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# To Be or Not to Be Vaccinated? The Perilous Evolution of COVID-19

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#### ABSTRACT

The COVID-19 classification and evolution through its multiple mutations have increased its transmissibility rate up to 70% or more globally, threatening to undermine the promise of a number of emerging medications and vaccines that primarily focus on the immune detection of the Spike trimer.

Mutations have been long considered as random events, or mistakes during the viral RNA replication. Usually, what can go wrong will go wrong; therefore, repeated transformations lead to the extinction of a virus. On the contrary, the aggregate result of over 300,000 COVID-19 variants have expanded its transmissibility and infectiousness. COVID-19 mutations do not degrade the virus; they empower and facilitate its disguise to evade detection. Unlike other coronaviruses, COVID-19 amino acid switches do not reflect the random unfolding of errors that eventually eradicate the disease. COVID-19 appears to use mutations adaptively in the service of its survival and expansion.

One of the COVID-19 primary strategies is to inhibit the production of interferon type (INF) that is involved in recognizing the virus. The deleterious consequences of the cytokine storm where the CD8<sup>+</sup> killer cells injure the vital organs of the host may well be collateral damage, as the blind immune system struggles to annihilate the unidentified COVID-19. It is probable that evolution has programmed COVID-19 with an adeptness designed to debilitate key systemic defences to secure its subsistence. To date the infectiousness of the COVID-19 pandemic is exponentially increasing, denoting the possibility of an even more dangerously elusive, inconspicuous, and sophisticated version of the disease.

#### **COVID-19 and Previous Viruses**

According to the latest live updates on world meter, the COVID-19 pandemic resulted in 192,974,202 cases and 4,145,502 deaths globally until July, 22 2021. Its lethal consequences have motivated a large body of evolving scientific research that often broadcasts contradictory results giving rise to personal opinions, misunderstandings and misinformation. That further obscures data interpretation, and obstructs the formation of a united front that would entail everyone in the world working together to combat the virus.

COVID-19 is a positive RNA virus classified under the Beta coronaviruses category along with SARS-CoV (Severe Acute Respiratory Syndrome) and MERS CoV (Middle East Respiratory Syndrome). There are other milder forms of beta type of human

infections, experienced during the common cold, such as the HCoV-OC43 and HCoV-HKU1. Other viruses responsible for flu like symptoms such as HCov-229D and HCoV-NL63 come under the Alpha classification. Feline (FCoVs) and canine corona viruses (CCoVs) are also sorted under the alpha group. The remaining coronaviruses fall under the genera of Gamma and Delta categories that primarily affect poultry, wildlife and other birds, although rather sparce information is available regarding the delta division [1,2]. The Delta section of coronaviruses should not be confused with the Delta COVID-19 variant, or B.1.167.2, that has demonstrated the highest transmissibility rate so far, and which was first detected in India towards the end of 2020. Very different types of viruses such as the Bafinivirus infects fish, while the Arterivirus is limited to specific species including mice, monkeys, horses and

coronaviruses that cause enteric and upper respiratory tract

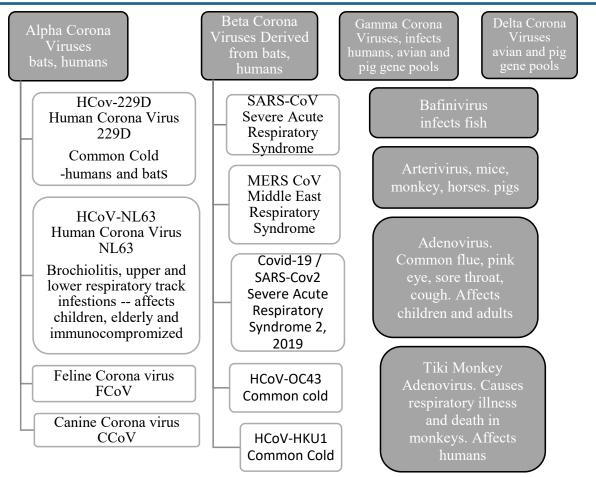


Figure 1: Corona virus classifications: Alpha, Beta, Gamma and Delta. Other viruses: Bafinivirus, Arterivirus, Adenovirus, Tiki Monkey Adenovirus.

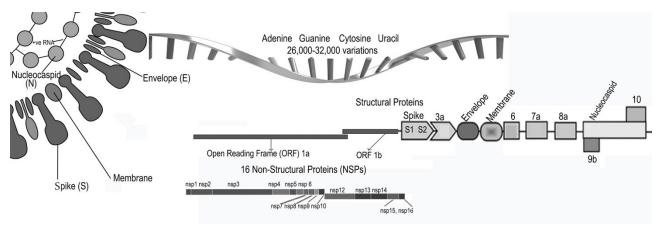


Figure 2: COVID-19 Composition.

pigs [3]. Adenovirus infects the lining of the eyes (pink eye), the intestine, resulting in gastrointestinal disturbances, the urinary track, the lungs and respiratory system, and the nervous system. It primarily infects children, however, it often infects adults as well. The Tiki Monkey Adenovirus (TMAdV) is currently used in the Astra Zeneca vaccine after its genome has been modified. Figure 1 offers a table that summarizes some basic information about different viruses and their target populations.

### **Coronavirus** Composition

The genome of corona viruses is composed by sequences of around 26,000-32,000 variations of the ribonucleic acid (RNA) nitrogenous bases: adenosine, cytosine, guanine, and uracil. It harbours 6-11 open reading frames (ORFs), 67% of which encode 16 non-structural proteins (nsps) that direct virus assembly, transcription and replication in connection with the host, and the rest encode the accessory and structural proteins.

Structural proteins include the main surface trimeric Spike glycoprotein (S) that binds and fuses with the ACE2 receptor, a key-to-lock process that releases the viral RNA into the cells; the smaller surface proteins are the envelope (E) protein, the membrane (M), while the nucleocapsid (N) defensively surrounds the genome. The N protein offers protection and signature sequences, equipping the virus with adaptation skills that enable it to survive the adversities of the host's environment. A graphical representation of COVID-19 structure is given in Figure 2.

The immune defence assembled against the antigen is composed by: A. The innate immune response during which antibodies prophylactically obstruct the Spike's contact and fusion with the human cells.

B. The adaptive immune response comprised by a number of cells including cytotoxic T-killer cells or CD8<sup>+</sup> that clasp onto the infected cells' antigens, and obliterate them by releasing perform and granzyme that is absorbed through the cellular pores [4,5].

