ESSAYS ON SURVIVING COVID-19

LESSONS FROM THE ANCIENTS TO THE PRESENT

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The Ultimate Trial By Combat

“Thus, though we have heard of stupid haste in war, cleverness has never been seen associated with long delays.” (Sun Tzu, The Art of War)

“Most of warfare is about convincing an enemy to give up. The greatest difference now is that the “enemy” is totally unthinking and unpersuadable, and will never give up.” (Christian Macedonia, MD)

Introduction

Both the U.S. Healthcare Agencies and the U.S. Military and have mutually supporting roles in maintaining strong security and safety measures for American citizens at home and abroad. The arrival of COVID-19 is an event of unprecedented strain on the health systems and security of our interconnected world.

COVID-19 is caused by coronavirus SARS-CoV-2. Older adults and people who have severe underlying medical conditions like heart disease, lung disease or diabetes seem to be at higher risk for developing more serious complications from contracting COVID-19.

Traditionally, clinical research is performed in a careful and meticulous manner to assure, first and foremost, the safety of the study participants. Secondarily, clinical research provides quality data to assure the safety and effectiveness of treatments which the FDA and other regulatory bodies then allow marketing of these novel therapies to the general public.

We are living in extraordinary times when infectivity of a relatively large proportion of the population is real, with a high risk of imminent death and disability within the global population. It is quite sad to hear, that the risk of COVID-19 is at the feet of the elderly, and those with heart disease, lung disease and diabetes. We are a civilized society, where it is unconscionable just say that because you are vulnerable, “tough luck.”

The Enemy

The enemy is a dangerous new virus, SARS-CoV-2. First of all, clinical trial stakeholders, including study participants, clinical care providers, sponsors, regulators, pharmacies, as well as CRO’s like Target Health are all under stress to deliver and complete high quality studies, now effectively in a war zone, with Covid-19 ravaging our citizens.

Years ago, Target Health met with the Defense Threat Reduction Agency (DTRA), a division of the US Army, for a product to treat neuroactive chemical agents in a war
zone. Besides being impressed by the quality and commitment of the DTRA team, it was very clear that first and foremost, the goal was to reduce mortality and morbidity by quick action in a war zone, while at the same time, get FDA to approve the product. For example, one requirement was to quickly administer the countermeasure and then evacuate the soldier to the nearest medical unit.

**The Pharmaceutical Industry**

Some of the very exciting phenomena we are seeing due to the current public health emergency is the behavior of the pharmaceutical industry as it reacts to devastating Covid-19 statistics, including:

1. repurposing of off-patent marketed drugs
2. repurposing of currently marketed novel drugs
3. identification of new indications of drugs currently in development
4. resurrection of drugs that have failed for one indication, which can be applied to COVID-19

**Study Endpoints**

Study endpoints are measures that often involve symptoms of a disease like reduction of blood pressure in hypertension, reduction of hemoglobin A1C in diabetes and joint pain in arthritis. Other endpoints may include patient reported outcome (PROs) such as “I can now play sports.”

In COVID-19 studies, virtually all studies have the same key endpoints with the following parameters:

1. NIAID ordinal assessment
2. WHO Ordinal Scale for Clinical Improvement
3. Death within certain number of days from first dose of study drug
4. Time to extubation
5. Length of hospitalization
6. Length of ICU stay
7. AEs and SAEs

**What is the Nature of the “Enemy”?**

1. SARS-CoV-2, a heartless enemy:
   a. Is like a roadside bomb, hiding ready to launch toward us at any moment.
   b. Is like a chameleon, changing its camouflage depending on the background of the environment
   c. Easily attacks the weak and vulnerable
   d. The virus itself knows no fear, has no regard for diplomacy, and cannot be placated with overtures of money or power.
   e. The “enemy” has only one mission and that is to reproduce as many copies as possible.
Managing a Study in a War Zone, and Why Do We Call It a War Zone?

a. Protective gear is needed to fend off attacks
b. Access to the zone of operations is often denied.
c. The situation is often fluid and chaotic and defenders and planners do not have the luxury of time.
d. Murphy’s Law applies: “What can go wrong will go wrong.”
e. Like a War Zone, even when the plan is executed perfectly there still innocent lives lost in the process.

To Combat the Enemy, We Must Cooperate as Humans

a. To identify and empower intelligent and capable leaders
b. To meet the virus head on while at the same time keeping a safe distance
c. To take risks to find its vulnerabilities
d. To develop countermeasures at all levels
e. To reward and indemnify leadership that is wise, bold, and decisive.
f. To eschew a “zero defects” mentality.

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2. Darwin Nailed It, but....

Part 1: Who Survives and Who Lives?

With the rapid and very deadly advent of COVID-19, it has been reported that certain subpopulations within our society are more vulnerable as to morbidity and mortality. The deaths in the nursing homes, the elderly, prisoners, people with concomitant diseases and the poor, show that Darwin in a certain sense was right when he said

“One general law, leading to the advancement of all organic beings, namely, multiply, vary, let the strongest live and the weakest die.” - Charles Darwin, The Origin of Species

However, as human beings, we do have alternatives to the basic notion of survival of the fittest. We have the ability, which we share with other species, to evolve socially, so that those most vulnerable amongst us, even though they may be viewed as physically “weak”, offer much to make us strong. Think of the theoretical physicist Steven Hawking who was diagnosed with ALS in 1963 at age 21. If we only lived by the dogma that the physically strongest live and the physically weakest die, then all the physically “sick” intellectuals and “disabled” leaders like FDR would be left to die, and all the bullies of the world, most of whom are mentally weak and emotionally disabled, would take over.

So what we are seeing now are 2 evolutionary forces at work. One is the killer battle with SARS-CoV-2 which we are fighting with all that we developed over time using our brains rather than our brawn. The second is a selection process using social and political pressures, and ultimately the power of “WE THE PEOPLE,” to select and elect leaders, who value life and all that it brings, rather than those who only believe in themselves in a zero-sum game society.

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Part 2: Learning From the Past

“One general law, leading to the advancement of all organic beings, namely, multiply, vary, let the strongest live and the weakest die.” - Charles Darwin, The Origin of Species (24 November 1859)

**Question 1:** There is a hurricane coming to Florida this weekend with incredible planning to save lives and property. Why the disconnect with the pandemic?

**Question 2:** If we are currently dealing with Darwin’s Origin of Species, who will be the strongest and who will be the weakest?

As part of the evolutionary process, we as humans, must learn from the past or as scholars have said quite clearly and to the point:

1. “Those who don’t know history are destined to repeat it.” (Edmund Burke: 1729-1797)
2. “Those who cannot remember the past are condemned to repeat it.” (George Santayana: 1863-1952)

Here are also some relevant and famous quotes from Nelson Mandela who spent 27 years in jail for fighting for human rights:

1. “Education is the most powerful weapon which you can use to change the world.”
2. “It always seems impossible until it’s done.”
3. “May your choices reflect your hopes, not your fears.”
4. “A winner is a dreamer who never gives up”
5. “It always seems impossible until it’s done.”

In order to manage the pandemic we must use all of the skills that human beings have developed over time, as cited above. The main reasons we must do this is that the SARS-CoV-2 virus knows how to:

1. Travel on airplanes without buying a ticket
2. Fly internationally without a passport
3. Asymptomatically hide in humans as it spreads
4. Kill healthcare workers who want to kill it
5. Enter the brains of decision-makers to have them make decisions to make it easier for the virus to transfect others. For example:
   a. There are no consistent mandates by global leaders for the population to wear masks
   b. Some individuals have stated that:
i. Wearing a mask challenges my rights under the American constitution
ii. Wearing a mask causes transfection
iii. It is not manly to wear a mask
iv. I do not look good in a mask
c. It is ok to party
d. Kids are immune

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Part 3: It is All About Education

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Think about it, why can the National Basketball Association (NBA) compel the Centers for Disease Control and Prevention (CDC) and common sense controls to ensure the
safety of their players, but our government cannot insist on the same controls to ensure
the safety of all of us.

