be taken into account: the transfusion risk associated with the use of convalescent serum and the effectiveness of the treatment about the temporal status and duration of viral infection (initial phase, intermediate phase, advanced phase) [1].

Other hypotheses, however, were soon discarded or traced to mere research hypotheses or as a preventive measure, to favour a vaccine approach, as in the case of interferon and colchicine, ACE inhibitors and angiotensin receptor blockers [48], in response to complications arising after administration. The use of ivermectin [49,93], despite excellent results, has not yet been investigated in detail in published studies with representative population samples. Finally, the hypothesis of the use of ozone therapy for severe patients with complementary oxygenation is also poorly investigated [50].

In all of the above hypotheses, however, the following are always fundamental (always in the writer’s opinion):

1) maintaining healthy eating and sports habits (balanced diet without excesses, prohibition of smoking and drugs, at least five thousand steps per day and drinking about two litres of water per day), in addition to the health and social ones of spacing at least 2 meters (preferably two meters), the use of surgical masks / disposable gloves to cover nose and mouth (taking care not to touch the mucous membranes), surgical handwashing (according to the procedure that provides for the use of certain actions lasting about 45-60 seconds) and the use of alcohol-based and antibacterial gels to be used frequently in case of public exposure. Extremely useful is the exposure to the Sun, for the development of vitamin D, even if not to prevent the infectious disease [51-53].

2) in agreement with your doctor, and unless otherwise indicated for previous or concomitant diseases, supplement your dietary plan with vitamins A, B (group), C, D and E, in addition to the use of prebiotic supplements, probiotics, omega 3-6-9, coenzyme q10, flavonoids (such as quercetin), glucosamine and lactoferrin, from the time of discovery of the state of positivity, even if asymptomatic (to further strengthen the immune and vascular system), maintaining this supplementation scheme for at least 4-6 months from the state of negativity, except to perform serological controls every 3 months to ensure the effectiveness of integration and the risk of over excess especially of vitamin D that would be toxic if in excess; The opposite is true for vitamin C and vitamin E that should be dosed with values around 1000-1500 mg for vitamin C and 1000 mg for vitamin E, as they are eliminated through urine. The purpose is to bring the inflammatory state of the body, also due to the frequent intestinal dysbiosis detected, to a state of eubiosis and positive levelling of the general state. The use of supplementary products should not be perceived as a substitute for drug therapy or medical prescriptions, but as complementary to a healthy and rigorous lifestyle, both in the preventive phase and during the management of active/acute infection, and for the subsequent phases (so-called “long covid”); This attention is necessary for light of the criticality of adverse events, clinical reactions and adverse effects from the administration of vaccine therapy (from the most common as tremors, fever, widespread and localized pain especially in the arm that received the dose, drowsiness, generalized weakness, excessive sweating, breathing difficulties, to those more serious as thrombotic events), which we will discuss below.

The data concerning pregnant women are not sufficient to be able to issue a systematic and scientifically rigorous assessment Table 1.

Collective clinical management profiles: Vaccines and gene therapies

Due to the prevention of COVID-19 contagion, as required by international protocols on the subject of epidemics and pandemics, from the very first weeks of the declaration of the pandemic status, a race began to find an experimental (and/or vaccine) therapy in the shortest possible time, able to counteract the pathological infectious phenomenon. Let’s analyze them individually:
Table 1: Integrated Pharmacologic Protocol.