#### **Methods of COVID-19 Transmission**

- Droplet transmission as a result of infected individuals coughing, sneezing, talking, singing, etc.
- Transmission via touch from contaminated surfaces where the virus may survive for hours outside the body of a host. Poor hygiene increases the probability of contracting COVID-19 via touch.
- Defective sewage system containing toxic sewage where the virus can sustain itself for days [6].
- Flushing waste water that may contain viral particles from COVID-19 patients' faeces. Infected faeces could increase COVID-19 escalation in countries like India where the "night soil," as it is historically referred to faeces and other human excretions, is widely utilized as a fertilizer.
- Airborne dust transporting the virus along with environmental pollution that undermines and compromises immunity.
- Evidence regarding vertical transmission is inconclusive. Some research has reported neonates testing positive to COVID19, while others manifested increased IgM and IgG levels, while testing negative to COVID19. These results are juxtaposed against research demonstrating no evidence of COVID19 in neonates of placentas of mothers infected by the virus [7-10].
- Transmission via saliva that generally appears to contain high concentrations of COVID-19 [11].
- Reports of COVID-19 in semen present contradictory evidence, depending on whether testing was completed during the acute phase of the disease or during recovery [12,13].
- Ocular route of transmission is rather controversial, with some studies evidencing pronounced ocular defects in several COVID-19 patients, and others reporting little or no ocular manifestations of COVID-19 [14,15].

Once COVID-19 has entered the body via any of the routes enumerated above, its Spike protein connects and fuses with the ACE2 (Angiotensin converting enzyme 2) receptors of the vital organs to release the COVID-19 into the human cells, where the virus is duplicated, inevitably spreading and overwhelming the body. This process will be described in more detail in later chapters.

#### **COVID-19 Neutralizing Antibodies**

COVID-19 neutralizing antibodies are Y shaped proteins that can recognize the S1 RBD and fit into the viral antigens like a key to a lock. This prohibits the virus from binding with the ACE2 cellular receptor, thus preventing viral entry. Other antibodies can neutralize the heptad repeat 2 (HR2) domains to impede S2 fusion with the ACE2 receptor, so even if the Spike protein can bind with the ACE2 receptor, the second step of antigen/receptor fusion is compromised, disallowing COVID-19 entry into the cells, without which the virus can neither replicate, nor spread inside the body [16].

A recent study experimented on a powerful monoclonal antibody, LY-CoV555, that binds with the COVID-19 spike protein obstructing it from fusing with the cells' ACE2 receptors. The results of 309 patients who received the LY-CoV555 antibody treatment were compared to 148 patients who received placebo. Eighty percent of all 452 participating patients had mild COVID-19 symptomatology. By the 11th day of clinical observation both experimental and placebo group had a significantly reduced viral load, with the treated patients exhibiting a modest advantage. The experimental group patients who received a 2800mg antibody dose had a -0.53 difference from the placebo group (p=0.02 / p<0.05), which is a statistically significant result. Neither a lower dose of 700mgs (p=0.38) nor a higher dose of 7000mgs (p=0.7) were statistically significant. Importantly, however, when the rate of hospitalizations was examined on the 29th day, the percentage of the viral load in the experimental group that was treated with LY-CoV555, was 1.6%, contrasted with the significantly higher viral load of the placebo / control group that was 6.3%. Further analysis focusing on high risk aged (>65) and obese (BMI>35) individuals denoted a diminished hospitalization rate of 4.2% for those receiving LY-CoV555, when compared to 14.6% of nontreated patients [17].

#### Antibodies: The Safest Avenue to Restrict Viral Entry

The immune memory of CD4+ and CD8+ T cells is an encouraging finding. However, allowing COVID-19 to enter the system which will occur in the absence of antibodies, may be already too late, especially in elderly, or immunosuppressed individuals. The optimum method of fighting COVID-19 is focusing on antibodies that can block viral invasion in the first place. This is important for two reasons:

1. Preventing viral entry into the cells is the safest option. Once Covid19 enters the cells, the CD8<sup>+</sup> cells must exterminate the infected cells, a necessary intervention, but a casualty nevertheless, that can often injure the host.

2. There is evidence that coronavirus inhibits the interferon type I production and therefore, it suppresses the ability of the adaptive immune system to recognize the virus, possibly leading to the destruction of healthy cells. This is illustrated by the cytokine storm that indiscriminately attacks and rampages the host's vital organs [18, 19, 20]. During the cytokine storm the adaptive immune system is informed about the lethal danger, but has

difficulty identifying the enemy that is evasive and imperceptible due to insufficient availability of Interferon I. As a result, immune counterattack is persistently fierce yet, undifferentiating, with deleterious consequences for the human body. The inhibition of the interferon type I production that compromises adaptive efficiency can be particularly detrimental to aged individuals with compromised immunity, who are faced by viral influx, and rely on the adaptive immune system for protection. This is why neutralizing antibody treatments have become so promising in the treatment of older COVID-19 patients.

#### **COVID-19 Mutations**

COVID-19 mutations appear to increase its contagiousness as if these evolving transformations occur as a result of predetermined calculations rather than merely representing random events. Viruses have a propensity to change in an effort to adjust and survive within their hosts. However, according to the second law of thermodynamics systemic changes from one state into another decrease energy and increase entropy, eventually driving a virus into extinction; There are millions of incorrect combinations and only one correct solution, therefore, during amino acid transpositions what can go wrong will go wrong. Inevitable extinction has been the inexorable fate of all previous life-threatening viruses. But COVID-19 stands alone. It defies the laws of physics to secure its sustenance, while increasing its transmissibility. Interestingly, unfolding mutations do not make COVID-19 more lethal, because that would be against the virus' interests, since it depends on its host for survival. Its evolving variants are more contagious, serving the virus' main purpose to proliferate and establish its ascendancy over the world.

# Vaccines: The Light at the End of the Tunnel? mRNA Vaccines

COVID-19 messenger ribonucleic acid (mRNA) based vaccines, like the two-dose Pfizer/BioNTech and Moderna vaccines, that have now received emergency use authorization from the FDA, are developed by first sequencing the gene of the S protein, they develop a transcription of its mRNA, they encapsulate the nucleotide-modified messenger in a lipid nanoparticle that is subsequently delivered within a sterile saline solution, acting as a dilutant, into the muscles of the host's upper arm. mRNA is a single stranded molecular sequence that can be read by the host's ribosomes. The intention is to introduce the immune system to the configuration of the Spike protein, provoking it to produce the specific antibodies that can defensively wrap around the Spike protein to prohibit viral binding, fusion and entry into the human cells [21]. The vaccine encodes the COVID-19 S1 subunit of the trimer that binds with the ACE2 receptors, as well as the S2 one that fuses with the ACE2 receptors, releasing the viral RNA into the cells. For additional safety, the S2 subunit is stabilized by substituting two amino acids at two consecutive positions, 986 and 987, by prolines which are secondary amines that do not contain the amino-group -NH, often used in the biosynthesis of proteins.