Most people think of Charles Darwin as the Father of Evolutionary Biology, and rightfully
so. The following is one of Darwin’s most noted quotes.

“One general law, leading to the advancement of all organic beings,
namely, multiply, vary, let the strongest live and the weakest die.” – Charles
Darwin, On The Origin of Species (24 November 1859)

Many are not aware that "Survival of the fittest" is not a Darwin quote, but rather a
phrase that Herbert Spencer first used after reading Charles Darwin's “On the Origin of
Species.” When confronted by Spencer, Darwin agreed that “survival of the fittest” more
clearly defined what he, Darwin, intended to convey when he coined the phrase "natural
selection”.

Last week, we wrote as part of our series on evolution, that we as humans must learn
from the past and become much better educated, cradle to grave. The following are
some memorable quotes.

1. “Those who don’t know history are destined to repeat it.” (Edmund Burke: 1729-
1797)
2. “Those who cannot remember the past are condemned to repeat it.” (George
Santayana: 1863-1952)
3. “Education is the most powerful weapon which you can use to change the world.”

What does all of this mean during the ongoing COVID-19 pandemic of 2020, just 100
years after the Spanish flu pandemic of 1918. The 1918 pandemic infected an
estimated 500 million people worldwide - about one-third of the planet’s population - and
killed an estimated 20 million to 50 million victims, including approximately 675,000
Americans.

To put the current crisis in perspective, the following are some of the great
accomplishments of modern times:

1. Humans have learned how to control and/or eliminate pandemic diseases such
   as smallpox, polio and measles
2. Humans landed on and returned from the moon
3. Humans invented the Internet, thus enabling Global connectivity and an unlimited
crossroads of creative ideas
4. Humans have invented multiple methods of alternative energy, namely, Solar
   energy
5. Humans are offered medical miracles from great institutions like the NIH, CDC
   and WHO
Yet, in spite of these and other success stories, we have failed miserably to educate people throughout the world to recognize the value of truth over lies, science over “wishful thinking,” and evidence-based decision making over “fake news.”

Being the strongest, most intelligent and the most adaptable to change are all noble traits, but without an educated society willing to take on civic responsibilities, societies acquiesce to the whims of the unscrupulous who may be strong and intelligent, but who also gain the power by forcing decent citizenry to comply with their imposed changes. Thus, without having an educated society there is no path to the survival of the human species. The reasons are that 1) none of us are totally self-sufficient, 2) we all need others to survive, and 3) we are all in this world together, with each person optimizing his/her contributions for the betterment of all.

Think of the complexity of societies where even the super elite, with all of their resources, cannot by themselves survive a planetary catastrophe such as the imminent climate change predicted in 1998 by James Hanson (then Director of the NASA Goddard Institute for Space Studies); or a global viral pandemic as we are currently experiencing.

While now defunct and debunked, Social Darwinism reflected various theories of society which emerged in the United Kingdom, North America, and Western Europe in the 1870s, claiming to apply biological concepts of natural selection and survival of the fittest to sociology, economics, and politics. Social Darwinists argued that the strong should see their wealth and power increase, while the weak do not deserve much of anything. Various social Darwinist groups had differing views regarding which groups are considered “the strong” and which groups should be considered the “weakest.” They also held different opinions about the precise mechanisms that should be used to reward strength and punish weakness.

Science and Learning From the Past are Bridges to a Healthy and Wealthy Society

Why during the COVID-19 pandemic or 2020, are some people asymptomatic while others are not? Why do some die and some survive with sequelae? Perhaps Biology tells a better story as to how advanced societies should and could manage and adapt to change. The following are 4 examples on how to optimally deal with change:

Wear Masks and Socially Distance – Lessons from the Past:

Almost 700 years ago, the overwhelmed physicians and health officials fighting a devastating outbreak of bubonic plague in medieval Italy had no notion of viruses or bacteria, but they understood enough about the Black Death to implement some of the world’s first anti-contagion measures. Starting in 1348, soon after the plague arrived in cities like Venice and Milan, city officials put emergency public health measures in place that foreshadowed today’s best practices of social distancing and disinfecting surfaces. The Adriatic port city of Ragusa (modern-day Dubrovnik) was the first to pass legislation...
requiring the mandatory quarantine of all incoming ships and trade caravans in order to screen for infection. The order, which survived in the Dubrovnik archives, reads that on July 27, 1377, the city’s Major Council passed a law “which stipulates that those who come from plague-infested areas shall not enter [Ragusa] or its district unless they spend a month on the islet of Mrkan or in the town of Cavtat, for the purpose of disinfection.”

Understanding Immunity: According to the scientific community, previous exposure to other coronaviruses, may provide “T-cell immunity” to similar viruses, thus resulting in a lower viral load with less severe or no symptoms. It has been observed that healthy people who have not been previously infected with SARS-CoV-2 have detectable T cells for the virus, and it is felt that this exposure to other common, seasonal coronaviruses may have induced the production of long-lasting T cells immunity.

Understand Risk Factors: People who are obese make more of something called “complement” proteins. These proteins can trigger out-of-control blood clotting, which is a problem in patients with severe COVID-19. People with obesity also have lower blood levels of a hormone called adiponectin. Recent studies in mice show that adiponectin protects the lungs. It has also been hypothesized that those with lower baseline levels of adiponectin may be more likely to have lung inflammation during an infection like COVID-19. Adiponectin also helps keep blood vessels clean and open.

The SARS-CoV-2 virus uses the angiotensin-converting enzyme 2 (ACE2) as a cell receptor to invade human cells. Those ACE2 receptors appear to be more prevalent in older people and those who are obese, than in younger people.

Famous Darwin Quotes:

Several Darwin quotes noted below are worth considering.

1. “…but if we were intentionally to neglect the weak and helpless, it could only be for a contingent benefit, with a certain and great present evil.”
2. “In the long history of humankind (and animal kind, too) those who learned to collaborate and improvise most effectively have prevailed.”
3. “Intelligence is based on how efficient a species became at doing the things they need to survive.”
4. “If I had my life to live over again, I would have made a rule to read some poetry and listen to some music at least once every week.”

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Part 4: Lessons to be Learned from Homo neanderthalensis

Planet Earth is now experiencing the COVID-19 global pandemic caused by the novel SARS-CoV-2 coronavirus. As a result, so we can perhaps better plan for what the future might or will bring, we thought it would be of interest to look at the causes of the “extinction” of Homo neanderthalensis. While violence from encroaching modern humans may have contributed, in part, to the extinction of the Neanderthals, infectious diseases from human encounters and climate change appear to be most critical factors. Thus, “word to the wise…,” and need we say more.

As mentioned previously:

1. “Those who don’t know history are destined to repeat it.” (Edmund Burke: 1729-1797)
2. “Those who cannot remember the past are condemned to repeat it.” (George Santayana: 1863-1952)
3. “Education is the most powerful weapon which you can use to change the world.” (Nelson Mandela: 1918-2013; quoted in 2003)

Homo sapiens, We Are Not Alone

Homo sapiens, (AKA “wise man”) is the species to which all of us humans belong to, and yes, is the only species within the genus Homo that is not “yet” extinct. All of the other Homo species are gone ……. have become extinct.