| Pathological stage                        | Best clinical therapy*                                                                 | Recommended integrative therapy* |
|-------------------------------------------|----------------------------------------------------------------------------------------|----------------------------------|
| 0: Absence of infectious conditions       | No pharmacological therapeutic indication                                               | 1) Vitamin A (Retinoic): 0.6 - 0.95 mg, 1/día                                  |
| 1: Positivity with the absence of symptoms (symptomatology) | Hydration, rest and isolation                                                            | 2) Vitamins B Complex: 
- B1 (Thiamine): 0.9-1.2 mg, 1/day
- B2 (Riboflavin): 0.6 mg for every 1,000 Kcal introduced into the diet, 1/day
- B3 (Niacin or PP): 14-18 mg, 1/day
- B5 (Pantothenic Acid): 5-7 mg, 1/day
- B6 (Pyridoxine): 1-1.5 mg, 1/day
- B7 (Inositol): 500 mg, 1/day |
| 2: Mild symptomatology                    | 1) Hydration, rest and isolation                                                         | - B8 (Biotin): 20-200 mg (depending on the type of activity practiced; the higher the higher the consumption, the higher the recommended), 1/day |
|                                           | 2) Paracetamol: a) 500 mg, 2/day (for mild febrile states up to 38°C); b) 1000 mg, 2/ day (for moderate and severe febrile state over 38°C), for 5 days. | - B9 (Folic acid): 1.2 mg (depending on the presence or absence of a state of pregnancy), 1/day |
|                                           | 3) In case of moderate or severe febrile persistence for more than 48h, supplement with Salicylic Acid, 500-1000 mg, 1/day, for 5 days. | - B12 (Cobalamin): 500-1000 mcg, 1/day |
| 3: Moderate symptomatology                | 1) Paracetamol: a) 500 mg, 2/day (for mild febrile states up to 38°C); b) 1000 mg, 2/ day (for moderate and severe febrile states above 38°C), for 5 days. | |
|                                           | 2) Dexamethasone, 6 mg/die, for 7-21 days, on a sliding scale.                          | |
|                                           | 3) Subcutaneous low-molecular-weight heparin, 40 mg (4000 U), 1/day (in case of high D-Dimer and need for supplemental oxygen therapy for hypoxia, in place of salicylic acid), according to therapeutic duration and serum control of coagulation times. | |
| 4: Severe and very severe symptomatology  | 1) Hydration, rest and isolation                                                         | 4) Vitamin D3: 1000-2000 IU (up to 4000 IU in case of deficiency), 1/day (must be monitored in serum to assess its level of toxicity) + Vitamin K2: 50-100 mcg, 1/day. |
|                                           | 2) Paracetamol: a) 500 mg, 2/daily (for mild febrile states up to 38°C); b) 1000 mg, 2/ daily (for moderate and severe febrile states above 38°C), for 5 days. | 5) Vitamin E: 1000 mg, 1/day |
|                                           | 3) Dexamethasone, 6 mg/daily, for 7 to 21 days, on a sliding scale.                     | 6) Prebiotics-Probiotics: 10-20 billion, 1/day |
|                                           | 4) Subcutaneous low-molecular-weight heparin, 40 mg (4000 U), 1/daily, according to therapeutic duration and serum control of clotting times. | 7) Omega 3 (alpha-linoleic acid) - 6 (oleic acid): 1000 mg, 1/day. |
|                                           | 5) Hydroxychloroquine, 200 mg, 1/daily, for 7-21 days, according to symptomatology.     | 8) Coenzyme q10: 100-200 mg, 1/day |
|                                           | 6) Azithromycin, 500-1000 mg, 2/day, for 7-21 days, according to symptomatology.        | 9) Quercitin: 500-1000 mg, 1/day |
|                                           | 7) Adenosine, in aerosol, 9 mg for 2/day the first 24 hours then 1/day for 4 days.        | 10) Glucosamine: 500-1500 mg, 1/day |
|                                           | 8) Integrative oxygen therapy, according to need and haemogasanalytic values.           | 11) Lactoferin: 500 mg, 1/day |
|                                           |                                                                                         | 12) Glutathione: 400 - 800 mg, 1/day |

*Doses are subject to change in the amount and prescriptive duration, based on the patient’s medical history and based on the physician’s history and clinical evaluation. Non-pharmacological integrations are suggested, however, with a doctor’s prescription, who evaluates the general physical state and any disease and drug interactions.

a) “Antivirals”: In addition to those already hypothesized and/or used in a non–systematic way, such as Remdesivir, Molnupiravir has recently appeared which seems to reduce the replication of SARS-CoV-2 and lung damage [54] and nafamostat mesylate, which seems to interact with the Spike protein (responsible for the entry of the virus into cells and its spread) avoiding thrombotic activation and vascular inflammatory state [55].