Although the Pfizer/BioNTech vaccine was recently approved for children over the age of 12, its effect on children under the age

of 12, pregnant women and individuals with certain specific preexisting conditions is currently unclear, since the above mentioned populations were mostly excluded from the clinical studies. Additional unknowns involve the vaccine's interaction with a wide range of medications; the durability of immune protection against viral infection; and the vaccine efficiency against new viral mutations [22].

### **DNA Vaccines**

Two other vaccines, the AstraZeneca and the Johnson and Johnson Janssen vaccines are produced by modifying the DNA of the Adenovirus and inserting the COVID-19 Spike protein molecular information into its genetic sequence. After being genetically altered that Adenovirus cannot replicate and it cannot integrate into the DNA of the host. It carries the mRNA message of the Spike protein into the cytoplasm like a Trojan horse where the cells synthesize the Spike protein which is manifested on the surface of the cell to instigate the formation of antibodies. Adenovirus is a group of common viruses infecting the lungs, intestine, urinary tract and nervous system. They primarily infect children more often than adults manifesting symptomatology that ranges from runny nose, fever and cough to gastrointestinal tract infections. The method of delivery is similar to the mRNA vaccines, with the exclusion that the Spike Protein mRNA is synthesized out of the genetic material of the Spike DNA that was previously inserted into the DNA of the Adenovirus. Theoretically, deleting part of the DNA sequence of the Adenovirus and altering it by inserting the genetic information of the Spike protein, renders the Adenovirus unable to duplicate. The genetic material of COVID-19 is not even available, except for the Spike protein that accounts for only one out of its 29 proteins. Besides, the COVID-19 Spike genetic material is incorporated within a completely different virus, the Adenovirus. Therefore, Covid-19 replication is impossible. Once the Spike mRNA serves as a template to compose the Spike protein in the cytoplasm, the process is the same as with the mRNA vaccines, where the mRNA is translated by the ribosomes to form Spike proteins which activate the production of antibodies and T-cells to efficiently defend against COVID-19 infection [23].

### **Protein Subunit Vaccines**

Other vaccine research companies like the Novavax and Sanofi-GlaxoSmithKline produce the spike protein vaccines in insect cells out of recombinant baculovirus [24]. Protein subunit vaccines utilise an isolated protein, in this case the Spike protein, which is purified from any viral infectious components to establish safety. The problem arises when the isolated protein becomes denatured, losing its quaternary, tertiary or secondary structure as well as its functionality, thus failing to stimulate the immune production of the necessary antibodies that can ultimately protect the system against COVID-19. Therefore, its high safety may be undermined by its potentially compromised efficiency [25].

### **Deactivated Virus Vaccines**

An alternative method is vaccination with a COVID-19 virus that has been deactivated and therefore, it is unable to replicate. This type of vaccine research has obtained different COVID-19

strains from hospitalized patients around the world including China, Italy, Switzerland, United Kingdom and Spain, and has chemically inactivated the hazardous viral features, leaving a purified, disarmed COVID-19 version that can no longer assail the body. Introducing the sight of the inactivated virus in terms of the new PiCoVacc, or otherwise known as Sinovac vaccine, prepares the body to anticipate future viral invasion and encompass immune defences by eliciting potent antibodies, which have so far demonstrated an ability to neutralize at least 10 viral mutations in mice, rats and nonhuman primates. The PiCoVacc was formed by deactivating the CN2 strain and testing it against CN3, CN5 and OS6, as well as the CN1 and OS1, which are closely related to the COVID-19 mutations observed in Wuhan that evinced severe clinical symptoms. These investigators report that the purified inactivated virus exhibited genetic stability, despite multiple passages. The comparison of the different purification stages unveiled minor amino acid substitutions in the Envelope protein - residue 32, which replaced Alanine (A) with Aspartate (D). It also presented an interchange between Threonine (T) with Isoleucine (I) in the non-structural protein nsp10 - residue 49. Genetic stability persisting despite inactivation, signified that the immune system should be able to recognize and create antibodies to potentially protect the cells from future mutations. Immune recognition should occur despite future alternations of the Spike protein, designed to disguise it, so that it eludes antibodies, inconspicuously succeeding in infecting the cells [26, 27]. The PicoVacc is currently better known as the Sinovac or Coronavac.

#### **Live Attenuated Virus Vaccines**

Live attenuated virus vaccines are based on whole viruses that have been modified and hence weakened. A single dosage can stimulate immune responses against a wide variety of viral proteins, without infecting the body with the disease. However, a mutation in live attenuated viral compounds could potentially reinstate their harmful potency; or they may have deleterious consequences in individuals with compromised immunity. Moreover, in light that COVID-19 is excreted in the faeces, there is a risk of transmitting the attenuated viral compound to healthy individuals. Lastly, there is the potential of COVID-19 fusion with alternative wild-type versions of coronavirus [28].

Table 2: Comparison of Vaccines' efficacy and safety. It should be noted that new research continuously revises the percentages presented in this table. Therefore these are only estimated percentages offering contradictory evidence.

	Pfizer/BioNTech BioNTech / BNT162b2	Moderna	Astra Zeneca	Johnson & Johnson	Sinovac / Coronavac/ PiCoVacc
Type of Vaccine	mRNA of Spike protein embedded in lipid nanoparticle	mRNA of Spike protein embedded in lipid nanoparticle	Part of the monkey Adenovirus genetic sequence deleted to insert the Spike DNA (non-replicating)	Part of the human Adenovirus genetic sequence deleted to insert the Spike DNA (non-replicating)	Purified inactivated virus with genetic stability to allow immune recognition (non-replicating)
Safety	Benefits outweigh the risks	Benefits outweigh the risks	Benefits outweigh the risks	Benefits outweigh the risks	Benefits outweigh the risks
Additional Safety	Two amino acid substitution in positions 986 & 987 by prolines	Two amino acid substitution in positions 986 & 987 by prolines			Several purification stages
Two-dosage effectiveness	93-95%	93-95%	66.7- 70%	66.7-70%	50.7-56.5%
One-dosage effectiveness	52-83%	52-83%	58.9%	58.9%	3-27%
Adverse Reactions (AE)	pain at the injection site (65-80%), fatigue, (35-60%) headache (25- 50%), fever (10-15%)	pain at the injection site (65-80%), fatigue, (35-60%) headache (25- 50%), fever (10-15%)	pain at the injection site (40-70%), fatigue, headache, fever (15- 20%) Rare blood clots 10 cases in 100,000	pain at the injection site (40-70%), fatigue, headache and fever (15- 20%) Rare blood clots 10 cases in 100,000	pain at the injection site (60%), fatigue (15%), headache (35%), fever (<1%)
Approved Age	12 and over most countries	16 and over most countries	18 and over most countries	18 and over most countries	18 and over most countries
Two-dosage against B.1.1.7 (UK) P1 (Brazil)	93%	93%	65%	65%	50.7-56.5%
Two-dosage against B.1.1.7 (UK) P1 (Brazil)	51.1%	51.1%	51.1%	51.1%	3-27%
Two Dosage B.1.351 (South Africa)	90% Mostly susceptible within 14 days after 2 <sup>nd</sup> dose but not after that	90%	65%	65%	Undetermined
Two-dosage against B.1.617.1 B.1.617.2 (India)	88% England 76% Scotland 64% Israel	88% USA 65% Canada	59.8% England 60% Scotland	59.8%	21% (no valid data)
One-dosage against B.1.617.1 B.1.617.2 (India)	33% England 37% Scotland Canada 58%	33% England 37% Scotland 65% Canada	70% Canada	33%	Undetermined