On a positive note, humans have the ability to 1) write books, create music and appreciate the arts; invent mathematics and time; 2) create a knowledge base of science and technology; 3) innovate medical cures; 4) take a round trip to the moon; and 5) show empathy towards others. Interestingly, these traits, other than to take a round trip to the moon, although who knows for sure, are not unique to humans, since birds like eagles fly high. Think of 1) the Bower Bird mating displays; 2) the sadness displayed by primates and elephants when death occurs; 3) the behavior of cleaner wrasses that live in a cleaning symbiosis with larger, often predatory, fish, grooming them and benefiting by eating what is cleaned; 4) the gorgeous sounds of birds; and 5) the engineering magnificence of an ant hill and termite mound, including farming of aphids and “air conditioning.”
The Genus Homo (AKA “man”)

The genus Homo emerged from the extinct genus Australopithecus (Lucy), about 3 million years ago. Homo encompasses modern humans, plus several extinct species most notably Homo erectus and Homo neanderthalensis. The following are species within the genus Homo:

1. Homo antecessor
2. Homo erectus
3. Homo ergaster
4. Homo floresiensis
5. Homo habilis
6. Homo heidelbergensis
7. Homo luzonensis
8. Homo naledi
9. Homo neanderthalensis
10. Homo rudolfensis

Homo habilis appeared just over 2 million years Before the Present (BP), and in several early migrations, spread throughout Africa (where it is designated as Homo ergaster) and Eurasia. Homo erectus was likely the first human species to live in a hunter-gatherer society and to control fire. Homo erectus was an adaptive and successful species which persisted for more than a million years, and then gradually diverged into new species around 500,000 years ago.

Based on the fossil record, Homo sapiens emerged close to 300,000 to 200,000 years ago in Africa, while Homo neanderthalensis emerged at around the same time in Europe and Western Asia. Homo sapiens left Africa in several waves, possibly as early as 250,000 years ago, for sure by 130,000 years ago, and also during the so-called Southern Dispersal beginning about 70-50,000 years ago. This latter migration led to the lasting colonization of Eurasia and Oceania by 50,000 years ago.

Both in Africa and Eurasia, Homo sapiens met with and interbred with archaic (non-sapiens) humans. Separate archaic human species are thought to have survived until around 40,000 years ago. This is the time of the so-called Neanderthal extinction, with possible late survival of hybrid species as late as 12,000 years ago (e.g. the Red Deer Cave people, a prehistoric archaic human population).

Red Deer Cave People

Fossils dated to the Bølling-Allerød warming, an abrupt warm and moist interstadial period that occurred during the final stages of the last glacial period, ran from about 14,690 to 12,890 years BP. Interstadials are phases dividing the Quaternary period, or the last 2.6 million years, and are periods of warmer climate. Fossils during this period were found in Red Deer Cave and Longlin Cave in Southwest China. These fossils exhibit a mix of archaic and modern features and are tentatively thought to represent a
late survival of an archaic human species, or of a hybrid population of Denisovan hominin and modern humans. The Denisovans or Denisova hominins are an extinct species or subspecies of archaic human that ranged across Asia during the Lower and Middle Paleolithic (potentially surviving as late as 30,000 - 14,500 BP in New Guinea).

So, Why Exactly Did Neanderthals Go Extinct?

About 40,000 years ago, Neanderthals began disappearing from Europe, but exactly why they died out is still somewhat of a mystery. Hypotheses on the fate of the Neanderthals include violence from encroaching anatomically modern humans, parasites and pathogens, competitive exclusion, extinction by interbreeding with early modern human populations, natural catastrophes, and failure or inability to adapt to climate change. It is unlikely that any one of these hypotheses is sufficient on its own; rather, multiple factors probably contributed to the demise of an already widely-dispersed population. However, violence from encroaching modern humans is not considered by many to be a major factor.

Was the Extinction Due to Infectious Diseases Carried by Homo sapiens?

One possibility for the demise of the Neanderthals was the spread among the Neanderthal population of pathogens or parasites carried by Homo sapiens. Neanderthals would have limited immunity to diseases they had not been exposed to, so diseases carried into Europe by Homo sapiens could have been particularly lethal to them, while at the same time, Homo sapiens were relatively resistant. It might have been easy for pathogens to leap between these two similar species, perhaps because they lived in close proximity, then Homo sapiens would have provided a pool of individuals capable of infecting Neanderthals. On the other hand, the same mechanism could work in reverse, and the resistance of Homo sapiens to Neanderthal pathogens and parasites would need explanation. However, there is good reason to suppose that the net movement of novel human pathogens would have been overwhelmingly from Africa into the Eurasian landmass and not vice versa. For example, the most common source of novel human pathogens (like HIV today) would have been our closest phylogenetic relatives, namely other primates, of which there were many in Africa but only one known species in Europe, the Barbary Macaque, and only a few species in Southern Asia. As a result, African populations of humans would have been exposed to, and developed resistance to, and become carriers of, more novel pathogens than the Neanderthals. This unidirectional movement of pathogens immunologically challenged the naïve indigenous populations of Eurasia whenever they encountered more recent emigrants out of Africa. This putative "African advantage" would have persisted until the agricultural revolution about 10,000 years ago in Eurasia, after which domesticated animals overtook other primate species as the most common source of novel human pathogens, replacing the "African advantage" with a "Eurasian advantage".

While we are not currently concerned about infection transmission from another Homo species, as none exist, we are concerned about zoonotic diseases caused by harmful germs like viruses, bacteria, parasites, and fungi jumping from mammals and birds to
humans, and then the expansion of human to human transmission. We are also
cconcerned about possible mutations along the way, which can lead to improved
infectivity rates and lethality.

Remember that starting about 400,000 years ago Neanderthals were widespread
across Europe and Western Asia. But things began to change when early populations of
Homo sapiens migrated from Africa to Europe about 45,000 years ago. Five thousand
years later not a single Neanderthal remained. However, there is no evidence of direct
combat between the two species, but it is known that there were interactions, because
there was interbreeding. Some would say Neanderthals did not actually go extinct,
because everyone alive today whose ancestry is from outside of Africa, where
Neanderthals never lived, carries a little bit of the Neanderthal DNA genome.

**Was the Demise of the Neanderthals Due to Climate Change?**

It has been argued that the Campanian Ignimbrite Eruption, a volcanic eruption near
Naples, Italy, about 39,280 BP, contributed to the extinction of the Neanderthals. The
hypothesis is that although the Neanderthals had encountered several Interglacial
periods during 250,000 years in Europe, the inability to adapt their hunting methods
caued their extinction when Europe changed into a sparsely vegetated steppe and
semi-desert during the last Ice Age which started around 70,000 BP, during the Middle
Paleolithic period. The damage to plant life would have led to a corresponding decline in
plant-eating mammals hunted by the Neanderthals.

Neanderthals also had physical features that helped them survive cold climates, like
large noses to humidify and warm dry, cold air, as well as short, stout bodies to
conserve heat. In contrast, early Homo sapiens had technology that Neanderthals did
not, including sewing needles to make clothing, important during the colder periods of
the Ice Ages. Homo sapiens also had innovative tools like bows and arrows and
seemed to have a more diverse diet than Neanderthals.