b) “Superimmune Serum”: The convalescent serum is the serum obtained from subjects recovering from COVID–19 and which contains antibodies to SARS-CoV-2; they may also be available in plasma, which is called hyperimmune when antibodies are present in neutralizing concentrations. Convalescent serum treatment has not yet undergone the randomized controlled trials necessary to determine whether it is safe and effective for treating people with COVID–19, although in certain cases the agencies have granted temporary authorization as an experimental treatment with convalescent plasma or serum, in cases where the person’s life is seriously or immediately threatened, as already happened in the H1N1 flu a few years ago [1]. A Cochrane Collaboration research has been ongoing since December 2020 and could clarify the aspects about its real usefulness [56].

c) “Gene Therapies / Vaccines”: An important part of the scientific community is working on the preparation of an effective vaccine against Covid–19, net of the variants of the virus that in recent months are increasingly appearing on the international scene. Despite the strong pressure exerted by the COVID–19 pandemic, and the hope that each of us places in scientific research, the future use of a vaccine must necessarily be preceded by rigorous studies that require the time necessary to evaluate its efficacy and safety. Initially, the research
production of proteins from one part of the cell to another, which is why it is called “messenger”. In this case, the RNA carries the instructions for the production of the protein used by the virus to attach itself to cells, the protein called Spike. Thanks to vaccination, the body produces specific antibodies before coming into contact with the virus and immunizes itself against it. Of this type are the Pfizer–BioNTech vaccine, Moderna and CureVac.

cb) “DNA vaccine”: The mechanism is similar to the RNA vaccine. In this case, a fragment of DNA synthesized in the laboratory is introduced, capable of inducing the cells to synthesize a protein similar to the one to which the immune response is to be induced. One of the first vaccines of this type will be AstraZeneca, but studies have yet to be completed.

cc) “Protein vaccine”: Using the RNA sequence of the virus (in the laboratory), proteins or protein fragments of the viral capsid are synthesized. Consequently, by injecting them into the body combined with substances that enhance the immune response, the antibody response is induced by the individual. Of this type is the Novavax vaccine.

cd) “Inactivated vaccine”: It is obtained by killing the virus with chemicals, heat or radiation. The inactivated whole virus includes the entire virion that causes the disease, therefore it has different antigenic parts, which induce an immunological response against the pathogen in the host (vaccinated person). The inactivated whole virus has several advantages, including low manufacturing cost, safety, and does not involve genetic manipulation. This approach uses a technology that has been shown to work very well, vaccines against influenza and polio are produced with this methodology, but it requires specialized laboratory equipment and can have a relatively long production time than other methods. Of this type are the Sinovac vaccine and Sinopharm.

cc) “Non-replicating viral vector vaccine”: uses a safe virus such as adenovirus which is stable and non-replicating to carry genetic material or one or more antigens which thus induce a cell-mediated immunity as well as an immune response humoral. Vector vaccines are characterized by strong immunogenicity and safety. There are over 50 subtypes of human Adenovirus, including Adenovirus serotype 5 (Ad5) which is a stable and non-replicating virus used in the development of various vaccines. However, pre-existing immunity against human Ad5 is widespread, hindering its use as a vector for vaccine development. Chimpanzee adenovirus (used for example in the case of the ChAdOx1 vaccine) represents an alternative to the human adenovirus vector due to its safety and lack of pre-existing immunity in humans. Of this type are the vaccine AstraZeneca, Gamaleya, Janssen (Johnson & Johnson) and CanSino.

The costs per single dose range from $2 (AstraZeneca) to $7–8 (Janssen and Sanofi), up to $10–12 (CureVac and Pfizer), ending with $18 (Moderna). The vaccines authorized up to now have an efficacy ranging from 62% to 90% (based on the dosages) for AstraZeneca, 95% for Pfizer and Moderna; however, there are insufficient systematic data on administration and resolution in the case of Covid–19 variants.
except for the most studied English variant. Following dozens of thrombotic episodes, the AstraZeneca vaccine has been suspended in several European countries since March 2021.