#### Vaccines' Comparison on Safety and Effectiveness

All vaccines appear to demonstrate both safety and effectiveness, which, however, varies from vaccine to vaccine. The two dosage Pfizer / BioNTech / Comirnaty mRNA (messenger Ribonucleic Acid) vaccine has been 100% effective in preventing critical illness and death following COVID-19 infection as attested by the US Centres for Disease Control and Prevention. It is 95.3% effective in preventing severe symptomatology according to the standards of the US Food and Drug Administration. Recent evidence elucidated that two dosages of the Pfizer / BioNTech are 94% effective for adults over 65. The vaccine effectiveness is based on two applications, while only one application significantly reduces this percentage to 64% according to research findings on a multi ethnic sample of adults with a median age of 73 [64]. A large body of research has confirmed that overall, Pfizer / BioNTech / Comirnaty mRNA vaccine is effective around 52 - 83% after the first dose ascending to an optimal 95% after the second dosage. However, Pfizer opposed the idea of only administering one dose on the basis that vaccine efficacy cannot be guaranteed with a single dose [29, 30]. The Pfizer / BioNTech / Comirnaty vaccine consists of the nucleotide-modified messenger RNA of the Spike protein embedded in a lipid nanoparticle within a saline solution that is injected into the recipient's muscle. The messenger RNA represents a transcript recorded by the RNA polymerase that normally carries the DNA genetic information from the cell's nucleus into the cytoplasm, where it is translated by the ribosomes into functional proteins. The Pfizer/BioNTech mRNA vaccine that is injected into the human muscle, is limited to carrying only the genetic information of the Spike protein, which is one out of around 29 primary proteins that compose COVID-19. The virus cannot replicate when only one of its proteins is available, the way it is impossible to copy a book with only one of its pages at hand. After the ribosomes have translated the genetic information carried by the mRNA that serves as a template for the synthesis of the Spike protein, the mRNA is either stored for future translation or discarded. The presence of the Spike (S) protein activates naïve or memory B cells which produce spike protein-specific antibodies designed to defensively bind to the COVID-19 S protein disallowing the virus from releasing its contents into the cells. B cells are associated with receptors in the plasma membrane that stimulate intracellular signalling pathways in case antibodies fail to prevent the virus from binding to the ACE2 cellular receptors. B cells can proliferate and become differentiated into lymphocytes, phagocytes and other effector cells that can eventually obliterate any remaining pathogens that have managed to enter the system [31].

#### **Common Side Effects of Vaccination**

Vaccination results in temporary adverse effects, lasting from 3-7 days, that mostly include pain at the injection site, fatigue, headache and fever with serious adverse effects like facial paralysis noted in less than 1% of the studied population. The experience of mild or moderate transient symptoms following vaccination signifies the laborious activity of the immune production of antibodies which are later transformed into other defensive mechanisms that consume large amounts of biological energy to prepare and defend

the body from future viral invasion. Therefore, side effects is a necessary part of vaccination that denotes vaccine efficacy. Lack of any adverse reactions may either indicate greater tolerance or, in certain cases, that the vaccine is ineffective. A new variant that was first detected in India is now spreading around the world, diminishing the effectiveness of the Pfizer/BioNTech Comirnaty from 93% to 88% (or 64% according to more recent studies); and the AstraZeneca vaccine from 66% to 60%.

The DNA vaccine has had some rare life threatening side effects of blood clots that occur around 10-11 times per 100,000 vaccination. Other than that, it involves very similar symptomatology of temporary adverse reactions as the mRNA vaccines. Vaccine efficacy appears to be around 66.7-70% on the average, based on a number of different studies with moderately lower vaccine effectiveness following the first dose which is around 58.9% [32].

#### Vaccine Effectiveness. What can Go Wrong?

The DNA vaccine is not even based on the COVID-19 virus. It is based on the Adenovirus after its genetic sequence has been altered to disable reproduction within the cell. As a result of the vaccination, the B cells can produce antibodies for the particular S protein configuration presented, thus obstructing the COVID-19 spike protein from targeting and fusing with human cells. However, any formation of immune memory resulting from this process can be rendered ineffective by a viral mutation that substantially disguises the S protein to be unrecognizable by the immune system.

The genetic stability of inactivated vaccines could perhaps offer protection against several mutated strains; however, it is unclear whether accurately examining and mapping certain current strains can extend to future emerging ones. Additionally, it is unclear how many vaccine dosages will be warranted with the inactivated virus vaccines; and what will be their final level of effectiveness and durability [33]. So far, and up to July 22 2021, Sinovac has offered two doses.

Both mRNA and DNA vaccines have been proven to be effective against the UK/Kent variant, also known as B.1.1.7. However, the Delta mutation that is more transmissible than B.1.1.7, has been found to mildly compromise the effectiveness of the Pfizer/ BioNTech and AstraZeneca vaccines from 93% to 88% and from 66% to 59.8% respectively. However, one dose of both vaccines appears to reduce the vaccine effectiveness on B.1.617.2 down to 33%. These findings strongly urge for a two-dose administration of both vaccines to secure a higher protection against COVID-19, against the B.1.617.2 new variant [34].

The Sinovac or Coronavac vaccine has attained the lowest efficacy rate when compared against both its mRNA and DNA alternatives. The University of Chile study reported that Sinovac was effective around 56.5% after two weeks administration of the second dose and only 3% effective after only one dose that exponentially increased to 27% within two weeks. Brazilian researchers have

found that the Sinovac only has 50.7% overall efficacy that did not seem to be compromised by the Brazilian P1 variant, while Turkish studies reported an 83% efficacy. The Sinovac has not released data regarding its effectiveness against the Delta variant.