To investigate the climate of central Europe during the age of Neanderthals,
paleontologists looked at stalagmites in two Romanian caves. Like trees, stalagmites
grow thin new layers each year. Temperature influences the size and chemical
composition of the calcium carbonate layers. Each layer includes information about
rainfall, soil bacteria and other information that can help create a detailed annual climate
record. Results from these investigations demonstrated that paleoclimate records
indicate that a particularly cold, dry period began about 44,000 years ago and lasted
1,000 years. Another cold dry period began 40,800 years ago, lasting about 600 years.
It was cold enough that average temperatures dropped to below zero, creating year-
round permafrost. Interestingly, these climate disruptions correspond to the
archaeological record, which shows that at the same time Neanderthals began to
disappear from the Danube River Valley and in France, the heart of their territory, while
early signs of modern humans begin to appear. The double-dose of super-cold weather
likely radically changed the environment, transforming the open woodlands of central
Europe into Arctic-like steppes. Early humans with more adaptable strategies likely
moved into former Neanderthal territory, but did not actively kill the Neanderthals. It is possible that the Neanderthal population became markedly reduced during that first cold period. When the second one occurred, the remaining small bands of Neanderthals were likely absorbed into human populations, as evidenced by the Neanderthal DNA in the genome of modern humans.

So, the question needs to be asked why did Neanderthals die out during these climate shifts while modern humans survived? One hypothesis is that because Neanderthals relied heavily on protein from large game animals, they had trouble adapting when climate change impacted populations of those animals. Homo sapiens, on the other hand, were more adaptive, eating a variety of plants, fish and meat, enabling their survival on the cold steppes.

It is also thought that Homo sapiens had a competitive edge over Neanderthals. There is evidence that early Homo sapiens had long-distance trade networks, possibly buffering them against times of climate change when their preferred foods were not available. Archaeological evidence exists to suggest traveling bands of early humans interacted with each other and that inter-group trading emerged. Early humans, the Aurignations and the Gravettians, imported many raw materials over long ranges and their creative innovations and solutions were widely dispersed. Such exchanges of goods and ideas helped early humans to develop high level social mechanisms that kept both cultures going and generated new cultural opportunities. Neanderthals did not have these advantages.

Charles Darwin

1. “In the long history of humankind (and animal kind, too) those who learned to collaborate and improvise most effectively have prevailed.”
2. “Intelligence is based on how efficient a species becomes at doing the things they need to survive.”

Sources: Wikipedia; Smithsonian Insider; Smithsonian Magazine; Proceedings of the National Academy of Science.

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Is The Future Here Already? Growing Food Indoors

“My main concern on the food supply is the health of those working in the fields and processing plants. Is it any wonder they seem to be disproportionately affected? One wonders how long this can go on. What impact that will have on our food security remains the great unknown.” Anonymous 2020

Food security, as defined by the United Nations' Committee on World Food Security, means that all people, at all times, have physical, social, and economic access to sufficient, safe, and nutritious food that meets their food preferences and dietary needs for an active and healthy life.

Food Security also means that the people who produce our food are able to earn a decent, living wage growing, catching, producing, processing, transporting, retailing, and serving food. At the core of food security is access to healthy food and optimal nutrition for all. Food access is closely linked to food supply, so food security is dependent on a healthy and sustainable food system.

The food system includes the production, processing, distribution, marketing, acquisition, and consumption of food.

Growing Food on Fifth Avenue in New York City

A few days ago I took a walk up 5th Avenue to get some fresh air and check out the Central Park Reservoir.
On the way to the reservoir, I passed the Guggenheim Museum, an iconic landmark located at on the corner of East 89th Street just a few blocks from where I live with my darling wife Joyce.

When I passed by, I could not believe what I saw, yes tomatoes growing indoors on 5th Avenue. *Countryside, The Future, an Exhibition at the Guggenheim Museum, Grows and Donates Fresh Produce to Food Pantries in New York.* Although the exhibition *Countryside, The Future* is temporarily closed to the public due to the ongoing coronavirus (COVID-19) pandemic, the grow module located outside the museum continues to yield fresh produce on Fifth Avenue. Sort of amazing as with all the open spaces in Central Park to grow things, New Yorkers are growing tomatoes indoors. Also see the write-up in the NY Times on 17 May 2020, entitled “The Museum Is Closed, but Its Tomato Man Soldiers On.”

I took some photos to memorialize this incredible event. The first photo is from across 5th avenue, the second is closer and in the 3rd photo, you can see the tomatoes very clearly.
The Guggenheim Museum. View from the West Side of 89th Street and 5th Avenue NY, NY 10128. Note the Building on the Left and the Tractor (copyright Jules T. Mitchel 2020)

Tomato vines growing at the Guggenheim Museum. Closer view from the West Side of 89th street and 5th Avenue NY, NY 10128 (copyright Jules T. Mitchel 2020)
Tomato vines growing at the Guggenheim Museum. Even closer view from 89th Street and 5th Avenue NY, NY 10128 (copyright Jules T. Mitchel 2020)
Tomato vines growing at the Guggenheim Museum. And an even closer view from 89th street and 5th Avenue NY, NY 10128 (copyright Jules T. Mitchel 2020)

Note the citation in the above photo for 80 Acres Farms. The following is abstracted from their website:

The founders, Mike and Tisha, knew that food was not what it used to be. They wanted to make it better—and they did it by creating a new kind of farm. One capable of producing an abundance of crop varieties year-round. Completely indoors. Using 100% renewable energy. Without any pesticides or excessive food miles. “80 Acres” is inspired by the amount of food that can be grown, not the amount of land used to grow it. Thanks to super-efficient vertical farming techniques, 80 Acres Farms can produce a lot more in a much smaller space. About the equivalent of a farm with 80 acres of land, give or take. And the rest is history.

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7. Hope During the Current COVID-19 Pandemic

History of Pandemics and Hope

To all of you, no matter where you are in the planet, who love science, democracy, truth and the American experiment, we will get through this war, but not without a major battle against the coronavirus SARS-CoV-2, the pathogen that causes COVID-19. We must also battle for true global leadership during this historic pandemic, that is challenging our beloved families, friends and colleagues in so many ways, both physically and emotionally.

This topic was shared with a few in June, but a lot has happened since that time that makes this topic even more meaningful.

To be clear, while this is not first pandemic to hit humankind, best we learn from the past or as scholars have said quite clearly and to the point:

1. "Those who don't know history are destined to repeat it." (Edmund Burke: 1729-1797)
2. "Those who cannot remember the past are condemned to repeat it." (George Santayana: 1863-1952)

Here is a brief list of epidemics afflicting mankind since the Greeks.

1. **430 BCE: Athens** - The earliest recorded pandemic happened during the Peloponnesian War. After the disease passed through Libya, Ethiopia and Egypt, and the Athenian walls as the Spartans laid siege. As much as two-thirds of the population died.

2. **165 CE: Antonine Plague** - The Antonine plague was possibly an early appearance of smallpox that began with the Huns. The Huns then infected the Germans, who passed it to the Romans and then returning troops spread it throughout the Roman empire. The plague continued until 180 CE., claiming the life of Emperor Marcus Aurelius.

3. **250 CE: Cyprian Plague** - Named after the first known victim, the Christian bishop of Carthage, the Cyprian plague entailed diarrhea, vomiting, throat ulcers, fever and gangrenous hands and feet. In 444 CE, it afflicted Britain.

4. **541 CE: Justinian Plague** - First appearing in Egypt, the Justinian plague spread through Palestine and the Byzantine Empire, and then throughout the Mediterranean. Recurrences over the next two centuries eventually killed about 50 million people, 26% of the world population. It is believed to be the first significant appearance of the bubonic plague.

5. **11th Century: Leprosy** - Though it had been around for ages, leprosy grew into a pandemic in Europe in the Middle Ages. Now known as Hansen's disease, it
still afflicts tens of thousands of people a year and can be fatal if not treated with antibiotics.

6. **1350: The Black Death** - Responsible for the death of one-third of the world population, this second large outbreak of the bubonic plague. This pandemic entered through Sicily in 1347 CE when plague sufferers arrived in the port of Messina.