The vaccine issue presents, concerning COVID-19 immunization, several criticalities that the scientific community is still unable to unravel; in particular, the preparations authorized for dissemination to the population:

a) have an efficacy that is always inferior to natural immunization and does not guarantee lasting coverage over time, except to the extent of 6–9 months to be repeated practically annually (maybe 2/year) on a par with seasonal influenza vaccines;

b) do not guarantee safe immunization over time concerning potential new reactivations and variants of the virus itself. It is no coincidence that we have seen new positivity in subjects already immunized or with the inoculation carried out.

c) do not guarantee certain data concerning individual health, in the medium and long term, as well as we do not know the actual degree of toxicity of the same, always in the medium and long term. It is not by chance that inoculation is preceded by the stipulation of an administrative document in which the citizen states that he is aware of the risks to his health and assumes direct responsibility by declaring to undergo the inoculation voluntarily.

d) do not exempt the citizen from the use of the disposable surgical mask, from the social distancing and the hygienic-sanitary norms foreseen.

e) vaccinating the mass population during the pandemic peak promotes the adaptation of the virus which thus generates new variants that are potentially more dangerous and lethal. [98–100].

“Monoclonal therapies”. Monoclonal antibodies are particular types of antibodies, produced with recombinant DNA techniques starting from a single type of immune cell. More correctly, monoclonal antibodies can be defined as hybrid homogeneous proteins, obtained from a single engineered lymphocyte clone. Monoclonal antibodies are widely used in the clinical setting, both for diagnostic and therapeutic purposes. Antibodies (or immunoglobulins) are glycoproteins produced by the B lymphocytes of the humoral immune system. These proteins can recognize and bind in a specific way to other types of substances called “antigens” (antigens can be various; for example, protein, polysaccharide, lipidic, etc). The function of antibodies is to recognize and neutralize foreign agents and/or pathogens, such as, for example, viruses, bacteria or toxins. This is possible thanks to the particular structure of these molecules. Antibodies are globular proteins with a particular “Y” conformation. Within this protein structure, there are a so-called constant region and variable regions, corresponding to the arms of the “Y”. It is precisely at the level of the variable regions that the specific binding sites for the antigen are found. Each B lymphocyte is capable of producing millions of antibodies, in turn, capable of recognizing different types of antigens (polyclonal antibodies). Once the antibody binds to the antigen for which it is specific, the antibody itself is activated and gives rise to the immune response that will lead to the elimination of the foreign agent. Monoclonal antibodies act with the same mechanism of action just described for polyclonal antibodies. Monoclonal antibodies possess a highly specific affinity for a certain type of antigen and bind to it, thus allowing to obtain a marked immune response against that toxin, protein, chemical mediator, malignant cell or pathogen, which is the target of therapy. To try to simplify the concept as much as possible, we can divide these active ingredients according to the activity they exert: Monoclonal antibodies with anti-inflammatory action: drugs such as infliximab and adalimumab belong to this group. These monoclonal antibodies exert an anti-inflammatory action since their antigen is constituted by human TNF-α, one of the pro-inflammatory cytokines most involved in the symptoms of inflammatory diseases on an autoimmune basis, such as, for example, rheumatoid arthritis and arthritis. psoriatic. Monoclonal antibodies with immunosuppressive action; the target of these active ingredients is mainly constituted by defence cells such as B lymphocytes and T lymphocytes and by proteins essential for their differentiation and activation, such as interleukin–2. The drugs used in the treatment of autoimmune diseases and in the prevention of rejection in organ transplants belong to this group of monoclonal antibodies, including rituximab (also used in the treatment of some types of lymphomas) and basiliximab. In addition, omalizumab also belongs to this group, the target of which is human IgE and is used in the treatment of allergic asthma. Monoclonal antibodies with antitumor action; numerous active ingredients are belonging to this group. The target of these monoclonal antibodies is mostly constituted by factors fundamental for the development of malignant cells, or by proteins that are overexpressed when certain types of tumours are present, as is the case, for example, in the case of HER–2 positive breast tumours. In this case, the monoclonal antibody trastuzumab is used for the treatment of this tumour form. Rituximab, cetuximab and bevacizumab also belong to this group of monoclonal antibodies. Furthermore, there are monoclonal antibodies capable of exerting activities different from those just described. This is the case with abciximab, which has antiplatelet activity. The antigen of this monoclonal antibody is, in fact, the glycoprotein IIb / IIIa present in the platelets and involved, in fact, in the processes of platelet aggregation. The side effects that may occur during therapy based on monoclonal antibodies depend on many variables, such as the type of active ingredient chosen, the pathology to be treated, whether or not the antibody is conjugated with other drugs or radioactive isotopes, general conditions and the sensitivity of patients towards the same drug. However, there are limitations shared by all types of monoclonal antibody-based therapy, regardless of the type of active ingredient chosen. More precisely, we are talking about the high cost of production and the possible immune response that these molecules could trigger. The patient’s organism itself may develop antibodies to counteract the monoclonal antibodies.
introduced with the therapy, since it recognizes them as foreign agents, thus leading to the ineffectiveness of the treatment.