Overall, around 2.12 billion people have been vaccinated around the world by June 2021 with very rare serious adverse effects, leading to the conclusion that the benefits of any vaccine available today are greater than the risks involved in contracting the COVID-19 [35].

# Questions and Answers

# **Q: Should I be vaccinated?**

A: Clinical trials gathered by the U.S. National Institute of Allergy and Infectious Diseases [36] report that 95.5% of individuals with severe COVID-19 symptomatology resulting in death are unvaccinated. Only 0.05% of vaccinated individual suffer life threatening or fatal COVID-19 infections. According to the World Health Organization a total of 3,696,135,440 people have been vaccinates as of July 25, 2021 [37]. The vaccines have high efficacy. Reported serious adverse effects are rare. Temporary pain and swelling limited to the vaccination side, transient headaches and fatigue attest to the exhaustive insurmountable labour of the immune system as it reassembles for a winning battle. Overall, the benefits of the vaccines available appear to be greater than the risks involved in contracting any of the highly contagious COVID-19 variants [38].

## Q: Why be vaccinated?

A: All evidence indicates that the benefits of vaccination surpass its risks. COVID-19 transmissibility rate is generally lower among vaccinated individuals. Importantly, this disease is not like cancer or diabetes that advance or improve affecting primarily the individual without endangering the community. Anyone infected by COVID-19 puts everyone around them at risk: both friends and enemies, family members and strangers. The diagnosis of cancer is frightening because as the malignancy spreads, it tarnishes the vital organs destroying life. COVID-19 does not only target one person but everything and everyone around us, including the surfaces we touch and the air we breathe. COVID-19 is a public cancer that can ravage families, societies, economies, expanding to devastate the planet Earth. Vaccines can reinforce the immune system with antibodies which ultimately restrict or prevent viral entry. Vaccines provide the keys to seal our doors and keep the invisible enemy outside. A detailed explanation on vaccines' safety and effectiveness is given in section 1, along with their importance, in light of an uprise of progressively more infectious variants.

# Q: What can Stop COVID-19 from Entering our Bodies?

A: One of the most significant goals of the vaccine is to promote immune production of antibodies that will restrict or prevent COVID-19 entry. 80% of vaccines trigger antibodies that can bind with the Spike protein after only 10 days of the first dose. 100% of vaccines induce T-cells, specifically designed to target the Spike protein and defend us against the multifaceted manifestations of COVID-19 [39].

Antibodies are Y shaped proteins. Certain antibodies recognize the S1 glycoprotein and fit onto the viral antigens like a key to a lock. This prohibits the virus from binding with the ACE2 cellular receptor, thus preventing viral entry. Other ones can neutralize the heptad repeat 2 (HR2) domain to impede the fusion between the Spike subunit S2 with the ACE2 receptor, thus avoiding the release of the viral contents into the cells. So even if the S1 subunit of Spike protein binds with the ACE2 receptor, the second step of antigen/receptor fusion is compromised, disallowing COVID-19 entry into the cells. Prohibiting COVID-19 invasion into the cells impedes the virus from highjacking our cellular machinery and exploiting it for the purpose of its replication. In short, the antibodies obstruct COVID-19 from entering and spreading within the body [40].

# Q: Do I still need to wear a face covering after I have been vaccinated?

A: The data so far suggests that developing antibodies or T-cells that specialize in the Spike protein can protect us against developing severe COVID-19 symptomatology or dying. However, whether or not a vaccine completely protects us from being infected by COVID-19 is altogether a different story. Besides, statistics pertain to large numbers of people but not to individuals. 95% efficacy means that there is a small 5% of individuals that remain unprotected. The consensus from several clinical studies seems to be that vaccinated people do not infect others with regards to the Alpha variant that manifested the highest transmissibility rate until the Delta variant came along. However, there is always a small percentage that reacts unlike what is considered statistically significant. Moreover, it is possible that vaccinated but unmasked individuals can contract COVID-19, have no symptoms because of the protective antibodies and T-cells developed as a result of the vaccination, and therefore, be incognizant that they endanger others. Because they have refused to wear a mask, they can contaminate people in their proximity who are not yet fully vaccinated, because it takes at least two doses of most vaccines to shield the body from the virus. Or there may be cases where unmasked vaccinated people are infected with COVID-19 and transmit the virus to those who cannot be vaccinated due to health reasons, or children, turning them into COVID-19 carriers propagating the COVID-19 epidemic. By being unmasked, such vaccinated individuals will start a chain reaction, merely by carrying the virus and transmitting it to others, perpetuating the destructive vicious circle of the pandemic, and giving COVID-19 one yet opportunity to invent new ways to adapt in a human body, forming novel, incrementally more contagious mutations that come back to attack us with a vengeance. In other words there may be a future unprecedented COVID-19 mutant that suddenly appears, evading antibody detection and escalating COVID-19 transmissibility among vaccinated people. All this nightmarish downfall can stop by wearing a face covering to protect both ourselves from the onset of next generation, yet unknown mutations, and protect others from being infected from asymptomatic individuals. A face mask is a small price to pay to keep ourselves and our communities safe.

Recent unpublished data regarding the increased transmissibility of the Delta variant was cited on July 28, 2021 by Dr Antony Fauci, the director of the US National Institute of Allergy and Infectious Diseases, and chief medical advisor to the US president. So far, the data indicated that vaccinated individuals infected by the Alpha variant have very low viral loads in their nasal fairings, and therefore, are not contagious. On the other hand, vaccinated people infected by the Delta variant have a viral load in their nasal fairing that is 1000 greater than what was formerly observed with the Alpha variant. When vaccinated individuals are infected by the Delta variant, they will contaminate everyone around them, unless they are wearing a face mask. Additionally, earlier data supported the assumption that the Alpha variant did not afflict children. The current statistics suggest that children are quite susceptible to the Delta variant. Now, that the Delta variant is spreading around the world, both vaccinated and unvaccinated adults should take precautions, that can be very easily accomplished by a face covering, to avoid infecting their children or other people's children.

#### Q: If I can still contract COVID-19 then why get vaccinated?

A: According to research, 95.5% of vaccinated people avoid noxious symptomatology and survive. Simply contracting the virus and shaking it off in a few days, cannot be compared with being debilitated for weeks or months or leaving your last breath in some hospital. It is the degree of infection and the severity of symptomatology that make the crucial distinction between vaccination and the lack of it. The goal is for the world to fight this COVID-19 pandemic together. Non-compliance with vaccines or face coverings does nothing more than help COVID-19 evolve into more contagious and dangerous versions of itself.