7. **1492: The Columbian Exchange** - Following the arrival of the Spanish in the Caribbean, diseases such as smallpox, measles and bubonic plague were passed along to the native populations. With no previous exposure, these diseases devastated indigenous people, with as many as 90% dying throughout the north and south continents. Upon arrival on the island of Hispaniola, Christopher Columbus encountered the Taino people, population 60,000. By 1548, the population stood at less than 500.

8. **1817: First Cholera Pandemic** – This was the first of seven cholera pandemics over the next 150 years, which originated in Russia, where one million people died. Spreading through feces-infected water and food, the bacterium was passed along to British soldiers who brought it to India where millions more died.

9. **1855: The Third Plague Pandemic** - The bubonic plague claimed 15 million victims. The pandemic was considered active until 1960 when cases dropped below a couple hundred.

10. **1875: Fiji Measles Pandemic** - After Fiji ceded to the British Empire, a royal party visited Australia as a gift from Queen Victoria. Arriving during a measles outbreak, the royal party brought the disease back to where one-third of Fiji’s population, a total of 40,000 people, died.

11. **1889: Russian Flu** - The first significant flu pandemic started in Siberia and Kazakhstan, traveled to Moscow, and made its way into Finland and then Poland, where it moved into the rest of Europe. By the following year, it had crossed into North America and Africa. By the end of 1890, 360,000 had died.

12. **1918: Spanish Flu** – This flu resulted in 50 million deaths worldwide. By October 1918, hundreds of thousands of Americans died.


We know that this is a difficult time for all, including our friends and colleagues all over the world. However, it is important that no matter what is going on, and as troubling as life can be, we must have HOPE, as HOPE has driven humans in the past to deal with adversity. Think of FDR during the great depression when he spoke in 1932 and said, "There is nothing to fear than fear itself." Remember Mahatma Gandhi’s Do or Die Speech in 1942 when he launched the non-violent Quit India movement to demand India’s freedom from the 200-year British colonial rule. Of course, we all remember Dr. Martin Luther King, when in 1963 he gave his very famous, I Have a Dream Speech. And just last week, a major hero of the civil rights movement in the United States, Congressman John Lewis of Georgia, died. Here is what he wrote in 1998: “I was so inspired by Dr. King that in 1956 with my brothers and sisters and first cousins, I was only 16 years old, we went down to the public library trying to check out some books and we were told by the librarian that the library was for whites only and not for colors! It
was a public library! I never went back to that public library until July 5th, 1998, by this time I am in the Congress, for a book signing of my book "Walking with the Wind."

**SHARING MUSIC DURING THESE MOST CHALLENGING TIMES**

A suggestion to do around dinner time to deal with the pandemic, without any negotiations, each member at the breakfast, lunch or dinner table picks a piece of music and everyone listens. This week, picks at our table were “Wonderful World” (Louis Armstrong), “Una furtiva lagrima” (A furtive tear) from the great and fun Italian opera L’elisir d’amore (Elixir of Love) by Gaetano Donizetti, and Paganini’s Violin Concerto #1 performed by Ruggiero Ricci, a transformational exposure to classical music. Please share your selections with friends, family and colleagues. Clearly, humans can be caring and empathetic. Let us make it catchy.

Also, if you are in a cooking mood, go to https://targethealthyeating.com/ for the best and healthiest recipes in the world from our Founder and Master Chef Joyce Hays.

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8. The Destiny of Homo sapiens

Lessons from Evolutionary Biology, Immunology and Human Behavior

What is a Positive Natural Antibody and a Negative Human “ANTI-BODY?”

According to Charles Darwin, “Intelligence is based on how efficient a species becomes at doing the things they need to survive.” Need we say more?

According to Christian Macedonia, MD, “A Systems Response to COVID 19 is not all about antibodies. It also includes:”

1. “Individual human immune responses”
2. “Individual behavioral responses”
3. “Group and societal responses”
4. “How COVID-19 jumped quickly from humans to the internet, and how it now wreaks havoc on societal norms”

Planet Earth is now experiencing the COVID-19 global pandemic caused by the novel SARS-CoV-2 coronavirus. In order to better plan for what the future might or will bring, we thought it would be of interest to look at the biological response to viruses on the molecular level, and the overwhelming “ANTI-BODY” response of Homo sapiens on the macro level.

In order to assess the current approaches by humans to COVID-19 global viral pandemic, some brilliant and some flawed, lessons can surely be learned from human history and basic biology. The positive natural antibody response is what protects us from outside insults from nature, while the “Negative Human “ANTI-BODY” Response,” as manifested by human behavior, does its best to negate the beautiful and profound efforts of our biological and evolutionary history. Through evolution, the human body has masterfully designed extraordinary defense mechanisms to pathogens, while at the same time, human beings have destroyed more people through warfare and other nefarious means than all diseases combined.

And now, with the COVID-19 pandemic, some political leaders seem to be helping the virus to harm or kill its host. To be crystal clear, by not empowering medical experts to lead the complex fight against this dangerous virus, we surrender our species and become an ally to the virus. Because of pathological inaction by leaders in the United States, more Americans have died of COVID-19 than the virus would have normally killed as part of its lifecycle.
Lessons from the Past

Almost 700 years ago, the overwhelmed physicians and health officials fighting a devastating outbreak of bubonic plague in medieval Italy had no notion of viruses or bacteria, but they understood enough about the Black Death to implement some of the world's first anti-contagion measures. Starting in 1348, soon after the plague arrived in cities like Venice and Milan, city officials put emergency public health measures in place that foreshadowed today's best practices of social distancing and disinfecting surfaces. In order to screen for infection, the Adriatic port city of Ragusa (modern-day Dubrovnik, a city on the Adriatic Sea in southern Croatia) was the first to pass legislation requiring the mandatory quarantine of all incoming ships and trade caravans. The order, which survived in the Dubrovnik archives, reads that on July 27, 1377, the city's Major Council passed a law “which stipulates that those who come from plague-infested areas shall not enter [Ragusa] or its district unless they spend a month on the islet of Mrkan or in the town of Cavtat, for the purpose of disinfection.”

Paul Ehrlich Conceives of the Concept of Antibody in 1891

The first use of the term "antibody" occurred in a text by Paul Ehrlich in his article "Experimental Studies on Immunity," published in October 1891. However, the study of antibodies began in 1890 when Emil von Behring and Kitasato Shibasaburo described antibody activity against diphtheria and tetanus toxins. They then put forward the theory of humoral immunity, proposing that a mediator in serum could react with a foreign antigen. This idea prompted Paul Ehrlich to propose the side-chain theory for antibody and antigen interaction in 1897, when he hypothesized that receptors (described as "side-chains") on the surface of cells could bind specifically to toxins - in a "lock-and-key" interaction - and that this binding reaction is the trigger for the production of antibodies. In 1904, Almroth Wright suggested that soluble antibodies coated bacteria (pathogens) to label them more susceptible to phagocytosis and killing by white cells; process that he named opsonization. In the 1920's, Michael Heidelberger and Oswald Avery observed that antigens could be precipitated by antibodies and went on to show that antibodies are made of protein. The biochemical properties of antigen-antibody-binding interactions were then examined in more detail in the late 1930s by John Marrack. The next major advance was in the 1940s, when Linus Pauling confirmed the lock-and-key theory proposed by Ehrlich by showing that the interactions between antibodies and antigens depend more on their shape than their chemical composition. In 1948, Astrid Fagraeus discovered that B cells, in the form of plasma cells, were responsible for generating antibodies.