Compared to COVID, several studies are trying to prove their effectiveness but the problem lies in their high costs per dose (approximately $2,000 per dose) and duration between 1 and 3 months. Under discussion, we find the following antibodies or associations of them: Bamlanivimab, Bamlanivimab–Etesevimab and Casirivimab–Indevimab [57,58].

e) “Parvulan” [59]. Based on a study by Prof. Palmieri, and recently used in Brazil, the researcher suggests exploiting the antiviral activity of the bacterium C. Parvum, as prevention and therapy of Covid–19. Parvulan, as an antiviral immunostimulant (registered in Brazil), may be useful, although studies on representative population samples are lacking on this point.

Psychological and psychopathological profiles related to Covid–19

The writer, in research [1] published in February 2021, highlighted how the Covid–19 problem is not only health and medical but that it holistically concerns the whole person, massively interfering even on his psychological well-being. The data on a representative Italian sample reported three important criticalities:

1) the first criticality linked to a little (if not absent, at least compared to the Italian territory), attention to the problem of mental health, with the aggravation of anxious symptoms, depressive and humoral, two, four and six months from the end of the hospitalization and positive infection [60–79], also taking into account the worsening of symptoms in personal and psychotic disorders, as well as the adolescent drama of isolation and abuse of the through the internet [80–95];

2) the second criticality linked to a direct correlation between psychiatric symptoms and intestinal dysbiosis, the subject of a subsequent publication nearing completion, capable of favouring and aggravating the precipitate of symptoms related to serotonin and dopamine;

3) the underestimation by the scientific community of the correlation between the Covid–19 Pandemic and the immunity of family ascendants up to the second generation obtained through the three main pandemics of the 20th century, and consequently an underestimation of the use of super immune serum/convalescent serum to replace a dubious gene therapy based on preparations (the so–called anticovid vaccines) whose medium and long–term effects are unknown, in terms of private and public health. These criticalities are still evident and increasingly emerging, also taking into account the continuous “lockdowns” to contain the spread of the virus; this solution is lacking or seriously insufficient, taking into account that the curves often have a trend contrary to the “all too optimistic” expectations of government consultants.

Critical issues, these, which could be solved by implementing the following solutions

1) concerning the first problem, recognizing the profession of Psychologists the dignity of health professionals (which in Italy has held only on paper and on a few other factual circumstances since 2018), massive recruitment at the hospitals and bodies responsible for welcoming the patient, guaranteeing the latter a cycle of free sessions (and reimbursed by local territorial or national bodies);

2) concerning the second problem, preparing a series of researches aimed at correlating intestinal dysbiosis with the effects on neurotransmitters, serotonin and dopamine, with statistical data obtained on relevant samples, to allow greater knowledge and knowledge of immunoneurobiological phenomena;

3) concerning the third problem, preparing a series of researches aimed at correlating with statistical data obtained on relevant samples the immunity of family ascendants compared to previous pandemics (for genetic profiles) with convalescent serum, and its concrete use in replacements of gene therapies/vaccines not yet sufficiently tested in a medium–long period and therefore of dubious if not dangerous and harmful efficacy.