### **Q: How Do Humans Empower COVID-19?**

A: COVID-19 is more cunning, multifaceted and resourceful than other coronaviruses. In the pursuit of its endurance and subsistence, COVID-19 evolves within our bodies. It mutates strategically, revising errors that extinguished previous coronaviruses. Several people within certain countries are oblivious, ignoring the facts unfolded in front of them that delineate the speedy extraordinary adaptation of COVID-19 that continuously increases its transmissibility. They refuse to adjust to the grave risk that COVID-19 poses. In other words, they do not take COVID-19 seriously. They are under the impression that they can still go about their lives as if nothing has changed. They see COVID-19 as a passing nuisance, despite flagrant evidence that this pandemic is becoming progressively more transmissible with every new emerging variant. They refuse to be vaccinated or use face coverings to protect themselves and others. They do not believe that the danger is real until the virus has infiltrated their lives bringing desolation and despair in its passage. Therefore, the answer to this question is yes. COVID-19 is only part of the problem. Misinformation, ignorance and individuals who defy the need to sacrifice convenience for the safety of their communities is the other side of the problem.

### Q: What makes COVID-19 so Dangerous?

A: COVID-19 places the immune system on check. It has a tenfold stronger hold on ACE2 receptors that its predecessor, SARS- CoV. ACE2 receptors catalyse Angiotensin II into Angiotensin 1-7 which is anti-inflammatory and lowers blood pressure. This process is compromised when COVID-19 seizes and occupies ACE2 receptors leaving the system with excess Angiotensin II. Angiotensin II constricts the blood vessels, obstructing blood flow, thus increasing blood pressure, while inducing an inflammatory response in the vascular wall. Increased blood pressure is deleterious to a number of medical conditions including hypertension, cardiovascular disease and diabetes, which manifest the highest mortality rates after COVID-19 infection. So just by binding to the ACE2 receptors COVID-19, debilitates the antiinflammatory and anti-fibrotic functions of ACE2 receptors that can no longer catalyse Angiotensin II. The inevitable result of this process is escalated inflammation, vasoconstriction and high blood pressure, preluding the eventual catastrophic immune reaction termed "cytokine storm."

### Q: COVID-19 disables the Immune System. How?

A: COVID-19 blinds the immune system by impairing its capacity to recognize the virus and target it directly. Shooting in the dark, the white blood cells indiscriminately attack the vital organs that contain the virus, failing to distinguish self from non-self. This consists of two processes: Under normal circumstances, the innate response emerges immediately in the presence of a foreign agent's invasion. Innate immune system is largely non-specific and serves as a general defensive strategy. Subsequently, the adaptive immune response is activated that is specifically designed to recognize and attack the virus. A recent review suggests that coronavirus is designed to hinder the critical process of viral recognition, and suppress the production of Interferon (IFN) type I, ultimately impairing the competence of the adaptive immune system to identify the position of the virus within the organism and distinguish it from the host's healthy cells [41,42]. If the adaptive system cannot discover the virus' hiding place, then exterminating the virus will most likely fail. The immune system will attack, destroy healthy cells, yet the virus, safely concealed from the blind giant, shall survive. The immune system, will mobilize all its defensive mechanisms, interferons, interleukins, cytokines, leukocytes or white blood cells, colony stimulating factors, tumour necrosis factors, the protagonist of the cytokine storm, along with CD8-T cells or killer cells. But the virus will remain out of sight and the onslaught will end up annihilating the host.

Another possibility is that COVID-19 affects the Immunoglobulin (IG) gene that regulates the antigen receptors of B cells which secrete antibodies and are a crucial aspect of the immune system [43]. Without antibodies, the body cannot defend against COVID-19 invasion.

A third possibility is that COVID-19 interferes with the major histocompatibility complex (HMC) genes that encode many proteins involved in T-cells antigens, which are part of the adaptive immune response. This is directly related to undermining the adaptive immune system. T-cells are like immune soldiers unleashed against the viral assault. Proteins within the cell are like the brains of a cell. Immune soldiers shall suffer "brain damage" as COVID-19 disqualifies the HMC gene that encodes the proteins (the brains) necessary for the T-cells to function. Inevitably, the immune system will lose both the battle and the war because its soldiers are deficient. Unable to defend against the virus the host will collapse.

Defects related to the INF type 1 and the IG gene, which subsequently affects the antibody production by B cells, interferes with the switch from the innate to the adaptive sector of immunity, leaving the adaptive immune response in a state of disarray especially if the HMC gene is damaged. The adaptive immune system shall predictably fail to recognize the virus, firing against anything in sight, ravaging the vital organs and killing the host [43,44]. This phenomenon termed "cytokine storm" is discussed in greater detail below.

### Q: What is a cytokine storm?

A: It is what kills us. The virus does not want the host to die. Mortality is collateral damage during the immune system's war against the invisible enemy.

# Q: How is COVID-19 more sophisticated than other coronaviruses?

A: Viruses randomly mutate in order to adapt within the diverse biological environments of different hosts, so that they avoid detection. Mutations are like a disguise that helps a virus hide unobserved, to get out of the radar of the immune system, and cunningly mislead it. The word "random" entails that several of these transformation will lead to mistakes on the part of the virus, and as the errors pile up, the virus will be eventually extinguished.

In real situations we are observing that after over 300,000 transformation, COVID-19 has achieved the unthinkable which is the exact opposite. Rather than eradicating itself, COVID-19 empowers itself with every new variant. Novel mutants have expanded the COVID-19 infectiousness, increasing its transmissibility from 70% to 100% globally with this next generation Delta variant. Uprising COVID-19 mutants are now challenging the effectiveness of several emerging medications and vaccines.

The question is how could that happen during a random process, where what can go wrong will go wrong? A mutation is basically the result of at least one amino acid substitution from one position to another. How can COVID-19 manoeuvre away from all amino acid rearrangements that could potentially obliterate it and only adopt amino acid swapping that enhance its efficacy and potency? The answer is that we "don't know." All we can suggest is that this is exactly what COVID-19 seems to be doing.

An example is Van Dorp et al (2020) study that reported changes in the COVID-19 non-structural proteins Nsp6, Nsp11, Nsp13 as well as the trimeric spike [45]. However, if instead of the Nsp6, Nsp11 and Nsp13, the non-structural proteins Nsp7, Nsp8, and Nsp12 in association with Nsp14 were involved, the COVID-19 capacity to replicate long viral RNA would have been compromised, eventually leading to the degradation of the virus [46]. COVID-19 Non-structural protein (Nsp) transformations are adaptive allowing the virus to survive, in contrast to other coronavirus Nsp transformations that lead to the eventual extinction of the disease.