Physical Barriers as Our Initial Biological Defenses to the Assault by Coronavirus SARS-CoV-2

Think about how the simple use of masks, gloves, hand washing and physical distancing, as recommended by the CDC and all infectious disease experts, totally mimic the initial use of a physical barrier as the initial tactic against a pathogenic attack. In war-time, as first lines of defense, soldiers also stay at protective bases, move
around in armored cars, wear body armor and use gas masks against biological and chemical attacks. Also think about how we tackled the risk of HIV/AIDS, currently still with no vaccine. Once the pattern of the infectious nature of HIV/AIDS became apparent, we started by identifying those at risk to infection, the potential carriers of the virus and then creating an environment for physical isolation.

The following shows how biology addresses the physical attack by assaults of all kind.

**Physical Barriers:** To address the assault of viruses and other pathogens to our survival, the human body starts with physical barriers which includes the skin, eyes, nose, throat, and gastrointestinal, urinary tract and reproductive systems.

**The skin** prevents invasion by microorganisms unless it is damaged, for example, as we all know about infection potential post skin injuries such as a 3rd degree burn or bullet wound.

**Mucous membranes**, such as the lining of the mouth, nose, and eyelids, are also effective barriers. Typically, mucous membranes are coated with secretions that fight microorganisms. For example, the mucous membranes of the eyes are bathed in tears, which contain an enzyme called lysozyme that attacks bacteria and helps protect the eyes from infection.

**The airways** filter out particles that are present in the air that is inhaled. The walls of the passages in the nose and airways are coated with mucus. Microorganisms in the air become stuck to the mucus, which is coughed up or blown out of the nose. Mucus removal is aided by the coordinated beating of tiny hair-like projections (cilia) that line the airways. The cilia sweep the mucus up the airways, away from the lungs.

**The digestive tract** has a series of effective barriers, including stomach acid, pancreatic enzymes, bile, and intestinal secretions. These substances can kill bacteria or prevent them from multiplying. The contractions of the intestine (peristalsis, which moves contents of the bowel through the digestive tract), and the normal shedding of cells lining the intestine help remove harmful microorganisms.

**The urinary tract** also has several effective barriers. The bladder is protected by the urethra, the tube that drains urine from the body. In males, the urethra is long enough that bacteria are seldom able to pass through it to reach the bladder, unless the bacteria are unintentionally placed there by catheters or surgical instruments. In females, the urethra is shorter, occasionally allowing external bacteria to pass into the bladder. In both genders, when the bladder empties, it flushes out any bacteria that reach it.

**Therapeutics as Our Second Defense to the SARS-CoV-2 Coronavirus Assault**

During the initial response of physical isolation and the body’s generation of the immune response, in parallel, it is time for the lab scientists to take over developing treatments to simulate and stimulate the body’s attempt to manage/kill the virus using chemical
means (aka therapeutics). Therapeutics can include 1) a currently approved drugs such as dexamethasone with possibly new indications for use; 2) novel drugs in development for other indications with a possible mechanism of action to attack the SARS-CoV-2 coronavirus such as remdesivir; and 3) drugs that were never marketed, but are sitting in the libraries of pharmaceutical companies, with animal and human data indicating that they may be safe and efficacious.

**Human Generated Therapeutics and Regulatory Strategies**

Sometimes called “compassionate use,” expanded access is a potential pathway for a patient with an immediately life-threatening condition, or serious disease or condition, to gain access to an *investigational medical product* (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.

Emergency Authorization USE (EUA), on the other hand, is an authority granted to the US FDA under sections of the Federal Food, Drug, and Cosmetic Act as added to and amended by various Acts of Congress, including by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, to allow early marketing approval of a drug with limited but encouraging data. It does not constitute approval of a drug in the full statutory meaning of the term, but instead authorizes FDA to facilitate availability of an unapproved product, or an unapproved use of an approved product, during a declared state of emergency from one of several agencies or of a "material threat" by the Secretary of Homeland Security.

Currently remdesivir and convalescent plasma have received EUA for marketing by FDA for the treatment of COVID-19 patients. It should be noted that while convalescent plasma is a natural product, it needs to be manipulated to obtain its therapeutic effect. Dexamethasone, a currently marketed generic corticosteroid drug, has been studied in large controlled clinical trials in COVID-19 with results published in peer-reviewed journals.

**Remdesivir:** Remdesivir was originally developed as an Ebola antiviral but never approved by any regulatory body. On 28 August 2020, the FDA expanded its emergency use authorization for antiviral remdesivir to allow it to be used on all hospitalized patients. The FDA’s previous EUA in May allowed for the use of the drug on only hospitalized adult and pediatric patients with “severe” COVID-19. Now, all hospitalized patients with suspected or laboratory confirmed coronavirus may receive the drug regardless of the severity of the disease.

**Convalescent Plasma:** Convalescent plasma means plasma that comes from people who have recovered from an infection, like the coronavirus that causes COVID-19. This plasma may contain antibodies against the virus. The plasma of recovered COVID-19 donors contains specific IgG and IgM anti–SARS-CoV-2 antibodies, which can neutralize the virus. However, implementation of a convalescent plasma transfusion program needs comprehensive planning as it involves use of blood banks. There are
currently no data from well-controlled, adequately powered randomized clinical trials that demonstrate the efficacy and safety of convalescent plasma for the treatment of COVID-19. The FDA analysis of data on a subset of hospitalized patients from the Mayo Clinic’s Expanded Access Program (EAP) compared outcomes in patients who received convalescent plasma with high titers of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) neutralizing antibodies to outcomes in patients who received plasma with low titers and found no difference in 7-day survival overall. Among patients who were not intubated, 11% of those who received convalescent plasma with high antibody titers died within 7 days of transfusion compared with 14% of those who received convalescent plasma with low antibody titers. Among those who were intubated, there was no difference in 7-day survival.

**Dexamethasone:** The following study entitled: “Dexamethasone in Hospitalized Patients with Covid-19,” was published in the *New England Journal of Medicine* (17 July 2020). In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) and among those receiving oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72 to 0.94), but not among those who were receiving no respiratory support at randomization (17.8% vs. 14.0%; rate ratio, 1.19; 95% CI, 0.91 to 1.55). According to the NIH, On the basis of the preliminary report from the RECOVERY trial, the COVID-19 Treatment Guidelines Panel recommends using dexamethasone 6 mg per day for up to 10 days or until hospital discharge, whichever comes first, for the treatment of COVID-19 in hospitalized patients who are mechanically ventilated (AI) and in hospitalized patients who require supplemental oxygen but who are not mechanically ventilated (BI).

**Types of Immune Responses - The Complement System and Lymphocytes vs Phagocytes**

The mammalian immune system can be broadly divided into two main disciplines: innate and adaptive immunity. The key difference between innate and adaptive immunity is that innate immunity is a fast immune response that provides the first line of immunological defense against infections while adaptive immunity is a slow immune response mediated by the T and B lymphocytes.

The complement system is a constituent of the innate immunity that serves as a vital link between the innate and the adaptive immunity. This ancient system, established about 500-1,000,000 million years ago, has the ability to recognize and eliminate varied invading pathogens including viruses. The elimination of viruses by the complement system is owing to direct neutralization of cell-free viruses, lysis of the virus-infected cells, induction of antiviral state, and boosting of virus-specific immune responses due to recognition of effector fragments of complement along with viral antigens by the immune cells. The complement system represents the first response of the host immune system to SARS-CoV-2 infection, but there is growing evidence that unrestrained activation of complement induced by the virus in the lungs and other
organs plays a major role in acute and chronic inflammation, endothelial cell dysfunction, thrombus formation, and intravascular coagulation, and ultimately contributes to multiple organ failure and death (Nature Reviews, Immunology, June 2020). According to a paper recently published (Kidney International (Aug. 2020), the relative role of the different complement activation products in the pathogenesis of COVID-19–associated tissue inflammation and thrombosis are discussed and a hypothesis is proposed that blockade of the terminal complement pathway may represent a potential therapeutic option for the prevention and treatment of lung and multiorgan damage.