Socio-economic and political profiles

It is a social, economic and political phenomenon common to all the nations affected by this pandemic: the continuous and pressing lockdowns, to limit the contagion, although functional to the objective, do not have the desired effect and on the contrary, are increasingly impoverishing. families who live off commercial activities and free professions. The journalistic data indicate and depict what it describes up to now (even more so in the Italian reality) and predicting leopard–spotted closures does not eradicat the problem at the root, just as vaccination administration is not giving the expected results, despite a slight improvement compared to hospitalizations and intensive care wards. There are therefore three critical issues in this sense:

1) a national social policy, already in serious crisis, which tries to close the gaps by dedicating itself to the symptom and without intervening on the primary causes;

2) an international social and economic policy which is proclaimed united and cohesive only in principles, but which in fact (and especially in economic and health matters) is profoundly individualistic and asynchronous concerning daily events;

3) an economic policy that blindly follows the rules that have self–imposed and that is leading to the collapse of the system and the impoverishment of those who were already in crisis for other reasons, affecting, even more, the middle–poor social class.

The solution, therefore, which appears drastic but necessary (for the writer) is exclusively one and is structured in three simultaneous actions. If this solution were put into practice, they could truly resolve the pandemic situation definitively (avoiding further periodic and ineffective patchy lockdowns, with traffic bans after a certain time –effective only to avoid gatherings in commercial premises in the evening or at night–)

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and the resulting socio-economic and political consequences; or to prepare a “global socio-health-economic action plan”, identical for all nations, which provides for the following:

1) Total lockdown, for 3 consecutive months, preventing people from going out of the house. Essential items and drugs would be mailed or delivered by military forces at specific times. Those who are already hospitalized or those in need of hospital medical intervention would be accompanied by the military police and military medical personnel. The only ones exempt from the obligation to stay at home are medical and health personnel operating in public and private structures. Every family is obliged to undergo a swab to check for any positivity. The obligation to stay at home could be extended in the case of a persistent positive or non-negative state for at least 3 tests, for the individual and the entire family. Arranging a lockdown of this type would make sense, however, only if all nations implemented the same policy and for the same period; otherwise, the problem would eradicate only in the Nation that implements it but would find itself infected again in a short time due to the entry of foreign third parties into the territory, perhaps for work or vacation, effectively cancelling all efforts.

2) Preparation of a single world currency, valid only for the pandemic period, printed by every single nation without charges or debts towards third parties. Every month, every single person would find on their bank account the necessity to buy food, medicines, necessary goods and pay for utilities and expenses. All would be exempt from work services except for the medical, health and administrative staff necessary to meet the health demand. At this point, the temporary hiring of the necessary personnel is arranged by direct call and by titles, as if the need were not health war but war.

3) Preparation of a single therapeutic protocol in all nations to counter Covid–19 symptoms and the preparation of biological therapy or convalescent plasma, pending the preparation of an effective monoclonal or pharmacological therapy different from the economic and political commodification of this last year on gene and vaccine therapies, with related risks for health in the medium and long term. The vaccination issue becomes problematic, not due to the inoculation of the serum itself but because the direct and indirect effects in the medium and long term are not known, as admitted by the same pharmaceutical manufacturers that have obtained specific authorization for the treatment “voluntary” by the patient. Therefore, if vaccines, as biological preparations consisting of killed or attenuated microorganisms, or of some of their antigens, or of substances produced by microorganisms and made safe (such as tetanus toxoid resulting from the treatment of tetanus toxin) or, again, from proteins obtained with genetic engineering techniques, they are “safe” within the limits of their function, in the case of Covid–19 this certainty is not possessed even by the manufacturers themselves and therefore the inoculation represents in all respects a violation of the law constitutional to health that cannot be sufficiently overcome by the state of necessity resulting from the pandemic situation. A different reconciliation of rights and needs, therefore, appears evident. Finally, the “green card” to return free to circulate would be issued only under the following conditions: a) healing demonstrated with at least 3 instrumental tests; b) state of negativity for at least 2 months and at least 3 instrumental tests.

Considerations conclusions

Because of the foregoing, the writer recognizes the extraordinary need to suggest to political institutions to interact at the EU and international level, to prepare the suggested plan or other plans with the same purposes, to definitively eradicate the pandemic problem and ensure everyone citizens have their rights, constitutionally guaranteed by law and by the legal system, first of all preserving the right to health, present and future, with an increased focus on pharmacological and integrative therapies, which have demonstrated greater stability, cost-effectiveness, and individual health and safety.

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