### Q: Why there are more deaths among men than women?

A: Initially scientists thought that oestradiol protects women. However, according to the contradictory results of recent published data oestradiol does not appear to be a reliable protective shield against COVID-19. On the other hand, male testes have an abundance of ACE2 receptors which serve as the COVID-19 entry points into the cells. Additionally, research on human tissues has revealed that the immune responses between males and females are different. For example ACE2 expression in male vital organs was associated with an elevation of immune cells, such as B cells that develop antibodies, NK or natural killer cells and CD8+ or cytotoxic T cells. Specifically, this exacerbated immune response in males involved positive correlations between immune cells and ACE2 receptors in the following vital organs: lungs, thyroid, live, colon, kidney, stomach, pancreas, skin, adipose tissue and testes. While females' ACE2 receptors in the lungs and thyroid was associated with decreased levels of B, NK, CD8+ T cells. On the other hand, upregulated ACE2 expression in the female heart tissues was accompanied by increased B, NK, CE8+ T cells and Interferons, unlike male heart tissues, where ACE2 receptors and immune cells featured a negative correlation. ACE2 receptors in the kidneys, skin, stomach, and adipose tissue were associated with increased levels of immune cells in both sexes. [47]. Basically, males appear to be biologically more vulnerable to COVID-19 than females as a result of the relatively higher positive correlations between ACE2 receptors and immune cells in a greater number of male rather than female vital organs.

There may be additional reasons associated to toxicity such as smoking that some countries report to be more frequent among males than females, environmental pollution or higher exposure for working men who support women that are sheltered at home due to pregnancy or other social arrangement.

**Q:** Is there an affinity between adipose tissue and COVID-19? A: Fat cells are abundant in ACE2 receptors, which are the chosen COVID-19 portal into the cells. The greater the number of ACE2 receptors, the higher the chance of being targeted by COVID-19.

Additionally, both subcutaneous and visceral adiposity withhold toxicity. In general, toxic stressors, including neurotoxic, biological, physical, chemical, psychological and psychosocial irritants, may lead to immune degradation, rendering the body an easy prey to COVID-19.

Reducing BMI and increasing fitness appear to be some of the most fundamental protective methods against COVID-19. We emphasize optimal BMI rather than merely recommending weight loss, because there are several ways to reduce fat that may be deleterious to health, because they increase inflammation or result in systemic hyperstimulation as it happens with some slimming products. Some diet pills that speed up metabolism and suppress appetite can lead to increased blood pressure, lung and heart problems that will provoke rather than prevent COVID-19 severe symptomatology.

Health and hormonal balance are the cornerstones of a preventive strategy against COVID-19 and anything that can undermine health or disorganize hormones into a disequilibrium is detrimental exposing the body to all kinds of medical issues, in addition to increasing vulnerability to becoming severely ill with COVID-19. Research has reported that prescribed slimming preparations may cause pulmonary hypertension and serotonin neurotoxicity that can be expressed in anxiety and depression, sleep disturbances and cognitive defects [48].

## **Q: How about RF and Laser lipolysis?**

A: Weight loss is only one aspect of health that largely depends on fitness, optimal lifestyle choices, hormonal balance, the absence of stress and so much more. Both laser and RF can offer fast lipolysis, but results will rebound with lipolysis alone. Without detoxification or the fitness factor, toxicity will disorganize the hormonal reciprocity of leptin and ghrelin resulting in constant hunger. Hormonal equilibrium is crucial in balancing disproportional levels of complementary hormones like the appetite regulating leptin and ghrelin or optimize cortisol to control food consumption. Neither lasers nor RF is in anyway designed to balance hormones, increase fitness or detox.

The sparce studies that report visceral fat reduction following laser or radiofrequency procedures, combine lasers with exercise, making it impossible to distinguish which contributed to the result. Moreover, they manifest methodological difficulties, such as internal validity flaws related to instrumentation or failure to duplicate the study which is a threat to external validity.

Importantly, there are several reports of eventual escalated inflammation following radiofrequency procedures [49-53]. Radiofrequency replaces pre-existing inflammation inherent in adipose tissue with radiofrequency induced inflammation. Whether inflammation is the result of excess adipose tissue or the after effect of the radiofrequency procedure, the outcome will be the same. Inflammation, irrespective of its source, will most likely exacerbate the deleterious immune response termed "cytokine storm" that is detected in COVID-19 severe cases with often lethal consequences. This line of reasoning renders any procedure that increases inflammation counterproductive. and conceivably dangerous during this pandemic.

### **Q: What is the Importance of Fitness?**

A: During exercise, or its alternative that was introduced by a series of clinical trials, the body uses fat as an energy source to build muscle. As previously reported, adipose tissue displays an abundance of ACE2 receptors. COVID-19 Spike protein binds and fuses with the ACE2, releasing its viral contents into the cells. Fat is to COVID-19 what a flower field is to the bees. However, the more sparce the ACE2 receptors are, the less the opportunities

COVID-19 will have to enter into the cells and commandeer our molecular machineries to duplicate itself. ACE2 receptors' expression is very limited in the muscle, according to research in human tissues [54]. The premise should be now clarified: The greater the number of ACE2 receptors as it is in the adipose tissue, the more the chances of COVID-19 spreading and overwhelming the body. The diminished ACE2 expression in muscle tissues, reduces the COVID-19 chances to proliferate, and gives the immune system more time to assemble its defences. In a war, the size of the armed forces attacking, and the time of gathering recourses to defend and counterattack is crucial. Similarly, the COVID-19 rate of transmissibility within the human body will depend on the number of COVID-19 receptors the virus can seize. There are many in the fat, and a relatively low number in the muscles. This does not mean that muscular individuals cannot contract COVID-19. Anyone can be prey to this savvy new virus. It is not whether or not we can be infected, but the speed of duplication and the magnitude of the viral contagion in our cellular networks that determine the difference between mild and severe symptomatology, or between life and death.

## Q: What are the COVID-19 key vulnerability factors?

A: Several factors that undermine health contribute to increased COVID-19 vulnerability, some of which are listed below.

- 1. Elevated low-density lipoprotein (LDL)
- 2. Upraised very low-density lipoprotein (VLDL)
- 3. Inadequate levels of high-density lipoprotein (HDL)
- 4. Testosterone below the normal range
- 5. Escalated Cortisol
- 6. Reduced thyroid function and compromised metabolism. Low T3.
- 7. Excess Visceral Adipose Tissue
- 8. Excess overall fat and obesity
- 9. Sedentary lifestyles

10. Absence of Fitness via either regular physical exercise or its effortless alternative

- 11. Growth Factor below the normal range
- 12. Elevated Bilirubin
- 13. Abnormal levels of Creatinine
- 14. Upraised C reactive protein (CRP)
- 16. Elevated proinflammatory Interleukins
- 17. Upheaved tumour necrosis factor

18. Heightened numbers of leucocytes, or white blood cells that are involved in both the adaptive and the immune system response to invading microorganisms.