Phagocytes can be either macrophages, neutrophils, monocytes, dendritic cells or mast cells. They destroy pathogens by phagocytosis. The main difference between lymphocytes and phagocytes is that lymphocytes generate specific immune responses against pathogens whereas phagocytes generate the same response to any pathogen. This means that phagocytes are the tools of innate immunity and lymphocytes are the tools of the adaptive immunity.

Once the adaptive immune system has vanquished the invader, a pool of long-lived memory T and B cells are made. These memory lymphocytes remain dormant until the next time they encounter the same pathogen. This time, though, they produce a much faster and stronger immune reaction. Memory is the key feature of the adaptive immune system, enabling long-term protection. Thus, the major advantages of an adaptive response to the host are twofold. First, it allows the host to form an immune response that is specifically tailored to the invading pathogen. Second, it forms a pool of memory cells from these specific effectors that can last for many years, capable of protecting the host against reinfection by their rapid response. This combination of specificity and memory are also the mechanistic underpinnings for the clinical success of vaccination.

Vaccine-Based Therapeutics Mimic Nature

In standard viral vaccines, either inactivated (or attenuated) virus or viral proteins known to cause infection are used to immunize. However, the mRNA vaccines do not use this conventional model to immunize. mRNA vaccine carries the molecular instructions to make the protein in the body through a synthetic RNA of the virus. The host body uses this to produce the viral protein that is recognized by the immune system, thereby making the body ready to fight against the disease.

Attenuated Virus Vaccine

1. AstraZenecca & University of Oxford: A COVID-19 vaccine has been made from a weakened version of a common cold virus, the adenovirus, taken from chimpanzees. The adenovirus is genetically altered so it cannot reproduce itself. The vaccine is combined with genes of the spike protein to trigger production of antibodies against it, which allows the immune system to destroy the SARS-CoV-2 virus.
2. **Sinopharm:** The vaccine, from the Sinopharm Wuhan Biological Products Research Institute in China, was tested previously in 1,120 people ages 18-59 in phase I/II clinical trials and produced a strong neutralizing antibody response of 97.6% to 100%, depending on the timing and dosing of the injections. The vaccine uses an inactivated version of the virus.

3. **Sinovac Biotech:** Sinovac Biotech's vaccine, CoronaVac, uses an inactivated version of the virus. Early results of a Phase II clinical trial released in June show that the vaccine induced antibodies to neutralize the virus after 14 days in 90% of people who received it. Sinovac Biotech, based in Beijing, said it will develop the vaccine for global use.

**Messenger RNA Vaccines**

1. **BioNTech & Fosun Pharma:** BioNTech and Fosun Pharma are jointly developing the COVID-19 vaccine candidate in China.

2. **BioNTech and Pfizer:** BioNTech and Pfizer are jointly developing the COVID-19 vaccine candidate. The Pfizer/BioNTech vaccine development program is evaluating at least four experimental vaccines, each of which represents a unique combination of messenger RNA (mRNA) format and target antigen.

3. **Moderna:** According to Moderna, Catalent will handle large-scale vial filling and packaging for the vaccine candidate mRNA-1273 at its biologics facility in Bloomington, Indiana to support the production of an initial 100 million doses of the vaccine. If the vaccine gets approved, Moderna intends to supply it to the US market beginning the third quarter of 2020.

Sources: Wikipedia; CDC; NIH; Merck Manual.

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9. Getting Through the Challenge of COVID-19
Lessons from Ebola
Music as the Healer

From the 1993 founding of Target Health, one of the favorite traditions has been celebrating birthdays of our esteemed employees. When the company was smaller, we did individual birthday celebrations, but as we grew, the celebration became the last Friday of each month. In addition to cakes and fruit, our esteemed professional opera tenor, Adam Harris (regulatory department), always had an aria or song to share. This party has been one of the happiest highlights of our company and we miss it. Thus, let music be a part of the recovery of all of us!

Music and Humanity  ~  Famous Quotes

- Music in the soul can be heard by the universe. - Lao Tzu (604-531 BCE)
- Music is a moral law. It gives soul to the universe, wings to the mind, flight to the imagination, and charm and gaiety to life and to everything. - Plato (428-328 BCE)
- Beautiful music is the art of the prophets that can calm the agitations of the soul; it is one of the most magnificent and delightful presents God has given us. - Martin Luther (1483-1536)
- If music be the food of love, play on. - William Shakespeare (1564 – 1616)
- Music has charms to soothe a savage breast, to soften rocks, or bend a knotted oak. - William Congreve (1670-1729)
- Music is a higher revelation than all wisdom and philosophy. - Ludwig van Beethoven (1770 – 1827)
- Music can name the unnamable and communicate the unknowable. - Leonard Bernstein (1918-1990)

A Bit of History: Just Seven Years Ago We knew How to Prevent a Pandemic
The Story of Ebola Virus Disease (EVD)

The great tragedy of our times is not that COVID-19 is amongst us, terrible and horrific as it is, it is that we as a people, our leaders, and society at large have failed to take the most obvious steps, even without a vaccine, to mitigate this enormous social impact on all of us. Is the challenge of climate change coming next? Nevertheless, there is enormous hope based on human resilience to do the right thing.

The initial case, or index patient of Ebola Virus Disease (EVD) was reported in December 2013. An 18-month-old boy from a small village in Guinea is believed to have been infected by bats. After five additional cases of fatal diarrhea, an official medical alert was issued on January 24, 2014, to the district health officials. On March 23, 2014, with 49 confirmed cases and 29 deaths, the WHO officially declared an
outbreak of EVD. Finally, on August 8, 2014, WHO declared the deteriorating situation in West Africa a Public Health Emergency of International Concern (PHEIC), which is designated only for events with a risk of potential international spread or that require a coordinated international response.

The following May Sound Familiar: The scope of the outbreak in Africa, both in terms of cases and geography, was most likely attributed to the unprecedented circulation of EVD into crowded urban areas, increased mobilization across borders, conflicts between key infection control practices, as well as prevailing cultural and traditional practices in West Africa.

Eventually, along with careful policy implementation at the national and global levels and engaging local leaders in prevention programs and messaging, the spread of the virus was contained and an end was put to the outbreak.

Outcomes in Africa: Two and a half years after the first case was discovered, the outbreak ended with more than 28,600 cases and 11,325 deaths. Liberia first declared it to be Ebola-free in May 2015, but made its final declaration on June 1, 2016. However, during the epidemic, Liberia lost 8% of its doctors, nurses, and midwives to EVD. Sierra Leone announced it was Ebola-free on March 17, 2016, and Guinea in June 2016.

Outcomes in the US: The first case of EVD was reported in the US in September 2014. Four laboratory-confirmed cases of EVD occurred in 2014, with seven cases medically evacuated from other countries. Nine of the people contracted the disease outside the US and traveled into the US, either as regular airline passengers or as medical evacuees; of those nine, two died. Two people also contracted Ebola in the US. Both were nurses who treated an Ebola patient; both recovered.

Bravo to the CDC Response: In July 2014, the CDC activated its Emergency Operations Center to help coordinate technical assistance and disease control activities. CDC personnel were deployed to West Africa to assist with response efforts, including surveillance, contact tracing, data management, laboratory testing, and health education. During the height of the response, CDC trained 24,655 healthcare workers in West Africa on infection prevention and control practices. Laboratory capacity was also expanded in Guinea, Liberia, and Sierra Leone with 24 laboratories able to test for Ebola virus by the end of 2015. In the US, more than 6,500 people were trained during live training events throughout the response. To prevent cross-border transmission, the CDC implemented enhanced entry screening for travelers coming from Guinea, Liberia, Sierra Leone, and Mali by routing them to designated airports better able to assess travelers for risk, and travelers leaving West Africa were screened at local airports.
Music and the Brain

The human species possesses two complementary, yet distinct, universal communication systems—language, music and the arts. Music, in contrast to language itself, affects many aspects of human behavior, especially in encouraging prosocial interactions and promoting trust and cooperation within groups of culturally compatible but not necessarily genetically related individuals.

Music and the arts are believed to have been a part of civilizations that existed as long as 50,000 years ago. Music began with basic rhythm, and the arts began with cave paintings and amulets, and over time have become an integral part of the human lifestyle. It is very interesting to note that music and rhythm evolved as a means of expression and communication and generally reflect the social, economic, environmental, religious, and other activities related to humans. Music enables the expression of a range of emotions and feelings, and provides relief for many of us by calming our entire nervous system.

The good news is, that you do not need to be a musicologist, performer or composer, to reap the benefits of music! Listening to music releases endorphins in your system. When listening to music that you enjoy, dopamine, the “feel-good” chemical and serotonin, the ”happy” chemical are released in your brain giving a sense of pleasure and boosting your mood. Music, the great motivator, may with a strong beat, encourage you to move, due to a psychological phenomenon called entrainment. This is why many listen to music when exercising.

Biology of Our Pleasure Receptors

Music, presumably via its impact on the limbic system, is also rewarding and motivating, and can facilitate aspects of learning and memory. The limbic system, also known as the paleomammalian cortex, is a set of brain structures located on both sides of the thalamus, immediately beneath the medial temporal lobe of the cerebrum primarily in the forebrain. It supports a variety of functions including emotion, behavior, motivation, long-term memory, and olfaction. Emotional life is largely housed in the limbic system, and it critically aids the formation of memories.

Chemical Modulators of Mood, Emotion and Pleasure

Music encourages interactions in infancy and adulthood, aids in the development of perceptual, cognitive, and motor skills, promotes trust and reduces a sense of social vulnerability, and is rewarding and motivating, as well as having a beneficial effect on aspects of learning and memory. Music, pure rhythm and dance, which most likely developed in parallel, also promotes synchrony and social interaction, thus contributing to cultural identity, and encouraging the formation of cooperative networks. Along with dopamine and serotonin which are released by the brain when listening to music, oxytocin, a hormone that is released while singing, has been shown to alleviate stress.
and anxiety. Studies have also found that listening to music and singing decreases feelings of depression and loneliness.

**Oxytocin:** Lullabies are a universal way of soothing infants, and it is thus of interest that vocalization by mothers increases levels of salivary oxytocin, and reduces cortisol in their children.

Oxytocin is a nine amino-acid peptide that is enzymatically derived from a larger peptide precursor made from the oxytocin gene. In mammals, oxytocin is universally involved in reproductive biology, modulating social learning and related behaviors, as well as modifying responses to adverse conditions. Prosocial behavior, in contrast to anti-social behavior, is behavior that benefits other people or society as a whole, such as helping, sharing, donating, cooperating, and volunteering. In Homo sapiens, it has been postulated that the unique prosocial and harmonizing activities of music and dance are elements of this pre-existing oxytocinergic network. Based on the above, it should be apparent that many of these musical influences on human behavior are also characteristic of many of the psychological and sociological effects of oxytocin. These associations become even clearer when comparing the neural networks that are: (i) activated when listening to music perceived as being rewarding and pleasurable with; (ii) regions that process behaviors that involve social cooperation, empathy and altruism; and (iii) the distribution of oxytocinergic fibers and oxytocin receptors (OXTR) in the human brain.

**Dopamine:** Dopamine is a type of neurotransmitter that our nervous system uses it to send messages between nerve cells. Dopamine also plays a role in how we feel pleasure and is a big part of our unique human ability to think and plan. In addition, Dopamine helps us strive, focus, and find things interesting. Too much or too little dopamine can lead to a vast range of serious health issues like Parkinson’s disease, Schizophrenia, ADHD and Drug Addiction. For example, decades ago, it was hypothesized that symptoms of Schizophrenia stemmed from a hyperactive dopamine system. Now we know that too much dopamine in certain parts of the brain results in hallucinations and delusions, while a lack of it in other parts of the brain can cause outcomes, such as lack of motivation and desire. However, dopamine overabundance is not the complete explanation for Schizophrenia. Rather, the overactivation of dopamine D2 receptors, specifically, is one effect of the global chemical synaptic dysregulation observed in Schizophrenia.

A study from The Montreal Neurological Institute and Hospital — The Neuro at McGill University published in their Journal Nature Neuroscience, 9 January 2011 revealed that the pleasurable experience of listening to music releases dopamine in the brain. These results indicated that intense pleasure in response to music can lead to dopamine release in the striatal system. These results help to explain why music is of such high value across all human societies. The study used positron emission tomography (PET) scanning, combined with psychophysiological measures of autonomic nervous system activity, and found endogenous dopamine release in the striatum at peak emotional arousal during music listening. In addition, the anticipation of an abstract reward can
result in dopamine release in an anatomical pathway distinct from that associated with the peak pleasure itself.

A key element of the study was to measure the release of dopamine, when the participants were feeling their highest emotional response to the music. To achieve this, the study marked the point at which participants felt a shiver down the spine of the sort that many people feel in response to a favorite piece of music. This "chill" or "musical frisson" pinpointed when the volunteers were feeling maxim pleasure. The scans showed increased endogenous dopamine transmission when the participants felt a "chill". Conversely, when they were listening to music which did not produce a "chill", less dopamine was released.

**Serotonin:** Serotonin is a mood regulator in vertebrate animals, including humans. Activation of one form of serotonin receptor in the brain called the 5-HT1A receptor has been shown to prevent aggression. A study was conducted to track patient's ratings of their own anxiety. Before undergoing surgery, subjects were randomly assigned to listen to music or take antianxiety pills. Results showed that patients who listened to music had less anxiety compared to those who took pills.

**What Tips Are There to Have an Optimal Experience?**

It is important to set up your environment for an optimal experience when listening to music. This means dim the lights, make sure the temperature is just right, turn off your phone, get into a comfortable position and minimize all distractions to use music mindfully and purposefully. You can also add other sensory stimuli to your music listening experience such as candles, scented lotion, essential oils or a heated blanket. Be sure to listen to music that satisfies your preference; if you listen to Mozart and you do not like classical music, it will not help you. There is no one-size-fits-all when it comes to music selection and no special genre that works the best. So listen to what you enjoy! 15-20 minutes a day is all you need to actively listen, relax, and reset.

**We share some of our favorites:**

1. **COVID Cello Project 10 "Adagio for Strings"** by Samuel Barber
   The exigencies of the Covid-19 global pandemic require that we become quarantined and/or keep a social distance from others, in order to protect each other. Music like this first piece, performed by musicians from 29 countries, each performing from home, hopefully, brought you into the realization, that you are not alone. During this crisis, music along with new technologies, and social media has brought the planet together, harmoniously. We are the world; we are the same; we are all global citizens.

2. **Una Furtiva Lagrima** from Elixir of Love, Donizetti. Matthew Polenzani

3. **Wonderful World:** Louis Armstrong

4. **Paganini Violin Concerto # 1** Hilary Hahn

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