19. Hyperleptinemia

20. A disturbance in the balance of appetite hormone leptin and ghrelin resulting in hunger that inevitably leads to weight gain

- 21. Hyperglycaemia.
- 22. Insulin Resistance
- 23. Low BMR
- 25. High BMI
- 26. Old Age
- 27. Hormonal Imbalance
- 28. Being a Male
- 29. Fatty Liver

30. Increased lymphocytes, a type of white blood cells designed to recognize antigens that is primarily involved in the adaptive immune response. Lymphocytes indicate the presence of an infection or inflammation.

31. Pre-existing medical disorders, some of which are: Asthma, Diabetes, Cardiovascular illness, Hypertension, chronic respiratory disease, chronic liver disease, immunosuppressed conditions, lupus, rheumatoid arthritis, psoriasis, cancer, organ transplant, asplenia, stroke or other neurological conditions [55].

32. Increased oxidative stress. Toxicity. Environmental pollution, smoking.

33. Psychological Stress

34. Crowded places

35. Coughing, sneezing, talking, socially interacting without a facial covering.

# Q: What are the advantages of exercising?

**A:** Individuals with medical disorders have demonstrated the highest COVID-19 susceptibility rate. Exercise is the golden rule most frequently recommended by most medical professionals as part of empowering immunity [56-59]. There is a large body of research specifically postulating that exercise:

1. Uses fat as an energy source to build muscle

2. It decreases low density lipoprotein [60,61]

3. It reduces inflammation [62]

4. It is necessary to treat hyperlipidemia and obesity [63,64]

5. It decreases hyperglycaemia [65-67]

6. It enhances the growth hormone response (HGH). HGH is not only involved in muscle building but bone integrity, collagen regulation and increased fat metabolism [68].

7. Animal studies have postulated that exercise influences lymphocyte function.

8. It decreases visceral fat that can be deleterious to vital organs

9. It reduces the incidence of fatty liver

10. It reduces overall fat

11. After 9 days of repeated physical activity fat oxidation was increased to an additional 24% within one hour, the equivalent to 4.5 kilograms of burned fat [69].

# Q: Are there any adverse effects related to exercise?

A: Exercise has many advantages. There are, however, some disadvantages.

 In the above study [70], training was reported to upregulate the gene expression of the fatty acid translocase (FAT/ CD36) that mediates fatty acid effects on insulin secretion, but it also enhanced the constitutive expression of PR gene 1, (CPR1) that is a suppressor of pathogen signalling.
Prolonged exercise decreases leptin concentrations by 32% and increases free fatty acids as expected by the understanding that free fatty acids act as an energy replenishment mechanism after energy expenditure [71]. However, leptin reduction will reinforce increased food consumption after exercise, undermining the weight loss benefits.

**3.** Excessive exercise is perceived by the body as a form of stress and stimulates the release of cortisol that may cause tissue breakdown with over training leading to stress eating behaviours

that are bound to compromise the benefits of exercise [72].

4. Cortisol is involved in the conversion of protein to glucose potentially predisposing older individuals to type II diabetes [73]. 5. Strenuous exercise, necessary to reduce visceral adipose tissue, is associated with a negative relationship between cortisol and testosterone. In other words, cortisol increases with a reciprocal decrease of testosterone. High cortisol may precipitate weight gain, a higher susceptibility to infections, puffy or flushed face, mood swings, anxiety, acne and other skin disorders and a higher risk for bone fractures and osteoporosis. Low testosterone will induce weight gain, fatigue, depression, joint pain, muscle weakness, respiratory problems and compromised sexual drive. Therefore, both of these complementary hormonal fluctuations are in the wrong direction leading to hormonal imbalance that may ultimately offset the benefits obtained during exercise [74].

**6.** Importantly, during overtraining, which is often necessary for visceral fat reduction muscle-derived IL-6 is released into the circulation in high amounts resulting in increased inflammation [75,76].

# Q: Is there an alternative to exercise?

A: A number of clinical studies have indicated that there is an alternative to exercise, a technology discovered in London University by the co-inventor of the first pacemaker, Gerald Pollock. This effortless exercise technique appears to solve the inverse negative cortisol / testosterone problem by demonstrating an increase in testosterone and a decrease of cortisol, but without any of these two variables falling outside the normal range. In short, cortisol appears to descend towards the bottom of the normal range in subjects with high cortisol, yet remain stable in individuals whose cortisol was already closer to the lower end of this dimension. In contrast, testosterone appeared to climb towards the peak of the normal range in subjects with low testosterone or remain unchanged in those who already manifested high testosterone levels [78-88]. Other observed benefits following a course of treatments that varied from 12 to 20 treatments depending on the research project were as follows:

1. Growth Hormone ascended towards the peak of the normal range.

2. T3 was also elevated toward the top of the normal range.

3. There was a significant decrease in inflammation as indicated by the C reactive protein (CRP).

4. The very low density lipoprotein (VLDL) was significantly reduced.

5. The very high density lipoprotein (HDL) was significantly increased.

6. Triglycerides indicated a decline, returning into normalcy.

- 7. Creatine dropped down to be within the normal range.
- 8. Bilirubin was significantly reduced to be within normalcy.

9. Both fasting and postprandial glucose in diabetic patients descended to either prediabetic levels or within normalcy.

10. Both fasting and postprandial insulin in prediabetic patients descended to either prediabetic levels or within normalcy.

- 11. There was a significant decrease in visceral fat.
- 12. Subcutaneous fat was also significantly reduced.
- 13. A significant decrease in BMI was demonstrated.
- 14. The basal metabolic rate (BMR) was optimally elevated.

- 15. There was a significant increase in skeletal muscle mass.
- 16. Leptin and Ghrelin returned to optimal levels.
- 17. Subjects reported normal appetite without cravings.

18. There was a substantial weight loss in kgs and upper abdomen, waist and lower abdomen reduction in cm.

19. No adverse reactions or side effects were observed or reported by any of the subjects.

# Q: Can a healthy lifestyle, exercise or its alternative prevent COVID-19 infection?

A: Fitness and optimal lifestyle choices are the shield of health. But we are still at war with COVID-19. In a war casualties can happen at any time. The survival of the fittest is the golden rule that applies here. But that alone is not enough. We need sophisticated defences like the vaccines, and effective pharmaceuticals to combat this cunning multifaceted virus. Everyone exposed to the virus will contract it. But what determines the severity of symptomatology or the chance of fatality is what comes next. Fitness and hormonal balance enhance our health status along with our immunity. Vaccines trigger the production of immune defences, the weapons we can use to prohibit or restrict viral entry or survive its deleterious consequences. Hence the importance of taking all precautions possible against this inconspicuous invisible enemy that is always a step ahead.

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